

COMPLETE CASE HISTORIES FROM TEXTBOOK: *INTEGRATED NEUROSCIENCES*

PART III. CASES – CEREBRAL HEMISPHERE MOTOR SYSTEM, CEREBELLUM, BASAL GANGLIA

CHAPTER 18: MOTOR SYSTEM I:

The following case 18-1 presents an example of focal seizures beginning in the motor cortex.

Case 18-1. This 29-year-old, right-handed, white woman was in her usual state of good health until three months prior to admission when she developed an intermittent “pulling sensation” over the anterior aspect of the left thigh, lasting a few minutes. This recurred without other symptoms about twice a week. On the evening of admission, while sitting on a couch, she again had the onset of this same sensation in her left. She stood up, noted that her left leg felt “numb” and then started to have “jerky movements” in her left foot which progressed to involve the whole left lower extremity. She sat down, pressed on her left thigh in an attempt to stop the movement. At this point, her husband and a friend came to her (the patient is amnesic for these events), and saw her have tonic extension then clonus of all four limbs associated with grunting respiration, clenched jaw, and rolling of the eyes. She was placed on the floor and after a few seconds she regained consciousness, though she still appeared dazed and slightly confused for the next 5 minutes.

Past history and family history: noncontributory.

Physical Exam: Normal except for bite marks on the left lateral aspect of the tongue.

Neurological Exam: Significant only a slight asymmetry of deep tendon reflexes: left > right.

Clinical Diagnosis: Focal seizures originating right parasagittal motor cortex (foot area), with ? of parasagittal meningioma.

Laboratory Data:

(1) *Electroencephalogram* (Fig.29-1B) demonstrated rare focal spikes, right Rolandic parasagittal consistent with the focal source of the secondarily generalized seizure and rare focal slow waves in the right Rolandic and mid temporal area - consistent with minor damage in this area

2) *CT scan* (Fig.18-13) demonstrated an enhancing lesion in the right parasagittal region just anterior to the central sulcus.

- (3) *Arteriograms* (Fig.18-14) demonstrated a circumscribed vascular tumor in the right parasagittal rolandic area which was supplied by the right anterior cerebral artery (A,B) and the right middle meningeal branch of the external carotid artery©. The venous phase of the study demonstrated a significant draining vein from this area of tumor blush(D). All of these findings were consistent with a right parasagittal meningioma.

Hospital Course: A well-circumscribed right parasagittal meningioma was removed by Doctor Bernard Stone. A distal weakness of the left lower extremity was present in the immediate postoperative period but this improved rapidly so that by two months after surgery, a foot drop brace was no longer required and strength had returned to normal. During all of the pre and post operative period, the patient received diphenylhydantoin (Phenytoin) to prevent additional seizures. A possible sensory seizure involving the hand occurred 2 years later. Four years after surgery, the patient attempted to reduce her dosage of anticonvulsant and experienced a recurrence of focal motor seizure activity beginning in the left leg with subsequent secondary generalization. When evaluated 6 years after surgery, she had experienced no additional seizure activity. Her neurological examination continued to demonstrate an increase in deep tendon reflexes on the left and a left sign of Babinski. Her CT scan demonstrated no recurrence of tumor, there was very minor atrophy at the site of the previous meningioma. The EEG continued to demonstrate bursts of blunt spikes and slow waves in the right parasagittal Rolandic and parietal areas. Follow-up 10.5 years after surgery indicated no additional seizures.

Comment: The onset of focal seizure activity should always raise the question of focal pathology. When these seizures begin at age 29, without a prior medical history, there is always a strong possibility of a primary brain tumor. In general gliomas are much more common than meningiomas but the odds of a meningioma are increased by the parasagittal location and the gender of the patient. In this case, there was a very close correlation of the clinical phenomena with the laboratory data regarding the anatomical location of the lesion. Surgical therapy eliminated the underlying benign tumor - the parasagittal meningioma, but the predisposition to focal seizures remained. Thus, the tumor in compression of cerebral cortex had produced alterations in neuronal excitability which persisted following the removal of the tumor.

Case 18-2 provides an example of a slow growing tumor involving the premotor and supplementary motor cortex from the standpoint of focal seizure activity. The motor effects of frontal lesions are presented in case histories 22-2 and 22-3 which follows the discussion of the prefrontal areas.

Case 18-2: This 57-year-old right-handed single nun and occupational therapist, had the onset of her first generalized convulsive seizure at age 47, ten years prior to consultation. This occurred without warning with sudden loss of consciousness and an observed generalized tonic clonic seizure. Both an EEG and CT scan were reported to have been normal. Approximately 4 additional generalized convulsive seizures occurred over the next 4 years. Shortly after the onset of the grand mal seizures, the patient began to have focal seizures. She described these as beginning with the abduction and raising of the right arm at the side, over her head, then a jerking of the right arm, and then she would fall to the ground. She would remain fully conscious but she would be unable to talk. She would have an awareness that something strange was occurring. She had a sinking sensation. She denied any impairment of memory after the episode. But, she would be aware that her right arm and leg were tingling and weak for perhaps 5 minutes afterwards and she would be unable to speak for 10-30 minutes afterwards. These focal seizures occurred once a month, but for the last 2 years, they had been occurring once a week. The patient indicated that over the last 10 years she has had problems with her memory.

She was reported to have had three “negative” CT scans over the years, and yearly EEG’s which did not reveal focal features or electrical seizure discharges although some bilateral slow wave activity was present. The patient has been treated with a variety of medications over the years without attaining seizure control. Her initial evaluation 4 years after onset of seizures at another neurological center indicated some increased activity in the finger jerks on the right with withdrawal of both plantar responses, and a diminished swing of the right arm.

Past history and family history were negative: she was the product of a full-term delivery weighing 9 pounds and had excellent developmental and educational milestones.

Neurological examination :The following abnormalities were present:

1. *Mental Status*: Although orientation and language functions were all intact, delayed recall without assistance, was 0 out of 5; and with assistance 2 out of 5. Proverb interpretation was abstract for 1/3 proverbs, but similarity testing was abstract.
2. *Cranial Nerves* II through XII were intact.
3. *Motor System* was intact except for a decreased swing of the right arm in walking.
4. *Reflexes*: deep tendon reflexes were increased on the right at biceps and patellar. Plantar response was extensor on the right and equivocally extensor on the left.
5. Sensory system was intact.

Clinical diagnosis: Seizures of focal origin left premotor/supplementary motor cortex possibly secondary to low grade glioma. A meningioma was less likely due to the reports of “normal CT scans”.

Laboratory data:

1. **CT scan** (Fig.18-16),demonstrated an area of calcification with surrounding edema in the left premotor area .

2. **MRI scan** (Fig.18-17),demonstrated extensive involvement of the premotor and supplementary areas by tumor and edema.

Subsequent course: Subtotal resection of this tumor was performed by Doctor Bernard Stone. Histological examination of the tissue confirmed the preoperative impression of an infiltrating glioma - predominantly oligodendroglioma in type. The patient received postoperative radiotherapy, 5000 rads to the left hemisphere and an additional 1000 rads to area of tumor. When last seen in follow-up 4 years after surgery, the patient was still experiencing infrequent (1-2 per month) short focal seizures of the same type involving focal movements of right arm, plus speech arrest. The neurological examination demonstrated some decrease in spontaneous speech and some blunting of affect. However, she was fluent; naming of objects and repetitions was intact. Strength was intact. Reflexes were symmetrical but bilateral extensor plantar responses were present. She had a moderate frontal type apraxia of gait and required a cane to avoid falls.

Comment :This patient presented with seizures of focal origin. The description of the posture adopted by the arm at the very beginning of the seizure, raised the possibility that her seizures were originating in the supplementary motor cortex of the left hemisphere and then spreading into the motor and sensory area. The arrest of speech would be compatible with such an origin since there is a superior speech area located in relationship to supplementary motor cortex. The fact that the patient remembered much of the seizure would also be consistent with such an origin. The post ictal depression of motor and sensory function in right arm and right leg and the depression of speech would all be consistent with post ictal phenomena involving the left hemisphere, particularly its sensory, motor and speech areas. The fact that the EEG's had not been particularly remarkable would also be consistent with such an origin of discharge. Thus, the discharging focus may well be buried on the parasagittal surface and not accessible to recording electrodes at the surface.

As regards the underlying nature of the pathology, when the patient was seen 10 years after onset of symptoms, she now has some focal findings; in terms of a right Babinski sign and increased reflexes in the right arm raising the question of a low grade glioma such as an oligodendroglioma in this area. The previous “negative” CT scans would have ruled out a meningioma or arteriovenous malformation. The long history and the finding of calcification within the tumor all made oligodendroglioma the most likely diagnosis. Low grade gliomas of this type often produce seizures without producing major neurological findings .Thus frontal release signs were minimal.

The following case history provide an example of normal pressure hydrocephalus producing the triad of a gait apraxia, urinary incontinence and problems in memory.

Case 18-3: This 72-year-old retired white handed carpenter was referred for evaluation of progressive impairment of gait, and more recent problems, in memory. The gait problems began insidiously five years previously but had become more significant in the past six months. He described his walking as involving small steps and then “going forward at too fast a rate, with difficulty in stopping”. As a result, he would stumble and tend to fall forward, losing his balance. He had considerable fear of falling and made use of a cane to avoid falling. For the last four to five months, the patient had noted urinary frequency and incontinence. He kept a bucket with him at all times. “Once I have to go, I can’t hold on.” Memory problems had developed during the last two to three months related to the recall of recent events and new material. He would enter a room and be

unable to recall why he had entered the room. Emotional lability had also developed during the past year. It was difficult not to cry when he heard a sad story.

Past history indicated at least three myocardial infarctions.

Neurological examination:

1. Mental Status:

- a. Oriented for time, place and person.
- b. Delayed recall, even with assistance, was limited to 1/3 in five minutes.
- c. The patient often lost track of what he was saying or doing.
- d. Serial 7 subtractions was slowly performed but intact.
- e. Reading, writing, drawing and naming of objects were intact but spelling was poor.
- e. Abstract reasoning was intact.
- g. Affect demonstrated changes: At times, he was tearful; at times, inappropriately jocular.

2. Cranial Nerves: Intact except bilateral decrease in hearing - long standing.

3. Motor System: Intact except for gait. The patient walked on a broad base with small steps. He was slow in starting and then picked up speed. He was unsteady on the turns and tended to turn "en bloc". No rigidity and no tremor were present. Finger to nose and heel to shin tests were normal.

4. Reflexes: Deep tendon reflexes were hyperactive at patellar. Plantar responses were equivocal. No definite frontal release signs were present.

Clinical diagnosis: Frontal lobe syndrome with involvement of premotor and prefrontal areas. The combination of a frontal gait apraxia, memory impairment and urinary incontinence raised the question of normal pressure hydrocephalus.

Laboratory data:

- 1. *CT scan (Fig. 18-21):* Demonstrated markedly dilated lateral; third and fourth ventricles but with no enlargement of the sulci.

Figure 18-21 Normal Pressure Hydrocephalus - CT Scan - Case 18-3 A. Ventricular Enlargement B. Section Through Vertex: Demonstrating No Enlargement of Sulci PART II: Comparison patient with progressive multiple sclerosis involving cerebral hemispheres at relatively comparable levels of section demonstrating A. Ventricular Enlargement B. Accompanied by Enlargement of Cortical Sulci

- 2. Lumbar puncture studies were normal.

- 3. *Radio-isotope cisternogram (Fig 18-22)* demonstrated continued presence of isotope within the ventricular system with no reabsorption over the convexities - subarachnoid space at 24, 48, and 72 hours.

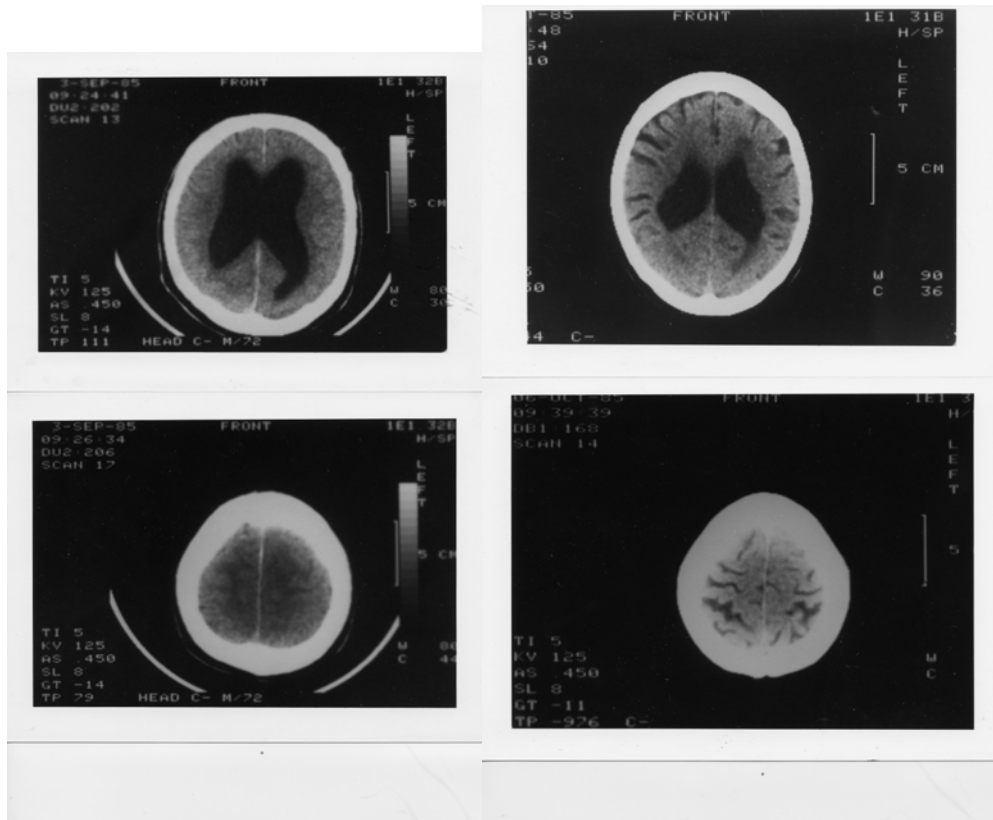
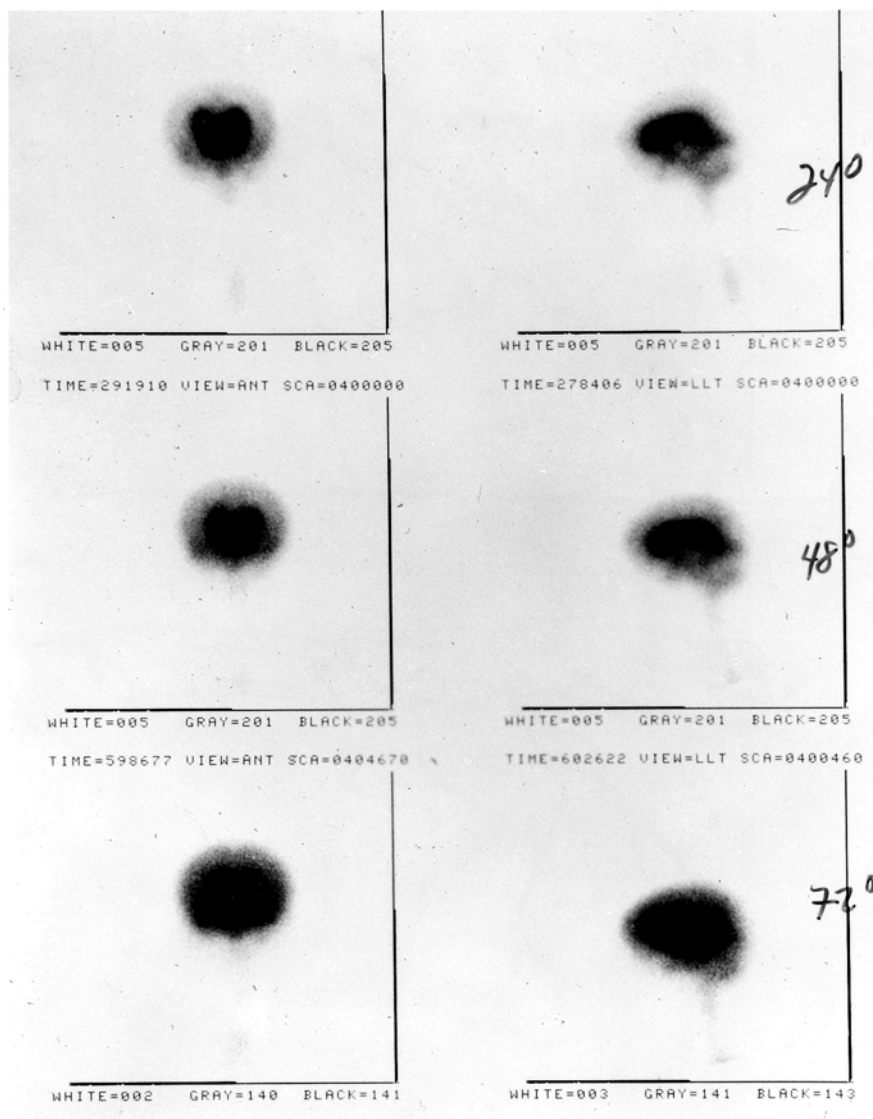


Figure 18-21. Normal Pressure Hydrocephalus Figure 18-21. Comparison Scan.

Figure 18-22: Normal Pressure Hydrocephalus: Isotope Flow Study: Lumbar CSF Injection Case 18-3 Isotope remaining in ventricular system at 24, 48 and 72 hours B. Comparison Case: Progressive multiple sclerosis of

cerebral hemispheres with enlargement of ventricular system but with enlargement of sulci. Isotope has begun to leave ventricles at 24 hours - appearing over the convexity and this is even more apparent at 48 and 72 hours.

Fig 18- 22. Normal Pressure Hydrocephalus; Isotope Flow Study



Subsequent course: Doctor Alex Danylevich performed a ventriculo-peritoneal shunt procedure (right lateral ventricle to peritoneal cavity). The patient did well with clearing of his triad of symptoms: Ataxia, dementia and urinary incontinence and was able to return to work as a carpenter , 12 hours per day. Subsequently , symptoms recurred due to infection of the peritoneal component of the shunt tube. Following revision of the shunt, symptoms improved only to worsen again in 6 months later. The patient had to use a wheelchair at times. A more marked apraxia of gait, frontal release signs, bilateral Babinski signs and urinary incontinence were present on examination 6 months after the revision. CT scan indicated a greater degree of ventricular enlargement. Following removal of 30 cc. of CSF, the patient was more responsive, and better oriented. Myocardial problems prevented additional neurosurgical revision of the shunt at that time. Subsequently, Doctor Robert Ojemann, of the Massachusetts General Hospital, revised the shunt utilizing a valve which allowed greater flow. At last evaluation, two years after admission, gait had improved (he was using a walker). Mentation was clearer (he was still described as showing aspects of a “frontal lobe syndrome”). Urinary incontinence was no longer present.

Comment: This patient presented a premotor/prefrontal syndrome .The imaging studies allowed a more specific delineation of the etiology of the syndrome. In most cases of normal pressure hydrocephalus, the gait disturbance is out of proportion to any change in mental status.

CHAPTER 19: MOTOR SYSTEM II: BASAL GANGLIA AND MOVEMENT DISORDERS

The following case presents an example of a patient with Parkinson's disease followed for 19 years.

Case 19-1 : This 48-year-old married white male, left-handed school master and physics teacher, was referred on 08/16/82 by his orthopedic surgeon for neurological evaluation of problems of control of the left arm and dragging of the left leg. Symptoms had begun 3 months previously with a sense of fatigue, stiffness and lack of control in the left arm. After a period of prolonged writing, he would have to make a conscious effort to continue writing. Approximately one month prior to the evaluation, he first noted a slowing down in movements of the left leg. "I have to remember to lift it."

Past medical history: Negative except for neck pain eight years previously related to cervical spondylosis, which cleared with the use of collar and traction except for occasional tingling in the 4th and 5th fingers of the left arm. Family history was unremarkable.

Neurological examination:

1. Mental Status: intact
2. *Cranial Nerves I-XII:* Intact except for a tremor of the closed eyelids and a positive glabellar sign (he was unable to suppress eye lid blinking on tap of forehead).
3. Motor System:
 - a. Strength : intact
 - b. Gait : There was a tendency to turn en bloc and a decreased swing of the left arm. However he could walk a tandem gait without difficulty.
 - c. There was a slight increase in resistance to passive motion at the left elbow, wrist and knee (rigidity without definite cogwheel component).
 - d. Although the patient was left-handed, there was a slowness of alternating finger movements of the left hand.
 - e. No tremor was present.
 - f. Handwriting was intact with no evidence of micrographia.
4. *Reflexes:* deep tendon stretch reflexes and plantar responses were physiologic
5. *Sensation:* all modalities were intact.

Clinical diagnosis: early Parkinson's disease, predominantly unilateral.

Laboratory data: all studies were normal including CT Scan of the brain, thyroid studies, blood chemistries, erythrocyte sedimentation rate, antinuclear antibody and serologic test for syphilis.

Subsequent course⁴: The patient did not wish to begin any treatment at that point in time. When evaluated 3 months later progression had occurred. He occasionally had the sense of moving slowly. He was now aware that with continuous writing, the writing became smaller, that is, micrographia emerged, evident on examination of handwriting. In addition, a minimal tremor was noted in the Archimedean spiral. A greater, but still minor, degree of cogwheel rigidity was now present at left wrist and elbow. Again, the patient was reluctant to begin therapy. On evaluation 1 year after onset of symptoms, additional progression was evident with significant micrographia (Fig. 19-6) and cogwheel rigidity now evident at left shoulder, elbow and wrist. Therapy with Sinemet (10-100 mg., t.i.d.)⁵ was begun. Re-evaluation one week later demonstrated a marked improvement in handwriting (Fig. 19-6) and decreased cogwheel rigidity.

⁴ This patient was followed for a total of 19 years after disease onset, initially for the first 13 years by the author, subsequently by Dr Paula Ravin at the University of Massachusetts Medical Center, Dr. David Standeart at the Massachusetts General Hospital and Dr. Warren Olanow at the Mount Sinai Hospital in New York.

⁵ This is a combination of 10 mg. of carbidopa (Dopa decarboxylase inhibitor) and 100 mg. of L-Dopa. Higher dosage combinations are a) 25 mg. of carbidopa with 100 mg L-Dopa, and b) 25 mg. carbidopa with 250 mg. L-Dopa. A sustained release form is also available (50 mg. of carbidopa with 200 mg. of L-Dopa), and is marketed as Sinemet CR.

As the dose of Sinemet was increased to (10-100) mg.5x/day over the next week, occasional choreiform movements of the fingers of the left hand and occasional backward flinging (hemi ballistic) movements of the left arm occurred. As the dose reached 10-100 mg. 6x/day, the patient reported that his handwriting now was back to normal. Examination confirmed the significant improvement in handwriting and in gait - with a better movement of the left leg. He no longer turned en bloc. Cogwheel rigidity was still present at left shoulder but to only a minimal degree at left wrist and elbow. The patient did experience 90 minutes after a Sinemet dose - a tremor of the left shoulder and an exaggerated grasp of the left foot toes on lifting the leg (possible form of dyskinetic or dystonic reaction).

The patient did well. When seen one year later, he had only a minimal degree of cogwheel rigidity. No tremor was evident. In walking he had a good swing of the arms and no longer turned en bloc. He was aware that some symptoms of his underlying disease would emerge 3-4 hours after a dose of Sinemet.

He continued to have progression of disease despite the use of all of the known anti Parkinson medications. He eventually underwent a fetal cell transplant in 1997 with apparently little improvement but with a significant increase in dyskinesias.

Re-evaluation, three years after onset of symptoms, indicated a minor progression with decreased swing of the arm and movements of the left leg, which were less smooth. The patient had increased his daily dosage of Sinemet to (10-100 mg) 6 (or) 7 tabs and noted that duration of action was approximately three hours. Re-evaluation, five years after onset of symptoms, indicated that despite having increased his dosage of Sinemet to 25-100 mg. tablets, 7 or 8 x/day, more resting tremor of the left hand had emerged. (In actuality 75-100mg of carbidopa is probably sufficient to saturate the peripheral dopa decarboxylase system). Moreover, choreiform movements of the left arm occurred 60 to 90 minutes after each dose of Sinemet. Examination demonstrated a pill-rolling tremor of the left hand as the patient walked down the hall. The choreiform movements disappeared when the dosage of Sinemet was reduced to 25/100mg 6/day. The increased rigidity and tremor responded to the addition of a DOPA agonist Bromocriptine (Parlodel) - Initial dosage 1.25 mg. 2x/day then increased to a total dose of 5.0 mg., and subsequently to 7.5 mg./day. Despite increasing dosage of the Bromocriptine to 17.5 mg/day - no additional improvement occurred. Additional reduction of Sinemet to (25-100) 5x/day - eliminated sudden myoclonic jerks and dyskinetic movement of the left lower extremity, which would occur - 45 minutes after a dose of Sinemet. Examination 6 years after onset of symptoms, examination and 3.5 hours after last dose of Sinemet demonstrated a coarse pill rolling tremor of the left hand and a shuffling of the left foot in walking. Marked cogwheel rigidity was present at left wrist and elbow. Considerable slowness of alternating finger movements was present. Handwriting was small and slow. Amantadine (an antiviral agent with mild ant parkinsonian effects), 200 mg./day was added at this point with a considerable improvement in symptomatology.

When examined 7 years after onset of symptoms, and 2.5 hours after Sinemet dosage and he now had a prominent tremor of the left hand at rest and a minor tremor of the right hand. Only minor cogwheel rigidity of left wrist and elbow were present. There was mild facial akinesia, tremor of the closed lids and a positive glabellar sign. As he walked he had a problem with sequential movements of the left leg. He reported that initially in the mornings, he had considerable problems in the initiation of movements of his left hand. Because effects of the Sinemet were wearing off in a shorter period of time - the dosing interval was altered to every three hours, in the process increasing total intake to 6 and then 7 tablets per day, with transient improvement. When seen 8 years after onset of symptoms, he was having sudden "kick in of the on effects" at 30-45 minutes and wearing off effects of greater degree at 3 hours after Sinemet dosage. As a result balance had shown some deterioration. Although tremor and cogwheel rigidity were primarily present left arm lesser symptoms were present in the right arm. At this point, a monoamine oxidase B. inhibitor was added: Selegiline (Deprenyl) in a total dose of 10 mg./day (5 mg., b.i.d.). When seen 6months later, the patient was uncertain that any benefit had been achieved. A major symptom was now "freezing" - he would have times in going over the threshold of a door when he would suddenly freeze. This, at times, related to the wearing off of medication (Sinemet) effect but at other times, usually in the afternoon, was unrelated to time of last dose. In the morning, freezing effect was clearly related to time of dosage. He remained relatively stable for the next year and then had a progression of symptoms - increasing tremor, increasing dragging of the left leg and more wearing off of dose effect - usually after 2.5 hours. In addition, "freezing" episodes were occurring more frequently in between dose wear off periods, usually in going through a doorway or even in hallways. At this point, the patient was switched to the sustained release form of Sinemet (50/200 mg carbidopa/L-Dopa) taken three times a day. Amantadine, Bromocriptine and Selegiline were continued unchanged. When evaluated 6 weeks later, there had been a remarkable improvement. He had a smoother day with fewer ups and downs, less dyskinesia and less stiffness. Effects of the medication were lasting 5-6 hours. When seen 3.5 hours after his last Sinemet dosage, he had

very little cogwheel rigidity. He could walk with a good swing of the arms. Handwriting was good with little tremor and little dyskinesia. On the other hand, when seen several weeks later, approximately 5.5 hours after his dose of sustained release Sinemet, he had marked difficulty, walked with small steps, and would arrest going through a doorway. Balance was poor, requiring a cane. There was a marked tremor of the left hand and to a lesser degree, of the right hand. A marked akinesia was present. However, within 20 minutes of his taking an additional tablet of sustained release Sinemet, a marked improvement again occurred. Despite this long course, the patient had been able to continue in his usual occupation. The patient subsequently was treated with a COMT inhibitor and was switched to another dopamine agonist pergolide with little apparent benefit. Eventually, in 1997 he was entered into the NIH sponsored fetal transplant study (subsequent imaging study did indicate that the patient was in the transplant and not the placebo group). It was unclear that this had produced any decrease in his disability. However evaluation 3 years after the transplant did demonstrate a marked increase in the dyskinesias involving head arms and torso. Some improvement in dyskinesias occurred when dopaminergic medications were reduced

Comment: Parkinson's disease is a progressive disorder of motor function, with variable manifestations of tremor, rigidity, akinesia, bradykinesia, and impairment of postural reflexes. Patients vary in the type of major involvement and in the rate of progression. Pharmacological management has rapidly evolved and in the process has provided considerable insights into the nature of basal ganglia function. For the specific patient, therapy must still be individualized. As this case history illustrates the pharmacological effects are time limited. Evaluation of therapy must always record the time of drug intake and the time of examination.

It is important to note that the disease remains progressive, despite the impressive pharmacological achievements. To prevent progression would require arresting or reversing the loss of the nigral cells producing dopamine or of introducing another source of dopamine producing neurons into the basal ganglia as discussed above. The future of fetal transplantation remains uncertain. Surgical procedures particularly deep brain stimulation involving the subthalamic nucleus or the globus pallidus may offer benefit to specific patients.

The following case, 19-2 provides an example of hemichorea.

Case 19-2 : This 88-year-old, right-handed, widowed white female with a past medical history of profound hearing impairment, adult onset diabetes, euthyroid goiter, coronary artery disease, and hypertension was brought by her daughter to Saint Vincent's Hospital because of uncontrollable movements ("twitching") of her left foot and shoulder. The daughter described the insidious onset of involuntary rotary movement in the left foot five days prior to admission, which increased in intensity and progressed to involve the left shoulder. The movements were constantly present, even during sleep. The movement was accompanied by a "shooting" pain on the left side of the body which the patient was not able to further describe. She denied loss of consciousness, dizziness, change in mental status, weakness, sensory impairment, visual changes, aphasia, or dysphagia associated with the movement disorder, but did describe a dull headache greater on the left side than on the right during the last few days prior to admission, not accompanied by nausea or vomiting. There was no history of a past movement disorder. Progression rather than spontaneous resolution of the choreiform movements which had begun to impair the patient's ability to ambulate with her walker prompted her daughter to seek medical attention.

Past history: The patient had been admitted briefly one year previously with confusion. and hyperglycemic state related to diabetes mellitus.

Physical Examination: vital signs were all normal.. Patient was alert and cooperative, though profoundly hard of hearing and exhibited involuntary twisting movements of her left foot and upward jerking movements of her left shoulder.

Neurological examination:

1. *Mental Status:* The patient was oriented x3. Memory and language were grossly intact, questions were answered appropriately, and mental status was consistent with the patient's baseline according to her daughter.
2. *Cranial Nerves:* Intact except: for Left eye blindness (cataracts), and gross impairment of hearing such that shouting was necessary to communicate.
3. *Motor System:*
 - a. Tone and strength in upper and lower extremities were normal except for minimal weakness in the left upper extremity(5-/5) .
 - b. Finger tapping, finger-to-nose and heel-to-shin were grossly intact with only slight left-sided difficulty due to involuntary movements.

- c. There was a persistent hemichorea without flinging motions in the left foot, more marked than the left shoulder. There were rotary, twisting movements at the left ankle and upward and rotary motions at the left shoulder. The movement was exacerbated by motor—tasks but did dissipate with sleep.
 - d. Gait was slightly unsteady due to hesitant placement of the left foot. She did quite well with minimal assistance.
 - e. Romberg was negative.
4. *Reflexes*: Deep tendon reflexes were symmetrical, and physiologic except for decreased Achilles secondary to diabetes. The right plantar response was flexor, the left ;extensor.
 5. *Sensation*: Intact except for symmetrically diminished vibration sense in toes.

Clinical diagnosis: hemichorea

Laboratory data:

1. *Electrolytes creatinine, and CBC* were normal. *Glucose* was elevated to 168; *ESR* - 36 mm/hr. *RPR* non-reactive. *ANA* was 1:80(not significant) .*Urine culture* was positive for group B Streptococcal - infection sensitive to Ampicillin. *EKG and chest X-ray* were unchanged from last admission.
2. *CT scan* on admission revealed bilateral basal ganglia calcification, bifrontal atrophy consistent with age, but no evidence of infarction, hemorrhage, or tumor and revealed no change from previous CT scan of 2 months previously.
3. *MRI scan* 3 days after admission, revealed mild cortical atrophy and a hyperdense area without mass effect or enhancement on gadolinium in the right basal ganglia (particularly the head of caudate and putamen) and external capsule consistent with subacute hemorrhage (Fig.19-7).

Hospital course: The patient was begun on haloperidol 0.5 mg by mouth every morning and advanced to 1 mg., by mouth., t.i.d. with some improvement in the hemichorea, particularly in the upper - extremity. Her hemichorea continued to improve over the next two weeks on haloperidol with only occasional twitching of the left shoulder and diminished but persistent, rotary movement of the left foot, both still exacerbated by motor tasks.

The following case 19-3 provides an example of hemiballismus

Case 19-3: This 79-year-old, right-handed, white housewife had the abrupt onset in the early morning hours, 2 days prior to admission, of almost constant flinging movements of the right arm over which she had no control. At the same time, she noted that her right arm felt numb and heavy. Over the next 2 days, the movements decreased markedly and she regained more control of the arm.

Past history: The patient had been a known diabetic for 21 years, receiving insulin - most recently, lente insulin, 25 units each morning.

Neurological examination:

1. *Mental Status*: intact ,the patient was alert and well oriented and without aphasia.
2. *Cranial Nerves*: All were intact.
3. *Motor System*:
 - a. Minimal weakness was present in the right upper extremity at the elbow, wrist and fingers
 - b. Alternating movements and finger-to-nose testing in the right hand were markedly impaired.
 - c. Gait was intact.
 - d. Occasional involuntary flinging movements occurred at the right shoulder.
4. *Sensory System*: Pain, touch, vibration and position sense were all absent in the right upper extremity to the elbow and decreased in this extremity above the elbow.

Clinical diagnosis: hemiballismus

Laboratory data: Chest and skull X-rays EEG, and cerebrospinal fluid studies were all normal.

Subsequent course: The flinging movements of the right arm subsided spontaneously, shortly after admission. Position sense returned and pain sensation showed a mild improvement. The ataxia on finger-to-nose testing disappeared.

Comment: The loss of pain, touch, vibration and position sense in the right upper extremity at the onset of symptoms in this case, would suggest a lesion involving the ventral posterior lateral nucleus of the thalamus, presumably as a result of occlusion of the penetrating branches of the

posterior cerebral artery. Such a lesion could have damaged the subthalamic nucleus as well. The severe dysmetria in the right upper extremity could well have reflected the severe sensory deficit in the right upper extremity. This would appear to be more likely than postulating a lacunar ataxic hemiplegia, due to involvement of the corona radiata in which the origin of the hemiballistic movements could have been in the adjacent caudate putamen. This however would not explain the severe sensory deficit. Note that the use of antidopaminergic agents will decrease or eliminate hemiballismus or hemichorea; however many patients as in this case resolve spontaneously.

The following case history provides an example of Huntington's disease.

Case 19-4: This 54-year-old right-handed divorced white female was referred for evaluation of a movement disorder. The patient lived alone and it was difficult to obtain much of any history from the patient. So far as she was concerned, she had no neurological problems. She denied any problem with her movements. She did indicate that she had worked for 10 years as a secretary/computer operator but had been fired 10 years ago because "she did not work fast enough". She did indicate that she had experienced problems with memory over the last year. The patient denied that she had never been treated on a psychiatric service. She denied receiving neuroleptics. She had a past history of hypertension but had not been reliable in taking her prescribed medication. The patient's son was aware that changes in emotion, personality, speech, gait and a movement disorder had been present for at least 3 years.

Family history: The patient denied any neurological family history except for a maternal uncle who had the "shakes". By contacting the patient's son age 27 and her mother now age 81 and then obtaining old records we were able to assemble additional information. The patient's father had been hospitalized at age 55 on the psychiatry service of St. Vincent Hospital. A review of that record indicated that for several years he had been showing irritability, had become suspicious and paranoid at work. He gave a history of choreiform movements of 20–30 years duration beginning with twitchings about the shoulders. This had progressed over the several years prior to admission, affecting his gait and the movements of the hands. The examination demonstrated that he was moderately depressed and impatient. As he sat, he had "purposeless" movements of his body particularly of the lower extremities. In walking he had "ballistic" movements. He walked on a broad base. Choreiform movements were noted in the tongue. The diagnosis of the neuropsychiatrist was Huntington's disease. He apparently died of cardiac disease shortly after that hospitalization.

The paternal grandfather had died at age 43 of pneumonia, the paternal grandmother at age 37 of gall bladder disease, neither was known to have Huntington's disease, but information was scanty. The patient's father had two siblings one alive at age 81, the other dead at age 68, both apparently unaffected. The patient's mother had a sister with essential tremor.

The patient had 2 siblings, a brother age 60, a sister age 44; both unaffected according to the patient's mother.

The patient had 4 children ages 34, 32, 30 and 27, and 3 grandchildren ages 13 years, 2 years, and 3 months. The eldest daughter age 34 had been depressed for 5 years and had problems with speech and walking for a number of years.

Neurological examination:

1. *Mental status*: the patient often avoided eye contact. Affect was usually inappropriate with laughter as the response to many questions. The overall mini-mental status score was 27/30. The only deficit related to delayed recall portion of the test (0/3 objects).

2. *Cranial nerves*: the patient had a hyperactive jaw jerk. She had frequent facial grimacing.

3. *Motor system*: the patient had decreased tone at wrists and elbows, but strength was intact.

As she sat she had frequent restless and at times choreiform movements of hands and feet.

Gait was often "bizarre" in terms of occasional sudden movements of a leg as moved down the hall and came to a stop. These same movements occurred as she remained standing. In addition in standing or walking, there were intermittent dystonic postures of either left or right arm.

4. *Reflexes*: Deep tendon stretch reflexes were everywhere hyperactive. Plantar responses were flexor. There was a minimal suggestion of grasp release.

5. *Sensory system*: intact

Clinical diagnosis: Huntington's disease.

Laboratory data:

1. *MRI scans of head* (Fig.19-13): The heads of the caudate nuclei were very atrophic. Cortical sulci were wide consistent with cortical atrophy. The lateral and third ventricles were secondarily dilated.
2. PCR testing for the CAG trinucleotide repeats of the Huntingtin gene.: allele 1=17; allele 2=42.
3. Thyroid studies, sedimentation rate, electrolytes, RPR, and antinuclear antibody were all normal.

Subsequent course: The patient refused any treatment for the movement disorder. The patient's son requested genetic testing and the issues were discussed. He and his siblings finally decided not to have the genetic testing performed. The patient's neurological status according to the son worsened to a moderate degree over the subsequent 3 years as regards speech, unsteadiness of gait, and mood swings but without any additional change in memory. The patient herself always appeared unaccompanied for follow up visits and reported no change in her condition.

Comment: Occasionally patients are encountered where changes in psychological function limit the information that the patient can provide.. In other cases denial of illness has a neurological as well as a psychological basis. In this case it was evident that this patient had not only symptoms relevant to the basal ganglia but also changes in cognitive function relevant to the cerebral cortex particularly the frontal areas. In such cases, information must be sought from other sources. In this case, the patient was willing to provide permission to contact those possible sources.

The clinical presentation in this case was clear-cut. In retrospect, many of the neurological features were similar to her father's findings on his admission 30 years previously. When did the patient's disease begin? This was uncertain, but we may presume that serious problems had been present at least 10 years earlier when she had been fired from her long time employment. Did this relate to motor problems, to changes in personality and interpersonal relations or to cognitive changes? Most likely, there were problems in all of these areas. According to her family, symptoms had been present for 2-3 years suggesting onset at age 51 or 52 years.

Case 19-5 provides an example of a patient with Huntington's disease followed over a longer period of time.

This 32 year old right-handed married white male spray painter at a computer factory, was referred for evaluation of a possible hereditary movement disorder. The patient was unclear about the reasons for his evaluation and much of the history was provided by his wife. She reported that the patient had undergone a personality change in the last several months. He had noticeable mood swings and on one occasion he reported people outside the window when no one actually had been there. He had some problems with remembering incidental matters, but no major problems and his job performance had remained intact. He was described as always having been "fidgety".

Past medical history - Mild hypertension for three years.

Family history - The patient's initial history indicated that the family had "Parkinson's" disease and his father had died in his 40's at the state hospital after a 10-15 year illness. The patient indicated that he was a child at the time and his mother never really told him much about the father or let him visit the father in the hospital but he did recall that perhaps his father had some excessive movements of the hands and face. The records were subsequently obtained and these indicated the father had been admitted to Worcester State Hospital in 1968 at age 37. At that time, he had already had three previous hospitalizations for "nervous breakdowns". At the time of his final admission, he had developed hallucinations, seeing people in his room. He had threatened his wife and other relatives. He had difficulty sleeping and he had also developed a problem with his legs "they are jumping". The father's examination had demonstrated a mumbled speech with repetition of the same phrases. His responses would often be tangential and then incoherent with impairment of memory and judgment. His mood was depressed. He was noted to have involuntary movements of the fingers and occasional facial grimacing. The deep tendon reflexes were hyperactive and the plantar responses were extensor. His gait was ataxic. The subsequent course indicated increasing ataxia, choreiform movements and rigidity with increasing weakness, difficulty swallowing and the final development of bronchial pneumonia with death at age 42. The diagnosis of Huntington's disease was confirmed at autopsy.

The paternal grandfather had expired at age 67 with a diagnosis of Huntington's disease, manifested by "nervous breakdowns, inability to sleep and movement disorder". The father's three siblings apparently did not manifest the disease. The patient had two siblings, brother age 28, a sister age 35, all without known disease. He had two children ages 9 and 5.

Neurological examination

1. *Mental Status* - The patient was anxious, often appeared blunted in emotional expression or in answering questions. He avoided eye contact. He was oriented for time, place and person. He was able to name objects and colors. His delayed recall was 2/5 without assistance and 4/5 with assistance.
2. *Cranial Nerves II-XII* were intact, except for the occurrence of occasional, sudden darting movements of the eyes to either left or right. In addition, occasional facial grimacing was noted occurring in a rather irregular manner.
3. *Motor System* : Strength and gait were intact . There were occasional, sudden, irregular, lateral, tremulous movements of the fingers of a choreiform-type.
4. *Reflexes* : Deep tendon reflexes including the jaw jerk were everywhere hyperactive. Plantar responses were bilaterally extensor (bilateral Babinski signs).
5. *Sensory system* : intact

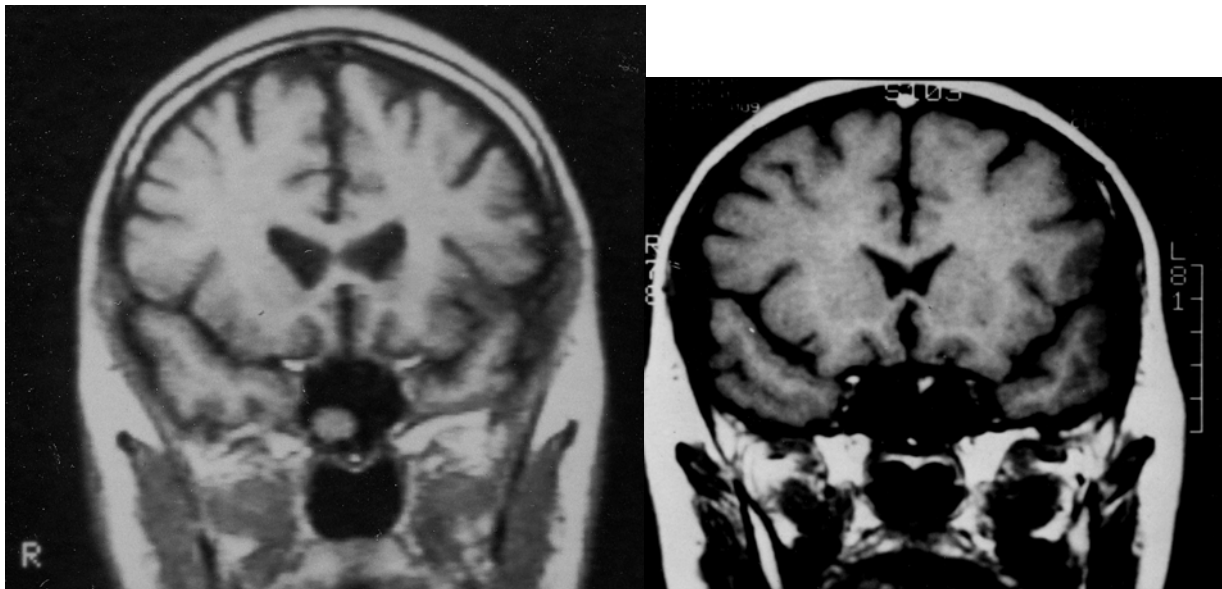
Clinical diagnosis: Huntington's disease

Laboratory Data :

1. All blood chemistries, including glucose; BUN, calcium, electrolytes, liver function studies, ceruloplasmin level, thyroid studies and serological test for syphilis were within normal limits. Ceruloplasmin levels are low in Wilson's disease but normal in Huntington's disease.
2. *Electroencephalogram* was normal with a dominant awake background activity of 10 Hz alpha rhythm.
3. *CT scan of the head* demonstrated enlargement of the ventricles with particular atrophy of the caudate. In addition the sulci were prominent for the age, suggesting some degree of cortical atrophy. The study was considered consistent with the clinical diagnosis of Huntington's disease.
4. The *MRI scan* (fig 19-11A) demonstrated mild enlargement of the ventricles and deepening of the cortical sulci, as well as a very significant atrophy of the head of the caudate nucleus. The MRI from this patient is compared to a similar section from a patient without signs of neurological disease (Figure 19-B)..

Figure 19-11A ;Case 19-5. Huntington's Disease

Figure 19-11B. Normal, age matched



Subsequent course :The patient subsequently developed increased paranoid ideation, increasing dependency with regard to his wife. He was treated with Haloperidol (a neuroleptic, tranquilizer) with considerable improvement with regard to personality. When evaluated, 3 years after onset of disease, it was evident that in the interim, the patient's personality problems had decreased. Attacks of anger and paranoid features had subsided. Mood swings were less. Memory problems, however, were worse and choreiform movements were worse. Dysarthria was now present. The patient had been divorced in the interim and he was on social security disability and no longer working. The examination now showed an exacerbation of many of those features noted at the time of his initial evaluation. He had occasional, sporadic movements of head or eyes of a

choreiform nature. He had frequent choreiform movements involving the fingers as he was sitting, also a similar type of movement appeared to involve the abdominal musculature. He had a moderate degree of dysarthria. He could walk a tandem gait but as he did so, the left arm came up in an somewhat flexed position. When last seen 4 years after onset of disease, he had more dysarthria and his speech was more difficult to interpret. There had been some increase in degree of rigidity but this had decreased when the dose of haloperidol had been decreased. The decrease in this medication, however, then resulted in a greater prominence of the choreiform movements. He could still handle a deck of cards, although he was dropping objects more often than previously. His neurological examination showed a significant degree of dysarthria, a greater degree of facial akinesia, more frequent choreiform movements of hands and face. He had difficulty in mimicking facial expression. As before, all of his deep tendon reflexes were hyperactive and the plantar responses were extensor. The patient walked in a flexed position and tended to turn en bloc. He had a mild degree of cogwheel rigidity at wrist and elbows. His memory remained remarkably good for delayed recall. Final telephone follow-up with his primary physician (approximately 7 years after apparent clinical onset of disease) indicated that the patient was no longer able to drive. He had continued weight loss. He had a marked dysarthria so that his speech was barely intelligible. Choreiform movements had increased. His gait was ataxic, but he could still walk without stumbling. He was relatively stable from a psychiatric standpoint. He was now living with his mother and brother.

Comment: This patient and his family demonstrate the relatively typical course of most patients with Huntington's disease. Patients and families do vary as to whether it is the psychiatric features or the movement disorder features that first bring the patient to medical attention. In this case, the psychiatric features, that is, the change in personality and the increasing paranoid ideation were the first features noted. Subsequently, involvement of the motor system became the most prominent feature. As in the previous case, the patient was unclear as to why he had come for neurological evaluation. Was this a neurological or a psychological denial of illness? Most likely both factors were operational. It was of considerable interest that this patient when first seen, although he was aware of some neurological problem that had occurred in the family, was unclear as to the specific diagnosis. It was also evident that almost no genetic counseling had been done in a disorder that was very clearly an autosomal dominant disorder. The significant family impact, social and economic impact of the disease are clearly evident in this patient. The implications of presymptomatic detection are discussed by Meisser et al (1988), and Klawans (1972).

The following Case 19-6 illustrates the clinical problem of hepatolenticular degeneration in a 21 year old female with a brother who had died at age 16 with hepatic disease, a Kayser Fleischer ring and choreoathetosis. The patient had serum elevation of free copper and a decrease in protein bound copper. She was successfully treated with penicillamine.

Case 19-6 (Patient of Doctor Huntington Porter) :This 21-year-old, single, white female shoe worker in January 1954 had the onset of a "shaking", or trembling of the fingers and hands which progressed to involve both arms and legs. The degree of involvement increased sufficiently to force her to give up her work. Nine months after onset of symptoms, she began to note increasing difficulty with balance and coordination and a slurring of speech. She had also noted increasing weakness and difficulty in doing repetitive tasks. One year after onset, the patient noted blurring of vision, occasional diplopia, and periods of "staring". She also had experienced increasing urgency and occasional urinary incontinence.

Family history: A brother of the patient had died in 1952, at age 16, of a disease with manifestations similar to this patient's. Evaluation of the sibling 2 years before his death by Drs. John Sullivan, Raymond Adams and D. Denny-Brown, had indicated the presence of choreoathetosis with lapses in posture of the hands. In addition, a brownish green ring at the corneal -

scleral junction was noted. Liver disease was present in this sibling and possibly other members of the family.

Neurological examination:

1. Mental status:

- a. The patient was anxious, at times crying, at other times, euphoric.
- b. Digit span was limited to 6 forward, 3 in reverse.
- c. Serial 7 subtractions were poorly performed.

2. Cranial Nerves:

- a. A brown rim was present at the limbus of the cornea, more evidence inferiorly and superiorly.
- b. Extraocular movements were impaired by involuntary jerk movements, The patient was unable to track a moving finger.
- c. Facial expression was mask-like.
- d. Speech was dysarthric and of a nasal quality with slurring and slowness of articulation.

3. Motor System:

- a. No actual weakness was present. However, this patient had difficulty maintaining the limbs in a fixed posture.
- b. There was a rigidity to passive movement of the limbs.
- c. A coarse arrhythmic tremor was present which was most marked proximally and more marked on sustained posture and on movement than at rest.
- d. Alternating movements were poorly performed.
- e. Gait was ataxic. Romberg test was negative.

4. Reflexes: Deep tendon stretch reflexes were hyperactive but plantar responses were flexor

5. Sensation: Intact

Clinical diagnosis: Wilson's disease: hepatolenticular degeneration.

Laboratory data:

1. Liver function tests were normal.
2. *Glucose tolerance test* was normal, but glycosuria occurred.
3. *Total plasma copper* 52 ug/100 ml. (normal range in a young adult is 65 to 150 ug/100 ml).
Direct reacting copper (unbound to ceruloplasmin) 31 ug/100ml (normal 10 ug/100 ml).
Indirect copper (ceruloplasmin bound) 21 ug/100 ml, normal 105 ug/ ml).

Subsequent course: The patient did relatively well following the use of the chelating agents, BAL and calcium versenate and the institution of a copper free diet. A liver biopsy performed at the time of a cesarean section 18 months after beginning treatment was compatible with perihepatitis with a question of post-necrotic cirrhosis.

Re-evaluation 6 years after onset revealed, in addition to the earlier findings, the presence of "continual spontaneous involuntary movements of the limbs; at the feet, characterized by alternating flexion and extension at the ankle and a waving of the toes". A broad amplitude coarse tremor was noted when the patient was asked to abduct arms, flex elbows, and hold hands just before her nose (wing beating position). A side-to-side tremor of the head was also present. The gait was slightly wide-based and associated with continual dystonic movements of the hands and arms. Treatment with d-penicillamine (which had just become available) was begun at that time.

Urine copper excretion increased from 700 ug per 24 hours to 3240 ug per 24 hours. Normal 24-hour urinary copper in the adult is less than 40 ug. Neurological symptoms soon demonstrated improvement from the previously noted status. The patient was now able to do her house work and take care of her children.

Follow-up 2 years later, indicated significant improvement as regards the findings noted in 1960; dystonic facies and dysarthria was less marked. No tremor was present in the left hand; that in the right hand was evident only when under tension. Dystonic posturing of the hands was present only to a minimal degree. At last report 4 years later, and 12 years after onset of the disease, the patient continued to do well. She had remarried and was expecting another child.

Comment:

This patient presents a typical case of Wilson's disease with onset in the young adult years and with a definite familial background. The copper levels were consistent with the diagnosis (an increased unbound fraction and a decreased bound fraction). At the time that this patient was seen in the mid 1950's and early 1960's, ceruloplasmin levels were not available. Early establishment of a specific diagnosis in this case allowed for specific therapy with improvement of neurological symptoms and the prevention of progression of hepatic disease. With a specific diagnosis established in the patient, periodic blood tests were performed on her offspring to determine whether they also had inherited this genetic disease. (The child born 18 months after onset of the disease had not the disorder.)

An acquired form of non-Wilsonian hepatic and cerebral degeneration occurs in patients who have had multiple episodes of hepatic coma. Degenerative changes occur in the astrocytes and neurons of the basal ganglia. This disorder which was first described by Adams and Victor is discussed in greater detail above.

CHAPTER 20. MOTOR SYSTEMS III: CEREBELLUM

The following case provides an example of a child with a medulloblastoma.

Case 20-1: This 27-month old white female was referred for evaluation of ataxia. The mother had noted that the child had been unsteady in gait, with poor balance, falling frequently since the age of 13 months, when she began to walk. Three months prior to admission, in relation to a viral infection manifested by fever and diarrhea, the patient developed increasing anorexia and lethargy. One-month prior to admission, vomiting increased, and the patient also became more irritable. Perinatal history had been normal, and head circumference had remained normal.

Neurologic examination:

1. *Mental Status:* The child was irritable but cooperative.
2. *Cranial Nerves:* The fundi could not be visualized. Bobbing of the head was present in the sitting position.
3. *Motor System:* A significant ataxia of the trunk was present when sitting or standing. Gait was broad-based and ataxic, requiring assistance. No ataxia or tremor of the extremities was present. Strength and tone were normal.
4. *Reflexes:* Deep tendon reflexes were symmetric and plantar responses were flexor.
5. *Sensory System:* All modalities were intact.

Clinical diagnosis: Probable midline cerebellar tumor, most likely based on age a medulloblastoma

Laboratory data:

1. *Left brachial arteriogram* indicated an avascular area in the posterior fossa. The superior cerebellar artery was elevated. The inferior cerebellar arteries were depressed.
2. *Air-contrast ventriculogram* demonstrated enlargement of the lateral and third ventricles. The cerebral aqueduct was displaced forward to a marked degree. The fourth ventricle was deformed by a mass overlying the posterior wall (essentially located in the nodulus).

Hospital Course: Doctor Peter Carney performed a suboccipital craniotomy. The dura was bulging. The cerebellar tonsils were herniated to a minor degree. On gentle retraction of the inferior posterior vermis, a pinkish gray tumor, originating from a higher point in the fourth ventricle, was visualized at the obex. Limited biopsies of this tumor were taken, revealing a medulloblastoma. Samples of cerebrospinal fluid obtained at surgery revealed the presence of many malignant cells. A permanent shunt from the lateral ventricle to the jugular vein was not installed because of the possibility of spread of tumor cells into systemic circulation. Instead, a catheter was connected from the lateral ventricle to a small reservoir inserted under the skin of the scalp to allow daily drainage. Radiation therapy to the entire central nervous axis was begun one week after surgery. By the time of hospital discharge two weeks after the operation, the patient was able to walk unassisted, with only a moderate degree of ataxia. Three months after the operation, the patient was readmitted because of recurrent irritability and vomiting. A mild degree of papilledema was present. Horizontal nystagmus was present on lateral gaze bilaterally. A wide-base ataxic gait was still present. Various antineoplastic agents were employed (methotrexate into the cerebrospinal fluid and vincristine intravenously) without significant improvement. One month later, respirations became slow, deep, and irregular and death occurred. The findings at autopsy are demonstrated in Fig. 20-4.

In the following case a metastatic tumor in the midline cerebellum produced vertigo, ataxia of gait and headaches.

Case 20-2: This 67 year old white female 6 weeks prior to admission developed intermittent vertigo. Two weeks prior to admission she developed an ataxia of gait. Two days later headaches and true vertigo developed, ataxia increased and vomiting occurred. On the day of admission severe vertigo, headache and nausea and vomiting resulted in her visit to the emergency room

Past history: The patient had a lumpectomy 6 years prior to admission for carcinoma of the left breast. She had undergone a radical mastectomy followed by radiation therapy 3 years prior to admission for a recurrence of malignancy. Histologic examination of the excised tissue indicated a very poorly differentiated (high grade of malignancy) infiltrating ductal tumor which was negative for estrogen and progesterone receptors. On both occasions, the patient refused chemotherapy. The patient had multiple other medical problems including non insulin dependent diabetes mellitus, coronary artery disease, mild hypertension, and prior hip replacement surgery.

Neurological examination (in the emergency room)

1. **Mental Status:** Intact
2. **Cranial Nerves:** Intact except for an absence of venous pulsations on funduscopic examination suggesting a mild increase in intracranial pressure without frank papilledema.
3. **Motor System:** The patient had difficulty standing tending to fall to the right. She was unable to walk because of severe ataxia. There was no limb dysmetria.
4. **Reflexes:** Deep tendon stretch reflexes were symmetrical. The right plantar response was equivocal.
5. **Sensory system:** Intact

Clinical diagnosis: Midline cerebellar tumor metastatic from breast.

Laboratory data :

1. **CT scan of brain:** A large (3-4 cm) enhancing tumor was present involving the midline vermis and right paramedian cerebellum and compressing the fourth ventricle.

2. **MRI of brain** (3 days after admission): An enhancing midline mass involved the cerebellar vermis extended into the right cerebellar hemisphere, and produced mass effect upon 4th ventricle (Fig. 20-5).

3. **CT scan of abdomen** demonstrated two solitary possible metastatic lesions in the liver.

Subsequent course: The patient was immediately placed on dexamethasone with significant improvement. Within 12 hours the examination demonstrated only a mild ataxia tandem gait on turns and bilateral extensor plantar responses. The patient strongly insisted on removal of the solitary central nervous system metastases. Histological examination of the tumor resected by Dr. Gerald McGullicuddy demonstrated poorly differentiated adenocarcinoma with extensive necrosis similar to the tumor which previously had been removed from the breast. Following surgery she received 3000cGy(rads) whole brain radiation and was begun on the antitumor agent tamoxifen. She continued to manifest some unsteadiness on gait but had no difficulty in finger to nose or heel to shin tests. Three months after her admission, a repeat CT scan of the abdomen and pelvis demonstrated diffuse hepatic metastases with mesenteric and retroperitoneal lymphadenopathy. She expired at home, four

months after surgery before she was to start additional treatment with the antineoplastic combination of Cytosan, methotrexate and 5-fluorouracil.

Comment : This patient had a highly malignant poorly differentiated adenocarcinoma of the breast and was clearly at risk for the development of distant metastases, a risk that was likely increased by her unwillingness to receive antitumor medication. Six years after the lumpectomy she presented with vertigo, ataxia headache and nausea and vomiting, without limb dysmetria. These symptoms suggested involvement of those areas of cerebellum related to the vestibular system and the axis of the body: the floccular nodular area and vermis. Certainly, the best treatment of a solitary metastatic brain tumor where systemic metastases are not present is the combination of total resection of the brain lesion followed by radiotherapy. However at the time of surgery, this patient already had evidence of two probable metastatic lesions in the liver. Except for the strong insistence of the patient that the tumor in brain be removed, an alternate course of radiotherapy, dexamethasone and chemotherapy might have been pursued. Nevertheless the patient had several additional months of life during which she was able to travel to visit various relatives for a last time. Consistent with the highly malignant character of the tumor, this patient succumbed to the non neurologic effects of her disease.

The following case history 20-3 illustrates the problem of alcoholic cerebellar degeneration.

Case History 20-3: This 64-year-old, white male was admitted with a chief complaint of a slowly progressive incoordination of gait present for 8 years. The patient and others had noted that his gait was staggering. The patient denied weakness, numbness, diplopia, vertigo, or memory difficulty. The patient admitted to the consumption of one half pint (250cc) of brandy every 4 nights since symptoms had developed. He indicated that he used to drink more in his younger days, at least 6 to 8 beers in addition to brandy or other alcoholic beverages every night.

There was no history of pes cavus or neurological disease.

General physical examination : Blood pressure 140/80. Liver was enlarged with the inferior edge extending 2 finger breadths beyond the costal margin. Face was red with dilation of vessels.

Neurological examination:

1. *Mental status:* The patient was slightly disoriented for time. He gave the date as September 31. The date was actually October 19. Delayed recall was 0-out-of-5 objects in 5 minutes. He was unable to give the date of his birth, but he knew his phone number. Digit span was 7 forward, 4 in reverse. Calculations: The patient was unable to subtract 7 from 100 or 3 from 30; he could not add 14 and 13, although he had a fourth grade education.

2. *Cranial nerves:* All were intact. No nystagmus was present.

3. *Motor system:* Strength was intact. Gait was broad-based with an ataxia of trunk. The patient was unable to walk a tandem gait. His ataxia was accentuated by rapid walking. Small lateral nodding movements of the head were noted. He was relatively stable when sitting. There was a minimal tremor at rest. In addition, there was, to minor degree, a resistance to passive motion at the wrists and elbows with a suggestion of a cogwheel component. There was a minor tremor on finger-to-nose testing and a minor impairment of alternating hand movements.

There was, however, a very significant heel-to-shin ataxia which was out of proportion to any tremor or ataxia involving the upper extremities.

4. *Reflexes:* Deep tendon reflexes were physiological and symmetrical (2-3+). Plantar responses were flexor bilaterally.

5. *Sensory system:* Position, pain and touch were intact. There was a moderate decrease in vibratory sensation at the toes and ankles.

Clinical diagnosis: 1. Alcoholic cerebellar degeneration. 2. Mild dementia possible residuals of Wernicke's-Korsakoff syndrome.

Laboratory data: Complete blood count, albumin and total protein, sedimentation rate, cerebrospinal fluid, and skull and chest X-rays were normal.

Subsequent course: The patient received multiple B vitamins and was advised to discontinue any intake of alcohol. Neurological re-evaluation over the next 6 years indicated that no essential progression had occurred.

Comment: The major findings of the broad-based, staggering gait with truncal ataxia and heel-to-shin ataxia may be related to the anterior lobe of the cerebellum. In view of the absence of progression after the discontinuation of alcohol, a toxic or nutritional factor may be postulated (The reliability of the history obtained, in terms of the specific amount of alcohol intake is always open to question particularly in a patient

with significant problems in memory. The amount stated by the patient is usually assume to be the minimum amount.). The minor extrapyramidal findings of cogwheel rigidity may have represented unrelated disease. The lack of progression would be evidence against the diagnosis of a cerebellar degeneration of other etiology (see below). The minor degree of dementia may have related to previous nutritional problems with minor Wernicke-Korsakoff's syndrome or may have reflected a minor unrelated dementia or may have related to long standing retardation. At the present time, the diagnosis may be confirmed by CT scan or by MRI (midline sagittal section) (as in Fig. 20-7 or 20-8). As a result, evidence of cerebellar atrophy is now found in many patients presenting with other aspects of chronic alcoholism or other nutritional disease who do not necessarily present with initial symptoms of ataxia.

In the following case, a similar cerebellar gait disorder and heel to shin ataxia occurred o a genetic basis.

Case 20-4: A 45-year-old single white male carpenter presented with a 4 year history of progressive unsteadiness in walking, present during the daytime as well as at night. He had, during this period, noted minimal loss of coordinated movements in his hands, but felt that his greatest deficit was unsteadiness. The patient had noted no actual weakness but reported some numbness at the toes. He had also noted some minor difficulty in swallowing.

The patient lived in a small town in Virginia. Family historical information was incomplete His mother and father were second cousins. Several aunts and uncles had "trouble with their legs" in later life, resulting in a difficulty in walking. The patient admitted to a minimal intake of alcohol in the past. He had recently been under the care of a naturopath and had experienced a 7-pound weight loss.

Neurologic examination:

1. *Mental status:* Intact and consistent with his educational level.
2. *Cranial nerves:* Intact except for minimal dysarthria. Horizontal nystagmus was present on lateral gaze, vertical nystagmus on upward gaze.
3. *Motor system:* Strength was intact. The patient walked on a broad base with an ataxia of trunk, as though intoxicated, reeling from side to side, with marked unsteadiness on turns. He was unable to walk a tandem gait with eyes open. The patient was able to sit without significant ataxia of the trunk. A mild intention tremor was present, and there was minimal disorganization of alternating movements. In contrast a marked ataxia and tremor were evident on heel-to-shin test.
4. *Reflexes:* Deep tendon reflexes were intact, except for a relative decrease in ankle jerks compared to knee jerks. Plantar responses were flexor.
5. *Sensory system:* Intact, except for a minimal decrease in vibration sensation at the toes.

Clinical diagnosis: Hereditary cerebellar degeneration involving predominantly anterior lobe

Laboratory Data: Pneumoencephalogram performed at the University of Virginia Hospital (Doctor Stewart) confirmed the significant atrophy of cerebellum. Cerebrospinal fluid and other laboratory data were normal.

Comment: This patient had onset of ataxia at age 41 and was seen relatively early in his disease course. The most prominent features included the ataxia of gait and the heel to shin dysmetria. The patient also had a minor dysarthria, nystagmus and a mild asymptomatic peripheral neuropathy (decreased Achilles reflexes and decreased vibration at toes). There was a familial background but the information was incomplete. The subject of genetic cerebellar degeneration will be considered in a later section. Using older terminology, this patient would have been classified as olivopontocerebellar atrophy. Using more modern terminology, the patient might be included within the category of autosomal dominant cerebellar ataxia type I, had more genetic information regarding the family been available by history and or actual examination.

The following case history illustrates a focal lesion of the lateral hemisphere

Case 20-5 : This 36-year-old white male attorney was referred with a chief complaint of headaches and vomiting. The patient had frontal and biparietal headaches for approximately one month precipitated by coughing, sneezing, or bending. On at least one occasion, the patient had been awakened by the headache. The patient had nausea and vomiting independent of the headaches, at times, occurring suddenly without preceding nausea. For several weeks prior to admission, the patient had been unsteady on his feet, with a tendency to fall to the right, and had noted intermittent clumsiness of his right hand. For several days prior to admission, the

patient had double vision and had to keep one eye closed. During the week prior to admission, he had been excessively drowsy and constantly tired. The headaches had increased in frequency and were now occurring 3 to 4 times per day.

Neurologic examination:

1. Mental status: Intact.

2. *Cranial nerves:*

- a. On funduscopic examination there was evidence of bilateral papilledema.
- b. A bilateral paralysis of the sixth nerve was present.
- c. Horizontal nystagmus was present on right lateral gaze.

3. *Motor system:*

- a. Strength was everywhere intact.
- b. The patient's gait was wide-based. In walking, the patient tended to veer to the right. The patient was unable to stand independently on his right leg.
- c. There was a significant intention tremor of the right upper extremity on finger-to-nose test and of the right lower extremity on heel-to-shin test. Alternating movements of the right hand were disorganized.

4. *Reflexes:* Deep tendon stretch reflexes were normal and plantar responses were flexor.

5. *Sensory system:* All modalities were intact.

Clinical diagnosis: Tumor of the right cerebellar hemisphere with obstruction of ventricular system producing increased intracranial pressure and resulting in papilledema and bilateral cranial nerve VI palsy.

Laboratory Data:

1. Complete blood count and skull x-rays were normal.
2. *Right brachial arteriogram* revealed, in the late arterial phase, a blush in the right inferior and posterior cerebellar hemisphere consistent with a hemangioblastoma.
3. *Pantopaque ventriculogram* revealed a dilated third ventricle and a dilated aqueduct with obstruction to outflow from the fourth ventricle. The fourth ventricle and to a lesser degree, the aqueduct, were shifted to the left. These findings were consistent with a right cerebellar mass displacing and obstructing the fourth ventricle.

Hospital Course: The patient was placed on high dosage of dexamethasone to relieve increased intracranial pressure. Later that day a suboccipital craniectomy was performed by Doctor Samuel Brendler. When the dura was opened, bulging of the lower portion of the right cerebellar hemisphere was noted, with widening of the cerebellar folia. The widest area of the folia was tapped with a needle and a yellow cystic fluid was removed. A transcortical incision was then made, revealing a large cyst with a small strawberry-shaped hemangioma located within. The stalk of this tumor was ligated, and the hemangioma separated from the cystic capsule. Histologic examination of the tumor revealed a hemangioblastoma.

Postoperatively, the patient did well. His headache and diplopia disappeared. There was then improvement in the patient's tremor and ataxia, although there was a slight slowness on finger-to-nose testing on the right. A minor side-to-side tremor was present on right heel-to-shin testing. There was a tendency to veer to the right in walking, but tandem gait indicated only a minor unsteadiness. Evaluation six months after surgery, indicated only a minimal unsteadiness on tandem walking. Evaluation 9 months after surgery later indicated no significant neurologic findings. Re-evaluation three and one-half years after surgery, again indicated a completely intact neurologic status.

Comment: The headaches experienced by the patient, with pain occurring on coughing, sneezing, or mechanical changes, suggested a space-occupying lesion near the ventricular system or meninges. The tumor had produced a block of the ventricular system relatively early in its course, leading to an increase in intracranial pressure, with headache, vomiting and papilledema. The bilateral sixth-cranial nerve weakness was of moderate degree, and

its occurrence would not be unusual in a situation where intracranial pressure had rapidly increased.

The cerebellar symptoms experienced by the patient were lateralized in the sense that the patient was falling to the right side and had noted clumsiness of his right hand. Lateralized cerebellar disease was confirmed by the examination findings of intention tremor of the right arm and leg and disorganization of alternating movements on the right side.

In this case, the hemangioblastoma was in the lateral cerebellar hemisphere. In other cases of hemangioblastoma, the lesion is much more midline in location, and the symptoms are those of a midline cerebellar tumor. Thus, the patient may complain of an ataxia of gait and truncal ataxia and not display clearly lateralized symptoms involving the appendages, such as intention tremor and/or ataxia on heel-to-shin testing. The nodule of tumor often exists within a non-neoplastic cystic cavity. It is, therefore, possible to remove the tumor without sacrificing a large amount of the cerebellum. In some cases, both the mural nodule and the cyst are removed. In almost all cases a complete cure is obtained; recurrences are unlikely and the patients usually have a relatively complete resolution of symptoms and no residual disability.

In some cases, hemangioblastomas of the cerebellum are associated with angiomatous malformations of the retina (Landau-von-Hippel's disease). In some cases, there is an association with a secondary increase in red blood cell production (polycythemia). In rare cases, there is an association with tumors of the kidney. Other neoplasms may also involve the cerebellar hemispheres: cystic astrocytomas, metastatic tumors, and posterior fossa meningiomas. Meningiomas of the angioblastic type may be difficult to distinguish from hemangioblastomas.

At the present time, the diagnosis of these tumors may be readily made by means of MRI and CT scan (Fig. 20-11). Ventriculograms are no longer required. Arteriograms may still be of value in defining the vascularity and blood supply of the tumor.

The following case history presents a typical example of posterior inferior cerebellar artery infarct, the territory most frequently affected selectively.

Case 20-6: This 64-year-old right-handed married white male postmaster, on the morning prior to admission, awoke at 3:00 a.m. with severe posterior headache and severe vertigo, which was exacerbated by any head movement. Nausea, projectile vomiting and slurred speech soon developed. Shortly afterwards, he noted left facial paresthesias, clumsiness of the left upper extremity, and diplopia. He was admitted to his local hospital with a diagnosis of labyrinthine vertigo and then transferred to the neurology unit at Saint Vincent Hospital when symptoms began to evolve.

Two weeks previously, the patient had been seen for a transient episode of difficulty controlling the right arm, a hissing sensation, and impairment of speech.

Past history: The patient had evidence of significant vascular disease. He had hypertension and had undergone coronary artery bypass surgery. Beginning six years previously he had experienced episodes of transient weakness and numbness of the right arm with transient aphasia. He had normal aortic arch and carotid angiographic studies but EEG had demonstrated focal left frontal/temporal slow wave activity. He had been placed on long term anticoagulation. He had experienced migraine headaches without aura for many years.

Neurologic examination:

1. *Mental status:* Intact.
2. *Cranial nerves:* Conjugate lateral gaze to the left was impaired.
3. *Motor system:* Strength was intact. Significant lateralized cerebellar findings were present with marked dysmetria of left upper extremity on finger-to-nose testing and impairment of alternating hand movements. In attempting to stand, the patient was markedly ataxic.

4. *Reflexes*: Deep tendon stretch reflexes were decreased in both lower extremities. Plantar response was extensor on the right and flexor on the left.
5. *Sensory system*: Intact
- Clinical diagnosis**: Left cerebellar hemisphere infarct or hemorrhage with possible minor involvement of brainstem secondary to mass effect.

Laboratory data:

1. Duplex scans of carotids and vertebrals were normal.
2. *Transcranial Doppler studies* indicated normal flow velocities in the vertebral, basilar, anterior and middle cerebral arteries.
3. *Magnetic-resonance angiography* demonstrated occlusion of the left vertebral artery.
4. *CT scan* demonstrated a large left cerebellar infarct pressing the fourth ventricle to the right.
5. *MRI* (2 months after onset of symptoms): Infarction of the total cerebellar territory of the left posterior inferior cerebellar artery with no actual infarct of the brain stem (Fig. 20-12).

Subsequent course: The patient was somewhat vague with some difficulty in memory during the subsequent 8-day hospital course and remained ataxic. He was then transferred to the Fairlawn Rehabilitation Hospital where, over the next three weeks, he had a significant improvement. When re-evaluated two months after onset of symptoms, he was able to walk well with the use of a cane. A minor intention tremor was present on the left finger-to-nose test. An MRI study was obtained at this point, with results indicated above (because new symptoms suggested possible involvement of upper cervical nerve roots and spinal accessory nerve). Additional improvement was evident on evaluation three months after onset of symptoms. Evaluation 6 months after onset of symptoms demonstrated only a slight slowness of alternating movements of the left hand.

Comment: The acute onset of headache, vertigo, vomiting, ataxia of gait, and dysmetria of the left arm suggested an acute cerebrovascular problem involving the posterior circulation and the posterior fossa. (The syndrome of acute headache, vertigo, ataxia, nausea and vomiting is also seen in cases of acute cerebellar hemorrhage.) Numbness on the left side of the face and diplopia suggested, as well, possible brainstem involvement. The initial diagnosis at the local hospital of acute vestibular disturbance did not explain the headache, the diplopia or the lateralized findings. The presence of the left arm dysmetria suggested lateral hemispheric involvement rather than limited midline involvement.

In the era before CT scan and MRI, the distinction between acute cerebellar hemorrhage and acute cerebellar infarct was often difficult to make. Either lesion could produce block or distortion of the ventricular system and secondary hydrocephalus. Either lesion could be associated with the development of brainstem symptoms. The cerebellar infarct, often in the distribution of the posterior inferior cerebellar artery or the anterior inferior cerebellar artery, could also involve the medullary or pontine territories of these vessels. In addition, either type of lesion could cause significant edema with secondary distortion of the brainstem. Hemorrhage could also extend into the cerebellar peduncle and brainstem.

If significant clinical hydrocephalus or brainstem compromise develops, either type of lesion may require neurosurgical decompression or a shunt procedure.

A final note should be made regarding the considerable ability of the human nervous system to recover from extensive cerebellar lesions. Considerable recovery is possible because the cerebellum does not have a direct line role in the control of motor activity but instead, acts as a modulator of the motor control and motor planning circuits.

The following case history provides an example of a cerebellar hemorrhage secondary to an arteriovenous malformation.

Case 20-7: This 57-year-old right-handed married white female had the sudden onset of a severe left-sided pounding headache one afternoon. There was some stuffiness of the nose and tearing of the left eye. She had had a similar, but less severe, headache 20 years previously when taking birth-control pills. No headaches had occurred in the interim. As the current headache began to decrease, she noted that hearing in the left ear had decreased to a minor degree, and an echo sensation was present in the left ear. She also had the sensation that the environment was off balance, particularly if she was in a moving automobile. She subsequently reported a sense of unsteadiness. There was some sense of nausea when the symptoms first occurred. A vague blurring of vision was also present. She had a vague diplopia at the onset of symptoms but this then disappeared.

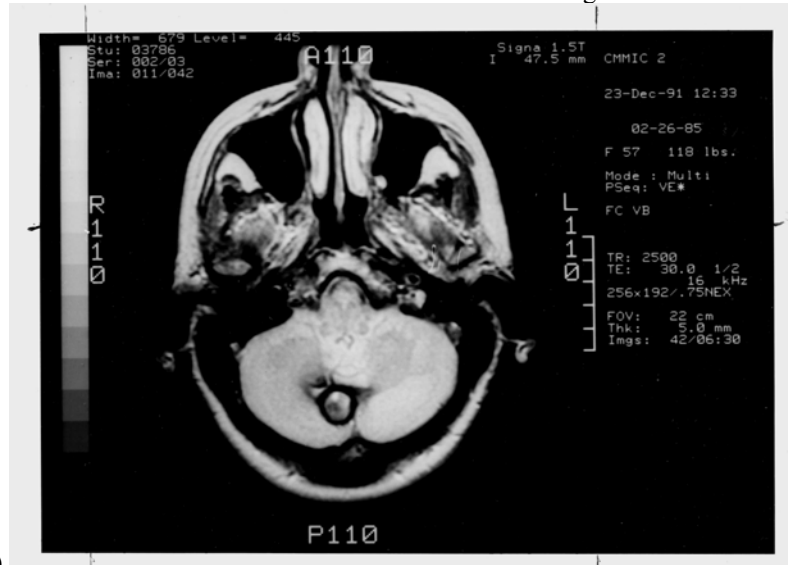
General physical examination: There were multiple pinpoint cavernous angiomas over the arms.

Neurologic examination: Entirely within normal limits.

Clinical diagnosis :Diagnosis unclear: possible migraine headache, or brain stem cerebrovascular event.

Laboratory data: 1. *CT scan of head* indicated hemorrhage in the right paramedian posterior cerebellum.

2. *MRI* showed a rim of hemosiderin stain around the residual hemorrhage in the cerebellar vermis



3. (Figure 20-14).

Subsequent course: The patient had no additional acute episodes. Because two episodes had occurred, she was referred for neurosurgical evaluation. A cavernous hemangioma of the right cerebellum was removed by Doctor Bernard Stone. Post-operatively, she had some right-sided clumsiness and ataxia, which gradually improved.

Evaluation by Doctor Stone one month following surgery, indicated minimal, if any, cerebellar signs. Finger-to-nose test showed no tremor. Gait demonstrated a minimal unsteadiness. Evaluation one year after surgery demonstrated no neurological findings, although some episodic symptoms of imbalance persisted.

CHAPTER 21: SENSORY FUNCTION AND PARIETAL LOBE

The following case demonstrates the localizing significance of focal sensory seizures beginning in the face of a 40 year old patient without prior neurological disease. As predicted, the etiology was neoplastic: a glioblastoma.

Case 21 -1:One week prior to evaluation, this 40-year old right-handed married white male had the onset of repeated 15-21 minute duration episodes of focal numbness (tingling or paresthesias) involving the left side of the face, head, ear, and posterior neck and occasionally spreading into the left hand and fingers, and rarely subsequently spreading into the left leg. There was no associated pain or headache or weakness or associated focal motor phenomena. Biting or eating would trigger the episodes. Past history was not remarkable.

Initial neurological examination: This was completely within normal limits as regards mental status, cranial nerves, motor system, reflexes, and sensory system.

Clinical diagnosis: Focal seizures originating lower third post central gyrus. In view of patient's age, a brain tumor must remain the prime consideration

Laboratory data:

- (1) *EEG*: no focal abnormalities were present. (The record, however, was abnormal because of bilateral bursts of spikes and slow waves - triggered by photic stimulation accompanied by myoclonic jerks - suggesting a predisposition to primary generalized epilepsy (refer to epilepsy chapter for the significance of this finding which was not relevant to this case).
- (2) *CT Scan* (Fig 21-2): The non-enhanced study was normal. The enhanced study demonstrated a small enhancing lesion just above the right Sylvian fissure.
- (3) *MRI* (Fig. 21 - 3): Demonstrated the more extensive nature of this process involving the operculum - above the right sylvian fissure including the lower end of the post central gyrus, the area of representation of the face. A probable infiltrating tumor was suggested as the most likely diagnosis.
- (4) *Arteriogram* - demonstrated a tumor blush at the right sylvian area, consistent with a glioblastoma, a rapidly growing infiltrating tumor - originating from astrocytic glia.

Subsequent Course: Treatment with an anticonvulsant reduced the frequency of the episodes. Neurosurgical consultation suggested an additional observation period and periodic CT scans in view of the normal neurological examination. Three months after onset of symptoms, the patient developed a numbness of the left arm and difficulty in coordination of left arm. Exam now demonstrated left central facial weakness, mild weakness of the left hand. A loss of stereognosis and graphesthesia with a relative alteration in pinprick perception was present in the left hand. The CT scan showed significant enlargement of the previous lesion. EEG now indicated focal 2-3 Hz Delta slow waves in the right frontal central Rolandic area. Subtotal resection of a glioblastoma - in the right temporal parietal area was performed by Dr. Bernard Stone. Radiation therapy was administered following surgery, 4000 rads total whole brain and 5210 rad total to the tumor area. Reevaluation 3 months after surgery, indicated only rare focal seizures involving the face. The neurological examination was normal. Repeat CT scans, however, continued to demonstrate a large area of enhancing tumor in the right temporal-frontal-parietal area. Despite the use of dexamethasone and arterial chemotherapy with cis-Platinum, he continued to progress. At the time of neurological follow-up, 29 months after onset of symptoms, he had developed a left field defect, left hemiparesis and a loss of all modalities of sensation on the left side. He subsequently developed significant changes in memory and cognition, as well as a complete left hemiplegia. CT scan demonstrated progression with extensive involvement of the right side of the brain and spread to the left hemisphere. Death occurred 33 months after onset of symptoms. **Postmortem examination of the brain:** almost the entire right hemisphere was replaced by necrotic infiltrating tumor. The tumor now had spread into the corpus callosum and temporal and occipital lobes. The internal capsule, thalamus, hypothalamus and basal ganglia were destroyed.

Comment: The initial occurrence of the limited focal sensory seizures involving the face and head in a patient of age 40 with no history of trauma or of vascular disease or hypertension clearly predicted the following conclusions (1) The location of the discharging lesion: the sensory cortex

just above the sylvian fissure. (Note that the actual extent of the pathology was more extensive but that is almost always the case in an infiltrating glioma). (2) The nature of the underlying pathology. The most common cause of focal seizures beginning at age 40 in a patient with no significant head trauma, vascular disease, hypertension or other medical disease is a tumor. Among tumors involving the cerebral hemispheres, an infiltrating glioma is by far the most common and on a statistical basis, a glioblastoma is by far the most likely histologic type. 3) The subsequent course was consistent with the natural history of a malignant glioma of the astrocytic series, a glioblastoma. The 33 month survival (30 months after surgery is beyond the median survival for this type of tumor.

The following patient (case 21-2) had a metastatic nodule in the post central gyrus producing a pseudo thalamic pain syndrome.

Case 21-2: This 62-year-old white, right-handed housewife, six years prior to admission

had undergone a left radical mastectomy for carcinoma of the breast. Five months prior to admission, the patient developed a persistent cough, left pleuritic pain and a collection of fluid in the left pleural space (pleural effusion) as well as daily headaches in the right orbit, occasionally awakening the patient from sleep. Four months prior to admission, over a 3 to 4 week period, the patient developed progressive "weakness" and difficulty in control of the right lower extremity. Several weeks later, the patient now experienced, aching pain in the right index finger in addition to a progressive deficit in the use of the right hand. This was more a "stiffness and incoordination" than any actual weakness. One month prior to admission the patient noted episodes of pain in the toes of the right foot and numbness of right foot occurred, lasting 2 to 3 days at a time. She subsequently developed, difficulty in memory and some minor language deficit, suggesting a nominal aphasia, prompting hospital admission.

Neurological examination:

1. *Mental status:* The patient was oriented for time, place, and person. Delayed recall was slightly reduced to 3-out-of-five in 5 minutes. A slowness in naming objects was present although she missed only one item of 6. Calculations, reading, and attention were normal. There was no left-right confusion.

2. Cranial nerves:

a. Nerve II: early papilledema was noted: absence of venous pulsations, indistinctness

of disc margins, and minimal elevation of vessels as they passed over the disc margin.

b. Nerve VII: right central facial weakness was present.

3. **Motor system:**

- a. Mild weakness of the right upper limb was present. A more marked weakness was present in the lower limb (most marked distally).
- b. Spasticity was present at the right elbow and knee.
- c. Gait: The right leg was circumducted; the right arm was held in a flexed posture.

4. **Reflexes:**

- a. Deep tendon reflexes were increased on the right.
- b. A right Babinski response was present.

5. **Sensory system:**

- a. Touch intact.
- b. An ill-defined alteration in pain perception was present in the right arm and leg - more of a relative difference in quality of the pain than any actual deficit.
- c. Repeated stimulation of the right lower extremity (pain or touch) produced dysesthesias (painful sensation).
- d. Vibratory sensation was decreased to a minor degree at the toes bilaterally but intact in the upper extremities.
- e. Position sense was markedly defective in the right fingers with errors in perception of fine and medium amplitude movement in the right toes.
- f. Simultaneous stimulation resulted in extinction in the right lower extremity.
- g. Graphesthesia (identification of numbers, e.g., 8, 5, 4 drawn on cutaneous surface) was absent in the right hand and fingers and poor in the right leg.
- h. Tactile localization and two-point discrimination were decreased on the right side.

Clinical diagnosis: Metastatic tumor to the left post central and precentral gyri with a cortical pain syndrome (pseudo thalamic pain syndrome).

Laboratory data:

1. *Skull x-rays:* the pineal was shifted from left to right. Demineralization of the dorsum sellae also had occurred: consistent with the increase in intracranial pressure.

2. *Chest x-ray:* Several metastatic nodules were present in the left lung.

3. *Electroencephalogram:* A focal disturbance, having the quality of damage, was present in the left posterior frontal central and parietal areas (almost continuous focal 4 to 7 cps slow wave activity).

4. *Left carotid arteriogram:* A left posterior frontal lobe lesion was suggested by a shift of the posterior portion of the anterior cerebral artery from the left to the right. The middle cerebral artery in the sylvian fissure was also depressed downwards.

5. *Brain scan:* The findings were consistent with a focal metastatic lesion with a focal uptake of radioisotope (Hg^{197}) in the left parietal area: high and close to the midline with uptake in the adjacent subcortical white matter.

6. **Erythrocyte sedimentation rate** was elevated to 90 mm., consistent with metastatic disease.

Subsequent course: There was evidence in this case that the disease had spread to multiple organs: brain (findings as noted), lung (chest x-rays and biopsy), and liver (abnormal laboratory tests of liver function). Radiation and hormonal therapy were, therefore, administered rather than any attempt at surgical removal of the left parietal metastatic lesion. Follow-up examination one month later indicated that a significant improvement had occurred in motor function in the arm. Sensory deficits persisted. Speech was slow but relatively intact. The patient eventually expired five months after admission.

Post mortem findings: Autopsy was performed by Dr. Humphrey Lloyd of the Beverly Hospital and disclosed extensive metastatic disease in the lungs, liver, and lymph nodes. A single necrotic metastatic lesion was present in

the brain. This was located in the upper postcentral gyrus of the left parietal area, 1.0 cm. below the pial surface and measuring 1.2 x 1.0 x 0.6 cm.

Comment: This patient had a progressive neurological deficit with headache and papilledema, a clinical course that clearly indicates the presence of a neoplasm. This case predated the era of CT and MRI scan. Today contrast-enhanced scans would be performed. This diagnosis was supported by the ancillary laboratory studies that were available at that time. Moreover this diagnosis however was clear based on the history and clinical-laboratory findings. The fact that motor findings in the arm relevant to the precentral gyrus improved with treatment might suggest that these findings were due to edema. In contrast the findings relevant to the area of the necrotic tumor, the post central gyrus, showed little improvement. In general, one should assume that a patient with a past history of carcinoma of the breast, carcinoma of the lung, malignant melanoma, or renal cell carcinoma, who develops symptoms of central nervous system disease, has metastatic disease until proven otherwise. Such symptoms at their onset may be minor and nonfocal and appear trivial: headache, subjective weakness, and a change in personality. On the other hand more focal symptoms and signs may be present: focal weakness, focal seizure. The metastatic lesions may be single or multiple.

A diagnosis of metastatic disease does not imply that no treatment of central nervous system lesions is possible. Surgical resection of single lesions may be successfully performed. Often the apparent deficits are far out of proportion to the actual size of the tumor because of the surrounding swelling (edema) in the adjacent tissues.

The pattern of sensory involvement in this case clearly localized this lesion to the cortex (or white matter close to cortical surface) rather than to the thalamus. The relative intactness of pain, touch, and vibration sensation should be contrasted to the significant deficits in position sense,

graphesthesia, tactile localization, and two-point discrimination with extinction on simultaneous stimulation. The occurrence of episodic pain in the involved arms and legs along with the production of an experienced painful sensation on repetitive tactile stimulation (dysesthesias) in patients with sensory pathway lesions is sometimes referred to as a "thalamic" or "pseudo thalamic" syndrome. (Refer to discussion of Wilkins and Brody, 1969). In this case, the anatomical locus for the pseudo thalamic syndrome is apparent.

The effects of deficits in cortical sensation on the total sensory motor function of a limb are apparent in this case. The actual disability and disuse of the right arm and leg were far out of proportion to any actual weakness. Such an extremity is often referred to as a "useless limb." The actual weakness that was present undoubtedly reflected pressure effects on the precentral gyrus and the descending motor fibers in adjacent white matter.

The following case (21-3) demonstrates many of the features of a non dominant parietal lobe lesion.

Case 21-3: This 70-year-old, single, white female, right-handed, retired candy maker underwent a left radical mastectomy for carcinoma of the breast, three years prior to admission. Four months prior to evaluation, the patient became unsteady with a sensation of rocking as though on a boat. She no longer attended to her housekeeping and to dressing. Over a three-week period, prior to evaluation, a relatively rapid progression occurred with deterioration of recent memory. A perseveration occurred in motor activities and speech. The patient was incontinent but was no longer concerned with urinary and fecal incontinence. For 2 weeks, right temporal headaches had been present. During this time, her sister noted the patient to be neglecting the left side of her body. She would fail to put on the left shoe when dressing. In undressing, the stocking on the left would be only half removed.

Family History: The patient's mother died of metastatic carcinoma of the breast.

Neurological examination:

1. Mental status:

- a. The patient was oriented for time, place and person.
- b. Delayed recall was 5-out-of-5 objects in 5 minutes.
- c. There was no evidence of aphasia.
 - d. The patient often wandered in her conversation. She often asked irrelevant questions and was often impersistent in motor activities.
- e. There was marked disorganization in the drawing of a house or of a clock. A similar marked disorganization was noted in attempts at copying the picture of a railroad engine (Fig 21-4).
- f. There was a marked neglect of the left side of space and of the left side of the body. The patient failed to read the left half of a page. When she put her glasses on, she did not put the left bow over the ear. When getting into bed, she did not move the left leg into bed. She had slipped off her dress on the right side, but was lying in bed with the dress still covering the left side.

- g. The patient had been reluctant to come for neurological consultation. Although she complained of headache and nausea, she denied any other deficits. Her relatives provided information concerning these problems. Much additional persuasion over a two-week period was required before the patient would agree to be hospitalized.

(2) *Cranial nerves:*

- a. Nerve II: A dense left homonymous hemianopsia was present. When reading, the patient left off the left side of a page. She bisected a line markedly off center. Disc margins were blurred and venous pulsations were absent, indicating papilledema.
- b. Nerve III: The right pupil was slightly larger than the left.
- c. Nerve VII: A minimal left central facial weakness was present.
3. *Motor system:* Strength was intact. There was, however, little spontaneous movement of the left arm and leg. Tone was normal.
4. *Reflexes:* deep tendon reflexes were symmetrical and physiologic and plantar responses, flexor.
5. *Gait:* The patient was ataxic on a narrow base with eyes open with a tendency to fall to the left, and was unable to stand with eyes closed even on a broad base.
6. *Sensory system:*
- a. Pain, touch and vibration were intact. At times, however, there was a decreased awareness of stimuli on the left side.
 - b. Errors were made in position sense at toes and fingers on the left.
 - c. With double simultaneous stimulation, the patient neglected stimuli on the left face, arm and leg.
 - d. Tactile localization was poor over the left arm and leg.

Clinical diagnosis: Metastatic tumor from breast to right non-dominant parietal cortex.

Laboratory data:

1. *Skull X-rays* were negative.
2. *Chest X-ray* indicated a possible metastatic lesion at the right hilum.
3. *Erythrocyte sedimentation rate* was elevated to 72 mm/hr, consistent with metastatic disease.
4. *Electroencephalogram* (Fig 21-5) was abnormal because of frequent focal 3 to 4 cps slow waves in the right temporal and parietal areas, suggesting focal damage in these areas.
5. *Brain scan (radioisotope)* (Fig 21-6) indicated that a large but well-defined area of increased uptake of isotope (Hg197) was present in the right parietal area extending from the midline to the lateral surface, measuring 7 x 5 x 7 cm. The most likely diagnosis was that of a solitary large metastatic lesion
6. *Right carotid arteriogram* showed that a large vascular tumor mass, probably metastatic, was present in the posterior section of the right temporal inferior parietal area. There was displacement of the middle cerebral artery upward and to the left.

Subsequent course: Treatment with steroids (dexamethasone and estrogens) resulted in temporary improvement. The patient refused surgery. Her condition soon deteriorated with increasing obtundation of consciousness. She expired two months following her initial neurological consultation.

Comment: This patient certainly presented a syndrome characterized by disturbance in concept of body image with a marked neglect of the left side, a denial of illness, and marked constructional apraxia. The various laboratory studies indicated a large lesion in the right posterior temporal parietal area. A CT scan from a more recent case demonstrating many aspects of this syndrome is illustrated in Figure 21-7. In many cases, the location of lesion may appear to be predominantly posterior temporal. Such large posterior temporal lesions would certainly compromise the cortex and subcortical white matter of the adjacent inferior parietal area.

In this case, marked deficits in perception of the cortical modalities of sensation were present. In other cases, as in the case demonstrated in Fig 21-7, such involvement is much less marked.

In some cases, involvement of the motor cortex is evident with an actual left hemiparesis accompanied by an increase in deep tendon reflexes and an extensor plantar response. At times in patients with neglect syndromes, there may be several indications in the clinical examination and in the laboratory studies that the involvement of the frontal lobe areas is more prominent than the parietal involvement. We have already indicated that the neglect components of this syndrome may also be noted in lesions of the anterior premotor

area (area 8). The premotor area as discussed above and in chapter 18, receives projection fibers from the multimodal area of the posterior parietal area. It is possible that in some cases the posterior temporal - inferior parietal location of the lesion may also be critical in interrupting these association fibers. For these several reasons, it is perhaps more appropriate to use the term, *syndrome of the non-dominant hemisphere*, rather than the more localized designation, non-dominant inferior parietal syndrome. Duffner et al, 1990 have presented the concept of a network for directed attention - with right frontal lesions leading to left hemi spatial neglect only for tasks that emphasize exploratory-motor components of directed attention whereas parietal lesions emphasize the perceptual-sensory aspects of neglect.

With lesions of the non-dominant hemisphere, there is a significant alteration of the patient's awareness of his environment. The behavior of an individual is in part determined by his or her own particular perception of the environment. If that perception is altered or disorganized, the behavioral responses of the patient may appear inappropriate to others. Obviously, not all individuals will respond in the same manner to a given environmental situation; part of the response will be determined by the past experience and personality of the individual. Thus, given the same lesion, one individual may be unaware of a hemiparesis, another may deny the hemiparesis but agree an illness is present, a third may claim to be healthy and claim that people are conspiring to keep him in the hospital.

CHAPTER 22: THE LIMBIC SYSTEM

In general, as we have indicated, there is mixed symptomatology during partial seizures of temporal lobe origin. The following case history (22-1) illustrates many of the points just discussed regarding seizures of temporal lobe origin.

Case 22-1: This 56-year-old white right-handed male baker was referred for evaluation of a seizure disorder. Three months before admission the patient had the onset of episodes of vertigo and tinnitus, each episode lasting 4 minutes and unrelated to position. The patient then noted increasing forgetfulness. Later that month he had a generalized convulsive seizure that occurred without any warning. The patient then developed episodes of confusion and unresponsiveness, followed by a left frontal headache. Several studies; EEG, pneumoencephalogram, and carotid arteriogram—were all negative at that point in time. One month before admission, the patient began to have minor episodes, characterized by lip smacking and a vertiginous sensation, during which he reported seeing several well-formed, colorful scenes. At times, he had hallucinations of “loaves of bread being laid out on the wall.” In addition, he would have a perceptual disturbance at the same time (e.g., objects would appear larger than normal) and “terrifying dreams.”

General physical examination: unremarkable.

Neurological examination: The essential neurological findings were as follows:

1. *General observations of seizures:* The patient was observed to have frequent transient episodes of distress characterized by saying, “Oh, oh, oh, my”. On occasion, these were accompanied by automatisms: fluttering of the eyelids, smacking of the lips, and repetitive picking at bedclothes with his right hand. Consciousness was not completely impaired during these episodes, which lasted from 30 seconds to 3 minutes, and the patient reported afterward that at the onset of the seizure he had seen loaves of bread on the wall and smelled a poorly described unpleasant odor. At other times, the olfactory hallucination was described as pleasant, resembling the aroma of baked bread.
2. *Mental status:* The patient was oriented to person but not dates. He could not recall his street address. He was unable to pronounce the name of the hospital correctly. Calculations were correctly performed.
3. *Cranial nerves:* Possible deficit in the periphery of the right visual field and a minor right central facial weakness.
4. *Motor system:* intact
5. *Reflexes:* Deep tendon reflexes were symmetrical and physiologic. A right Babinski sign was present.
6. *Sensory system:* intact.

Clinical diagnosis: Simple and complex partial seizures originating left temporal lobe probably involving at various times left lateral superior temporal gyrus, uncus, amygdala and hippocampus with tumor the most likely etiology in view of age and the focal neurological findings.

Laboratory data:

1. The *initial electroencephalographic recording* indicated frequent focal spike discharge throughout the left temporal and parietal areas, consistent with a focal seizure disorder originating in the left temporal/parietal areas (Fig. 29-1). A recording 6 days later indicated a decrease of focal spikes (i.e., a decrease in seizure activity) but the presence of frequent focal slow-wave activity in the left temporal area (almost continuous, 3 to 5 cps (Hz) slow-wave activity) suggesting that focal damage was present in the left temporal area .
2. *Brain scan* (H_g197) normal
3. *Left carotid arteriogram* indicated a possible avascular mass lesion left posterior frontal (the only abnormality was a 4-mm shift of the anterior cerebral artery).

Subsequent course: The patient continued to have multiple short episodes characterized by the sensation of odor and a sensation that he was looking at objects upon the wall. These episodes were eventually controlled with anticonvulsant medication: phenytoin (Dilantin) and primidone (Mysoline). However, 2 months later the patient had a day with several episodes with “crazy things occurring “ (colorful visions and terrifying nightmares).

The patient was readmitted to the hospital 7 months after onset of symptoms because of the recurrence of seizures. An aura of unpleasant odor was followed by a generalized convulsion followed by four or five

subsequent seizures of a somewhat different character (deviation of the head and eyes to the right, then tonic and clonic movements of the right hand spreading to the arm, foot, and leg lasting approximately 1 to 2 minutes, followed by a post-ictal right hemiparesis).

Neurologic examination now indicated a marked expressive aphasia, with little spontaneous speech and difficulty in naming objects. There was a dense right homonymous hemianopia, a flattening of the right nasolabial fold, and a right hemiparesis, with a right Babinski sign.

During a 2-week hospital period the patient continued to have minor seizures characterized by sensory phenomena on the right side of the body. A moderate degree of expressive aphasia persisted throughout the hospital course, although the right homonymous hemianopia largely disappeared. The symptoms and findings suggested that the basic disease process might well have spread to involve the adjacent areas across the sylvian fissure—the speech areas of the inferior frontal convolution, premotor areas, and sensory motor cortex.

The patient developed increasing expressive aphasia and right hemiparesis, with increasingly severe headache. An arteriogram indicated a large space-occupying tumor of the left temporal lobe, and surgery was undertaken by Dr. Robert Yuan 16 months after the onset of symptoms. The anterior and middle portions of the superior temporal gyrus appeared to be widened, and the anterior temporal area (the temporal tip) had an abnormal and discolored appearance. At a depth of 1 to 2 cm within the superior temporal gyrus and involving all of the deeper temporal areas, obvious necrotic glial tissue was found. The process had extended superficially under the Sylvian fissure to involve the adjacent posterior portion of the inferior frontal gyrus.

A temporal lobectomy was performed (from the anterior temporal pole posteriorly for a distance of 6 cm). The operative impression of a malignant glial tumor (glioblastoma) was confirmed by histologic examination.

Comment: This patient presented, at one time or another during his seizures, most of the phenomena associated with temporal lobe lesions: vertigo, tinnitus, visual distortions and hallucinations, olfactory hallucinations, fear, automatisms involving the lips and hands, and episodes of confusion. The visual and olfactory hallucinations are of interest in that both reflected the patient's occupation as a baker. As Halgren and colleagues (1978) note, the experiential phenomena of temporal-lobe seizures are often specific to the individual's experience and personality. The later progression clearly indicated spread across the sylvian fissure to involve the motor cortex and Broca's area in the inferior frontal gyrus areas. This patient had a highly malignant tumor, which clearly involved the cortex of the lateral surface, the deeper white matter, and presumably the medial temporal areas, including the amygdaloid-hippocampal regions. His clinical picture is highly reminiscent of the case described in 1887 by Hughlings Jackson of Emily M., a cook who experienced visual and olfactory hallucinations and who had a tumor arising in the "temporosphenoidal lobe" (the uncus). Such seizures have subsequently been referred to as uncinate epilepsy, but as we have indicated, the disease invariably involves more than just the uncus.

Today, CT scan and MRI would be employed for early diagnosis (see Figs. 22-17 and 22-18). Cases 22-2 and 22-3 which follow demonstrate the correlation of partial seizures with temporal lobe pathology.

Case 22-2. This 17-year-old right-handed male, at age 4 years began to have "staring spells and bizarre behavior". Some episodes had been preceded by the "sound of a musical rhythm". EEG at that time indicated a right temporal spike discharge. Seizures were controlled for ten years with anticonvulsants but then recurred and were poorly controlled occurring several times per day.

Neurological examination: The findings were limited to the following features:

1. *Observed 3 minute seizure:* The seizure began with loss of contact and a stare and then automatisms of the hands. He stood up, walked around the room, went to the physician's desk and attempted to pull open a nonexistent middle drawer. He answered questions vaguely with one or two word answers. Confusion was present for 1-2 minutes after the end of the episode.
2. *Cranial nerves:* a left central facial weakness was present.

Clinical diagnosis: Focal seizures originating right temporal lobe. Observed seizure was complex partial. The seizures beginning with the musical sound might be classified as simple partial with secondary complex partial.

Laboratory data:

1. *EEG*: Intermittent focal spike discharge anterior-middle temporal area.
2. *CT scan*: (Fig. 22-17) An area of focal atrophy was present in the right anterior temporal lobe with possible enhancement at the border.
3. *MRI*: At the Yale Epilepsy Center was more consistent with a tumor in the right anterior temporal lobe.

Subsequent course: Dr. Dennis Spencer at the Yale Epilepsy Center performed a temporal lobectomy. This demonstrated a cystic glial tumor with components of astrocytes and oligodendrocytes. Cerebral cortex also demonstrated abnormal lamination and dysplastic features. Seizures were fully controlled over the next three years.

Case 22-3. This 47-year-old ambidextrous male experienced his first seizure one month prior to admission. He felt light-headed and warm. Then he was observed to walk 100 feet down a hallway, appearing “dazed” and not recognizing people. He fell to the floor, with a loss of consciousness, bit his tongue and was confused afterwards for several minutes.

Neurological examination at 2, 16 and 48 hours after the episode: A persistent right Babinski sign, and slight right hyperreflexia were present. Otherwise the examinations were not remarkable.

Clinical diagnosis: Complex partial seizures. In view of age of onset and persistent focal signs a brain tumor was suspected as the etiology.

Laboratory diagnosis:

1. Sleep deprived EEG :normal.
2. *CT and MRI scans* (Fig. 22-18) demonstrated an extensive infiltrating tumor of the left temporal lobe most likely a glioblastoma.

Subsequent course: Despite Anticonvulsant therapy (phenytoin) additional episodes occurred over the next month: loss of train of thought while talking and several minutes of loss of memory. A subtotal resection by Dr. Bernard Stone (St. Vincent Hospital) demonstrated a Grade III-IV astrocytoma (glioblastoma). Despite radiotherapy and chemotherapy, the disease pursued a relentless course producing early and severe disability prior to death, approximately one year after onset of symptoms.

The following case histories illustrate many of the features of focal disease involving the prefrontal areas.

Case 22-4: This 69-year-old right handed white housewife; two years prior to neurological evaluation visited a relative (a physician) in Israel whom she had not seen in a number of years. The relative then wrote to the patient’s physician, (an old family friend) indicating concern over a change in the patient’s personality. The patient was described as apathetic with silly immature reactions. In retrospect, the patient’s husband felt that these alternations had begun insidiously a number of years previously. A year later, the same relative again wrote indicating that letters received from the patient had become incoherent. Letters became less frequent and then the patient no longer wrote letters. Ten months prior to evaluation, a left central facial weakness was first noted followed two months later by a decreased left arm swing. Six months prior to evaluation, her husband noted, she was purchasing items for which she had no need: 24 pairs of shoes, 15 brassieres. Subsequently she became careless in her housework. On occasions she lost her purse. Her ability to play bridge had decreased over the last year, although her golf game was unchanged.

Neurological examination:**1. Mental status**

- a. She was oriented x3
- b. There was a marked impersistence in motor activities. She was often inattentive. Her answers were often irrelevant. (According to her husband this had been present for many years.
- c. There was inappropriate joking.
- d. Delayed recall without assistance was 2/5 objects in 5 minutes. But 5/5 with assistance.
- e. Digit span was decreased to 5 forward and 3 in reverses.

- f. There were marked deficits in serial 7 subtractions. At times she began to subtract other numbers, at times she added rather than subtracted.
- g. There was a significant spatial disorientation. There was a marked impairment in the ability to copy a cube and deficits in drawing a house. There was disorientation in locating cities on a map.

2.Cranial nerves:

- a. There was a significant neglect of single stimulus objects in the left visual field; this was greater when bilateral simultaneous stimuli were utilized.
- b. At times there was a limitation of voluntary gaze to the left.
- c. A left central facial weakness was present.

3.Motor system:

- a. There was minimal weakness of the left arm and leg.
- b. Variable resistance was present on passive motion at left wrist and elbow suggesting the "gegenhalten" of frontal lobe disease.
- c. There was a decreased swing of the left arm in walking. The gait was initially apraxic but improved as the patient picked up speed.

4.Reflexes

- a. Deep tendon stretch reflexes were increased on the left.
- b. A left Babinski sign was present.
- c. There was a bilateral release of the grasp reflex.

5. Sensory system: intact.

Clinical diagnosis: Right frontal lobe tumor: probable meningioma based on the long history.

Laboratory data:

1.*Skull x-rays* there was a 5mm shift to the left of the calcified pineal gland. Long standing increased intracranial pressure was suggested by the demineralization of the sella turcica.

2.*EEG* demonstrated focal 2-5 Hz slow waves in the right frontal area most prominent in the parasagittal recording area

3.*Imaging study: radioactive brain scan (Hgl97):* there was a heavy uptake in the right frontal towards the midline measuring 5x5x4 cm (Fig.22-21).

4.*Arteriograms:* A parasagittal tumor was present in the right frontal area, with vascular supply derived from the left and right middle meningeal and left anterior meningeal arteries.

Hospital course: Following the arteriogram, the patient developed signs of increased intracranial pressure (vomiting, lethargy and papilledema). The patient received dexamethasone glucocorticoid used to reduce cerebral edema, with improvement in these symptoms. The right external carotid artery was ligated since the meningioma derived considerable blood supply from this source. Dr. Samuel Brendler performed a bilateral frontal craniotomy. Bulging of the dura was present requiring the administration of hyperosmotic agent (20% mannitol) with reduction of the swelling. When the dura was opened a large right posterior frontal meningioma was revealed measuring 8x8cm and attached to the right side of the superior sagittal sinus. On histological section this was a fibrous, meningothelial meningioma. During the course of removal of the tumor, it was necessary to ligate several bridging veins entering the superior sagittal sinus as well as the arteries feeding the tumor. At the conclusion of the procedure, it was noted that the right pupil was enlarged and neither responded to light. The patient failed to regain consciousness, remaining in a state of coma with bilateral extensor plantar responses, decerebrate postures on stimulation and bilateral fixed dilated pupils. The patient expired 2 weeks after surgery.

Comment: It is difficult to decide even in retrospect when the symptoms in this case began. It is clear that the initial symptoms involved an insidious change in personality. She was apathetic, her reactions were "silly" and judgment was impaired. Purchases were inappropriate. It would have been of interest to explore which aspects of her bridge playing were impaired in terms of planning and strategy etc. Her motor function was impaired only to a minor degree even late at the time of neurological evaluation, with minimal left-sided weakness and more prominent premotor release. The visual neglect syndrome may have reflected involvement of the premotor area or compromise of the parietal cortex by this large tumor. The fact that there was only minor evidence of involvement of motor cortex would make the premotor/SMA location more likely. While the spatial disorientation and deficits in drawing might

favor a nondominant parietal syndrome, such findings also could be consistent with a nondominant premotor/SMA location based on the close interaction between the posterior parietal and the premotor location. The impairment of voluntary gaze to the left would be consistent with area 8 involvement. There is little doubt that this patient required surgical intervention. The removal of large "benign" tumors of this type is not without risk. Hemorrhagic infarction with massive edema and tentorial herniation is a complication of ligation of bridging veins entering the superior sagittal sinus. In this case, serious brain swelling was already evident even before the dura was opened.

The following case history 22-3 provides an example of a patient with a slowly progressive subfrontal meningioma manifested by symptoms of apathy, loss of ambition, "depression" of mood, emotional lability, with a tendency to introspection and a slowness of mental processes. All of these symptoms were initially attributed to depression and a hypothyroid state. As gait and memory problems developed, these symptoms were attributed to Alzheimer's type senile dementia. When increased intracranial pressure and coma suddenly developed, neurological and neurosurgical intervention occurred.

Case 22-5: This white housewife and fashion designer was first admitted to the hospital at age 60 with a history of several years (?2 to 5) of fatigue, loss of ambition, lack of enthusiasm, and a tendency to readily cry over minor problems. A depression of mood and a tendency to introspection had developed. The patient also reported loss of her taste for food with a subsequent decrease in appetite and weight loss. These symptoms had progressed despite an adequate dosage of thyroid medication (60 mg., t.i.d.). Neurological examination was recorded as negative except for a slowness of speech and of thought processes. She was described by the psychiatric consultant as indecisive in her answers. Cerebrospinal fluid examination revealed no significant findings. Tests of thyroid function indicated hypothyroidism with protein bound iodine of 3.2 micrograms/100 ml. (normal; 4 to 8 micrograms/100 mg.) and a radioactive iodine uptake of 2.3 percent in 24 hours (normal 20 to 50 percent). Discharge diagnosis was chronic depression and hypothyroidism.

These symptoms continued to progress despite treatment with thyroid. The patient had increasing difficulty in walking. This had actually been first noted at age 57, 3 years prior to her initial hospital admission as a "phobia for heights". The patient would "freeze" at the top of a high flight of stairs. She then developed progressive difficulty in climbing stairs. Her husband reported that she would have marked difficulty in getting out of chairs. She would appear unsteady in gait after rising from a chair but would soon recover her equilibrium and would be able to walk in relatively normal manner. Increasingly, the patient's motor and mental activities became slower. She "procrastinated in making decisions". Occasional urinary incontinence developed at age 66 and was attributed to her neurological disease (apparent senile dementia). Although her husband reported her memory as initially well preserved, other observers at that point reported a progressive deficit in memory. At age 67, the patient began to complain of episodic fogging or blurring of vision.

Initial Neurological examination on re-admission to the hospital at age 67 was recorded as demonstrating the following features:

(a), slight disorientation for date and year, (b) slowness of speech and gait (c) deep tendon reflexes 2+, plantar responses flexor, and (d) no significant sensory finding except a slight decrease in position sense at the toes. No details as to the patient's gait were recorded. The sense of smell was apparently not tested and no notes as to the presence or absence of a grasp reflex were recorded.

On the day after admission, the patient developed headache and vomiting. She had difficulty walking unsupported and became increasingly more somnolent but could be roused by painful stimulation. Deep tendon reflexes were increased bilaterally with bilateral extensor plantar responses (bilateral Babinski signs). Grasp response was absent. Pupils responded to light but were sluggish.

Fundusoscopic examination was negative but lumbar puncture indicated a markedly increased pressure, greater than 400 mm. of csf. Cerebrospinal fluid protein was elevated to 125 mg/100 ml. The patient became unresponsive and emergency neurological and neurosurgical consultations were obtained.

Neurological examination:

1. *Mental Status:* The patient was semicomatose with periodic Cheyne-Stokes respirations.
2. *Cranial Nerves:* Pupils were fixed, the left dilated, the right constricted.
3. *Motor System:*
 - a. The patient moved all limbs in response to painful

stimulation, right more than left.

- b. There was a spastic resistance in the upper and lower left extremities.
4. Reflexes:
- a. A generalized hyperreflexia was present with bilateral ankle clonus.
 - b. Bilateral Babinski signs were present.
 - c. A bilateral grasp reflex was present. Note, however, that in a semicomatose patient this may have little localizing significance.
5. *Sensation*: Pain sensation was intact.

Clinical diagnosis: Subfrontal or parasagittal frontal tumor most likely a meningioma in view of the over 10 year course. Tentorial herniation had occurred possibly related to the lumbar puncture.

Laboratory data: An emergency bilateral carotid arteriograms revealed that a large subfrontal butterfly-shaped mass (probably meningioma) was present in the anterior cranial fossa bilaterally. The anterior cerebral arteries as well as the frontal polar, pericallosal and callosal marginal branches and the middle cerebral arteries were displaced backwards. The anterior cerebral arteries were also displaced upwards. The tumor mass derived blood supply from the ophthalmic arteries.

Hospital course:

A bifrontal craniotomy was immediately performed by Doctor Robert Yuan with total removal of a large bifrontal meningioma arising from the falx and olfactory groove. On the right side the tumor was estimated to occupy 75 percent of the anterior cranial fossa, measuring 7 x 5 x 6 cm. On the left the tumor was of approximately half this size, measuring 5 cm. in diameter. The thickness of the cerebral hemisphere covering the tumor in the right prefrontal area was reduced to 0.5 cm. Histological examination of the tumor indicated a benign meningioma (meningotheliomatous type).

The patient showed some immediate improvement at the conclusion of surgery, in the sense that both pupils were equal in size and reacted to light. By the time of discharge from the hospital, two months after surgery, considerable improvement had occurred. She could recognize the doctor by name but did not know the place, the season, or the month; she could, however, describe a picture she had just seen. A bilateral deficit in olfaction was present (anosmia). Assistance was required in walking. A bilateral grasp reflex was present.

Follow-up evaluation two years after surgery indicated continued improvement although the patient still had complaint relevant to impairment of recent memory and slight unsteadiness of gait. Deep tendon reflexes were symmetrical with plantar responses flexor. A bilateral grasp reflex was present and the patient was slow in walking and fell occasionally. Urinary incontinence occurred with wetting of the bed.

Comment: In retrospect, the evolution of symptoms in this patient clearly indicates a tumor initially compression both prefrontal areas and producing alterations in mood and personality. With continued growth of the tumor, compromise of the premotor areas with resultant apraxia of gait and release of grasp reflex began to occur, either as a result of direct compression or secondary to the distortion and compression of the anterior cerebral arteries. It is not unusual to witness the development of a dementia (deficit in recent memory) in large tumors in a subfrontal midline location. A similar dementia may occur in large aneurysms of the anterior communicating artery.

The problem of dementia will be considered in greater detail in the chapter on memory.

The development of headache, vomiting and increasing somnolence indicated the development of increasing intracranial pressure. The sudden unresponsiveness following the lumbar puncture with the development of periodic Cheyne-Stokes respirations, pupillary changes, and bilateral corticospinal tract signs all indicated an additional acute exacerbation of the already compromised brain stem functions, a compromise which had already resulted from the backward displacement of the intracranial contents with distortion of the brain stem. In retrospect, one might hypothesize that the patient's complaint of a loss of taste for her food at the time of her initial hospitalization might well have indicated some loss of olfactory sensation since much of our appreciation of food is dependent on olfaction. Specific tests for olfaction were not recorded.

CHAPTER 23: VISUAL SYSTEM

The following case is an example of a lesion involving the optic nerve, anterior to the optic chiasm.

Case History 23-1 (Fig 23-8).

This 53-year-old white right-handed housewife was referred for evaluation of progressive right-sided supraorbital headache of 23 years duration and decreasing acuity in the right eye. The loss of acuity had progressed to the point of almost total unilateral blindness. During the 3 years before admission, intermittent tingling paresthesia had been noted in the left face, arm, or leg. About 1 year before admission the patient had a sudden loss of consciousness and was amnesic for the events of the next 48

hours. She was hospitalized, but no explanation for the episode was clearly established, although cerebrospinal fluid protein was reported to be elevated (230 mg/dl).

The patient and her family reported some personality changes over a period of several years, including a loss of spontaneity and increasing apathy.

General Physical Examination: Unremarkable except for a minor degree of proptosis (downward protrusion of the right eye).

Neurologic Examination:

1. *Mental Status:* The patient was, in general, alert but at times would become lethargic. Her affect was flat. At times, she would laugh or joke in an inappropriate manner.
2. *Cranial Nerves:* There was anosmia for odors, such as cloves, on the right and a reduced sensitivity on the left.

Marked papilledema (increased intracranial pressure with protrusion of the optic disk and venous engorgement due to obstruction of the normal flow of CSF) was present in the left eye.

Pallor of the right optic disc was present, indicating optic atrophy. Visual acuity in the right eye was markedly reduced. The patient had only a small crescent of vision in the temporal field of the right eye, where only vague outlines of objects could be seen. A slight left central facial weakness was present.

3. *Motor Systems:* Intact although movements on the left side were slow.

4. *Reflexes:* A release of grasp reflex was present on the left side.

5. *Sensory system:* Intact

Clinical diagnosis: Subfrontal meningioma arising from olfactory groove or inner third sphenoid wing.

Laboratory data:

1. *Skull x-rays* demonstrated erosion of the dorsum sellae. Special lamniograms demonstrated hyperostosis of the sphenoid bone (planum sphenoidale) suggesting a meningioma originating from the sphenoid bone.

2. *EEG* demonstrated focal 2-4 Hz slow waves in the right anterior temporal and anterior lateral frontal area.

3. *Brain scan (H_g 197)* revealed a heavy uptake of isotope in the right posterior subfrontal area.

4. *Arteriograms* indicated that the anterior cerebral arteries were shifted backwards, posteriorly and the left. A tumor blush was present on the venous phase in the right subfrontal area extending back to the optic nerve groove (Fig 23-8). These findings were felt to be most consistent with an olfactory groove meningioma.

Hospital course: Dr. Samuel Brendler performed a bifrontal craniotomy which exposed a well-encapsulated smooth tumor attached to the medial third of the sphenoid wing. After intracapsular removal of 90 to 95% of the tumor, the right optic nerve could be visualized. The small portion of the tumor attached to the bone could not be removed because of considerable bleeding from the bone. Examination 4 months after surgery, indicated right anosmia and right optic atrophy were present.

Comment

If one considered only the patient's primary complaint, decreasing vision in the right eye, and the findings of right optic atrophy and left-sided papilledema (Foster-Kennedy syndrome), then the most probable diagnosis was inner-third sphenoid meningioma. The preservation of a small crescent of vision in the temporal field is consistent with compression of the optic nerve on its lateral surface. By the time of hospitalization, the lesion was quite large and had extended into the subfrontal area, producing anosmia on the right and some changes in personality. At this point, the various diagnostic studies suggested only a subfrontal mass and did not clearly differentiate between an olfactory-groove meningioma and a sphenoid-wing meningioma. One might suggest, in retrospect, that the degree of involvement of the right optic nerve was much more pronounced than the changes in prefrontal functions, and therefore, the inner-third sphenoid-wing location was more likely.

The surgical approach in any case was the same. The eventual recovery of vision in such cases is uncertain because the effects of compression often are not reversible

COMPLETE CASE HISTORIES FROM TEXTBOOK: *INTEGRATED NEUROSCIENCES*

PART III. CASES – CEREBRAL HEMISPHERE MOTOR SYSTEM, CEREBELLUM, BASAL GANGLIA

CHAPTER 18: MOTOR SYSTEM I:

The following case 18-1 presents an example of focal seizures beginning in the motor cortex.

Case 18-1. This 29-year-old, right-handed, white woman was in her usual state of good health until three months prior to admission when she developed an intermittent “pulling sensation” over the anterior aspect of the left thigh, lasting a few minutes. This recurred without other symptoms about twice a week. On the evening of admission, while sitting on a couch, she again had the onset of this same sensation in her left. She stood up, noted that her left leg felt “numb” and then started to have “jerky movements” in her left foot which progressed to involve the whole left lower extremity. She sat down, pressed on her left thigh in an attempt to stop the movement. At this point, her husband and a friend came to her (the patient is amnesic for these events), and saw her have tonic extension then clonus of all four limbs associated with grunting respiration, clenched jaw, and rolling of the eyes. She was placed on the floor and after a few seconds she regained consciousness, though she still appeared dazed and slightly confused for the next 5 minutes.

Past history and family history: noncontributory.

Physical Exam: Normal except for bite marks on the left lateral aspect of the tongue.

Neurological Exam: Significant only a slight asymmetry of deep tendon reflexes: left > right.

Clinical Diagnosis: Focal seizures originating right parasagittal motor cortex (foot area), with ? of parasagittal meningioma.

Laboratory Data:

(1) *Electroencephalogram* (Fig.29-1B) demonstrated rare focal spikes, right Rolandic parasagittal consistent with the focal source of the secondarily generalized seizure and rare focal slow waves in the right Rolandic and mid temporal area - consistent with minor damage in this area

2) *CT scan* (Fig.18-13) demonstrated an enhancing lesion in the right parasagittal region just anterior to the central sulcus.

- (3) *Arteriograms* (Fig.18-14) demonstrated a circumscribed vascular tumor in the right parasagittal rolandic area which was supplied by the right anterior cerebral artery (A,B) and the right middle meningeal branch of the external carotid artery©. The venous phase of the study demonstrated a significant draining vein from this area of tumor blush(D). All of these findings were consistent with a right parasagittal meningioma.

Hospital Course: A well-circumscribed right parasagittal meningioma was removed by Doctor Bernard Stone. A distal weakness of the left lower extremity was present in the immediate postoperative period but this improved rapidly so that by two months after surgery, a foot drop brace was no longer required and strength had returned to normal. During all of the pre and post operative period, the patient received diphenylhydantoin (Phenytoin) to prevent additional seizures. A possible sensory seizure involving the hand occurred 2 years later. Four years after surgery, the patient attempted to reduce her dosage of anticonvulsant and experienced a recurrence of focal motor seizure activity beginning in the left leg with subsequent secondary generalization. When evaluated 6 years after surgery, she had experienced no additional seizure activity. Her neurological examination continued to demonstrate an increase in deep tendon reflexes on the left and a left sign of Babinski. Her CT scan demonstrated no recurrence of tumor, there was very minor atrophy at the site of the previous meningioma. The EEG continued to demonstrate bursts of blunt spikes and slow waves in the right parasagittal Rolandic and parietal areas. Follow-up 10.5 years after surgery in indicated no additional seizures.

Comment: The onset of focal seizure activity should always raise the question of focal pathology. When these seizures begin at age 29, without a prior medical history, there is always a strong possibility of a primary brain tumor. In general gliomas are much more common than meningiomas but the odds of a meningioma are increased by the parasagittal location and the gender of the patient. In this case, there was a very close correlation of the clinical phenomena with the laboratory data regarding the anatomical location of the lesion. Surgical therapy eliminated the underlying benign tumor - the parasagittal meningioma, but the predisposition to focal seizures remained. Thus, the tumor in compression of cerebral cortex had produced alterations in neuronal excitability which persisted following the removal of the tumor.

Case 18-2 provides an example of a slow growing tumor involving the premotor and supplementary motor cortex from the standpoint of focal seizure activity. The motor effects of frontal lesions are presented in case histories 22-2 and 22-3 which follows the discussion of the prefrontal areas.

Case 18-2: This 57-year-old right-handed single nun and occupational therapist, had the onset of her first generalized convulsive seizure at age 47, ten years prior to consultation. This occurred without warning with sudden loss of consciousness and an observed generalized tonic clonic seizure. Both an EEG and CT scan were reported to have been normal. Approximately 4 additional generalized convulsive seizures occurred over the next 4 years. Shortly after the onset of the grand mal seizures, the patient began to have focal seizures. She described these as beginning with the abduction and raising of the right arm at the side, over her head, then a jerking of the right arm, and then she would fall to the ground. She would remain fully conscious but she would be unable to talk. She would have an awareness that something strange was occurring. She had a sinking sensation. She denied any impairment of memory after the episode. But, she would be aware that her right arm and leg were tingling and weak for perhaps 5 minutes afterwards and she would be unable to speak for 10-30 minutes afterwards. These focal seizures occurred once a month, but for the last 2 years, they had been occurring once a week. The patient indicated that over the last 10 years she has had problems with her memory.

She was reported to have had three “negative” CT scans over the years, and yearly EEG’s which did not reveal focal features or electrical seizure discharges although some bilateral slow wave activity was present. The patient has been treated with a variety of medications over the years without attaining seizure control. Her initial evaluation 4 years after onset of seizures at another neurological center indicated some increased activity in the finger jerks on the right with withdrawal of both plantar responses, and a diminished swing of the right arm.

Past history and family history were negative: she was the product of a full-term delivery weighing 9 pounds and had excellent developmental and educational milestones.

Neurological examination :The following abnormalities were present:

1. *Mental Status*: Although orientation and language functions were all intact, delayed recall without assistance, was 0 out of 5; and with assistance 2 out of 5. Proverb interpretation was abstract for 1/3 proverbs, but similarity testing was abstract.
2. *Cranial Nerves* II through XII were intact.
3. *Motor System* was intact except for a decreased swing of the right arm in walking.
4. *Reflexes*: deep tendon reflexes were increased on the right at biceps and patellar. Plantar response was extensor on the right and equivocally extensor on the left.
5. Sensory system was intact.

Clinical diagnosis: Seizures of focal origin left premotor/supplementary motor cortex possibly secondary to low grade glioma. A meningioma was less likely due to the reports of “normal CT scans”.

Laboratory data:

1. **CT scan** (Fig.18-16),demonstrated an area of calcification with surrounding edema in the left premotor area .

2. **MRI scan** (Fig.18-17),demonstrated extensive involvement of the premotor and supplementary areas by tumor and edema.

Subsequent course: Subtotal resection of this tumor was performed by Doctor Bernard Stone. Histological examination of the tissue confirmed the preoperative impression of an infiltrating glioma - predominantly oligodendroglioma in type. The patient received postoperative radiotherapy, 5000 rads to the left hemisphere and an additional 1000 rads to area of tumor. When last seen in follow-up 4 years after surgery, the patient was still experiencing infrequent (1-2 per month) short focal seizures of the same type involving focal movements of right arm, plus speech arrest. The neurological examination demonstrated some decrease in spontaneous speech and some blunting of affect. However, she was fluent; naming of objects and repetitions was intact. Strength was intact. Reflexes were symmetrical but bilateral extensor plantar responses were present. She had a moderate frontal type apraxia of gait and required a cane to avoid falls.

Comment :This patient presented with seizures of focal origin. The description of the posture adopted by the arm at the very beginning of the seizure, raised the possibility that her seizures were originating in the supplementary motor cortex of the left hemisphere and then spreading into the motor and sensory area. The arrest of speech would be compatible with such an origin since there is a superior speech area located in relationship to supplementary motor cortex. The fact that the patient remembered much of the seizure would also be consistent with such an origin. The post ictal depression of motor and sensory function in right arm and right leg and the depression of speech would all be consistent with post ictal phenomena involving the left hemisphere, particularly its sensory, motor and speech areas. The fact that the EEG's had not been particularly remarkable would also be consistent with such an origin of discharge. Thus, the discharging focus may well be buried on the parasagittal surface and not accessible to recording electrodes at the surface.

As regards the underlying nature of the pathology, when the patient was seen 10 years after onset of symptoms, she now has some focal findings; in terms of a right Babinski sign and increased reflexes in the right arm raising the question of a low grade glioma such as an oligodendroglioma in this area. The previous “negative” CT scans would have ruled out a meningioma or arteriovenous malformation. The long history and the finding of calcification within the tumor all made oligodendroglioma the most likely diagnosis. Low grade gliomas of this type often produce seizures without producing major neurological findings .Thus frontal release signs were minimal.

The following case history provide an example of normal pressure hydrocephalus producing the triad of a gait apraxia, urinary incontinence and problems in memory.

Case 18-3: This 72-year-old retired white handed carpenter was referred for evaluation of progressive impairment of gait, and more recent problems, in memory. The gait problems began insidiously five years previously but had become more significant in the past six months. He described his walking as involving small steps and then “going forward at too fast a rate, with difficulty in stopping”. As a result, he would stumble and tend to fall forward, losing his balance. He had considerable fear of falling and made use of a cane to avoid falling. For the last four to five months, the patient had noted urinary frequency and incontinence. He kept a bucket with him at all times. “Once I have to go, I can’t hold on.” Memory problems had developed during the last two to three months related to the recall of recent events and new material. He would enter a room and be

unable to recall why he had entered the room. Emotional lability had also developed during the past year. It was difficult not to cry when he heard a sad story.

Past history indicated at least three myocardial infarctions.

Neurological examination:

1. Mental Status:

- a. Oriented for time, place and person.
- b. Delayed recall, even with assistance, was limited to 1/3 in five minutes.
- c. The patient often lost track of what he was saying or doing.
- d. Serial 7 subtractions was slowly performed but intact.
- e. Reading, writing, drawing and naming of objects were intact but spelling was poor.
- e. Abstract reasoning was intact.
- g. Affect demonstrated changes: At times, he was tearful; at times, inappropriately jocular.

2. Cranial Nerves: Intact except bilateral decrease in hearing - long standing.

3. Motor System: Intact except for gait. The patient walked on a broad base with small steps. He was slow in starting and then picked up speed. He was unsteady on the turns and tended to turn "en bloc". No rigidity and no tremor were present. Finger to nose and heel to shin tests were normal.

4. Reflexes: Deep tendon reflexes were hyperactive at patellar. Plantar responses were equivocal. No definite frontal release signs were present.

Clinical diagnosis: Frontal lobe syndrome with involvement of premotor and prefrontal areas. The combination of a frontal gait apraxia, memory impairment and urinary incontinence raised the question of normal pressure hydrocephalus.

Laboratory data:

- 1. *CT scan (Fig. 18-21):* Demonstrated markedly dilated lateral; third and fourth ventricles but with no enlargement of the sulci.

Figure 18-21 Normal Pressure Hydrocephalus - CT Scan - Case 18-3 A. Ventricular Enlargement B. Section Through Vertex: Demonstrating No Enlargement of Sulci PART II: Comparison patient with progressive multiple sclerosis involving cerebral hemispheres at relatively comparable levels of section demonstrating A. Ventricular Enlargement B. Accompanied by Enlargement of Cortical Sulci

- 2. Lumbar puncture studies were normal.

- 3. *Radio-isotope cisternogram (Fig 18-22)* demonstrated continued presence of isotope within the ventricular system with no reabsorption over the convexities - subarachnoid space at 24, 48, and 72 hours.

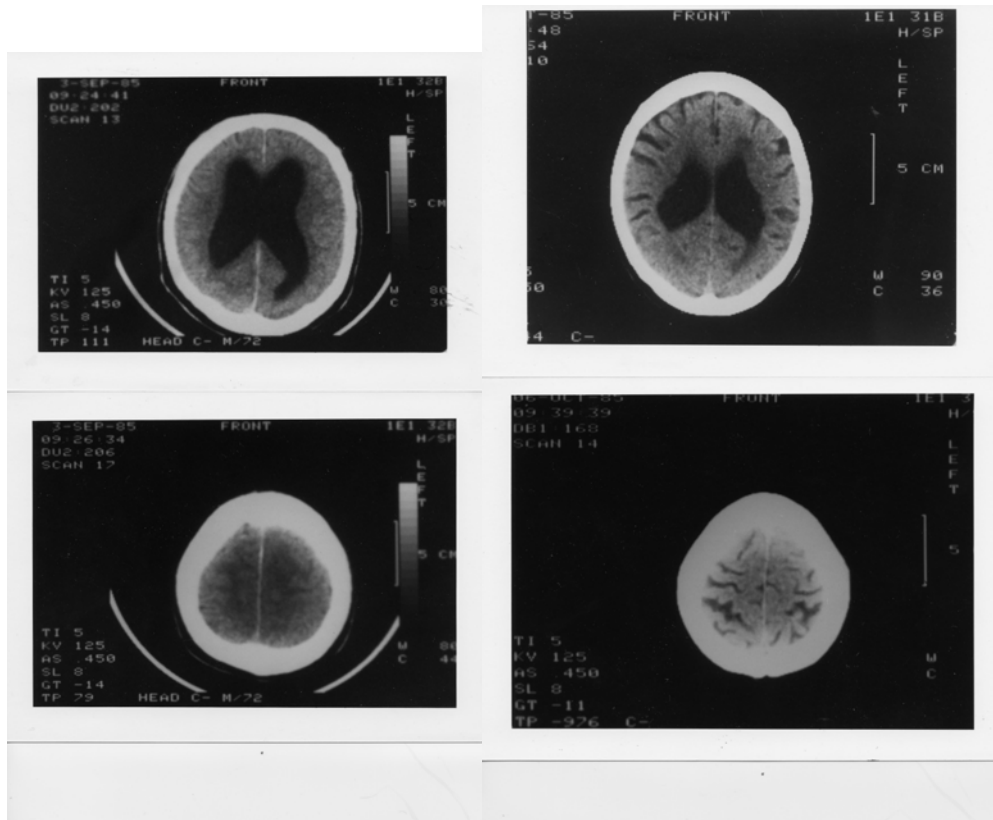
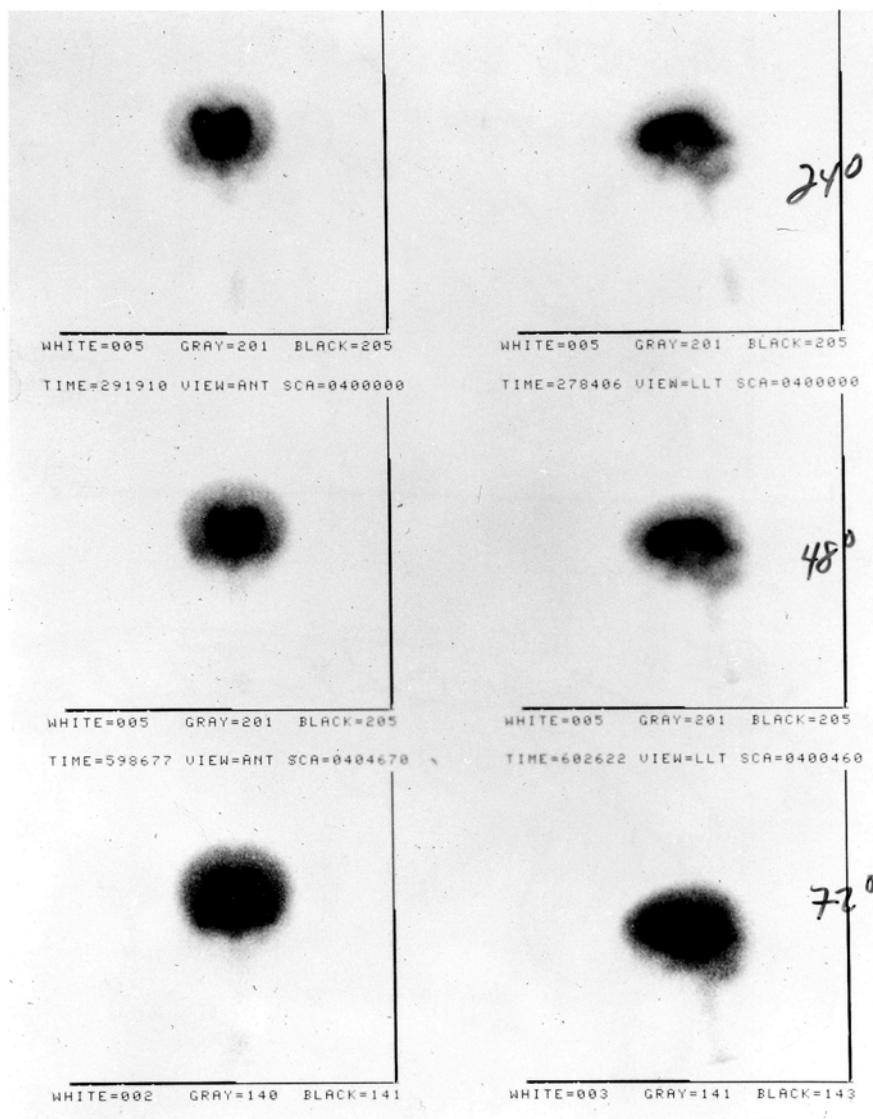


Figure 18-21. Normal Pressure Hydrocephalus Figure 18-21. Comparison Scan.

Figure 18-22: Normal Pressure Hydrocephalus: Isotope Flow Study: Lumbar CSF Injection Case 18-3 Isotope remaining in ventricular system at 24, 48 and 72 hours B. Comparison Case: Progressive multiple sclerosis of

cerebral hemispheres with enlargement of ventricular system but with enlargement of sulci. Isotope has begun to leave ventricles at 24 hours - appearing over the convexity and this is even more apparent at 48 and 72 hours.

Fig 18- 22. Normal Pressure Hydrocephalus; Isotope Flow Study



Subsequent course: Doctor Alex Danylevich performed a ventriculo-peritoneal shunt procedure (right lateral ventricle to peritoneal cavity). The patient did well with clearing of his triad of symptoms: Ataxia, dementia and urinary incontinence and was able to return to work as a carpenter , 12 hours per day. Subsequently , symptoms recurred due to infection of the peritoneal component of the shunt tube. Following revision of the shunt, symptoms improved only to worsen again in 6 months later. The patient had to use a wheelchair at times. A more marked apraxia of gait, frontal release signs, bilateral Babinski signs and urinary incontinence were present on examination 6 months after the revision. CT scan indicated a greater degree of ventricular enlargement. Following removal of 30 cc. of CSF, the patient was more responsive, and better oriented. Myocardial problems prevented additional neurosurgical revision of the shunt at that time. Subsequently, Doctor Robert Ojemann, of the Massachusetts General Hospital, revised the shunt utilizing a valve which allowed greater flow. At last evaluation, two years after admission, gait had improved (he was using a walker). Mentation was clearer (he was still described as showing aspects of a “frontal lobe syndrome”). Urinary incontinence was no longer present.

Comment: This patient presented a premotor/prefrontal syndrome .The imaging studies allowed a more specific delineation of the etiology of the syndrome. In most cases of normal pressure hydrocephalus, the gait disturbance is out of proportion to any change in mental status.

CHAPTER 19: MOTOR SYSTEM II: BASAL GANGLIA AND MOVEMENT DISORDERS

The following case presents an example of a patient with Parkinson's disease followed for 19 years.

Case 19-1 : This 48-year-old married white male, left-handed school master and physics teacher, was referred on 08/16/82 by his orthopedic surgeon for neurological evaluation of problems of control of the left arm and dragging of the left leg. Symptoms had begun 3 months previously with a sense of fatigue, stiffness and lack of control in the left arm. After a period of prolonged writing, he would have to make a conscious effort to continue writing. Approximately one month prior to the evaluation, he first noted a slowing down in movements of the left leg. "I have to remember to lift it."

Past medical history: Negative except for neck pain eight years previously related to cervical spondylosis, which cleared with the use of collar and traction except for occasional tingling in the 4th and 5th fingers of the left arm. Family history was unremarkable.

Neurological examination:

1. Mental Status: intact
2. *Cranial Nerves* I-XII: Intact except for a tremor of the closed eyelids and a positive glabellar sign (he was unable to suppress eye lid blinking on tap of forehead).
3. Motor System:
 - a. Strength : intact
 - b. Gait : There was a tendency to turn en bloc and a decreased swing of the left arm. However he could walk a tandem gait without difficulty.
 - c. There was a slight increase in resistance to passive motion at the left elbow, wrist and knee (rigidity without definite cogwheel component).
 - d. Although the patient was left-handed, there was a slowness of alternating finger movements of the left hand.
 - e. No tremor was present.
 - f. Handwriting was intact with no evidence of micrographia.
4. *Reflexes*: deep tendon stretch reflexes and plantar responses were physiologic
5. *Sensation*: all modalities were intact.

Clinical diagnosis: early Parkinson's disease, predominantly unilateral.

Laboratory data: all studies were normal including CT Scan of the brain, thyroid studies, blood chemistries, erythrocyte sedimentation rate, antinuclear antibody and serologic test for syphilis.

Subsequent course⁴: The patient did not wish to begin any treatment at that point in time. When evaluated 3 months later progression had occurred. He occasionally had the sense of moving slowly. He was now aware that with continuous writing, the writing became smaller, that is, micrographia emerged, evident on examination of handwriting. In addition, a minimal tremor was noted in the Archimedean spiral. A greater, but still minor, degree of cogwheel rigidity was now present at left wrist and elbow. Again, the patient was reluctant to begin therapy. On evaluation 1 year after onset of symptoms, additional progression was evident with significant micrographia (Fig. 19-6) and cogwheel rigidity now evident at left shoulder, elbow and wrist. Therapy with Sinemet (10-100 mg., t.i.d.)⁵ was begun. Re-evaluation one week later demonstrated a marked improvement in handwriting (Fig. 19-6) and decreased cogwheel rigidity.

⁴ This patient was followed for a total of 19 years after disease onset, initially for the first 13 years by the author, subsequently by Dr Paula Ravin at the University of Massachusetts Medical Center, Dr. David Standeart at the Massachusetts General Hospital and Dr. Warren Olanow at the Mount Sinai Hospital in New York.

⁵ This is a combination of 10 mg. of carbidopa (Dopa decarboxylase inhibitor) and 100 mg. of L-Dopa. Higher dosage combinations are a) 25 mg. of carbidopa with 100 mg L-Dopa, and b) 25 mg. carbidopa with 250 mg. L-Dopa. A sustained release form is also available (50 mg. of carbidopa with 200 mg. of L-Dopa), and is marketed as Sinemet CR.

As the dose of Sinemet was increased to (10-100) mg.5x/day over the next week, occasional choreiform movements of the fingers of the left hand and occasional backward flinging (hemi ballistic) movements of the left arm occurred. As the dose reached 10-100 mg. 6x/day, the patient reported that his handwriting now was back to normal. Examination confirmed the significant improvement in handwriting and in gait - with a better movement of the left leg. He no longer turned en bloc. Cogwheel rigidity was still present at left shoulder but to only a minimal degree at left wrist and elbow. The patient did experience 90 minutes after a Sinemet dose - a tremor of the left shoulder and an exaggerated grasp of the left foot toes on lifting the leg (possible form of dyskinetic or dystonic reaction).

The patient did well. When seen one year later, he had only a minimal degree of cogwheel rigidity. No tremor was evident. In walking he had a good swing of the arms and no longer turned en bloc. He was aware that some symptoms of his underlying disease would emerge 3-4 hours after a dose of Sinemet.

He continued to have progression of disease despite the use of all of the known anti Parkinson medications. He eventually underwent a fetal cell transplant in 1997 with apparently little improvement but with a significant increase in dyskinesias.

Re-evaluation, three years after onset of symptoms, indicated a minor progression with decreased swing of the arm and movements of the left leg, which were less smooth. The patient had increased his daily dosage of Sinemet to (10-100 mg) 6 (or) 7 tabs and noted that duration of action was approximately three hours. Re-evaluation, five years after onset of symptoms, indicated that despite having increased his dosage of Sinemet to 25-100 mg. tablets, 7 or 8 x/day, more resting tremor of the left hand had emerged. (In actuality 75-100mg of carbidopa is probably sufficient to saturate the peripheral dopa decarboxylase system). Moreover, choreiform movements of the left arm occurred 60 to 90 minutes after each dose of Sinemet. Examination demonstrated a pill-rolling tremor of the left hand as the patient walked down the hall. The choreiform movements disappeared when the dosage of Sinemet was reduced to 25/100mg 6/day. The increased rigidity and tremor responded to the addition of a DOPA agonist Bromocriptine (Parlodel) - Initial dosage 1.25 mg. 2x/day then increased to a total dose of 5.0 mg., and subsequently to 7.5 mg./day. Despite increasing dosage of the Bromocriptine to 17.5 mg/day - no additional improvement occurred. Additional reduction of Sinemet to (25-100) 5x/day - eliminated sudden myoclonic jerks and dyskinetic movement of the left lower extremity, which would occur - 45 minutes after a dose of Sinemet. Examination 6 years after onset of symptoms, examination and 3.5 hours after last dose of Sinemet demonstrated a coarse pill rolling tremor of the left hand and a shuffling of the left foot in walking. Marked cogwheel rigidity was present at left wrist and elbow. Considerable slowness of alternating finger movements was present. Handwriting was small and slow. Amantadine (an antiviral agent with mild ant parkinsonian effects), 200 mg./day was added at this point with a considerable improvement in symptomatology.

When examined 7 years after onset of symptoms, and 2.5 hours after Sinemet dosage and he now had a prominent tremor of the left hand at rest and a minor tremor of the right hand. Only minor cogwheel rigidity of left wrist and elbow were present. There was mild facial akinesia, tremor of the closed lids and a positive glabellar sign. As he walked he had a problem with sequential movements of the left leg. He reported that initially in the mornings, he had considerable problems in the initiation of movements of his left hand. Because effects of the Sinemet were wearing off in a shorter period of time - the dosing interval was altered to every three hours, in the process increasing total intake to 6 and then 7 tablets per day, with transient improvement. When seen 8 years after onset of symptoms, he was having sudden "kick in of the on effects" at 30-45 minutes and wearing off effects of greater degree at 3 hours after Sinemet dosage. As a result balance had shown some deterioration. Although tremor and cogwheel rigidity were primarily present left arm lesser symptoms were present in the right arm. At this point, a monoamine oxidase B. inhibitor was added: Selegiline (Deprenyl) in a total dose of 10 mg./day (5 mg., b.i.d.). When seen 6months later, the patient was uncertain that any benefit had been achieved. A major symptom was now "freezing" - he would have times in going over the threshold of a door when he would suddenly freeze. This, at times, related to the wearing off of medication (Sinemet) effect but at other times, usually in the afternoon, was unrelated to time of last dose. In the morning, freezing effect was clearly related to time of dosage. He remained relatively stable for the next year and then had a progression of symptoms - increasing tremor, increasing dragging of the left leg and more wearing off of dose effect - usually after 2.5 hours. In addition, "freezing" episodes were occurring more frequently in between dose wear off periods, usually in going through a doorway or even in hallways. At this point, the patient was switched to the sustained release form of Sinemet (50/200 mg carbidopa/L-Dopa) taken three times a day. Amantadine, Bromocriptine and Selegiline were continued unchanged. When evaluated 6 weeks later, there had been a remarkable improvement. He had a smoother day with fewer ups and downs, less dyskinesia and less stiffness. Effects of the medication were lasting 5-6 hours. When seen 3.5 hours after his last Sinemet dosage, he had

very little cogwheel rigidity. He could walk with a good swing of the arms. Handwriting was good with little tremor and little dyskinesia. On the other hand, when seen several weeks later, approximately 5.5 hours after his dose of sustained release Sinemet, he had marked difficulty, walked with small steps, and would arrest going through a doorway. Balance was poor, requiring a cane. There was a marked tremor of the left hand and to a lesser degree, of the right hand. A marked akinesia was present. However, within 20 minutes of his taking an additional tablet of sustained release Sinemet, a marked improvement again occurred. Despite this long course, the patient had been able to continue in his usual occupation. The patient subsequently was treated with a COMT inhibitor and was switched to another dopamine agonist pergolide with little apparent benefit. Eventually, in 1997 he was entered into the NIH sponsored fetal transplant study (subsequent imaging study did indicate that the patient was in the transplant and not the placebo group). It was unclear that this had produced any decrease in his disability. However evaluation 3 years after the transplant did demonstrate a marked increase in the dyskinesias involving head arms and torso. Some improvement in dyskinesias occurred when dopaminergic medications were reduced

Comment: Parkinson's disease is a progressive disorder of motor function, with variable manifestations of tremor, rigidity, akinesia, bradykinesia, and impairment of postural reflexes. Patients vary in the type of major involvement and in the rate of progression. Pharmacological management has rapidly evolved and in the process has provided considerable insights into the nature of basal ganglia function. For the specific patient, therapy must still be individualized. As this case history illustrates the pharmacological effects are time limited. Evaluation of therapy must always record the time of drug intake and the time of examination.

It is important to note that the disease remains progressive, despite the impressive pharmacological achievements. To prevent progression would require arresting or reversing the loss of the nigral cells producing dopamine or of introducing another source of dopamine producing neurons into the basal ganglia as discussed above. The future of fetal transplantation remains uncertain. Surgical procedures particularly deep brain stimulation involving the subthalamic nucleus or the globus pallidus may offer benefit to specific patients.

The following case, 19-2 provides an example of hemichorea.

Case 19-2 : This 88-year-old, right-handed, widowed white female with a past medical history of profound hearing impairment, adult onset diabetes, euthyroid goiter, coronary artery disease, and hypertension was brought by her daughter to Saint Vincent's Hospital because of uncontrollable movements ("twitching") of her left foot and shoulder. The daughter described the insidious onset of involuntary rotary movement in the left foot five days prior to admission, which increased in intensity and progressed to involve the left shoulder. The movements were constantly present, even during sleep. The movement was accompanied by a "shooting" pain on the left side of the body which the patient was not able to further describe. She denied loss of consciousness, dizziness, change in mental status, weakness, sensory impairment, visual changes, aphasia, or dysphagia associated with the movement disorder, but did describe a dull headache greater on the left side than on the right during the last few days prior to admission, not accompanied by nausea or vomiting. There was no history of a past movement disorder. Progression rather than spontaneous resolution of the choreiform movements which had begun to impair the patient's ability to ambulate with her walker prompted her daughter to seek medical attention.

Past history: The patient had been admitted briefly one year previously with confusion. and hyperglycemic state related to diabetes mellitus.

Physical Examination: vital signs were all normal.. Patient was alert and cooperative, though profoundly hard of hearing and exhibited involuntary twisting movements of her left foot and upward jerking movements of her left shoulder.

Neurological examination:

1. *Mental Status:* The patient was oriented x3. Memory and language were grossly intact, questions were answered appropriately, and mental status was consistent with the patient's baseline according to her daughter.
2. *Cranial Nerves:* Intact except: for Left eye blindness (cataracts), and gross impairment of hearing such that shouting was necessary to communicate.
3. *Motor System:*
 - a. Tone and strength in upper and lower extremities were normal except for minimal weakness in the left upper extremity(5-/5) .
 - b. Finger tapping, finger-to-nose and heel-to-shin were grossly intact with only slight left-sided difficulty due to involuntary movements.

- c. There was a persistent hemichorea without flinging motions in the left foot, more marked than the left shoulder. There were rotary, twisting movements at the left ankle and upward and rotary motions at the left shoulder. The movement was exacerbated by motor—tasks but did dissipate with sleep.
- d. Gait was slightly unsteady due to hesitant placement of the left foot. She did quite well with minimal assistance.
- e. Romberg was negative.
4. *Reflexes*: Deep tendon reflexes were symmetrical, and physiologic except for decreased Achilles secondary to diabetes. The right plantar response was flexor, the left ;extensor.
5. *Sensation*: Intact except for symmetrically diminished vibration sense in toes.

Clinical diagnosis: hemichorea

Laboratory data:

1. *Electrolytes creatinine, and CBC* were normal. *Glucose* was elevated to 168; *ESR* - 36 mm/hr. *RPR* non-reactive. *ANA* was 1:80(not significant) .*Urine culture* was positive for group B Streptococcal - infection sensitive to Ampicillin. *EKG and chest X-ray* were unchanged from last admission.
2. *CT scan* on admission revealed bilateral basal ganglia calcification, bifrontal atrophy consistent with age, but no evidence of infarction, hemorrhage, or tumor and revealed no change from previous CT scan of 2 months previously.
3. *MRI scan* 3 days after admission, revealed mild cortical atrophy and a hyperdense area without mass effect or enhancement on gadolinium in the right basal ganglia (particularly the head of caudate and putamen) and external capsule consistent with subacute hemorrhage (Fig.19-7).

Hospital course: The patient was begun on haloperidol 0.5 mg by mouth every morning and advanced to 1 mg., by mouth., t.i.d. with some improvement in the hemichorea, particularly in the upper - extremity. Her hemichorea continued to improve over the next two weeks on haloperidol with only occasional twitching of the left shoulder and diminished but persistent, rotary movement of the left foot, both still exacerbated by motor tasks.

The following case 19-3 provides an example of hemiballismus

Case 19-3: This 79-year-old, right-handed, white housewife had the abrupt onset in the early morning hours, 2 days prior to admission, of almost constant flinging movements of the right arm over which she had no control. At the same time, she noted that her right arm felt numb and heavy. Over the next 2 days, the movements decreased markedly and she regained more control of the arm.

Past history: The patient had been a known diabetic for 21 years, receiving insulin - most recently, lente insulin, 25 units each morning.

Neurological examination:

1. *Mental Status*: intact ,the patient was alert and well oriented and without aphasia.
2. *Cranial Nerves*: All were intact.
3. *Motor System*:
 - a. Minimal weakness was present in the right upper extremity at the elbow, wrist and fingers
 - b. Alternating movements and finger-to-nose testing in the right hand were markedly impaired.
 - c. Gait was intact.
 - d. Occasional involuntary flinging movements occurred at the right shoulder.
4. *Sensory System*: Pain, touch, vibration and position sense were all absent in the right upper extremity to the elbow and decreased in this extremity above the elbow.

Clinical diagnosis: hemiballismus

Laboratory data: Chest and skull X-rays EEG, and cerebrospinal fluid studies were all normal.

Subsequent course: The flinging movements of the right arm subsided spontaneously, shortly after admission. Position sense returned and pain sensation showed a mild improvement. The ataxia on finger-to-nose testing disappeared.

Comment: The loss of pain, touch, vibration and position sense in the right upper extremity at the onset of symptoms in this case, would suggest a lesion involving the ventral posterior lateral nucleus of the thalamus, presumably as a result of occlusion of the penetrating branches of the

posterior cerebral artery. Such a lesion could have damaged the subthalamic nucleus as well. The severe dysmetria in the right upper extremity could well have reflected the severe sensory deficit in the right upper extremity. This would appear to be more likely than postulating a lacunar ataxic hemiplegia, due to involvement of the corona radiata in which the origin of the hemiballistic movements could have been in the adjacent caudate putamen. This however would not explain the severe sensory deficit. Note that the use of antidopaminergic agents will decrease or eliminate hemiballismus or hemichorea; however many patients as in this case resolve spontaneously.

The following case history provides an example of Huntington's disease.

Case 19-4: This 54-year-old right-handed divorced white female was referred for evaluation of a movement disorder. The patient lived alone and it was difficult to obtain much of any history from the patient. So far as she was concerned, she had no neurological problems. She denied any problem with her movements. She did indicate that she had worked for 10 years as a secretary/computer operator but had been fired 10 years ago because "she did not work fast enough". She did indicate that she had experienced problems with memory over the last year. The patient denied that she had never been treated on a psychiatric service. She denied receiving neuroleptics. She had a past history of hypertension but had not been reliable in taking her prescribed medication. The patient's son was aware that changes in emotion, personality, speech, gait and a movement disorder had been present for at least 3 years.

Family history: The patient denied any neurological family history except for a maternal uncle who had the "shakes". By contacting the patient's son age 27 and her mother now age 81 and then obtaining old records we were able to assemble additional information. The patient's father had been hospitalized at age 55 on the psychiatry service of St. Vincent Hospital. A review of that record indicated that for several years he had been showing irritability, had become suspicious and paranoid at work. He gave a history of choreiform movements of 20–30 years duration beginning with twitchings about the shoulders. This had progressed over the several years prior to admission, affecting his gait and the movements of the hands. The examination demonstrated that he was moderately depressed and impatient. As he sat, he had "purposeless" movements of his body particularly of the lower extremities. In walking he had "ballistic" movements. He walked on a broad base. Choreiform movements were noted in the tongue. The diagnosis of the neuropsychiatrist was Huntington's disease. He apparently died of cardiac disease shortly after that hospitalization.

The paternal grandfather had died at age 43 of pneumonia, the paternal grandmother at age 37 of gall bladder disease, neither was known to have Huntington's disease, but information was scanty. The patient's father had two siblings one alive at age 81, the other dead at age 68, both apparently unaffected. The patient's mother had a sister with essential tremor.

The patient had 2 siblings, a brother age 60, a sister age 44; both unaffected according to the patient's mother.

The patient had 4 children ages 34, 32, 30 and 27, and 3 grandchildren ages 13 years, 2 years, and 3 months. The eldest daughter age 34 had been depressed for 5 years and had problems with speech and walking for a number of years.

Neurological examination:

1. *Mental status*: the patient often avoided eye contact. Affect was usually inappropriate with laughter as the response to many questions. The overall mini-mental status score was 27/30. The only deficit related to delayed recall portion of the test (0/3 objects).

2. *Cranial nerves*: the patient had a hyperactive jaw jerk. She had frequent facial grimacing.

3. *Motor system*: the patient had decreased tone at wrists and elbows, but strength was intact.

As she sat she had frequent restless and at times choreiform movements of hands and feet.

Gait was often "bizarre" in terms of occasional sudden movements of a leg as moved down the hall and came to a stop. These same movements occurred as she remained standing. In addition in standing or walking, there were intermittent dystonic postures of either left or right arm.

4. *Reflexes*: Deep tendon stretch reflexes were everywhere hyperactive. Plantar responses were flexor. There was a minimal suggestion of grasp release.

5. *Sensory system*: intact

Clinical diagnosis: Huntington's disease.

Laboratory data:

1. *MRI scans of head* (Fig.19-13): The heads of the caudate nuclei were very atrophic. Cortical sulci were wide consistent with cortical atrophy. The lateral and third ventricles were secondarily dilated.
2. PCR testing for the CAG trinucleotide repeats of the Huntingtin gene.: allele 1=17; allele 2=42.
3. Thyroid studies, sedimentation rate, electrolytes, RPR, and antinuclear antibody were all normal.

Subsequent course: The patient refused any treatment for the movement disorder. The patient's son requested genetic testing and the issues were discussed. He and his siblings finally decided not to have the genetic testing performed. The patient's neurological status according to the son worsened to a moderate degree over the subsequent 3 years as regards speech, unsteadiness of gait, and mood swings but without any additional change in memory. The patient herself always appeared unaccompanied for follow up visits and reported no change in her condition.

Comment: Occasionally patients are encountered where changes in psychological function limit the information that the patient can provide.. In other cases denial of illness has a neurological as well as a psychological basis. In this case it was evident that this patient had not only symptoms relevant to the basal ganglia but also changes in cognitive function relevant to the cerebral cortex particularly the frontal areas. In such cases, information must be sought from other sources. In this case, the patient was willing to provide permission to contact those possible sources.

The clinical presentation in this case was clear-cut. In retrospect, many of the neurological features were similar to her father's findings on his admission 30 years previously. When did the patient's disease begin? This was uncertain, but we may presume that serious problems had been present at least 10 years earlier when she had been fired from her long time employment. Did this relate to motor problems, to changes in personality and interpersonal relations or to cognitive changes? Most likely, there were problems in all of these areas. According to her family, symptoms had been present for 2-3 years suggesting onset at age 51 or 52 years.

Case 19-5 provides an example of a patient with Huntington's disease followed over a longer period of time.

This 32 year old right-handed married white male spray painter at a computer factory, was referred for evaluation of a possible hereditary movement disorder. The patient was unclear about the reasons for his evaluation and much of the history was provided by his wife. She reported that the patient had undergone a personality change in the last several months. He had noticeable mood swings and on one occasion he reported people outside the window when no one actually had been there. He had some problems with remembering incidental matters, but no major problems and his job performance had remained intact. He was described as always having been "fidgety".

Past medical history - Mild hypertension for three years.

Family history - The patient's initial history indicated that the family had "Parkinson's" disease and his father had died in his 40's at the state hospital after a 10-15 year illness. The patient indicated that he was a child at the time and his mother never really told him much about the father or let him visit the father in the hospital but he did recall that perhaps his father had some excessive movements of the hands and face. The records were subsequently obtained and these indicated the father had been admitted to Worcester State Hospital in 1968 at age 37. At that time, he had already had three previous hospitalizations for "nervous breakdowns". At the time of his final admission, he had developed hallucinations, seeing people in his room. He had threatened his wife and other relatives. He had difficulty sleeping and he had also developed a problem with his legs "they are jumping". The father's examination had demonstrated a mumbled speech with repetition of the same phrases. His responses would often be tangential and then incoherent with impairment of memory and judgment. His mood was depressed. He was noted to have involuntary movements of the fingers and occasional facial grimacing. The deep tendon reflexes were hyperactive and the plantar responses were extensor. His gait was ataxic. The subsequent course indicated increasing ataxia, choreiform movements and rigidity with increasing weakness, difficulty swallowing and the final development of bronchial pneumonia with death at age 42. The diagnosis of Huntington's disease was confirmed at autopsy.

The paternal grandfather had expired at age 67 with a diagnosis of Huntington's disease, manifested by "nervous breakdowns, inability to sleep and movement disorder". The father's three siblings apparently did not manifest the disease. The patient had two siblings, brother age 28, a sister age 35, all without known disease. He had two children ages 9 and 5.

Neurological examination

1. *Mental Status* - The patient was anxious, often appeared blunted in emotional expression or in answering questions. He avoided eye contact. He was oriented for time, place and person. He was able to name objects and colors. His delayed recall was 2/5 without assistance and 4/5 with assistance.
2. *Cranial Nerves II-XII* were intact, except for the occurrence of occasional, sudden darting movements of the eyes to either left or right. In addition, occasional facial grimacing was noted occurring in a rather irregular manner.
3. *Motor System* : Strength and gait were intact . There were occasional, sudden, irregular, lateral, tremulous movements of the fingers of a choreiform-type.
4. *Reflexes* : Deep tendon reflexes including the jaw jerk were everywhere hyperactive. Plantar responses were bilaterally extensor (bilateral Babinski signs).
5. *Sensory system* : intact

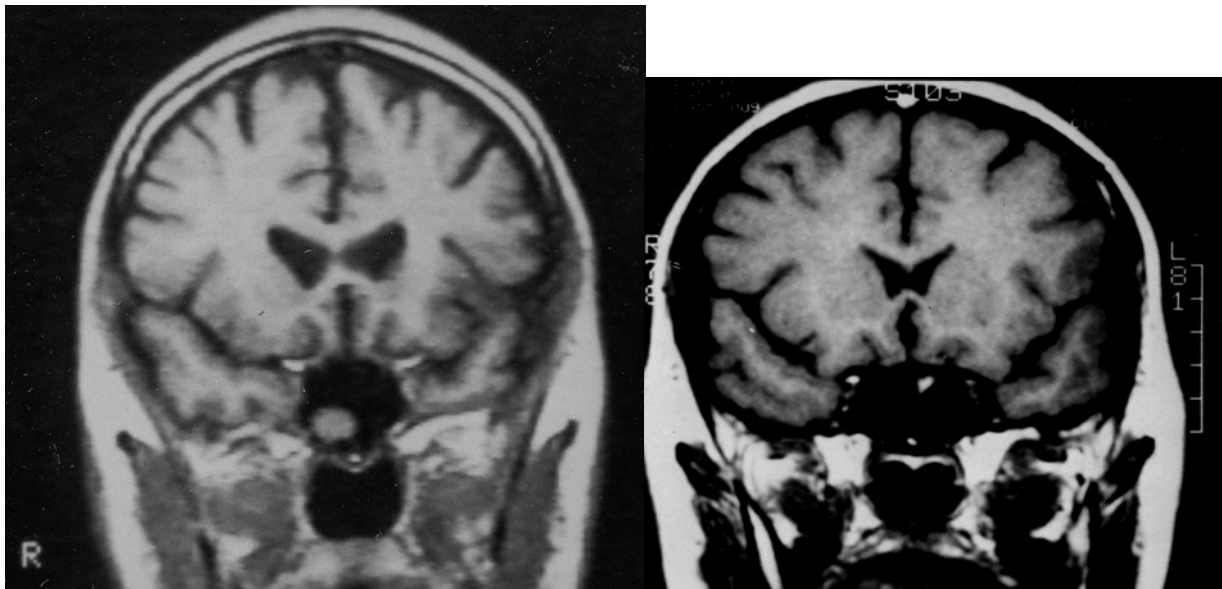
Clinical diagnosis: Huntington's disease

Laboratory Data :

1. All blood chemistries, including glucose; BUN, calcium, electrolytes, liver function studies, ceruloplasmin level, thyroid studies and serological test for syphilis were within normal limits. Ceruloplasmin levels are low in Wilson's disease but normal in Huntington's disease.
2. *Electroencephalogram* was normal with a dominant awake background activity of 10 Hz alpha rhythm.
3. *CT scan of the head* demonstrated enlargement of the ventricles with particular atrophy of the caudate. In addition the sulci were prominent for the age, suggesting some degree of cortical atrophy. The study was considered consistent with the clinical diagnosis of Huntington's disease.
4. The *MRI scan* (fig 19-11A) demonstrated mild enlargement of the ventricles and deepening of the cortical sulci, as well as a very significant atrophy of the head of the caudate nucleus. The MRI from this patient is compared to a similar section from a patient without signs of neurological disease (Figure 19-B)..

Figure 19-11A ;Case 19-5. Huntington's Disease

Figure 19-11B. Normal, age matched



Subsequent course :The patient subsequently developed increased paranoid ideation, increasing dependency with regard to his wife. He was treated with Haloperidol (a neuroleptic, tranquilizer) with considerable improvement with regard to personality. When evaluated, 3 years after onset of disease, it was evident that in the interim, the patient's personality problems had decreased. Attacks of anger and paranoid features had subsided. Mood swings were less. Memory problems, however, were worse and choreiform movements were worse. Dysarthria was now present. The patient had been divorced in the interim and he was on social security disability and no longer working. The examination now showed an exacerbation of many of those features noted at the time of his initial evaluation. He had occasional, sporadic movements of head or eyes of a

choreiform nature. He had frequent choreiform movements involving the fingers as he was sitting, also a similar type of movement appeared to involve the abdominal musculature. He had a moderate degree of dysarthria. He could walk a tandem gait but as he did so, the left arm came up in an somewhat flexed position. When last seen 4 years after onset of disease, he had more dysarthria and his speech was more difficult to interpret. There had been some increase in degree of rigidity but this had decreased when the dose of haloperidol had been decreased. The decrease in this medication, however, then resulted in a greater prominence of the choreiform movements. He could still handle a deck of cards, although he was dropping objects more often than previously. His neurological examination showed a significant degree of dysarthria, a greater degree of facial akinesia, more frequent choreiform movements of hands and face. He had difficulty in mimicking facial expression. As before, all of his deep tendon reflexes were hyperactive and the plantar responses were extensor. The patient walked in a flexed position and tended to turn en bloc. He had a mild degree of cogwheel rigidity at wrist and elbows. His memory remained remarkably good for delayed recall. Final telephone follow-up with his primary physician (approximately 7 years after apparent clinical onset of disease) indicated that the patient was no longer able to drive. He had continued weight loss. He had a marked dysarthria so that his speech was barely intelligible. Choreiform movements had increased. His gait was ataxic, but he could still walk without stumbling. He was relatively stable from a psychiatric standpoint. He was now living with his mother and brother.

Comment: This patient and his family demonstrate the relatively typical course of most patients with Huntington's disease. Patients and families do vary as to whether it is the psychiatric features or the movement disorder features that first bring the patient to medical attention. In this case, the psychiatric features, that is, the change in personality and the increasing paranoid ideation were the first features noted. Subsequently, involvement of the motor system became the most prominent feature. As in the previous case, the patient was unclear as to why he had come for neurological evaluation. Was this a neurological or a psychological denial of illness? Most likely both factors were operational. It was of considerable interest that this patient when first seen, although he was aware of some neurological problem that had occurred in the family, was unclear as to the specific diagnosis. It was also evident that almost no genetic counseling had been done in a disorder that was very clearly an autosomal dominant disorder. The significant family impact, social and economic impact of the disease are clearly evident in this patient. The implications of presymptomatic detection are discussed by Meisser et al (1988), and Klawans (1972).

The following Case 19-6 illustrates the clinical problem of hepatolenticular degeneration in a 21 year old female with a brother who had died at age 16 with hepatic disease, a Kayser Fleischer ring and choreoathetosis. The patient had serum elevation of free copper and a decrease in protein bound copper. She was successfully treated with penicillamine.

Case 19-6 (Patient of Doctor Huntington Porter) :This 21-year-old, single, white female shoe worker in January 1954 had the onset of a "shaking", or trembling of the fingers and hands which progressed to involve both arms and legs. The degree of involvement increased sufficiently to force her to give up her work. Nine months after onset of symptoms, she began to note increasing difficulty with balance and coordination and a slurring of speech. She had also noted increasing weakness and difficulty in doing repetitive tasks. One year after onset, the patient noted blurring of vision, occasional diplopia, and periods of "staring". She also had experienced increasing urgency and occasional urinary incontinence.

Family history: A brother of the patient had died in 1952, at age 16, of a disease with manifestations similar to this patient's. Evaluation of the sibling 2 years before his death by Drs. John Sullivan, Raymond Adams and D. Denny-Brown, had indicated the presence of choreoathetosis with lapses in posture of the hands. In addition, a brownish green ring at the corneal -

scleral junction was noted. Liver disease was present in this sibling and possibly other members of the family.

Neurological examination:

1. Mental status:

- a. The patient was anxious, at times crying, at other times, euphoric.
- b. Digit span was limited to 6 forward, 3 in reverse.
- c. Serial 7 subtractions were poorly performed.

2. Cranial Nerves:

- a. A brown rim was present at the limbus of the cornea, more evidence inferiorly and superiorly.
- b. Extraocular movements were impaired by involuntary jerk movements, The patient was unable to track a moving finger.
- c. Facial expression was mask-like.
- d. Speech was dysarthric and of a nasal quality with slurring and slowness of articulation.

3. Motor System:

- a. No actual weakness was present. However, this patient had difficulty maintaining the limbs in a fixed posture.
- b. There was a rigidity to passive movement of the limbs.
- c. A coarse arrhythmic tremor was present which was most marked proximally and more marked on sustained posture and on movement than at rest.
- d. Alternating movements were poorly performed.
- e. Gait was ataxic. Romberg test was negative.

4. Reflexes: Deep tendon stretch reflexes were hyperactive but plantar responses were flexor

5. Sensation: Intact

Clinical diagnosis: Wilson's disease: hepatolenticular degeneration.

Laboratory data:

1. Liver function tests were normal.
2. *Glucose tolerance test* was normal, but glycosuria occurred.
3. *Total plasma copper* 52 ug/100 ml. (normal range in a young adult is 65 to 150 ug/100 ml).
Direct reacting copper (unbound to ceruloplasmin) 31 ug/100ml (normal 10 ug/100 ml).
Indirect copper (ceruloplasmin bound) 21 ug/100 ml, normal 105 ug/ ml).

Subsequent course: The patient did relatively well following the use of the chelating agents, BAL and calcium versenate and the institution of a copper free diet. A liver biopsy performed at the time of a cesarean section 18 months after beginning treatment was compatible with perihepatitis with a question of post-necrotic cirrhosis.

Re-evaluation 6 years after onset revealed, in addition to the earlier findings, the presence of "continual spontaneous involuntary movements of the limbs; at the feet, characterized by alternating flexion and extension at the ankle and a waving of the toes". A broad amplitude coarse tremor was noted when the patient was asked to abduct arms, flex elbows, and hold hands just before her nose (wing beating position). A side-to-side tremor of the head was also present. The gait was slightly wide-based and associated with continual dystonic movements of the hands and arms. Treatment with d-penicillamine (which had just become available) was begun at that time.

Urine copper excretion increased from 700 ug per 24 hours to 3240 ug per 24 hours. Normal 24-hour urinary copper in the adult is less than 40 ug. Neurological symptoms soon demonstrated improvement from the previously noted status. The patient was now able to do her house work and take care of her children.

Follow-up 2 years later, indicated significant improvement as regards the findings noted in 1960; dystonic facies and dysarthria was less marked. No tremor was present in the left hand; that in the right hand was evident only when under tension. Dystonic posturing of the hands was present only to a minimal degree. At last report 4 years later, and 12 years after onset of the disease, the patient continued to do well. She had remarried and was expecting another child.

Comment:

This patient presents a typical case of Wilson's disease with onset in the young adult years and with a definite familial background. The copper levels were consistent with the diagnosis (an increased unbound fraction and a decreased bound fraction). At the time that this patient was seen in the mid 1950's and early 1960's, ceruloplasmin levels were not available. Early establishment of a specific diagnosis in this case allowed for specific therapy with improvement of neurological symptoms and the prevention of progression of hepatic disease. With a specific diagnosis established in the patient, periodic blood tests were performed on her offspring to determine whether they also had inherited this genetic disease. (The child born 18 months after onset of the disease had not the disorder.)

An acquired form of non-Wilsonian hepatic and cerebral degeneration occurs in patients who have had multiple episodes of hepatic coma. Degenerative changes occur in the astrocytes and neurons of the basal ganglia. This disorder which was first described by Adams and Victor is discussed in greater detail above.

CHAPTER 20. MOTOR SYSTEMS III: CEREBELLUM

The following case provides an example of a child with a medulloblastoma.

Case 20-1: This 27-month old white female was referred for evaluation of ataxia. The mother had noted that the child had been unsteady in gait, with poor balance, falling frequently since the age of 13 months, when she began to walk. Three months prior to admission, in relation to a viral infection manifested by fever and diarrhea, the patient developed increasing anorexia and lethargy. One-month prior to admission, vomiting increased, and the patient also became more irritable. Perinatal history had been normal, and head circumference had remained normal.

Neurologic examination:

1. *Mental Status:* The child was irritable but cooperative.
2. *Cranial Nerves:* The fundi could not be visualized. Bobbing of the head was present in the sitting position.
3. *Motor System:* A significant ataxia of the trunk was present when sitting or standing. Gait was broad-based and ataxic, requiring assistance. No ataxia or tremor of the extremities was present. Strength and tone were normal.
4. *Reflexes:* Deep tendon reflexes were symmetric and plantar responses were flexor.
5. *Sensory System:* All modalities were intact.

Clinical diagnosis: Probable midline cerebellar tumor, most likely based on age a medulloblastoma

Laboratory data:

1. *Left brachial arteriogram* indicated an avascular area in the posterior fossa. The superior cerebellar artery was elevated. The inferior cerebellar arteries were depressed.
2. *Air-contrast ventriculogram* demonstrated enlargement of the lateral and third ventricles. The cerebral aqueduct was displaced forward to a marked degree. The fourth ventricle was deformed by a mass overlying the posterior wall (essentially located in the nodulus).

Hospital Course: Doctor Peter Carney performed a suboccipital craniotomy. The dura was bulging. The cerebellar tonsils were herniated to a minor degree. On gentle retraction of the inferior posterior vermis, a pinkish gray tumor, originating from a higher point in the fourth ventricle, was visualized at the obex. Limited biopsies of this tumor were taken, revealing a medulloblastoma. Samples of cerebrospinal fluid obtained at surgery revealed the presence of many malignant cells. A permanent shunt from the lateral ventricle to the jugular vein was not installed because of the possibility of spread of tumor cells into systemic circulation. Instead, a catheter was connected from the lateral ventricle to a small reservoir inserted under the skin of the scalp to allow daily drainage. Radiation therapy to the entire central nervous axis was begun one week after surgery. By the time of hospital discharge two weeks after the operation, the patient was able to walk unassisted, with only a moderate degree of ataxia. Three months after the operation, the patient was readmitted because of recurrent irritability and vomiting. A mild degree of papilledema was present. Horizontal nystagmus was present on lateral gaze bilaterally. A wide-base ataxic gait was still present. Various antineoplastic agents were employed (methotrexate into the cerebrospinal fluid and vincristine intravenously) without significant improvement. One month later, respirations became slow, deep, and irregular and death occurred. The findings at autopsy are demonstrated in Fig. 20-4.

In the following case a metastatic tumor in the midline cerebellum produced vertigo, ataxia of gait and headaches.

Case 20-2: This 67 year old white female 6 weeks prior to admission developed intermittent vertigo. Two weeks prior to admission she developed an ataxia of gait. Two days later headaches and true vertigo developed, ataxia increased and vomiting occurred. On the day of admission severe vertigo, headache and nausea and vomiting resulted in her visit to the emergency room

Past history: The patient had a lumpectomy 6 years prior to admission for carcinoma of the left breast. She had undergone a radical mastectomy followed by radiation therapy 3 years prior to admission for a recurrence of malignancy. Histologic examination of the excised tissue indicated a very poorly differentiated (high grade of malignancy) infiltrating ductal tumor which was negative for estrogen and progesterone receptors. On both occasions, the patient refused chemotherapy. The patient had multiple other medical problems including non insulin dependent diabetes mellitus, coronary artery disease, mild hypertension, and prior hip replacement surgery.

Neurological examination (in the emergency room)

1. **Mental Status:** Intact
2. **Cranial Nerves:** Intact except for an absence of venous pulsations on funduscopic examination suggesting a mild increase in intracranial pressure without frank papilledema.
3. **Motor System:** The patient had difficulty standing tending to fall to the right. She was unable to walk because of severe ataxia. There was no limb dysmetria.
4. **Reflexes:** Deep tendon stretch reflexes were symmetrical. The right plantar response was equivocal.
5. **Sensory system:** Intact

Clinical diagnosis: Midline cerebellar tumor metastatic from breast.

Laboratory data :

1. **CT scan of brain:** A large (3-4 cm) enhancing tumor was present involving the midline vermis and right paramedian cerebellum and compressing the fourth ventricle.

2. **MRI of brain** (3 days after admission): An enhancing midline mass involved the cerebellar vermis extended into the right cerebellar hemisphere, and produced mass effect upon 4th ventricle (Fig. 20-5).

3. **CT scan of abdomen** demonstrated two solitary possible metastatic lesions in the liver.

Subsequent course: The patient was immediately placed on dexamethasone with significant improvement. Within 12 hours the examination demonstrated only a mild ataxia tandem gait on turns and bilateral extensor plantar responses. The patient strongly insisted on removal of the solitary central nervous system metastases. Histological examination of the tumor resected by Dr. Gerald McGullicuddy demonstrated poorly differentiated adenocarcinoma with extensive necrosis similar to the tumor which previously had been removed from the breast. Following surgery she received 3000cGy(rads) whole brain radiation and was begun on the antitumor agent tamoxifen. She continued to manifest some unsteadiness on gait but had no difficulty in finger to nose or heel to shin tests. Three months after her admission, a repeat CT scan of the abdomen and pelvis demonstrated diffuse hepatic metastases with mesenteric and retroperitoneal lymphadenopathy. She expired at home, four

months after surgery before she was to start additional treatment with the antineoplastic combination of Cytosan, methotrexate and 5-fluorouracil .

Comment : This patient had a highly malignant poorly differentiated adenocarcinoma of the breast and was clearly at risk for the development of distant metastases ,a risk that was likely increased by her unwillingness to receive antitumor medication. Six years after the lumpectomy she presented with vertigo, ataxia headache and nausea and vomiting, without limb dysmetria. These symptoms suggested involvement of those areas of cerebellum related to the vestibular system and the axis of the body: the floccular nodular area and vermis. Certainly ,the best treatment of a solitary metastatic brain tumor where systemic metastases are not present is the combination of total resection of the brain lesion followed by radiotherapy. However at the time of surgery ,this patient already had evidence of two probable metastatic lesions in the liver. Except for the strong insistence of the patient that the tumor in brain be removed ,an alternate course of radiotherapy, dexamethasone and chemotherapy might have been pursued. Never the less the patient had several additional months of life during which she was able to travel to visit various relatives for a last time. Consistent with the highly malignant character of the tumor, this patient succumbed to the non neurologic effects of her disease

The following case history 20-3 illustrates the problem of alcoholic cerebellar degeneration.

Case History 20-3: This 64-year-old, white male was admitted with a chief complaint of a slowly progressive incoordination of gait present for 8 years. The patient and others had noted that his gait was staggering. The patient denied weakness, numbness, diplopia, vertigo, or memory difficulty. The patient admitted to the consumption of one half pint (250cc) of brandy every 4 nights since symptoms had developed. He indicated that he use to drink more in his younger days, at least 6 to 8 beers in addition to brandy or other alcoholic beverages every night.

There was no history of pes cavus or neurological disease.

General physical examination ;Blood pressure 140/80.Liver was enlarged with the inferior edge extending 2 finger breadths beyond the costal margin. Face was red with dilation of vessels.

Neurological examination:

1.*Mental status:* The patient was slightly disoriented for time. He gave the date as September 31. The date was actually October 19. Delayed recall was 0-out-of-5 objects in 5 minutes. He was unable to give the date of his birth, but he knew his phone number. Digit span was 7 forward, 4 in reverse. Calculations: The patient was unable to subtract 7 from 100 or 3 from 30; he could not add 14 and 13, although he had a fourth grade education.

2.*Cranial nerves:* All were intact. No nystagmus was present.

3.*Motor system:* Strength was intact. Gait was broad-based with an ataxia of trunk. The patient was unable to walk a tandem gait. His ataxia was accentuated by rapid walking. Small lateral nodding movements of the head were noted. He was relatively stable when sitting. There was a minimal tremor at rest. In addition, there was, to minor degree, a resistance to passive motion at the wrists and elbows with a suggestion of a cogwheel component. There was a minor tremor on finger-to-nose testing and a minor impairment of alternating hand movements.

There was, however, a very significant heel-to-shin ataxia which was out of proportion to any tremor or ataxia involving the upper extremities.

4.*Reflexes:* Deep tendon reflexes were physiological and symmetrical (2-3+). Plantar responses were flexor bilaterally.

5.*Sensory system:* Position, pain and touch were intact. There was a moderate decrease in vibratory sensation at the toes and ankles.

Clinical diagnosis: 1. Alcoholic cerebellar degeneration. 2. Mild dementia possible residuals of Wernicke's-Korsakoff syndrome.

Laboratory data: Complete blood count, albumin and total protein, sedimentation rate, cerebrospinal fluid, and skull and chest X-rays were normal.

Subsequent course: The patient received multiple B vitamins and was advised to discontinue any intake of alcohol. Neurological re-evaluation over the next 6 years indicated that no essential progression had occurred.

Comment: The major findings of the broad-based, staggering gait with truncal ataxia and heel-to-shin ataxia may be related to the anterior lobe of the cerebellum. In view of the absence of progression after the discontinuation of alcohol, a toxic or nutritional factor may be postulated (The reliability of the history obtained, in terms of the specific amount of alcohol intake is always open to question particularly in a patient

with significant problems in memory. The amount stated by the patient is usually assume to be the minimum amount.). The minor extrapyramidal findings of cogwheel rigidity may have represented unrelated disease. The lack of progression would be evidence against the diagnosis of a cerebellar degeneration of other etiology (see below). The minor degree of dementia may have related to previous nutritional problems with minor Wernicke-Korsakoff's syndrome or may have reflected a minor unrelated dementia or may have related to long standing retardation. At the present time, the diagnosis may be confirmed by CT scan or by MRI (midline sagittal section) (as in Fig. 20-7 or 20-8). As a result, evidence of cerebellar atrophy is now found in many patients presenting with other aspects of chronic alcoholism or other nutritional disease who do not necessarily present with initial symptoms of ataxia.

In the following case, a similar cerebellar gait disorder and heel to shin ataxia occurred o a genetic basis.

Case 20-4: A 45-year-old single white male carpenter presented with a 4 year history of progressive unsteadiness in walking, present during the daytime as well as at night. He had, during this period, noted minimal loss of coordinated movements in his hands, but felt that his greatest deficit was unsteadiness. The patient had noted no actual weakness but reported some numbness at the toes. He had also noted some minor difficulty in swallowing.

The patient lived in a small town in Virginia. Family historical information was incomplete His mother and father were second cousins. Several aunts and uncles had "trouble with their legs" in later life, resulting in a difficulty in walking. The patient admitted to a minimal intake of alcohol in the past. He had recently been under the care of a naturopath and had experienced a 7-pound weight loss.

Neurologic examination:

1. *Mental status:* Intact and consistent with his educational level.
2. *Cranial nerves:* Intact except for minimal dysarthria. Horizontal nystagmus was present on lateral gaze, vertical nystagmus on upward gaze.
3. *Motor system:* Strength was intact. The patient walked on a broad base with an ataxia of trunk, as though intoxicated, reeling from side to side, with marked unsteadiness on turns. He was unable to walk a tandem gait with eyes open. The patient was able to sit without significant ataxia of the trunk. A mild intention tremor was present, and there was minimal disorganization of alternating movements. In contrast a marked ataxia and tremor were evident on heel-to-shin test.
4. *Reflexes:* Deep tendon reflexes were intact, except for a relative decrease in ankle jerks compared to knee jerks. Plantar responses were flexor.
5. *Sensory system:* Intact, except for a minimal decrease in vibration sensation at the toes.

Clinical diagnosis: Hereditary cerebellar degeneration involving predominantly anterior lobe

Laboratory Data: Pneumoencephalogram performed at the University of Virginia Hospital (Doctor Stewart) confirmed the significant atrophy of cerebellum. Cerebrospinal fluid and other laboratory data were normal.

Comment: This patient had onset of ataxia at age 41 and was seen relatively early in his disease course. The most prominent features included the ataxia of gait and the heel to shin dysmetria. The patient also had a minor dysarthria, nystagmus and a mild asymptomatic peripheral neuropathy (decreased Achilles reflexes and decreased vibration at toes). There was a familial background but the information was incomplete. The subject of genetic cerebellar degeneration will be considered in a later section. Using older terminology, this patient would have been classified as olivopontocerebellar atrophy. Using more modern terminology, the patient might be included within the category of autosomal dominant cerebellar ataxia type I, had more genetic information regarding the family been available by history and or actual examination.

The following case history illustrates a focal lesion of the lateral hemisphere

Case 20-5 : This 36-year-old white male attorney was referred with a chief complaint of headaches and vomiting. The patient had frontal and biparietal headaches for approximately one month precipitated by coughing, sneezing, or bending. On at least one occasion, the patient had been awakened by the headache. The patient had nausea and vomiting independent of the headaches, at times, occurring suddenly without preceding nausea. For several weeks prior to admission, the patient had been unsteady on his feet, with a tendency to fall to the right, and had noted intermittent clumsiness of his right hand. For several days prior to admission, the

patient had double vision and had to keep one eye closed. During the week prior to admission, he had been excessively drowsy and constantly tired. The headaches had increased in frequency and were now occurring 3 to 4 times per day.

Neurologic examination:

1. Mental status: Intact.

2. *Cranial nerves:*

- a. On funduscopic examination there was evidence of bilateral papilledema.
- b. A bilateral paralysis of the sixth nerve was present.
- c. Horizontal nystagmus was present on right lateral gaze.

3. *Motor system:*

- a. Strength was everywhere intact.
- b. The patient's gait was wide-based. In walking, the patient tended to veer to the right. The patient was unable to stand independently on his right leg.
- c. There was a significant intention tremor of the right upper extremity on finger-to-nose test and of the right lower extremity on heel-to-shin test. Alternating movements of the right hand were disorganized.

4. *Reflexes:* Deep tendon stretch reflexes were normal and plantar responses were flexor.

5. *Sensory system:* All modalities were intact.

Clinical diagnosis: Tumor of the right cerebellar hemisphere with obstruction of ventricular system producing increased intracranial pressure and resulting in papilledema and bilateral cranial nerve VI palsy.

Laboratory Data:

1. Complete blood count and skull x-rays were normal.
2. *Right brachial arteriogram* revealed, in the late arterial phase, a blush in the right inferior and posterior cerebellar hemisphere consistent with a hemangioblastoma.
3. *Pantopaque ventriculogram* revealed a dilated third ventricle and a dilated aqueduct with obstruction to outflow from the fourth ventricle. The fourth ventricle and to a lesser degree, the aqueduct, were shifted to the left. These findings were consistent with a right cerebellar mass displacing and obstructing the fourth ventricle.

Hospital Course: The patient was placed on high dosage of dexamethasone to relieve increased intracranial pressure. Later that day a suboccipital craniectomy was performed by Doctor Samuel Brendler. When the dura was opened, bulging of the lower portion of the right cerebellar hemisphere was noted, with widening of the cerebellar folia. The widest area of the folia was tapped with a needle and a yellow cystic fluid was removed. A transcortical incision was then made, revealing a large cyst with a small strawberry-shaped hemangioma located within. The stalk of this tumor was ligated, and the hemangioma separated from the cystic capsule. Histologic examination of the tumor revealed a hemangioblastoma.

Postoperatively, the patient did well. His headache and diplopia disappeared. There was then improvement in the patient's tremor and ataxia, although there was a slight slowness on finger-to-nose testing on the right. A minor side-to-side tremor was present on right heel-to-shin testing. There was a tendency to veer to the right in walking, but tandem gait indicated only a minor unsteadiness. Evaluation six months after surgery, indicated only a minimal unsteadiness on tandem walking. Evaluation 9 months after surgery later indicated no significant neurologic findings. Re-evaluation three and one-half years after surgery, again indicated a completely intact neurologic status.

Comment: The headaches experienced by the patient, with pain occurring on coughing, sneezing, or mechanical changes, suggested a space-occupying lesion near the ventricular system or meninges. The tumor had produced a block of the ventricular system relatively early in its course, leading to an increase in intracranial pressure, with headache, vomiting and papilledema. The bilateral sixth-cranial nerve weakness was of moderate degree, and

its occurrence would not be unusual in a situation where intracranial pressure had rapidly increased.

The cerebellar symptoms experienced by the patient were lateralized in the sense that the patient was falling to the right side and had noted clumsiness of his right hand. Lateralized cerebellar disease was confirmed by the examination findings of intention tremor of the right arm and leg and disorganization of alternating movements on the right side.

In this case, the hemangioblastoma was in the lateral cerebellar hemisphere. In other cases of hemangioblastoma, the lesion is much more midline in location, and the symptoms are those of a midline cerebellar tumor. Thus, the patient may complain of an ataxia of gait and truncal ataxia and not display clearly lateralized symptoms involving the appendages, such as intention tremor and/or ataxia on heel-to-shin testing. The nodule of tumor often exists within a non-neoplastic cystic cavity. It is, therefore, possible to remove the tumor without sacrificing a large amount of the cerebellum. In some cases, both the mural nodule and the cyst are removed. In almost all cases a complete cure is obtained; recurrences are unlikely and the patients usually have a relatively complete resolution of symptoms and no residual disability.

In some cases, hemangioblastomas of the cerebellum are associated with angiomatous malformations of the retina (Landau-von-Hippel's disease). In some cases, there is an association with a secondary increase in red blood cell production (polycythemia). In rare cases, there is an association with tumors of the kidney. Other neoplasms may also involve the cerebellar hemispheres: cystic astrocytomas, metastatic tumors, and posterior fossa meningiomas. Meningiomas of the angioblastic type may be difficult to distinguish from hemangioblastomas.

At the present time, the diagnosis of these tumors may be readily made by means of MRI and CT scan (Fig. 20-11). Ventriculograms are no longer required. Arteriograms may still be of value in defining the vascularity and blood supply of the tumor.

The following case history presents a typical example of posterior inferior cerebellar artery infarct, the territory most frequently affected selectively.

Case 20-6: This 64-year-old right-handed married white male postmaster, on the morning prior to admission, awoke at 3:00 a.m. with severe posterior headache and severe vertigo, which was exacerbated by any head movement. Nausea, projectile vomiting and slurred speech soon developed. Shortly afterwards, he noted left facial paresthesias, clumsiness of the left upper extremity, and diplopia. He was admitted to his local hospital with a diagnosis of labyrinthine vertigo and then transferred to the neurology unit at Saint Vincent Hospital when symptoms began to evolve.

Two weeks previously, the patient had been seen for a transient episode of difficulty controlling the right arm, a hissing sensation, and impairment of speech.

Past history: The patient had evidence of significant vascular disease. He had hypertension and had undergone coronary artery bypass surgery. Beginning six years previously he had experienced episodes of transient weakness and numbness of the right arm with transient aphasia. He had normal aortic arch and carotid angiographic studies but EEG had demonstrated focal left frontal/temporal slow wave activity. He had been placed on long term anticoagulation. He had experienced migraine headaches without aura for many years.

Neurologic examination:

1. *Mental status:* Intact.
2. *Cranial nerves:* Conjugate lateral gaze to the left was impaired.
3. *Motor system:* Strength was intact. Significant lateralized cerebellar findings were present with marked dysmetria of left upper extremity on finger-to-nose testing and impairment of alternating hand movements. In attempting to stand, the patient was markedly ataxic.

4. *Reflexes*: Deep tendon stretch reflexes were decreased in both lower extremities. Plantar response was extensor on the right and flexor on the left.
5. *Sensory system*: Intact
- Clinical diagnosis**: Left cerebellar hemisphere infarct or hemorrhage with possible minor involvement of brainstem secondary to mass effect.

Laboratory data:

1. Duplex scans of carotids and vertebrals were normal.
2. *Transcranial Doppler studies* indicated normal flow velocities in the vertebral, basilar, anterior and middle cerebral arteries.
3. *Magnetic-resonance angiography* demonstrated occlusion of the left vertebral artery.
4. *CT scan* demonstrated a large left cerebellar infarct pressing the fourth ventricle to the right.
5. *MRI* (2 months after onset of symptoms): Infarction of the total cerebellar territory of the left posterior inferior cerebellar artery with no actual infarct of the brain stem (Fig. 20-12).

Subsequent course: The patient was somewhat vague with some difficulty in memory during the subsequent 8-day hospital course and remained ataxic. He was then transferred to the Fairlawn Rehabilitation Hospital where, over the next three weeks, he had a significant improvement. When re-evaluated two months after onset of symptoms, he was able to walk well with the use of a cane. A minor intention tremor was present on the left finger-to-nose test. An MRI study was obtained at this point, with results indicated above (because new symptoms suggested possible involvement of upper cervical nerve roots and spinal accessory nerve). Additional improvement was evident on evaluation three months after onset of symptoms. Evaluation 6 months after onset of symptoms demonstrated only a slight slowness of alternating movements of the left hand.

Comment: The acute onset of headache, vertigo, vomiting, ataxia of gait, and dysmetria of the left arm suggested an acute cerebrovascular problem involving the posterior circulation and the posterior fossa. (The syndrome of acute headache, vertigo, ataxia, nausea and vomiting is also seen in cases of acute cerebellar hemorrhage.) Numbness on the left side of the face and diplopia suggested, as well, possible brainstem involvement. The initial diagnosis at the local hospital of acute vestibular disturbance did not explain the headache, the diplopia or the lateralized findings. The presence of the left arm dysmetria suggested lateral hemispheric involvement rather than limited midline involvement.

In the era before CT scan and MRI, the distinction between acute cerebellar hemorrhage and acute cerebellar infarct was often difficult to make. Either lesion could produce block or distortion of the ventricular system and secondary hydrocephalus. Either lesion could be associated with the development of brainstem symptoms. The cerebellar infarct, often in the distribution of the posterior inferior cerebellar artery or the anterior inferior cerebellar artery, could also involve the medullary or pontine territories of these vessels. In addition, either type of lesion could cause significant edema with secondary distortion of the brainstem. Hemorrhage could also extend into the cerebellar peduncle and brainstem.

If significant clinical hydrocephalus or brainstem compromise develops, either type of lesion may require neurosurgical decompression or a shunt procedure.

A final note should be made regarding the considerable ability of the human nervous system to recover from extensive cerebellar lesions. Considerable recovery is possible because the cerebellum does not have a direct line role in the control of motor activity but instead, acts as a modulator of the motor control and motor planning circuits.

The following case history provides an example of a cerebellar hemorrhage secondary to an arteriovenous malformation.

Case 20-7: This 57-year-old right-handed married white female had the sudden onset of a severe left-sided pounding headache one afternoon. There was some stuffiness of the nose and tearing of the left eye. She had had a similar, but less severe, headache 20 years previously when taking birth-control pills. No headaches had occurred in the interim. As the current headache began to decrease, she noted that hearing in the left ear had decreased to a minor degree, and an echo sensation was present in the left ear. She also had the sensation that the environment was off balance, particularly if she was in a moving automobile. She subsequently reported a sense of unsteadiness. There was some sense of nausea when the symptoms first occurred. A vague blurring of vision was also present. She had a vague diplopia at the onset of symptoms but this then disappeared.

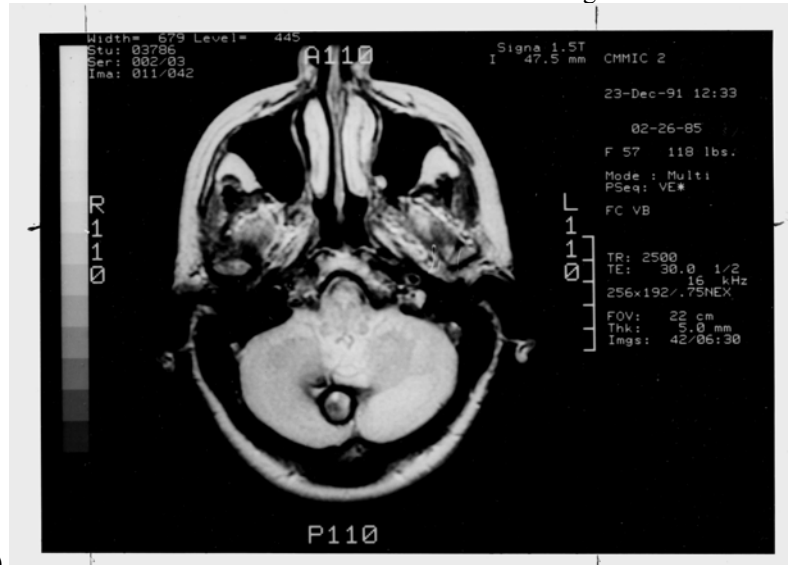
General physical examination: There were multiple pinpoint cavernous angiomas over the arms.

Neurologic examination: Entirely within normal limits.

Clinical diagnosis :Diagnosis unclear: possible migraine headache, or brain stem cerebrovascular event.

Laboratory data: 1. *CT scan of head* indicated hemorrhage in the right paramedian posterior cerebellum.

2. *MRI* showed a rim of hemosiderin stain around the residual hemorrhage in the cerebellar vermis



3. (Figure 20-14).

Subsequent course: The patient had no additional acute episodes. Because two episodes had occurred, she was referred for neurosurgical evaluation. A cavernous hemangioma of the right cerebellum was removed by Doctor Bernard Stone. Post-operatively, she had some right-sided clumsiness and ataxia, which gradually improved.

Evaluation by Doctor Stone one month following surgery, indicated minimal, if any, cerebellar signs. Finger-to-nose test showed no tremor. Gait demonstrated a minimal unsteadiness. Evaluation one year after surgery demonstrated no neurological findings, although some episodic symptoms of imbalance persisted.

CHAPTER 21: SENSORY FUNCTION AND PARIETAL LOBE

The following case demonstrates the localizing significance of focal sensory seizures beginning in the face of a 40 year old patient without prior neurological disease. As predicted, the etiology was neoplastic: a glioblastoma.

Case 21 -1:One week prior to evaluation, this 40-year old right-handed married white male had the onset of repeated 15-21 minute duration episodes of focal numbness (tingling or paresthesias) involving the left side of the face, head, ear, and posterior neck and occasionally spreading into the left hand and fingers, and rarely subsequently spreading into the left leg. There was no associated pain or headache or weakness or associated focal motor phenomena. Biting or eating would trigger the episodes. Past history was not remarkable.

Initial neurological examination: This was completely within normal limits as regards mental status, cranial nerves, motor system, reflexes, and sensory system.

Clinical diagnosis: Focal seizures originating lower third post central gyrus. In view of patient's age, a brain tumor must remain the prime consideration

Laboratory data:

- (1) *EEG*: no focal abnormalities were present. (The record, however, was abnormal because of bilateral bursts of spikes and slow waves - triggered by photic stimulation accompanied by myoclonic jerks - suggesting a predisposition to primary generalized epilepsy (refer to epilepsy chapter for the significance of this finding which was not relevant to this case).
- (2) *CT Scan* (Fig 21-2): The non-enhanced study was normal. The enhanced study demonstrated a small enhancing lesion just above the right Sylvian fissure.
- (3) *MRI* (Fig. 21 - 3): Demonstrated the more extensive nature of this process involving the operculum - above the right sylvian fissure including the lower end of the post central gyrus, the area of representation of the face. A probable infiltrating tumor was suggested as the most likely diagnosis.
- (4) *Arteriogram* - demonstrated a tumor blush at the right sylvian area, consistent with a glioblastoma, a rapidly growing infiltrating tumor - originating from astrocytic glia.

Subsequent Course: Treatment with an anticonvulsant reduced the frequency of the episodes. Neurosurgical consultation suggested an additional observation period and periodic CT scans in view of the normal neurological examination. Three months after onset of symptoms, the patient developed a numbness of the left arm and difficulty in coordination of left arm. Exam now demonstrated left central facial weakness, mild weakness of the left hand. A loss of stereognosis and graphesthesia with a relative alteration in pinprick perception was present in the left hand. The CT scan showed significant enlargement of the previous lesion. EEG now indicated focal 2-3 Hz Delta slow waves in the right frontal central Rolandic area. Subtotal resection of a glioblastoma - in the right temporal parietal area was performed by Dr. Bernard Stone. Radiation therapy was administered following surgery, 4000 rads total whole brain and 5210 rad total to the tumor area. Reevaluation 3 months after surgery, indicated only rare focal seizures involving the face. The neurological examination was normal. Repeat CT scans, however, continued to demonstrate a large area of enhancing tumor in the right temporal-frontal-parietal area. Despite the use of dexamethasone and arterial chemotherapy with cis-Platinum, he continued to progress. At the time of neurological follow-up, 29 months after onset of symptoms, he had developed a left field defect, left hemiparesis and a loss of all modalities of sensation on the left side. He subsequently developed significant changes in memory and cognition, as well as a complete left hemiplegia. CT scan demonstrated progression with extensive involvement of the right side of the brain and spread to the left hemisphere. Death occurred 33 months after onset of symptoms. **Postmortem examination of the brain:** almost the entire right hemisphere was replaced by necrotic infiltrating tumor. The tumor now had spread into the corpus callosum and temporal and occipital lobes. The internal capsule, thalamus, hypothalamus and basal ganglia were destroyed.

Comment: The initial occurrence of the limited focal sensory seizures involving the face and head in a patient of age 40 with no history of trauma or of vascular disease or hypertension clearly predicted the following conclusions (1) The location of the discharging lesion: the sensory cortex

just above the sylvian fissure. (Note that the actual extent of the pathology was more extensive but that is almost always the case in an infiltrating glioma). (2) The nature of the underlying pathology. The most common cause of focal seizures beginning at age 40 in a patient with no significant head trauma, vascular disease, hypertension or other medical disease is a tumor. Among tumors involving the cerebral hemispheres, an infiltrating glioma is by far the most common and on a statistical basis, a glioblastoma is by far the most likely histologic type. 3) The subsequent course was consistent with the natural history of a malignant glioma of the astrocytic series, a glioblastoma. The 33 month survival (30 months after surgery is beyond the median survival for this type of tumor.

The following patient (case 21-2) had a metastatic nodule in the post central gyrus producing a pseudo thalamic pain syndrome.

Case 21-2: This 62-year-old white, right-handed housewife, six years prior to admission

had undergone a left radical mastectomy for carcinoma of the breast. Five months prior to admission, the patient developed a persistent cough, left pleuritic pain and a collection of fluid in the left pleural space (pleural effusion) as well as daily headaches in the right orbit, occasionally awakening the patient from sleep. Four months prior to admission, over a 3 to 4 week period, the patient developed progressive "weakness" and difficulty in control of the right lower extremity. Several weeks later, the patient now experienced, aching pain in the right index finger in addition to a progressive deficit in the use of the right hand. This was more a "stiffness and incoordination" than any actual weakness. One month prior to admission the patient noted episodes of pain in the toes of the right foot and numbness of right foot occurred, lasting 2 to 3 days at a time. She subsequently developed, difficulty in memory and some minor language deficit, suggesting a nominal aphasia, prompting hospital admission.

Neurological examination:

1. *Mental status:* The patient was oriented for time, place, and person. Delayed recall was slightly reduced to 3-out-of-five in 5 minutes. A slowness in naming objects was present although she missed only one item of 6. Calculations, reading, and attention were normal. There was no left-right confusion.

2. Cranial nerves:

a. Nerve II: early papilledema was noted: absence of venous pulsations, indistinctness

of disc margins, and minimal elevation of vessels as they passed over the disc margin.

b. Nerve VII: right central facial weakness was present.

3. **Motor system:**

- a. Mild weakness of the right upper limb was present. A more marked weakness was present in the lower limb (most marked distally).
- b. Spasticity was present at the right elbow and knee.
- c. Gait: The right leg was circumducted; the right arm was held in a flexed posture.

4. **Reflexes:**

- a. Deep tendon reflexes were increased on the right.
- b. A right Babinski response was present.

5. **Sensory system:**

- a. Touch intact.
- b. An ill-defined alteration in pain perception was present in the right arm and leg - more of a relative difference in quality of the pain than any actual deficit.
- c. Repeated stimulation of the right lower extremity (pain or touch) produced dysesthesias (painful sensation).
- d. Vibratory sensation was decreased to a minor degree at the toes bilaterally but intact in the upper extremities.
- e. Position sense was markedly defective in the right fingers with errors in perception of fine and medium amplitude movement in the right toes.
- f. Simultaneous stimulation resulted in extinction in the right lower extremity.
- g. Graphesthesia (identification of numbers, e.g., 8, 5, 4 drawn on cutaneous surface) was absent in the right hand and fingers and poor in the right leg.
- h. Tactile localization and two-point discrimination were decreased on the right side.

Clinical diagnosis: Metastatic tumor to the left post central and precentral gyri with a cortical pain syndrome (pseudo thalamic pain syndrome).

Laboratory data:

1. *Skull x-rays:* the pineal was shifted from left to right. Demineralization of the dorsum sellae also had occurred: consistent with the increase in intracranial pressure.

2. *Chest x-ray:* Several metastatic nodules were present in the left lung.

3. *Electroencephalogram:* A focal disturbance, having the quality of damage, was present in the left posterior frontal central and parietal areas (almost continuous focal 4 to 7 cps slow wave activity).

4. *Left carotid arteriogram:* A left posterior frontal lobe lesion was suggested by a shift of the posterior portion of the anterior cerebral artery from the left to the right. The middle cerebral artery in the sylvian fissure was also depressed downwards.

5. *Brain scan:* The findings were consistent with a focal metastatic lesion with a focal uptake of radioisotope (Hg^{197}) in the left parietal area: high and close to the midline with uptake in the adjacent subcortical white matter.

6. **Erythrocyte sedimentation rate** was elevated to 90 mm., consistent with metastatic disease.

Subsequent course: There was evidence in this case that the disease had spread to multiple organs: brain (findings as noted), lung (chest x-rays and biopsy), and liver (abnormal laboratory tests of liver function). Radiation and hormonal therapy were, therefore, administered rather than any attempt at surgical removal of the left parietal metastatic lesion. Follow-up examination one month later indicated that a significant improvement had occurred in motor function in the arm. Sensory deficits persisted. Speech was slow but relatively intact. The patient eventually expired five months after admission.

Post mortem findings: Autopsy was performed by Dr. Humphrey Lloyd of the Beverly Hospital and disclosed extensive metastatic disease in the lungs, liver, and lymph nodes. A single necrotic metastatic lesion was present in

the brain. This was located in the upper postcentral gyrus of the left parietal area, 1.0 cm. below the pial surface and measuring 1.2 x 1.0 x 0.6 cm.

Comment: This patient had a progressive neurological deficit with headache and papilledema, a clinical course that clearly indicates the presence of a neoplasm. This case predated the era of CT and MRI scan. Today contrast-enhanced scans would be performed. This diagnosis was supported by the ancillary laboratory studies that were available at that time. Moreover this diagnosis however was clear based on the history and clinical-laboratory findings. The fact that motor findings in the arm relevant to the precentral gyrus improved with treatment might suggest that these findings were due to edema. In contrast the findings relevant to the area of the necrotic tumor, the post central gyrus, showed little improvement. In general, one should assume that a patient with a past history of carcinoma of the breast, carcinoma of the lung, malignant melanoma, or renal cell carcinoma, who develops symptoms of central nervous system disease, has metastatic disease until proven otherwise. Such symptoms at their onset may be minor and nonfocal and appear trivial: headache, subjective weakness, and a change in personality. On the other hand more focal symptoms and signs may be present: focal weakness, focal seizure. The metastatic lesions may be single or multiple.

A diagnosis of metastatic disease does not imply that no treatment of central nervous system lesions is possible. Surgical resection of single lesions may be successfully performed. Often the apparent deficits are far out of proportion to the actual size of the tumor because of the surrounding swelling (edema) in the adjacent tissues.

The pattern of sensory involvement in this case clearly localized this lesion to the cortex (or white matter close to cortical surface) rather than to the thalamus. The relative intactness of pain, touch, and vibration sensation should be contrasted to the significant deficits in position sense,

graphesthesia, tactile localization, and two-point discrimination with extinction on simultaneous stimulation. The occurrence of episodic pain in the involved arms and legs along with the production of an experienced painful sensation on repetitive tactile stimulation (dysesthesias) in patients with sensory pathway lesions is sometimes referred to as a "thalamic" or "pseudo thalamic" syndrome. (Refer to discussion of Wilkins and Brody, 1969). In this case, the anatomical locus for the pseudo thalamic syndrome is apparent.

The effects of deficits in cortical sensation on the total sensory motor function of a limb are apparent in this case. The actual disability and disuse of the right arm and leg were far out of proportion to any actual weakness. Such an extremity is often referred to as a "useless limb." The actual weakness that was present undoubtedly reflected pressure effects on the precentral gyrus and the descending motor fibers in adjacent white matter.

The following case (21-3) demonstrates many of the features of a non dominant parietal lobe lesion.

Case 21-3: This 70-year-old, single, white female, right-handed, retired candy maker underwent a left radical mastectomy for carcinoma of the breast, three years prior to admission. Four months prior to evaluation, the patient became unsteady with a sensation of rocking as though on a boat. She no longer attended to her housekeeping and to dressing. Over a three-week period, prior to evaluation, a relatively rapid progression occurred with deterioration of recent memory. A perseveration occurred in motor activities and speech. The patient was incontinent but was no longer concerned with urinary and fecal incontinence. For 2 weeks, right temporal headaches had been present. During this time, her sister noted the patient to be neglecting the left side of her body. She would fail to put on the left shoe when dressing. In undressing, the stocking on the left would be only half removed.

Family History: The patient's mother died of metastatic carcinoma of the breast.

Neurological examination:

1. Mental status:

- a. The patient was oriented for time, place and person.
- b. Delayed recall was 5-out-of-5 objects in 5 minutes.
- c. There was no evidence of aphasia.
 - d. The patient often wandered in her conversation. She often asked irrelevant questions and was often impersistent in motor activities.
- e. There was marked disorganization in the drawing of a house or of a clock. A similar marked disorganization was noted in attempts at copying the picture of a railroad engine (Fig 21-4).
- f. There was a marked neglect of the left side of space and of the left side of the body. The patient failed to read the left half of a page. When she put her glasses on, she did not put the left bow over the ear. When getting into bed, she did not move the left leg into bed. She had slipped off her dress on the right side, but was lying in bed with the dress still covering the left side.

- g. The patient had been reluctant to come for neurological consultation. Although she complained of headache and nausea, she denied any other deficits. Her relatives provided information concerning these problems. Much additional persuasion over a two-week period was required before the patient would agree to be hospitalized.

(2) Cranial nerves:

- a. Nerve II: A dense left homonymous hemianopsia was present. When reading, the patient left off the left side of a page. She bisected a line markedly off center. Disc margins were blurred and venous pulsations were absent, indicating papilledema.
- b. Nerve III: The right pupil was slightly larger than the left.
- c. Nerve VII: A minimal left central facial weakness was present.
3. *Motor system:* Strength was intact. There was, however, little spontaneous movement of the left arm and leg. Tone was normal.
4. *Reflexes:* deep tendon reflexes were symmetrical and physiologic and plantar responses, flexor.
5. *Gait:* The patient was ataxic on a narrow base with eyes open with a tendency to fall to the left, and was unable to stand with eyes closed even on a broad base.
6. *Sensory system:*
- a. Pain, touch and vibration were intact. At times, however, there was a decreased awareness of stimuli on the left side.
 - b. Errors were made in position sense at toes and fingers on the left.
 - c. With double simultaneous stimulation, the patient neglected stimuli on the left face, arm and leg.
 - d. Tactile localization was poor over the left arm and leg.

Clinical diagnosis: Metastatic tumor from breast to right non-dominant parietal cortex.

Laboratory data:

1. *Skull X-rays* were negative.
2. *Chest X-ray* indicated a possible metastatic lesion at the right hilum.
3. *Erythrocyte sedimentation rate* was elevated to 72 mm/hr, consistent with metastatic disease.
4. *Electroencephalogram* (Fig 21-5) was abnormal because of frequent focal 3 to 4 cps slow waves in the right temporal and parietal areas, suggesting focal damage in these areas.
5. *Brain scan (radioisotope)* (Fig 21-6) indicated that a large but well-defined area of increased uptake of isotope (Hg197) was present in the right parietal area extending from the midline to the lateral surface, measuring 7 x 5 x 7 cm. The most likely diagnosis was that of a solitary large metastatic lesion
6. *Right carotid arteriogram* showed that a large vascular tumor mass, probably metastatic, was present in the posterior section of the right temporal inferior parietal area. There was displacement of the middle cerebral artery upward and to the left.

Subsequent course: Treatment with steroids (dexamethasone and estrogens) resulted in temporary improvement. The patient refused surgery. Her condition soon deteriorated with increasing obtundation of consciousness. She expired two months following her initial neurological consultation.

Comment: This patient certainly presented a syndrome characterized by disturbance in concept of body image with a marked neglect of the left side, a denial of illness, and marked constructional apraxia. The various laboratory studies indicated a large lesion in the right posterior temporal parietal area. A CT scan from a more recent case demonstrating many aspects of this syndrome is illustrated in Figure 21-7. In many cases, the location of lesion may appear to be predominantly posterior temporal. Such large posterior temporal lesions would certainly compromise the cortex and subcortical white matter of the adjacent inferior parietal area.

In this case, marked deficits in perception of the cortical modalities of sensation were present. In other cases, as in the case demonstrated in Fig 21-7, such involvement is much less marked.

In some cases, involvement of the motor cortex is evident with an actual left hemiparesis accompanied by an increase in deep tendon reflexes and an extensor plantar response. At times in patients with neglect syndromes, there may be several indications in the clinical examination and in the laboratory studies that the involvement of the frontal lobe areas is more prominent than the parietal involvement. We have already indicated that the neglect components of this syndrome may also be noted in lesions of the anterior premotor

area (area 8). The premotor area as discussed above and in chapter 18, receives projection fibers from the multimodal area of the posterior parietal area. It is possible that in some cases the posterior temporal - inferior parietal location of the lesion may also be critical in interrupting these association fibers. For these several reasons, it is perhaps more appropriate to use the term, *syndrome of the non-dominant hemisphere*, rather than the more localized designation, non-dominant inferior parietal syndrome. Duffner et al, 1990 have presented the concept of a network for directed attention - with right frontal lesions leading to left hemi spatial neglect only for tasks that emphasize exploratory-motor components of directed attention whereas parietal lesions emphasize the perceptual-sensory aspects of neglect.

With lesions of the non-dominant hemisphere, there is a significant alteration of the patient's awareness of his environment. The behavior of an individual is in part determined by his or her own particular perception of the environment. If that perception is altered or disorganized, the behavioral responses of the patient may appear inappropriate to others. Obviously, not all individuals will respond in the same manner to a given environmental situation; part of the response will be determined by the past experience and personality of the individual. Thus, given the same lesion, one individual may be unaware of a hemiparesis, another may deny the hemiparesis but agree an illness is present, a third may claim to be healthy and claim that people are conspiring to keep him in the hospital.

CHAPTER 22: THE LIMBIC SYSTEM

In general, as we have indicated, there is mixed symptomatology during partial seizures of temporal lobe origin. The following case history (22-1) illustrates many of the points just discussed regarding seizures of temporal lobe origin.

Case 22-1: This 56-year-old white right-handed male baker was referred for evaluation of a seizure disorder. Three months before admission the patient had the onset of episodes of vertigo and tinnitus, each episode lasting 4 minutes and unrelated to position. The patient then noted increasing forgetfulness. Later that month he had a generalized convulsive seizure that occurred without any warning. The patient then developed episodes of confusion and unresponsiveness, followed by a left frontal headache. Several studies; EEG, pneumoencephalogram, and carotid arteriogram—were all negative at that point in time. One month before admission, the patient began to have minor episodes, characterized by lip smacking and a vertiginous sensation, during which he reported seeing several well-formed, colorful scenes. At times, he had hallucinations of “loaves of bread being laid out on the wall.” In addition, he would have a perceptual disturbance at the same time (e.g., objects would appear larger than normal) and “terrifying dreams.”

General physical examination: unremarkable.

Neurological examination: The essential neurological findings were as follows:

1. *General observations of seizures:* The patient was observed to have frequent transient episodes of distress characterized by saying, “Oh, oh, oh, my”. On occasion, these were accompanied by automatisms: fluttering of the eyelids, smacking of the lips, and repetitive picking at bedclothes with his right hand. Consciousness was not completely impaired during these episodes, which lasted from 30 seconds to 3 minutes, and the patient reported afterward that at the onset of the seizure he had seen loaves of bread on the wall and smelled a poorly described unpleasant odor. At other times, the olfactory hallucination was described as pleasant, resembling the aroma of baked bread.
2. *Mental status:* The patient was oriented to person but not dates. He could not recall his street address. He was unable to pronounce the name of the hospital correctly. Calculations were correctly performed.
3. *Cranial nerves:* Possible deficit in the periphery of the right visual field and a minor right central facial weakness.
4. *Motor system:* intact
5. *Reflexes:* Deep tendon reflexes were symmetrical and physiologic. A right Babinski sign was present.
6. *Sensory system:* intact.

Clinical diagnosis: Simple and complex partial seizures originating left temporal lobe probably involving at various times left lateral superior temporal gyrus, uncus, amygdala and hippocampus with tumor the most likely etiology in view of age and the focal neurological findings.

Laboratory data:

1. The *initial electroencephalographic recording* indicated frequent focal spike discharge throughout the left temporal and parietal areas, consistent with a focal seizure disorder originating in the left temporal/parietal areas (Fig. 29-1). A recording 6 days later indicated a decrease of focal spikes (i.e., a decrease in seizure activity) but the presence of frequent focal slow-wave activity in the left temporal area (almost continuous, 3 to 5 cps (Hz) slow-wave activity) suggesting that focal damage was present in the left temporal area .
2. *Brain scan* (H_g197) normal
3. *Left carotid arteriogram* indicated a possible avascular mass lesion left posterior frontal (the only abnormality was a 4-mm shift of the anterior cerebral artery).

Subsequent course: The patient continued to have multiple short episodes characterized by the sensation of odor and a sensation that he was looking at objects upon the wall. These episodes were eventually controlled with anticonvulsant medication: phenytoin (Dilantin) and primidone (Mysoline). However, 2 months later the patient had a day with several episodes with “crazy things occurring “ (colorful visions and terrifying nightmares).

The patient was readmitted to the hospital 7 months after onset of symptoms because of the recurrence of seizures. An aura of unpleasant odor was followed by a generalized convulsion followed by four or five

subsequent seizures of a somewhat different character (deviation of the head and eyes to the right, then tonic and clonic movements of the right hand spreading to the arm, foot, and leg lasting approximately 1 to 2 minutes, followed by a post-ictal right hemiparesis).

Neurologic examination now indicated a marked expressive aphasia, with little spontaneous speech and difficulty in naming objects. There was a dense right homonymous hemianopia, a flattening of the right nasolabial fold, and a right hemiparesis, with a right Babinski sign.

During a 2-week hospital period the patient continued to have minor seizures characterized by sensory phenomena on the right side of the body. A moderate degree of expressive aphasia persisted throughout the hospital course, although the right homonymous hemianopia largely disappeared. The symptoms and findings suggested that the basic disease process might well have spread to involve the adjacent areas across the sylvian fissure—the speech areas of the inferior frontal convolution, premotor areas, and sensory motor cortex.

The patient developed increasing expressive aphasia and right hemiparesis, with increasingly severe headache. An arteriogram indicated a large space-occupying tumor of the left temporal lobe, and surgery was undertaken by Dr. Robert Yuan 16 months after the onset of symptoms. The anterior and middle portions of the superior temporal gyrus appeared to be widened, and the anterior temporal area (the temporal tip) had an abnormal and discolored appearance. At a depth of 1 to 2 cm within the superior temporal gyrus and involving all of the deeper temporal areas, obvious necrotic glial tissue was found. The process had extended superficially under the Sylvian fissure to involve the adjacent posterior portion of the inferior frontal gyrus.

A temporal lobectomy was performed (from the anterior temporal pole posteriorly for a distance of 6 cm). The operative impression of a malignant glial tumor (glioblastoma) was confirmed by histologic examination.

Comment: This patient presented, at one time or another during his seizures, most of the phenomena associated with temporal lobe lesions: vertigo, tinnitus, visual distortions and hallucinations, olfactory hallucinations, fear, automatisms involving the lips and hands, and episodes of confusion. The visual and olfactory hallucinations are of interest in that both reflected the patient's occupation as a baker. As Halgren and colleagues (1978) note, the experiential phenomena of temporal-lobe seizures are often specific to the individual's experience and personality. The later progression clearly indicated spread across the sylvian fissure to involve the motor cortex and Broca's area in the inferior frontal gyrus areas. This patient had a highly malignant tumor, which clearly involved the cortex of the lateral surface, the deeper white matter, and presumably the medial temporal areas, including the amygdaloid-hippocampal regions. His clinical picture is highly reminiscent of the case described in 1887 by Hughlings Jackson of Emily M., a cook who experienced visual and olfactory hallucinations and who had a tumor arising in the "temporosphenoidal lobe" (the uncus). Such seizures have subsequently been referred to as uncinate epilepsy, but as we have indicated, the disease invariably involves more than just the uncus.

Today, CT scan and MRI would be employed for early diagnosis (see Figs. 22-17 and 22-18). Cases 22-2 and 22-3 which follow demonstrate the correlation of partial seizures with temporal lobe pathology.

Case 22-2. This 17-year-old right-handed male, at age 4 years began to have "staring spells and bizarre behavior". Some episodes had been preceded by the "sound of a musical rhythm". EEG at that time indicated a right temporal spike discharge. Seizures were controlled for ten years with anticonvulsants but then recurred and were poorly controlled occurring several times per day.

Neurological examination: The findings were limited to the following features:

1. *Observed 3 minute seizure:* The seizure began with loss of contact and a stare and then automatisms of the hands. He stood up, walked around the room, went to the physician's desk and attempted to pull open a nonexistent middle drawer. He answered questions vaguely with one or two word answers. Confusion was present for 1-2 minutes after the end of the episode.
2. *Cranial nerves:* a left central facial weakness was present.

Clinical diagnosis: Focal seizures originating right temporal lobe. Observed seizure was complex partial. The seizures beginning with the musical sound might be classified as simple partial with secondary complex partial.

Laboratory data:

1. *EEG*: Intermittent focal spike discharge anterior-middle temporal area.
2. *CT scan*: (Fig. 22-17) An area of focal atrophy was present in the right anterior temporal lobe with possible enhancement at the border.
3. *MRI*: At the Yale Epilepsy Center was more consistent with a tumor in the right anterior temporal lobe.

Subsequent course: Dr. Dennis Spencer at the Yale Epilepsy Center performed a temporal lobectomy. This demonstrated a cystic glial tumor with components of astrocytes and oligodendrocytes. Cerebral cortex also demonstrated abnormal lamination and dysplastic features. Seizures were fully controlled over the next three years.

Case 22-3. This 47-year-old ambidextrous male experienced his first seizure one month prior to admission. He felt light-headed and warm. Then he was observed to walk 100 feet down a hallway, appearing “dazed” and not recognizing people. He fell to the floor, with a loss of consciousness, bit his tongue and was confused afterwards for several minutes.

Neurological examination at 2, 16 and 48 hours after the episode: A persistent right Babinski sign, and slight right hyperreflexia were present. Otherwise the examinations were not remarkable.

Clinical diagnosis: Complex partial seizures. In view of age of onset and persistent focal signs a brain tumor was suspected as the etiology.

Laboratory diagnosis:

1. Sleep deprived EEG :normal.
2. *CT and MRI scans* (Fig. 22-18) demonstrated an extensive infiltrating tumor of the left temporal lobe most likely a glioblastoma.

Subsequent course: Despite Anticonvulsant therapy (phenytoin) additional episodes occurred over the next month: loss of train of thought while talking and several minutes of loss of memory. A subtotal resection by Dr. Bernard Stone (St. Vincent Hospital) demonstrated a Grade III-IV astrocytoma (glioblastoma). Despite radiotherapy and chemotherapy, the disease pursued a relentless course producing early and severe disability prior to death, approximately one year after onset of symptoms.

The following case histories illustrate many of the features of focal disease involving the prefrontal areas.

Case 22-4: This 69-year-old right handed white housewife; two years prior to neurological evaluation visited a relative (a physician) in Israel whom she had not seen in a number of years. The relative then wrote to the patient’s physician, (an old family friend) indicating concern over a change in the patient’s personality. The patient was described as apathetic with silly immature reactions. In retrospect, the patient’s husband felt that these alternations had begun insidiously a number of years previously. A year later, the same relative again wrote indicating that letters received from the patient had become incoherent. Letters became less frequent and then the patient no longer wrote letters. Ten months prior to evaluation, a left central facial weakness was first noted followed two months later by a decreased left arm swing. Six months prior to evaluation, her husband noted, she was purchasing items for which she had no need: 24 pairs of shoes, 15 brassieres. Subsequently she became careless in her housework. On occasions she lost her purse. Her ability to play bridge had decreased over the last year, although her golf game was unchanged.

Neurological examination:**1. Mental status**

- a. She was oriented x3
- b. There was a marked impersistence in motor activities. She was often inattentive. Her answers were often irrelevant. (According to her husband this had been present for many years.
- c. There was inappropriate joking.
- d. Delayed recall without assistance was 2/5 objects in 5 minutes. But 5/5 with assistance.
- e. Digit span was decreased to 5 forward and 3 in reverses.

- f. There were marked deficits in serial 7 subtractions. At times she began to subtract other numbers, at times she added rather than subtracted.
- g. There was a significant spatial disorientation. There was a marked impairment in the ability to copy a cube and deficits in drawing a house. There was disorientation in locating cities on a map.

2.Cranial nerves:

- a. There was a significant neglect of single stimulus objects in the left visual field; this was greater when bilateral simultaneous stimuli were utilized.
- b. At times there was a limitation of voluntary gaze to the left.
- c. A left central facial weakness was present.

3.Motor system:

- a. There was minimal weakness of the left arm and leg.
- b. Variable resistance was present on passive motion at left wrist and elbow suggesting the "gegenhalten" of frontal lobe disease.
- c. There was a decreased swing of the left arm in walking. The gait was initially apraxic but improved as the patient picked up speed.

4.Reflexes

- a. Deep tendon stretch reflexes were increased on the left.
- b. A left Babinski sign was present.
- c. There was a bilateral release of the grasp reflex.

5. Sensory system: intact.

Clinical diagnosis: Right frontal lobe tumor: probable meningioma based on the long history.

Laboratory data:

1.*Skull x-rays* there was a 5mm shift to the left of the calcified pineal gland. Long standing increased intracranial pressure was suggested by the demineralization of the sella turcica.

2.*EEG* demonstrated focal 2-5 Hz slow waves in the right frontal area most prominent in the parasagittal recording area

3.*Imaging study: radioactive brain scan (Hgl97):* there was a heavy uptake in the right frontal towards the midline measuring 5x5x4 cm (Fig.22-21).

4.*Arteriograms:* A parasagittal tumor was present in the right frontal area, with vascular supply derived from the left and right middle meningeal and left anterior meningeal arteries.

Hospital course: Following the arteriogram, the patient developed signs of increased intracranial pressure (vomiting, lethargy and papilledema). The patient received dexamethasone glucocorticoid used to reduce cerebral edema, with improvement in these symptoms. The right external carotid artery was ligated since the meningioma derived considerable blood supply from this source. Dr. Samuel Brendler performed a bilateral frontal craniotomy. Bulging of the dura was present requiring the administration of hyperosmotic agent (20% mannitol) with reduction of the swelling. When the dura was opened a large right posterior frontal meningioma was revealed measuring 8x8cm and attached to the right side of the superior sagittal sinus. On histological section this was a fibrous, meningothelial meningioma. During the course of removal of the tumor, it was necessary to ligate several bridging veins entering the superior sagittal sinus as well as the arteries feeding the tumor. At the conclusion of the procedure, it was noted that the right pupil was enlarged and neither responded to light. The patient failed to regain consciousness, remaining in a state of coma with bilateral extensor plantar responses, decerebrate postures on stimulation and bilateral fixed dilated pupils. The patient expired 2 weeks after surgery.

Comment: It is difficult to decide even in retrospect when the symptoms in this case began. It is clear that the initial symptoms involved an insidious change in personality. She was apathetic, her reactions were "silly" and judgment was impaired. Purchases were inappropriate. It would have been of interest to explore which aspects of her bridge playing were impaired in terms of planning and strategy etc. Her motor function was impaired only to a minor degree even late at the time of neurological evaluation, with minimal left-sided weakness and more prominent premotor release. The visual neglect syndrome may have reflected involvement of the premotor area or compromise of the parietal cortex by this large tumor. The fact that there was only minor evidence of involvement of motor cortex would make the premotor/SMA location more likely. While the spatial disorientation and deficits in drawing might

favor a nondominant parietal syndrome, such findings also could be consistent with a nondominant premotor/SMA location based on the close interaction between the posterior parietal and the premotor location. The impairment of voluntary gaze to the left would be consistent with area 8 involvement. There is little doubt that this patient required surgical intervention. The removal of large "benign" tumors of this type is not without risk. Hemorrhagic infarction with massive edema and tentorial herniation is a complication of ligation of bridging veins entering the superior sagittal sinus. In this case, serious brain swelling was already evident even before the dura was opened.

The following case history 22-3 provides an example of a patient with a slowly progressive subfrontal meningioma manifested by symptoms of apathy, loss of ambition, "depression" of mood, emotional lability, with a tendency to introspection and a slowness of mental processes. All of these symptoms were initially attributed to depression and a hypothyroid state. As gait and memory problems developed, these symptoms were attributed to Alzheimer's type senile dementia. When increased intracranial pressure and coma suddenly developed, neurological and neurosurgical intervention occurred.

Case 22-5: This white housewife and fashion designer was first admitted to the hospital at age 60 with a history of several years (?2 to 5) of fatigue, loss of ambition, lack of enthusiasm, and a tendency to readily cry over minor problems. A depression of mood and a tendency to introspection had developed. The patient also reported loss of her taste for food with a subsequent decrease in appetite and weight loss. These symptoms had progressed despite an adequate dosage of thyroid medication (60 mg., t.i.d.). Neurological examination was recorded as negative except for a slowness of speech and of thought processes. She was described by the psychiatric consultant as indecisive in her answers. Cerebrospinal fluid examination revealed no significant findings. Tests of thyroid function indicated hypothyroidism with protein bound iodine of 3.2 micrograms/100 ml. (normal; 4 to 8 micrograms/100 mg.) and a radioactive iodine uptake of 2.3 percent in 24 hours (normal 20 to 50 percent). Discharge diagnosis was chronic depression and hypothyroidism.

These symptoms continued to progress despite treatment with thyroid. The patient had increasing difficulty in walking. This had actually been first noted at age 57, 3 years prior to her initial hospital admission as a "phobia for heights". The patient would "freeze" at the top of a high flight of stairs. She then developed progressive difficulty in climbing stairs. Her husband reported that she would have marked difficulty in getting out of chairs. She would appear unsteady in gait after rising from a chair but would soon recover her equilibrium and would be able to walk in relatively normal manner. Increasingly, the patient's motor and mental activities became slower. She "procrastinated in making decisions". Occasional urinary incontinence developed at age 66 and was attributed to her neurological disease (apparent senile dementia). Although her husband reported her memory as initially well preserved, other observers at that point reported a progressive deficit in memory. At age 67, the patient began to complain of episodic fogging or blurring of vision.

Initial Neurological examination on re-admission to the hospital at age 67 was recorded as demonstrating the following features:

(a), slight disorientation for date and year, (b) slowness of speech and gait (c) deep tendon reflexes 2+, plantar responses flexor, and (d) no significant sensory finding except a slight decrease in position sense at the toes. No details as to the patient's gait were recorded. The sense of smell was apparently not tested and no notes as to the presence or absence of a grasp reflex were recorded.

On the day after admission, the patient developed headache and vomiting. She had difficulty walking unsupported and became increasingly more somnolent but could be roused by painful stimulation. Deep tendon reflexes were increased bilaterally with bilateral extensor plantar responses (bilateral Babinski signs). Grasp response was absent. Pupils responded to light but were sluggish.

Fundusoscopic examination was negative but lumbar puncture indicated a markedly increased pressure, greater than 400 mm. of csf. Cerebrospinal fluid protein was elevated to 125 mg/100 ml. The patient became unresponsive and emergency neurological and neurosurgical consultations were obtained.

Neurological examination:

1. *Mental Status:* The patient was semicomatose with periodic Cheyne-Stokes respirations.
2. *Cranial Nerves:* Pupils were fixed, the left dilated, the right constricted.
3. *Motor System:*
 - a. The patient moved all limbs in response to painful

stimulation, right more than left.

- b. There was a spastic resistance in the upper and lower left extremities.
4. Reflexes:
- a. A generalized hyperreflexia was present with bilateral ankle clonus.
 - b. Bilateral Babinski signs were present.
 - c. A bilateral grasp reflex was present. Note, however, that in a semicomatose patient this may have little localizing significance.
5. *Sensation*: Pain sensation was intact.

Clinical diagnosis: Subfrontal or parasagittal frontal tumor most likely a meningioma in view of the over 10 year course. Tentorial herniation had occurred possibly related to the lumbar puncture.

Laboratory data: An emergency bilateral carotid arteriograms revealed that a large subfrontal butterfly-shaped mass (probably meningioma) was present in the anterior cranial fossa bilaterally. The anterior cerebral arteries as well as the frontal polar, pericallosal and callosal marginal branches and the middle cerebral arteries were displaced backwards. The anterior cerebral arteries were also displaced upwards. The tumor mass derived blood supply from the ophthalmic arteries.

Hospital course:

A bifrontal craniotomy was immediately performed by Doctor Robert Yuan with total removal of a large bifrontal meningioma arising from the falx and olfactory groove. On the right side the tumor was estimated to occupy 75 percent of the anterior cranial fossa, measuring 7 x 5 x 6 cm. On the left the tumor was of approximately half this size, measuring 5 cm. in diameter. The thickness of the cerebral hemisphere covering the tumor in the right prefrontal area was reduced to 0.5 cm. Histological examination of the tumor indicated a benign meningioma (meningotheliomatous type).

The patient showed some immediate improvement at the conclusion of surgery, in the sense that both pupils were equal in size and reacted to light. By the time of discharge from the hospital, two months after surgery, considerable improvement had occurred. She could recognize the doctor by name but did not know the place, the season, or the month; she could, however, describe a picture she had just seen. A bilateral deficit in olfaction was present (anosmia). Assistance was required in walking. A bilateral grasp reflex was present.

Follow-up evaluation two years after surgery indicated continued improvement although the patient still had complaint relevant to impairment of recent memory and slight unsteadiness of gait. Deep tendon reflexes were symmetrical with plantar responses flexor. A bilateral grasp reflex was present and the patient was slow in walking and fell occasionally. Urinary incontinence occurred with wetting of the bed.

Comment: In retrospect, the evolution of symptoms in this patient clearly indicates a tumor initially compression both prefrontal areas and producing alterations in mood and personality. With continued growth of the tumor, compromise of the premotor areas with resultant apraxia of gait and release of grasp reflex began to occur, either as a result of direct compression or secondary to the distortion and compression of the anterior cerebral arteries. It is not unusual to witness the development of a dementia (deficit in recent memory) in large tumors in a subfrontal midline location. A similar dementia may occur in large aneurysms of the anterior communicating artery.

The problem of dementia will be considered in greater detail in the chapter on memory.

The development of headache, vomiting and increasing somnolence indicated the development of increasing intracranial pressure. The sudden unresponsiveness following the lumbar puncture with the development of periodic Cheyne-Stokes respirations, pupillary changes, and bilateral corticospinal tract signs all indicated an additional acute exacerbation of the already compromised brain stem functions, a compromise which had already resulted from the backward displacement of the intracranial contents with distortion of the brain stem. In retrospect, one might hypothesize that the patient's complaint of a loss of taste for her food at the time of her initial hospitalization might well have indicated some loss of olfactory sensation since much of our appreciation of food is dependent on olfaction. Specific tests for olfaction were not recorded.

CHAPTER 23: VISUAL SYSTEM

The following case is an example of a lesion involving the optic nerve, anterior to the optic chiasm.

Case History 23-1 (Fig 23-8).

This 53-year-old white right-handed housewife was referred for evaluation of progressive right-sided supraorbital headache of 23 years duration and decreasing acuity in the right eye. The loss of acuity had progressed to the point of almost total unilateral blindness. During the 3 years before admission, intermittent tingling paresthesia had been noted in the left face, arm, or leg. About 1 year before admission the patient had a sudden loss of consciousness and was amnesic for the events of the next 48

hours. She was hospitalized, but no explanation for the episode was clearly established, although cerebrospinal fluid protein was reported to be elevated (230 mg/dl).

The patient and her family reported some personality changes over a period of several years, including a loss of spontaneity and increasing apathy.

General Physical Examination: Unremarkable except for a minor degree of proptosis (downward protrusion of the right eye).

Neurologic Examination:

1. *Mental Status:* The patient was, in general, alert but at times would become lethargic. Her affect was flat. At times, she would laugh or joke in an inappropriate manner.
2. *Cranial Nerves:* There was anosmia for odors, such as cloves, on the right and a reduced sensitivity on the left.

Marked papilledema (increased intracranial pressure with protrusion of the optic disk and venous engorgement due to obstruction of the normal flow of CSF) was present in the left eye.

Pallor of the right optic disc was present, indicating optic atrophy. Visual acuity in the right eye was markedly reduced. The patient had only a small crescent of vision in the temporal field of the right eye, where only vague outlines of objects could be seen. A slight left central facial weakness was present.

3. *Motor Systems:* Intact although movements on the left side were slow.

4. *Reflexes:* A release of grasp reflex was present on the left side.

5. *Sensory system:* Intact

Clinical diagnosis: Subfrontal meningioma arising from olfactory groove or inner third sphenoid wing.

Laboratory data:

1. *Skull x-rays* demonstrated erosion of the dorsum sellae. Special lamniograms demonstrated hyperostosis of the sphenoid bone (planum sphenoidale) suggesting a meningioma originating from the sphenoid bone.

2. *EEG* demonstrated focal 2-4 Hz slow waves in the right anterior temporal and anterior lateral frontal area.

3. *Brain scan (H_g 197)* revealed a heavy uptake of isotope in the right posterior subfrontal area.

4. *Arteriograms* indicated that the anterior cerebral arteries were shifted backwards, posteriorly and the left. A tumor blush was present on the venous phase in the right subfrontal area extending back to the optic nerve groove (Fig 23-8). These findings were felt to be most consistent with an olfactory groove meningioma.

Hospital course: Dr. Samuel Brendler performed a bifrontal craniotomy which exposed a well-encapsulated smooth tumor attached to the medial third of the sphenoid wing. After intracapsular removal of 90 to 95% of the tumor, the right optic nerve could be visualized. The small portion of the tumor attached to the bone could not be removed because of considerable bleeding from the bone. Examination 4 months after surgery, indicated right anosmia and right optic atrophy were present.

Comment

If one considered only the patient's primary complaint, decreasing vision in the right eye, and the findings of right optic atrophy and left-sided papilledema (Foster-Kennedy syndrome), then the most probable diagnosis was inner-third sphenoid meningioma. The preservation of a small crescent of vision in the temporal field is consistent with compression of the optic nerve on its lateral surface. By the time of hospitalization, the lesion was quite large and had extended into the subfrontal area, producing anosmia on the right and some changes in personality. At this point, the various diagnostic studies suggested only a subfrontal mass and did not clearly differentiate between an olfactory-groove meningioma and a sphenoid-wing meningioma. One might suggest, in retrospect, that the degree of involvement of the right optic nerve was much more pronounced than the changes in prefrontal functions, and therefore, the inner-third sphenoid-wing location was more likely.

The surgical approach in any case was the same. The eventual recovery of vision in such cases is uncertain because the effects of compression often are not reversible

COMPLETE CASE HISTORIES FROM TEXTBOOK: *INTEGRATED NEUROSCIENCES*

PART III. CASES – CEREBRAL HEMISPHERE MOTOR SYSTEM, CEREBELLUM, BASAL GANGLIA

CHAPTER 18: MOTOR SYSTEM I:

The following case 18-1 presents an example of focal seizures beginning in the motor cortex.

Case 18-1. This 29-year-old, right-handed, white woman was in her usual state of good health until three months prior to admission when she developed an intermittent “pulling sensation” over the anterior aspect of the left thigh, lasting a few minutes. This recurred without other symptoms about twice a week. On the evening of admission, while sitting on a couch, she again had the onset of this same sensation in her left. She stood up, noted that her left leg felt “numb” and then started to have “jerky movements” in her left foot which progressed to involve the whole left lower extremity. She sat down, pressed on her left thigh in an attempt to stop the movement. At this point, her husband and a friend came to her (the patient is amnesic for these events), and saw her have tonic extension then clonus of all four limbs associated with grunting respiration, clenched jaw, and rolling of the eyes. She was placed on the floor and after a few seconds she regained consciousness, though she still appeared dazed and slightly confused for the next 5 minutes.

Past history and family history: noncontributory.

Physical Exam: Normal except for bite marks on the left lateral aspect of the tongue.

Neurological Exam: Significant only a slight asymmetry of deep tendon reflexes: left > right.

Clinical Diagnosis: Focal seizures originating right parasagittal motor cortex (foot area), with ? of parasagittal meningioma.

Laboratory Data:

(1) *Electroencephalogram* (Fig.29-1B) demonstrated rare focal spikes, right Rolandic parasagittal consistent with the focal source of the secondarily generalized seizure and rare focal slow waves in the right Rolandic and mid temporal area - consistent with minor damage in this area

2) *CT scan* (Fig.18-13) demonstrated an enhancing lesion in the right parasagittal region just anterior to the central sulcus.

- (3) *Arteriograms* (Fig.18-14) demonstrated a circumscribed vascular tumor in the right parasagittal rolandic area which was supplied by the right anterior cerebral artery (A,B) and the right middle meningeal branch of the external carotid artery©. The venous phase of the study demonstrated a significant draining vein from this area of tumor blush(D). All of these findings were consistent with a right parasagittal meningioma.

Hospital Course: A well-circumscribed right parasagittal meningioma was removed by Doctor Bernard Stone. A distal weakness of the left lower extremity was present in the immediate postoperative period but this improved rapidly so that by two months after surgery, a foot drop brace was no longer required and strength had returned to normal. During all of the pre and post operative period, the patient received diphenylhydantoin (Phenytoin) to prevent additional seizures. A possible sensory seizure involving the hand occurred 2 years later. Four years after surgery, the patient attempted to reduce her dosage of anticonvulsant and experienced a recurrence of focal motor seizure activity beginning in the left leg with subsequent secondary generalization. When evaluated 6 years after surgery, she had experienced no additional seizure activity. Her neurological examination continued to demonstrate an increase in deep tendon reflexes on the left and a left sign of Babinski. Her CT scan demonstrated no recurrence of tumor, there was very minor atrophy at the site of the previous meningioma. The EEG continued to demonstrate bursts of blunt spikes and slow waves in the right parasagittal Rolandic and parietal areas. Follow-up 10.5 years after surgery in indicated no additional seizures.

Comment: The onset of focal seizure activity should always raise the question of focal pathology. When these seizures begin at age 29, without a prior medical history, there is always a strong possibility of a primary brain tumor. In general gliomas are much more common than meningiomas but the odds of a meningioma are increased by the parasagittal location and the gender of the patient. In this case, there was a very close correlation of the clinical phenomena with the laboratory data regarding the anatomical location of the lesion. Surgical therapy eliminated the underlying benign tumor - the parasagittal meningioma, but the predisposition to focal seizures remained. Thus, the tumor in compression of cerebral cortex had produced alterations in neuronal excitability which persisted following the removal of the tumor.

Case 18-2 provides an example of a slow growing tumor involving the premotor and supplementary motor cortex from the standpoint of focal seizure activity. The motor effects of frontal lesions are presented in case histories 22-2 and 22-3 which follows the discussion of the prefrontal areas.

Case 18-2: This 57-year-old right-handed single nun and occupational therapist, had the onset of her first generalized convulsive seizure at age 47, ten years prior to consultation. This occurred without warning with sudden loss of consciousness and an observed generalized tonic clonic seizure. Both an EEG and CT scan were reported to have been normal. Approximately 4 additional generalized convulsive seizures occurred over the next 4 years. Shortly after the onset of the grand mal seizures, the patient began to have focal seizures. She described these as beginning with the abduction and raising of the right arm at the side, over her head, then a jerking of the right arm, and then she would fall to the ground. She would remain fully conscious but she would be unable to talk. She would have an awareness that something strange was occurring. She had a sinking sensation. She denied any impairment of memory after the episode. But, she would be aware that her right arm and leg were tingling and weak for perhaps 5 minutes afterwards and she would be unable to speak for 10-30 minutes afterwards. These focal seizures occurred once a month, but for the last 2 years, they had been occurring once a week. The patient indicated that over the last 10 years she has had problems with her memory.

She was reported to have had three “negative” CT scans over the years, and yearly EEG’s which did not reveal focal features or electrical seizure discharges although some bilateral slow wave activity was present. The patient has been treated with a variety of medications over the years without attaining seizure control. Her initial evaluation 4 years after onset of seizures at another neurological center indicated some increased activity in the finger jerks on the right with withdrawal of both plantar responses, and a diminished swing of the right arm.

Past history and family history were negative: she was the product of a full-term delivery weighing 9 pounds and had excellent developmental and educational milestones.

Neurological examination :The following abnormalities were present:

1. *Mental Status*: Although orientation and language functions were all intact, delayed recall without assistance, was 0 out of 5; and with assistance 2 out of 5. Proverb interpretation was abstract for 1/3 proverbs, but similarity testing was abstract.
2. *Cranial Nerves* II through XII were intact.
3. *Motor System* was intact except for a decreased swing of the right arm in walking.
4. *Reflexes*: deep tendon reflexes were increased on the right at biceps and patellar. Plantar response was extensor on the right and equivocally extensor on the left.
5. Sensory system was intact.

Clinical diagnosis: Seizures of focal origin left premotor/supplementary motor cortex possibly secondary to low grade glioma. A meningioma was less likely due to the reports of “normal CT scans”.

Laboratory data:

1. **CT scan** (Fig.18-16),demonstrated an area of calcification with surrounding edema in the left premotor area .

2. **MRI scan** (Fig.18-17),demonstrated extensive involvement of the premotor and supplementary areas by tumor and edema.

Subsequent course: Subtotal resection of this tumor was performed by Doctor Bernard Stone. Histological examination of the tissue confirmed the preoperative impression of an infiltrating glioma - predominantly oligodendroglioma in type. The patient received postoperative radiotherapy, 5000 rads to the left hemisphere and an additional 1000 rads to area of tumor. When last seen in follow-up 4 years after surgery, the patient was still experiencing infrequent (1-2 per month) short focal seizures of the same type involving focal movements of right arm, plus speech arrest. The neurological examination demonstrated some decrease in spontaneous speech and some blunting of affect. However, she was fluent; naming of objects and repetitions was intact. Strength was intact. Reflexes were symmetrical but bilateral extensor plantar responses were present. She had a moderate frontal type apraxia of gait and required a cane to avoid falls.

Comment :This patient presented with seizures of focal origin. The description of the posture adopted by the arm at the very beginning of the seizure, raised the possibility that her seizures were originating in the supplementary motor cortex of the left hemisphere and then spreading into the motor and sensory area. The arrest of speech would be compatible with such an origin since there is a superior speech area located in relationship to supplementary motor cortex. The fact that the patient remembered much of the seizure would also be consistent with such an origin. The post ictal depression of motor and sensory function in right arm and right leg and the depression of speech would all be consistent with post ictal phenomena involving the left hemisphere, particularly its sensory, motor and speech areas. The fact that the EEG's had not been particularly remarkable would also be consistent with such an origin of discharge. Thus, the discharging focus may well be buried on the parasagittal surface and not accessible to recording electrodes at the surface.

As regards the underlying nature of the pathology, when the patient was seen 10 years after onset of symptoms, she now has some focal findings; in terms of a right Babinski sign and increased reflexes in the right arm raising the question of a low grade glioma such as an oligodendroglioma in this area. The previous “negative” CT scans would have ruled out a meningioma or arteriovenous malformation. The long history and the finding of calcification within the tumor all made oligodendroglioma the most likely diagnosis. Low grade gliomas of this type often produce seizures without producing major neurological findings .Thus frontal release signs were minimal.

The following case history provide an example of normal pressure hydrocephalus producing the triad of a gait apraxia, urinary incontinence and problems in memory.

Case 18-3: This 72-year-old retired white handed carpenter was referred for evaluation of progressive impairment of gait, and more recent problems, in memory. The gait problems began insidiously five years previously but had become more significant in the past six months. He described his walking as involving small steps and then “going forward at too fast a rate, with difficulty in stopping”. As a result, he would stumble and tend to fall forward, losing his balance. He had considerable fear of falling and made use of a cane to avoid falling. For the last four to five months, the patient had noted urinary frequency and incontinence. He kept a bucket with him at all times. “Once I have to go, I can’t hold on.” Memory problems had developed during the last two to three months related to the recall of recent events and new material. He would enter a room and be

unable to recall why he had entered the room. Emotional lability had also developed during the past year. It was difficult not to cry when he heard a sad story.

Past history indicated at least three myocardial infarctions.

Neurological examination:

1. Mental Status:

- a. Oriented for time, place and person.
- b. Delayed recall, even with assistance, was limited to 1/3 in five minutes.
- c. The patient often lost track of what he was saying or doing.
- d. Serial 7 subtractions was slowly performed but intact.
- e. Reading, writing, drawing and naming of objects were intact but spelling was poor.
- e. Abstract reasoning was intact.
- g. Affect demonstrated changes: At times, he was tearful; at times, inappropriately jocular.

2. Cranial Nerves: Intact except bilateral decrease in hearing - long standing.

3. Motor System: Intact except for gait. The patient walked on a broad base with small steps. He was slow in starting and then picked up speed. He was unsteady on the turns and tended to turn "en bloc". No rigidity and no tremor were present. Finger to nose and heel to shin tests were normal.

4. Reflexes: Deep tendon reflexes were hyperactive at patellar. Plantar responses were equivocal. No definite frontal release signs were present.

Clinical diagnosis: Frontal lobe syndrome with involvement of premotor and prefrontal areas. The combination of a frontal gait apraxia, memory impairment and urinary incontinence raised the question of normal pressure hydrocephalus.

Laboratory data:

- 1. *CT scan (Fig. 18-21):* Demonstrated markedly dilated lateral; third and fourth ventricles but with no enlargement of the sulci.

Figure 18-21 Normal Pressure Hydrocephalus - CT Scan - Case 18-3 A. Ventricular Enlargement B. Section Through Vertex: Demonstrating No Enlargement of Sulci PART II: Comparison patient with progressive multiple sclerosis involving cerebral hemispheres at relatively comparable levels of section demonstrating A. Ventricular Enlargement B. Accompanied by Enlargement of Cortical Sulci

- 2. Lumbar puncture studies were normal.

- 3. *Radio-isotope cisternogram (Fig 18-22)* demonstrated continued presence of isotope within the ventricular system with no reabsorption over the convexities - subarachnoid space at 24, 48, and 72 hours.

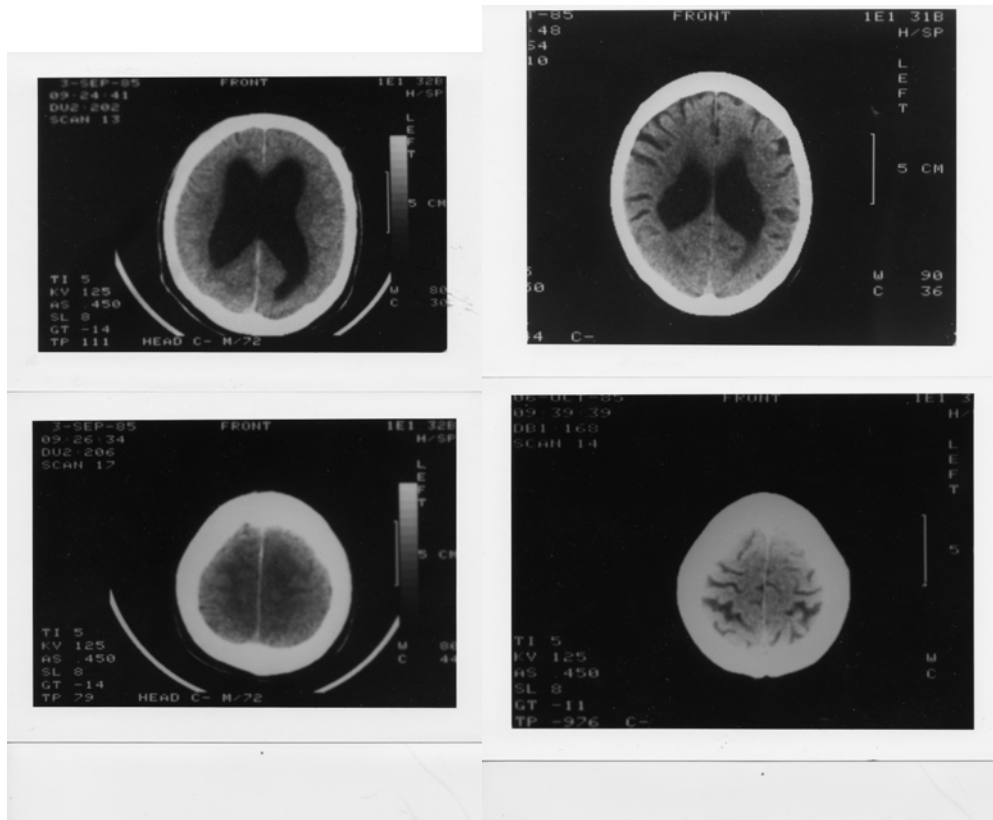
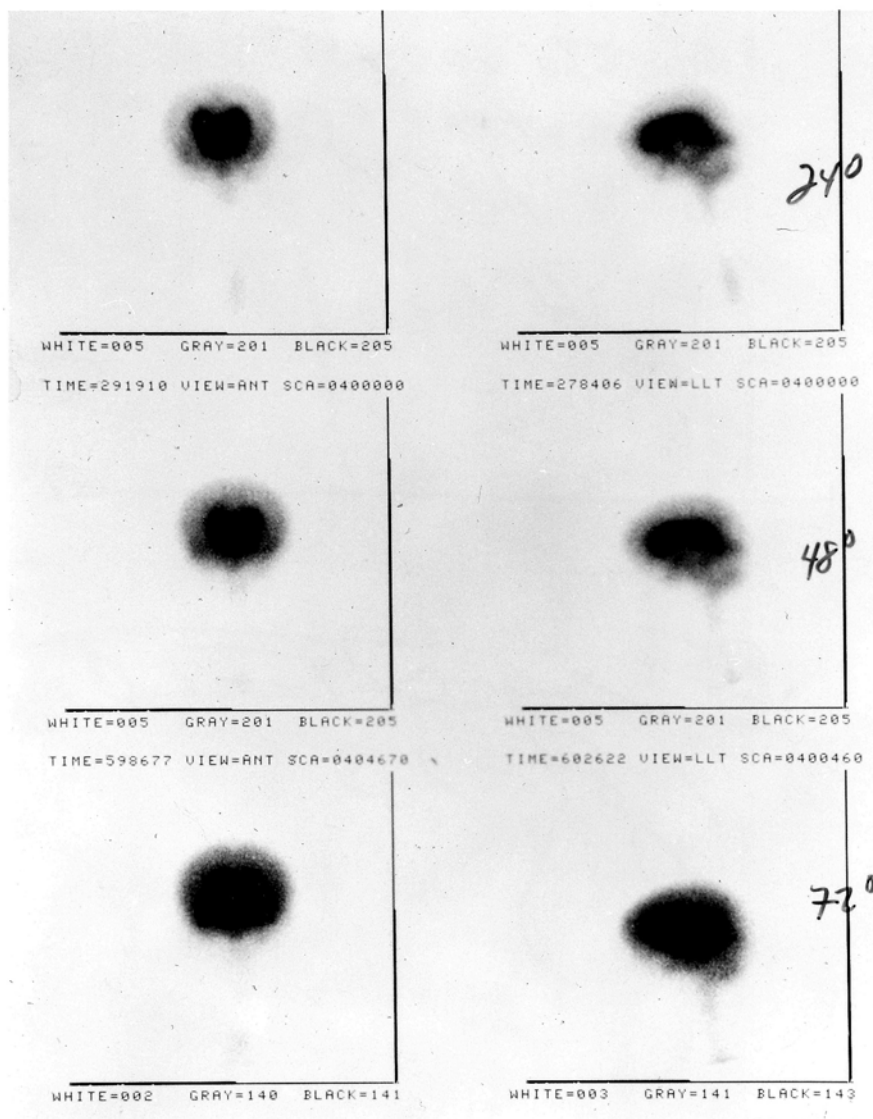


Figure 18-21. Normal Pressure Hydrocephalus Figure 18-21. Comparison Scan.

Figure 18-22: Normal Pressure Hydrocephalus: Isotope Flow Study: Lumbar CSF Injection Case 18-3 Isotope remaining in ventricular system at 24, 48 and 72 hours B. Comparison Case: Progressive multiple sclerosis of

cerebral hemispheres with enlargement of ventricular system but with enlargement of sulci. Isotope has begun to leave ventricles at 24 hours - appearing over the convexity and this is even more apparent at 48 and 72 hours.

Fig 18- 22. Normal Pressure Hydrocephalus; Isotope Flow Study



Subsequent course: Doctor Alex Danylevich performed a ventriculo-peritoneal shunt procedure (right lateral ventricle to peritoneal cavity). The patient did well with clearing of his triad of symptoms: Ataxia, dementia and urinary incontinence and was able to return to work as a carpenter , 12 hours per day. Subsequently , symptoms recurred due to infection of the peritoneal component of the shunt tube. Following revision of the shunt, symptoms improved only to worsen again in 6 months later. The patient had to use a wheelchair at times. A more marked apraxia of gait, frontal release signs, bilateral Babinski signs and urinary incontinence were present on examination 6 months after the revision. CT scan indicated a greater degree of ventricular enlargement. Following removal of 30 cc. of CSF, the patient was more responsive, and better oriented. Myocardial problems prevented additional neurosurgical revision of the shunt at that time. Subsequently, Doctor Robert Ojemann, of the Massachusetts General Hospital, revised the shunt utilizing a valve which allowed greater flow. At last evaluation, two years after admission, gait had improved (he was using a walker). Mentation was clearer (he was still described as showing aspects of a “frontal lobe syndrome”). Urinary incontinence was no longer present.

Comment: This patient presented a premotor/prefrontal syndrome .The imaging studies allowed a more specific delineation of the etiology of the syndrome. In most cases of normal pressure hydrocephalus, the gait disturbance is out of proportion to any change in mental status.

CHAPTER 19: MOTOR SYSTEM II: BASAL GANGLIA AND MOVEMENT DISORDERS

The following case presents an example of a patient with Parkinson's disease followed for 19 years.

Case 19-1 : This 48-year-old married white male, left-handed school master and physics teacher, was referred on 08/16/82 by his orthopedic surgeon for neurological evaluation of problems of control of the left arm and dragging of the left leg. Symptoms had begun 3 months previously with a sense of fatigue, stiffness and lack of control in the left arm. After a period of prolonged writing, he would have to make a conscious effort to continue writing. Approximately one month prior to the evaluation, he first noted a slowing down in movements of the left leg. "I have to remember to lift it."

Past medical history: Negative except for neck pain eight years previously related to cervical spondylosis, which cleared with the use of collar and traction except for occasional tingling in the 4th and 5th fingers of the left arm. Family history was unremarkable.

Neurological examination:

1. Mental Status: intact
2. *Cranial Nerves I-XII:* Intact except for a tremor of the closed eyelids and a positive glabellar sign (he was unable to suppress eye lid blinking on tap of forehead).
3. Motor System:
 - a. Strength : intact
 - b. Gait : There was a tendency to turn en bloc and a decreased swing of the left arm. However he could walk a tandem gait without difficulty.
 - c. There was a slight increase in resistance to passive motion at the left elbow, wrist and knee (rigidity without definite cogwheel component).
 - d. Although the patient was left-handed, there was a slowness of alternating finger movements of the left hand.
 - e. No tremor was present.
 - f. Handwriting was intact with no evidence of micrographia.
4. *Reflexes:* deep tendon stretch reflexes and plantar responses were physiologic
5. *Sensation:* all modalities were intact.

Clinical diagnosis: early Parkinson's disease, predominantly unilateral.

Laboratory data: all studies were normal including CT Scan of the brain, thyroid studies, blood chemistries, erythrocyte sedimentation rate, antinuclear antibody and serologic test for syphilis.

Subsequent course⁴: The patient did not wish to begin any treatment at that point in time. When evaluated 3 months later progression had occurred. He occasionally had the sense of moving slowly. He was now aware that with continuous writing, the writing became smaller, that is, micrographia emerged, evident on examination of handwriting. In addition, a minimal tremor was noted in the Archimedean spiral. A greater, but still minor, degree of cogwheel rigidity was now present at left wrist and elbow. Again, the patient was reluctant to begin therapy. On evaluation 1 year after onset of symptoms, additional progression was evident with significant micrographia (Fig. 19-6) and cogwheel rigidity now evident at left shoulder, elbow and wrist. Therapy with Sinemet (10-100 mg., t.i.d.)⁵ was begun. Re-evaluation one week later demonstrated a marked improvement in handwriting (Fig. 19-6) and decreased cogwheel rigidity.

⁴ This patient was followed for a total of 19 years after disease onset, initially for the first 13 years by the author, subsequently by Dr Paula Ravin at the University of Massachusetts Medical Center, Dr. David Standeart at the Massachusetts General Hospital and Dr. Warren Olanow at the Mount Sinai Hospital in New York.

⁵ This is a combination of 10 mg. of carbidopa (Dopa decarboxylase inhibitor) and 100 mg. of L-Dopa. Higher dosage combinations are a) 25 mg. of carbidopa with 100 mg L-Dopa, and b) 25 mg. carbidopa with 250 mg. L-Dopa. A sustained release form is also available (50 mg. of carbidopa with 200 mg. of L-Dopa), and is marketed as Sinemet CR.

As the dose of Sinemet was increased to (10-100) mg.5x/day over the next week, occasional choreiform movements of the fingers of the left hand and occasional backward flinging (hemi ballistic) movements of the left arm occurred. As the dose reached 10-100 mg. 6x/day, the patient reported that his handwriting now was back to normal. Examination confirmed the significant improvement in handwriting and in gait - with a better movement of the left leg. He no longer turned en bloc. Cogwheel rigidity was still present at left shoulder but to only a minimal degree at left wrist and elbow. The patient did experience 90 minutes after a Sinemet dose - a tremor of the left shoulder and an exaggerated grasp of the left foot toes on lifting the leg (possible form of dyskinetic or dystonic reaction).

The patient did well. When seen one year later, he had only a minimal degree of cogwheel rigidity. No tremor was evident. In walking he had a good swing of the arms and no longer turned en bloc. He was aware that some symptoms of his underlying disease would emerge 3-4 hours after a dose of Sinemet.

He continued to have progression of disease despite the use of all of the known anti Parkinson medications. He eventually underwent a fetal cell transplant in 1997 with apparently little improvement but with a significant increase in dyskinesias.

Re-evaluation, three years after onset of symptoms, indicated a minor progression with decreased swing of the arm and movements of the left leg, which were less smooth. The patient had increased his daily dosage of Sinemet to (10-100 mg) 6 (or) 7 tabs and noted that duration of action was approximately three hours. Re-evaluation, five years after onset of symptoms, indicated that despite having increased his dosage of Sinemet to 25-100 mg. tablets, 7 or 8 x/day, more resting tremor of the left hand had emerged. (In actuality 75-100mg of carbidopa is probably sufficient to saturate the peripheral dopa decarboxylase system). Moreover, choreiform movements of the left arm occurred 60 to 90 minutes after each dose of Sinemet. Examination demonstrated a pill-rolling tremor of the left hand as the patient walked down the hall. The choreiform movements disappeared when the dosage of Sinemet was reduced to 25/100mg 6/day. The increased rigidity and tremor responded to the addition of a DOPA agonist Bromocriptine (Parlodel) - Initial dosage 1.25 mg. 2x/day then increased to a total dose of 5.0 mg., and subsequently to 7.5 mg./day. Despite increasing dosage of the Bromocriptine to 17.5 mg/day - no additional improvement occurred. Additional reduction of Sinemet to (25-100) 5x/day - eliminated sudden myoclonic jerks and dyskinetic movement of the left lower extremity, which would occur - 45 minutes after a dose of Sinemet. Examination 6 years after onset of symptoms, examination and 3.5 hours after last dose of Sinemet demonstrated a coarse pill rolling tremor of the left hand and a shuffling of the left foot in walking. Marked cogwheel rigidity was present at left wrist and elbow. Considerable slowness of alternating finger movements was present. Handwriting was small and slow. Amantadine (an antiviral agent with mild ant parkinsonian effects), 200 mg./day was added at this point with a considerable improvement in symptomatology.

When examined 7 years after onset of symptoms, and 2.5 hours after Sinemet dosage and he now had a prominent tremor of the left hand at rest and a minor tremor of the right hand. Only minor cogwheel rigidity of left wrist and elbow were present. There was mild facial akinesia, tremor of the closed lids and a positive glabellar sign. As he walked he had a problem with sequential movements of the left leg. He reported that initially in the mornings, he had considerable problems in the initiation of movements of his left hand. Because effects of the Sinemet were wearing off in a shorter period of time - the dosing interval was altered to every three hours, in the process increasing total intake to 6 and then 7 tablets per day, with transient improvement. When seen 8 years after onset of symptoms, he was having sudden "kick in of the on effects" at 30-45 minutes and wearing off effects of greater degree at 3 hours after Sinemet dosage. As a result balance had shown some deterioration. Although tremor and cogwheel rigidity were primarily present left arm lesser symptoms were present in the right arm. At this point, a monoamine oxidase B. inhibitor was added: Selegiline (Deprenyl) in a total dose of 10 mg./day (5 mg., b.i.d.). When seen 6months later, the patient was uncertain that any benefit had been achieved. A major symptom was now "freezing" - he would have times in going over the threshold of a door when he would suddenly freeze. This, at times, related to the wearing off of medication (Sinemet) effect but at other times, usually in the afternoon, was unrelated to time of last dose. In the morning, freezing effect was clearly related to time of dosage. He remained relatively stable for the next year and then had a progression of symptoms - increasing tremor, increasing dragging of the left leg and more wearing off of dose effect - usually after 2.5 hours. In addition, "freezing" episodes were occurring more frequently in between dose wear off periods, usually in going through a doorway or even in hallways. At this point, the patient was switched to the sustained release form of Sinemet (50/200 mg carbidopa/L-Dopa) taken three times a day. Amantadine, Bromocriptine and Selegiline were continued unchanged. When evaluated 6 weeks later, there had been a remarkable improvement. He had a smoother day with fewer ups and downs, less dyskinesia and less stiffness. Effects of the medication were lasting 5-6 hours. When seen 3.5 hours after his last Sinemet dosage, he had

very little cogwheel rigidity. He could walk with a good swing of the arms. Handwriting was good with little tremor and little dyskinesia. On the other hand, when seen several weeks later, approximately 5.5 hours after his dose of sustained release Sinemet, he had marked difficulty, walked with small steps, and would arrest going through a doorway. Balance was poor, requiring a cane. There was a marked tremor of the left hand and to a lesser degree, of the right hand. A marked akinesia was present. However, within 20 minutes of his taking an additional tablet of sustained release Sinemet, a marked improvement again occurred. Despite this long course, the patient had been able to continue in his usual occupation. The patient subsequently was treated with a COMT inhibitor and was switched to another dopamine agonist pergolide with little apparent benefit. Eventually, in 1997 he was entered into the NIH sponsored fetal transplant study (subsequent imaging study did indicate that the patient was in the transplant and not the placebo group). It was unclear that this had produced any decrease in his disability. However evaluation 3 years after the transplant did demonstrate a marked increase in the dyskinesias involving head arms and torso. Some improvement in dyskinesias occurred when dopaminergic medications were reduced

Comment: Parkinson's disease is a progressive disorder of motor function, with variable manifestations of tremor, rigidity, akinesia, bradykinesia, and impairment of postural reflexes. Patients vary in the type of major involvement and in the rate of progression. Pharmacological management has rapidly evolved and in the process has provided considerable insights into the nature of basal ganglia function. For the specific patient, therapy must still be individualized. As this case history illustrates the pharmacological effects are time limited. Evaluation of therapy must always record the time of drug intake and the time of examination.

It is important to note that the disease remains progressive, despite the impressive pharmacological achievements. To prevent progression would require arresting or reversing the loss of the nigral cells producing dopamine or of introducing another source of dopamine producing neurons into the basal ganglia as discussed above. The future of fetal transplantation remains uncertain. Surgical procedures particularly deep brain stimulation involving the subthalamic nucleus or the globus pallidus may offer benefit to specific patients.

The following case, 19-2 provides an example of hemichorea.

Case 19-2 : This 88-year-old, right-handed, widowed white female with a past medical history of profound hearing impairment, adult onset diabetes, euthyroid goiter, coronary artery disease, and hypertension was brought by her daughter to Saint Vincent's Hospital because of uncontrollable movements ("twitching") of her left foot and shoulder. The daughter described the insidious onset of involuntary rotary movement in the left foot five days prior to admission, which increased in intensity and progressed to involve the left shoulder. The movements were constantly present, even during sleep. The movement was accompanied by a "shooting" pain on the left side of the body which the patient was not able to further describe. She denied loss of consciousness, dizziness, change in mental status, weakness, sensory impairment, visual changes, aphasia, or dysphagia associated with the movement disorder, but did describe a dull headache greater on the left side than on the right during the last few days prior to admission, not accompanied by nausea or vomiting. There was no history of a past movement disorder. Progression rather than spontaneous resolution of the choreiform movements which had begun to impair the patient's ability to ambulate with her walker prompted her daughter to seek medical attention.

Past history: The patient had been admitted briefly one year previously with confusion. and hyperglycemic state related to diabetes mellitus.

Physical Examination: vital signs were all normal.. Patient was alert and cooperative, though profoundly hard of hearing and exhibited involuntary twisting movements of her left foot and upward jerking movements of her left shoulder.

Neurological examination:

1. *Mental Status:* The patient was oriented x3. Memory and language were grossly intact, questions were answered appropriately, and mental status was consistent with the patient's baseline according to her daughter.
2. *Cranial Nerves:* Intact except: for Left eye blindness (cataracts), and gross impairment of hearing such that shouting was necessary to communicate.
3. *Motor System:*
 - a. Tone and strength in upper and lower extremities were normal except for minimal weakness in the left upper extremity(5-/5) .
 - b. Finger tapping, finger-to-nose and heel-to-shin were grossly intact with only slight left-sided difficulty due to involuntary movements.

- c. There was a persistent hemichorea without flinging motions in the left foot, more marked than the left shoulder. There were rotary, twisting movements at the left ankle and upward and rotary motions at the left shoulder. The movement was exacerbated by motor—tasks but did dissipate with sleep.
- d. Gait was slightly unsteady due to hesitant placement of the left foot. She did quite well with minimal assistance.
- e. Romberg was negative.
4. *Reflexes*: Deep tendon reflexes were symmetrical, and physiologic except for decreased Achilles secondary to diabetes. The right plantar response was flexor, the left ;extensor.
5. *Sensation*: Intact except for symmetrically diminished vibration sense in toes.

Clinical diagnosis: hemichorea

Laboratory data:

1. *Electrolytes creatinine, and CBC* were normal. *Glucose* was elevated to 168; *ESR* - 36 mm/hr. *RPR* non-reactive. *ANA* was 1:80(not significant) .*Urine culture* was positive for group B Streptococcal - infection sensitive to Ampicillin. *EKG and chest X-ray* were unchanged from last admission.
2. *CT scan* on admission revealed bilateral basal ganglia calcification, bifrontal atrophy consistent with age, but no evidence of infarction, hemorrhage, or tumor and revealed no change from previous CT scan of 2 months previously.
3. *MRI scan* 3 days after admission, revealed mild cortical atrophy and a hyperdense area without mass effect or enhancement on gadolinium in the right basal ganglia (particularly the head of caudate and putamen) and external capsule consistent with subacute hemorrhage (Fig.19-7).

Hospital course: The patient was begun on haloperidol 0.5 mg by mouth every morning and advanced to 1 mg., by mouth., t.i.d. with some improvement in the hemichorea, particularly in the upper - extremity. Her hemichorea continued to improve over the next two weeks on haloperidol with only occasional twitching of the left shoulder and diminished but persistent, rotary movement of the left foot, both still exacerbated by motor tasks.

The following case 19-3 provides an example of hemiballismus

Case 19-3: This 79-year-old, right-handed, white housewife had the abrupt onset in the early morning hours, 2 days prior to admission, of almost constant flinging movements of the right arm over which she had no control. At the same time, she noted that her right arm felt numb and heavy. Over the next 2 days, the movements decreased markedly and she regained more control of the arm.

Past history: The patient had been a known diabetic for 21 years, receiving insulin - most recently, lente insulin, 25 units each morning.

Neurological examination:

1. *Mental Status*: intact ,the patient was alert and well oriented and without aphasia.
2. *Cranial Nerves*: All were intact.
3. *Motor System*:
 - a. Minimal weakness was present in the right upper extremity at the elbow, wrist and fingers
 - b. Alternating movements and finger-to-nose testing in the right hand were markedly impaired.
 - c. Gait was intact.
 - d. Occasional involuntary flinging movements occurred at the right shoulder.
4. *Sensory System*: Pain, touch, vibration and position sense were all absent in the right upper extremity to the elbow and decreased in this extremity above the elbow.

Clinical diagnosis: hemiballismus

Laboratory data: Chest and skull X-rays EEG, and cerebrospinal fluid studies were all normal.

Subsequent course: The flinging movements of the right arm subsided spontaneously, shortly after admission. Position sense returned and pain sensation showed a mild improvement. The ataxia on finger-to-nose testing disappeared.

Comment: The loss of pain, touch, vibration and position sense in the right upper extremity at the onset of symptoms in this case, would suggest a lesion involving the ventral posterior lateral nucleus of the thalamus, presumably as a result of occlusion of the penetrating branches of the

posterior cerebral artery. Such a lesion could have damaged the subthalamic nucleus as well. The severe dysmetria in the right upper extremity could well have reflected the severe sensory deficit in the right upper extremity. This would appear to be more likely than postulating a lacunar ataxic hemiplegia, due to involvement of the corona radiata in which the origin of the hemiballistic movements could have been in the adjacent caudate putamen. This however would not explain the severe sensory deficit. Note that the use of antidopaminergic agents will decrease or eliminate hemiballismus or hemichorea; however many patients as in this case resolve spontaneously.

The following case history provides an example of Huntington's disease.

Case 19-4: This 54-year-old right-handed divorced white female was referred for evaluation of a movement disorder. The patient lived alone and it was difficult to obtain much of any history from the patient. So far as she was concerned, she had no neurological problems. She denied any problem with her movements. She did indicate that she had worked for 10 years as a secretary/computer operator but had been fired 10 years ago because "she did not work fast enough". She did indicate that she had experienced problems with memory over the last year. The patient denied that she had never been treated on a psychiatric service. She denied receiving neuroleptics. She had a past history of hypertension but had not been reliable in taking her prescribed medication. The patient's son was aware that changes in emotion, personality, speech, gait and a movement disorder had been present for at least 3 years.

Family history: The patient denied any neurological family history except for a maternal uncle who had the "shakes". By contacting the patient's son age 27 and her mother now age 81 and then obtaining old records we were able to assemble additional information. The patient's father had been hospitalized at age 55 on the psychiatry service of St. Vincent Hospital. A review of that record indicated that for several years he had been showing irritability, had become suspicious and paranoid at work. He gave a history of choreiform movements of 20–30 years duration beginning with twitchings about the shoulders. This had progressed over the several years prior to admission, affecting his gait and the movements of the hands. The examination demonstrated that he was moderately depressed and impatient. As he sat, he had "purposeless" movements of his body particularly of the lower extremities. In walking he had "ballistic" movements. He walked on a broad base. Choreiform movements were noted in the tongue. The diagnosis of the neuropsychiatrist was Huntington's disease. He apparently died of cardiac disease shortly after that hospitalization.

The paternal grandfather had died at age 43 of pneumonia, the paternal grandmother at age 37 of gall bladder disease, neither was known to have Huntington's disease, but information was scanty. The patient's father had two siblings one alive at age 81, the other dead at age 68, both apparently unaffected. The patient's mother had a sister with essential tremor.

The patient had 2 siblings, a brother age 60, a sister age 44; both unaffected according to the patient's mother.

The patient had 4 children ages 34, 32, 30 and 27, and 3 grandchildren ages 13 years, 2 years, and 3 months. The eldest daughter age 34 had been depressed for 5 years and had problems with speech and walking for a number of years.

Neurological examination:

1. *Mental status*: the patient often avoided eye contact. Affect was usually inappropriate with laughter as the response to many questions. The overall mini-mental status score was 27/30. The only deficit related to delayed recall portion of the test (0/3 objects).

2. *Cranial nerves*: the patient had a hyperactive jaw jerk. She had frequent facial grimacing.

3. *Motor system*: the patient had decreased tone at wrists and elbows, but strength was intact.

As she sat she had frequent restless and at times choreiform movements of hands and feet.

Gait was often "bizarre" in terms of occasional sudden movements of a leg as moved down the hall and came to a stop. These same movements occurred as she remained standing. In addition in standing or walking, there were intermittent dystonic postures of either left or right arm.

4. *Reflexes*: Deep tendon stretch reflexes were everywhere hyperactive. Plantar responses were flexor. There was a minimal suggestion of grasp release.

5. *Sensory system*: intact

Clinical diagnosis: Huntington's disease.

Laboratory data:

1. *MRI scans of head* (Fig.19-13): The heads of the caudate nuclei were very atrophic. Cortical sulci were wide consistent with cortical atrophy. The lateral and third ventricles were secondarily dilated.
2. PCR testing for the CAG trinucleotide repeats of the Huntingtin gene.: allele 1=17; allele 2=42.
3. Thyroid studies, sedimentation rate, electrolytes, RPR, and antinuclear antibody were all normal.

Subsequent course: The patient refused any treatment for the movement disorder. The patient's son requested genetic testing and the issues were discussed. He and his siblings finally decided not to have the genetic testing performed. The patient's neurological status according to the son worsened to a moderate degree over the subsequent 3 years as regards speech, unsteadiness of gait, and mood swings but without any additional change in memory. The patient herself always appeared unaccompanied for follow up visits and reported no change in her condition.

Comment: Occasionally patients are encountered where changes in psychological function limit the information that the patient can provide. In other cases denial of illness has a neurological as well as a psychological basis. In this case it was evident that this patient had not only symptoms relevant to the basal ganglia but also changes in cognitive function relevant to the cerebral cortex particularly the frontal areas. In such cases, information must be sought from other sources. In this case, the patient was willing to provide permission to contact those possible sources.

The clinical presentation in this case was clear-cut. In retrospect, many of the neurological features were similar to her father's findings on his admission 30 years previously. When did the patient's disease begin? This was uncertain, but we may presume that serious problems had been present at least 10 years earlier when she had been fired from her long time employment. Did this relate to motor problems, to changes in personality and interpersonal relations or to cognitive changes? Most likely, there were problems in all of these areas. According to her family, symptoms had been present for 2-3 years suggesting onset at age 51 or 52 years.

Case 19-5 provides an example of a patient with Huntington's disease followed over a longer period of time.

This 32 year old right-handed married white male spray painter at a computer factory, was referred for evaluation of a possible hereditary movement disorder. The patient was unclear about the reasons for his evaluation and much of the history was provided by his wife. She reported that the patient had undergone a personality change in the last several months. He had noticeable mood swings and on one occasion he reported people outside the window when no one actually had been there. He had some problems with remembering incidental matters, but no major problems and his job performance had remained intact. He was described as always having been "fidgety".

Past medical history - Mild hypertension for three years.

Family history - The patient's initial history indicated that the family had "Parkinson's" disease and his father had died in his 40's at the state hospital after a 10-15 year illness. The patient indicated that he was a child at the time and his mother never really told him much about the father or let him visit the father in the hospital but he did recall that perhaps his father had some excessive movements of the hands and face. The records were subsequently obtained and these indicated the father had been admitted to Worcester State Hospital in 1968 at age 37. At that time, he had already had three previous hospitalizations for "nervous breakdowns". At the time of his final admission, he had developed hallucinations, seeing people in his room. He had threatened his wife and other relatives. He had difficulty sleeping and he had also developed a problem with his legs "they are jumping". The father's examination had demonstrated a mumbled speech with repetition of the same phrases. His responses would often be tangential and then incoherent with impairment of memory and judgment. His mood was depressed. He was noted to have involuntary movements of the fingers and occasional facial grimacing. The deep tendon reflexes were hyperactive and the plantar responses were extensor. His gait was ataxic. The subsequent course indicated increasing ataxia, choreiform movements and rigidity with increasing weakness, difficulty swallowing and the final development of bronchial pneumonia with death at age 42. The diagnosis of Huntington's disease was confirmed at autopsy.

The paternal grandfather had expired at age 67 with a diagnosis of Huntington's disease, manifested by "nervous breakdowns, inability to sleep and movement disorder". The father's three siblings apparently did not manifest the disease. The patient had two siblings, brother age 28, a sister age 35, all without known disease. He had two children ages 9 and 5.

Neurological examination

1. *Mental Status* - The patient was anxious, often appeared blunted in emotional expression or in answering questions. He avoided eye contact. He was oriented for time, place and person. He was able to name objects and colors. His delayed recall was 2/5 without assistance and 4/5 with assistance.
2. *Cranial Nerves II-XII* were intact, except for the occurrence of occasional, sudden darting movements of the eyes to either left or right. In addition, occasional facial grimacing was noted occurring in a rather irregular manner.
3. *Motor System* : Strength and gait were intact . There were occasional, sudden, irregular, lateral, tremulous movements of the fingers of a choreiform-type.
4. *Reflexes* : Deep tendon reflexes including the jaw jerk were everywhere hyperactive. Plantar responses were bilaterally extensor (bilateral Babinski signs).
5. *Sensory system* : intact

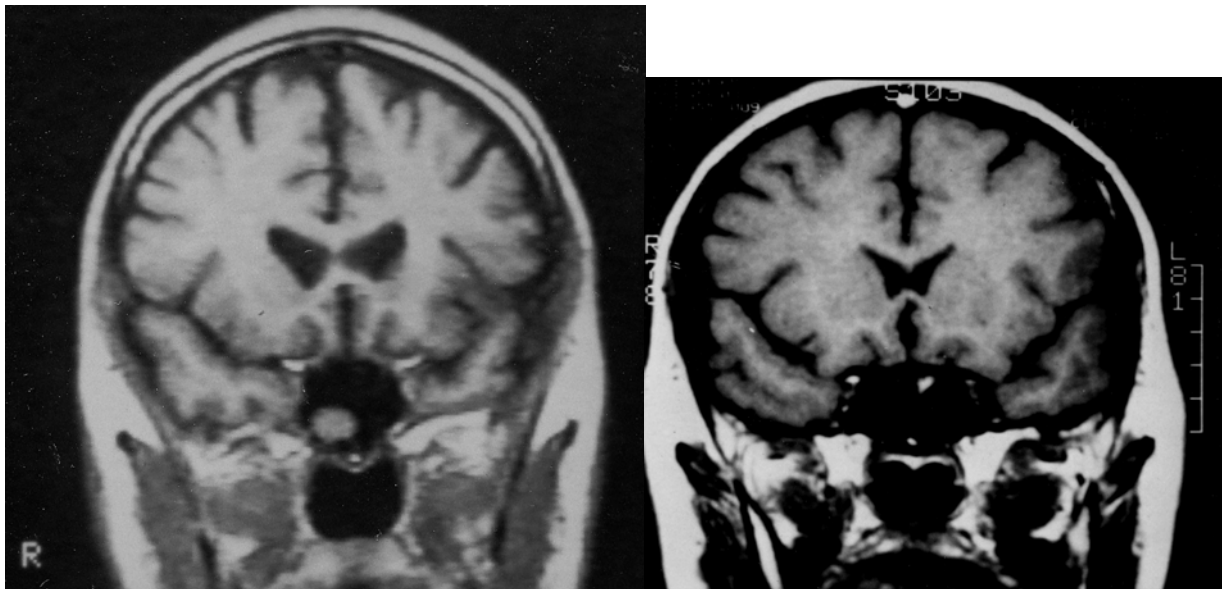
Clinical diagnosis: Huntington's disease

Laboratory Data :

1. All blood chemistries, including glucose; BUN, calcium, electrolytes, liver function studies, ceruloplasmin level, thyroid studies and serological test for syphilis were within normal limits. Ceruloplasmin levels are low in Wilson's disease but normal in Huntington's disease.
2. *Electroencephalogram* was normal with a dominant awake background activity of 10 Hz alpha rhythm.
3. *CT scan of the head* demonstrated enlargement of the ventricles with particular atrophy of the caudate. In addition the sulci were prominent for the age, suggesting some degree of cortical atrophy. The study was considered consistent with the clinical diagnosis of Huntington's disease.
4. The *MRI scan* (fig 19-11A) demonstrated mild enlargement of the ventricles and deepening of the cortical sulci, as well as a very significant atrophy of the head of the caudate nucleus. The MRI from this patient is compared to a similar section from a patient without signs of neurological disease (Figure 19-B)..

Figure 19-11A ;Case 19-5. Huntington's Disease

Figure 19-11B. Normal, age matched



Subsequent course :The patient subsequently developed increased paranoid ideation, increasing dependency with regard to his wife. He was treated with Haloperidol (a neuroleptic, tranquilizer) with considerable improvement with regard to personality. When evaluated, 3 years after onset of disease, it was evident that in the interim, the patient's personality problems had decreased. Attacks of anger and paranoid features had subsided. Mood swings were less. Memory problems, however, were worse and choreiform movements were worse. Dysarthria was now present. The patient had been divorced in the interim and he was on social security disability and no longer working. The examination now showed an exacerbation of many of those features noted at the time of his initial evaluation. He had occasional, sporadic movements of head or eyes of a

choreiform nature. He had frequent choreiform movements involving the fingers as he was sitting, also a similar type of movement appeared to involve the abdominal musculature. He had a moderate degree of dysarthria. He could walk a tandem gait but as he did so, the left arm came up in an somewhat flexed position. When last seen 4 years after onset of disease, he had more dysarthria and his speech was more difficult to interpret. There had been some increase in degree of rigidity but this had decreased when the dose of haloperidol had been decreased. The decrease in this medication, however, then resulted in a greater prominence of the choreiform movements. He could still handle a deck of cards, although he was dropping objects more often than previously. His neurological examination showed a significant degree of dysarthria, a greater degree of facial akinesia, more frequent choreiform movements of hands and face. He had difficulty in mimicking facial expression. As before, all of his deep tendon reflexes were hyperactive and the plantar responses were extensor. The patient walked in a flexed position and tended to turn en bloc. He had a mild degree of cogwheel rigidity at wrist and elbows. His memory remained remarkably good for delayed recall. Final telephone follow-up with his primary physician (approximately 7 years after apparent clinical onset of disease) indicated that the patient was no longer able to drive. He had continued weight loss. He had a marked dysarthria so that his speech was barely intelligible. Choreiform movements had increased. His gait was ataxic, but he could still walk without stumbling. He was relatively stable from a psychiatric standpoint. He was now living with his mother and brother.

Comment: This patient and his family demonstrate the relatively typical course of most patients with Huntington's disease. Patients and families do vary as to whether it is the psychiatric features or the movement disorder features that first bring the patient to medical attention. In this case, the psychiatric features, that is, the change in personality and the increasing paranoid ideation were the first features noted. Subsequently, involvement of the motor system became the most prominent feature. As in the previous case, the patient was unclear as to why he had come for neurological evaluation. Was this a neurological or a psychological denial of illness? Most likely both factors were operational. It was of considerable interest that this patient when first seen, although he was aware of some neurological problem that had occurred in the family, was unclear as to the specific diagnosis. It was also evident that almost no genetic counseling had been done in a disorder that was very clearly an autosomal dominant disorder. The significant family impact, social and economic impact of the disease are clearly evident in this patient. The implications of presymptomatic detection are discussed by Meisser et al (1988), and Klawans (1972).

The following Case 19-6 illustrates the clinical problem of hepatolenticular degeneration in a 21 year old female with a brother who had died at age 16 with hepatic disease, a Kayser Fleischer ring and choreoathetosis. The patient had serum elevation of free copper and a decrease in protein bound copper. She was successfully treated with penicillamine.

Case 19-6 (Patient of Doctor Huntington Porter) :This 21-year-old, single, white female shoe worker in January 1954 had the onset of a "shaking", or trembling of the fingers and hands which progressed to involve both arms and legs. The degree of involvement increased sufficiently to force her to give up her work. Nine months after onset of symptoms, she began to note increasing difficulty with balance and coordination and a slurring of speech. She had also noted increasing weakness and difficulty in doing repetitive tasks. One year after onset, the patient noted blurring of vision, occasional diplopia, and periods of "staring". She also had experienced increasing urgency and occasional urinary incontinence.

Family history: A brother of the patient had died in 1952, at age 16, of a disease with manifestations similar to this patient's. Evaluation of the sibling 2 years before his death by Drs. John Sullivan, Raymond Adams and D. Denny-Brown, had indicated the presence of choreoathetosis with lapses in posture of the hands. In addition, a brownish green ring at the corneal -

scleral junction was noted. Liver disease was present in this sibling and possibly other members of the family.

Neurological examination:

1. Mental status:

- a. The patient was anxious, at times crying, at other times, euphoric.
- b. Digit span was limited to 6 forward, 3 in reverse.
- c. Serial 7 subtractions were poorly performed.

2. Cranial Nerves:

- a. A brown rim was present at the limbus of the cornea, more evidence inferiorly and superiorly.
- b. Extraocular movements were impaired by involuntary jerk movements, The patient was unable to track a moving finger.
- c. Facial expression was mask-like.
- d. Speech was dysarthric and of a nasal quality with slurring and slowness of articulation.

3. Motor System:

- a. No actual weakness was present. However, this patient had difficulty maintaining the limbs in a fixed posture.
- b. There was a rigidity to passive movement of the limbs.
- c. A coarse arrhythmic tremor was present which was most marked proximally and more marked on sustained posture and on movement than at rest.
- d. Alternating movements were poorly performed.
- e. Gait was ataxic. Romberg test was negative.

4. Reflexes: Deep tendon stretch reflexes were hyperactive but plantar responses were flexor

5. Sensation: Intact

Clinical diagnosis: Wilson's disease: hepatolenticular degeneration.

Laboratory data:

- 1. Liver function tests were normal.
- 2. *Glucose tolerance test* was normal, but glycosuria occurred.
- 3. *Total plasma copper* 52 ug/100 ml. (normal range in a young adult is 65 to 150 ug/100 ml).
Direct reacting copper (unbound to ceruloplasmin) 31 ug/100 ml (normal 10 ug/100 ml).
Indirect copper (ceruloplasmin bound) 21 ug/100 ml, normal 105 ug/ ml).

Subsequent course: The patient did relatively well following the use of the chelating agents, BAL and calcium versenate and the institution of a copper free diet. A liver biopsy performed at the time of a cesarean section 18 months after beginning treatment was compatible with perihepatitis with a question of post-necrotic cirrhosis.

Re-evaluation 6 years after onset revealed, in addition to the earlier findings, the presence of "continual spontaneous involuntary movements of the limbs; at the feet, characterized by alternating flexion and extension at the ankle and a waving of the toes". A broad amplitude coarse tremor was noted when the patient was asked to abduct arms, flex elbows, and hold hands just before her nose (wing beating position). A side-to-side tremor of the head was also present. The gait was slightly wide-based and associated with continual dystonic movements of the hands and arms. Treatment with d-penicillamine (which had just become available) was begun at that time.

Urine copper excretion increased from 700 ug per 24 hours to 3240 ug per 24 hours. Normal 24-hour urinary copper in the adult is less than 40 ug. Neurological symptoms soon demonstrated improvement from the previously noted status. The patient was now able to do her house work and take care of her children.

Follow-up 2 years later, indicated significant improvement as regards the findings noted in 1960; dystonic facies and dysarthria was less marked. No tremor was present in the left hand; that in the right hand was evident only when under tension. Dystonic posturing of the hands was present only to a minimal degree. At last report 4 years later, and 12 years after onset of the disease, the patient continued to do well. She had remarried and was expecting another child.

Comment:

This patient presents a typical case of Wilson's disease with onset in the young adult years and with a definite familial background. The copper levels were consistent with the diagnosis (an increased unbound fraction and a decreased bound fraction). At the time that this patient was seen in the mid 1950's and early 1960's, ceruloplasmin levels were not available. Early establishment of a specific diagnosis in this case allowed for specific therapy with improvement of neurological symptoms and the prevention of progression of hepatic disease. With a specific diagnosis established in the patient, periodic blood tests were performed on her offspring to determine whether they also had inherited this genetic disease. (The child born 18 months after onset of the disease had not the disorder.)

An acquired form of non-Wilsonian hepatic and cerebral degeneration occurs in patients who have had multiple episodes of hepatic coma. Degenerative changes occur in the astrocytes and neurons of the basal ganglia. This disorder which was first described by Adams and Victor is discussed in greater detail above.

CHAPTER 20. MOTOR SYSTEMS III: CEREBELLUM

The following case provides an example of a child with a medulloblastoma.

Case 20-1: This 27-month old white female was referred for evaluation of ataxia. The mother had noted that the child had been unsteady in gait, with poor balance, falling frequently since the age of 13 months, when she began to walk. Three months prior to admission, in relation to a viral infection manifested by fever and diarrhea, the patient developed increasing anorexia and lethargy. One-month prior to admission, vomiting increased, and the patient also became more irritable. Perinatal history had been normal, and head circumference had remained normal.

Neurologic examination:

1. *Mental Status:* The child was irritable but cooperative.
2. *Cranial Nerves:* The fundi could not be visualized. Bobbing of the head was present in the sitting position.
3. *Motor System:* A significant ataxia of the trunk was present when sitting or standing. Gait was broad-based and ataxic, requiring assistance. No ataxia or tremor of the extremities was present. Strength and tone were normal.
4. *Reflexes:* Deep tendon reflexes were symmetric and plantar responses were flexor.
5. *Sensory System:* All modalities were intact.

Clinical diagnosis: Probable midline cerebellar tumor, most likely based on age a medulloblastoma

Laboratory data:

1. *Left brachial arteriogram* indicated an avascular area in the posterior fossa. The superior cerebellar artery was elevated. The inferior cerebellar arteries were depressed.
2. *Air-contrast ventriculogram* demonstrated enlargement of the lateral and third ventricles. The cerebral aqueduct was displaced forward to a marked degree. The fourth ventricle was deformed by a mass overlying the posterior wall (essentially located in the nodulus).

Hospital Course: Doctor Peter Carney performed a suboccipital craniotomy. The dura was bulging. The cerebellar tonsils were herniated to a minor degree. On gentle retraction of the inferior posterior vermis, a pinkish gray tumor, originating from a higher point in the fourth ventricle, was visualized at the obex. Limited biopsies of this tumor were taken, revealing a medulloblastoma. Samples of cerebrospinal fluid obtained at surgery revealed the presence of many malignant cells. A permanent shunt from the lateral ventricle to the jugular vein was not installed because of the possibility of spread of tumor cells into systemic circulation. Instead, a catheter was connected from the lateral ventricle to a small reservoir inserted under the skin of the scalp to allow daily drainage. Radiation therapy to the entire central nervous axis was begun one week after surgery. By the time of hospital discharge two weeks after the operation, the patient was able to walk unassisted, with only a moderate degree of ataxia. Three months after the operation, the patient was readmitted because of recurrent irritability and vomiting. A mild degree of papilledema was present. Horizontal nystagmus was present on lateral gaze bilaterally. A wide-base ataxic gait was still present. Various antineoplastic agents were employed (methotrexate into the cerebrospinal fluid and vincristine intravenously) without significant improvement. One month later, respirations became slow, deep, and irregular and death occurred. The findings at autopsy are demonstrated in Fig. 20-4.

In the following case a metastatic tumor in the midline cerebellum produced vertigo, ataxia of gait and headaches.

Case 20-2: This 67 year old white female 6 weeks prior to admission developed intermittent vertigo. Two weeks prior to admission she developed an ataxia of gait. Two days later headaches and true vertigo developed, ataxia increased and vomiting occurred. On the day of admission severe vertigo, headache and nausea and vomiting resulted in her visit to the emergency room

Past history: The patient had a lumpectomy 6 years prior to admission for carcinoma of the left breast. She had undergone a radical mastectomy followed by radiation therapy 3 years prior to admission for a recurrence of malignancy. Histologic examination of the excised tissue indicated a very poorly differentiated (high grade of malignancy) infiltrating ductal tumor which was negative for estrogen and progesterone receptors. On both occasions, the patient refused chemotherapy. The patient had multiple other medical problems including non insulin dependent diabetes mellitus, coronary artery disease, mild hypertension, and prior hip replacement surgery.

Neurological examination (in the emergency room)

1. **Mental Status:** Intact
2. **Cranial Nerves:** Intact except for an absence of venous pulsations on funduscopic examination suggesting a mild increase in intracranial pressure without frank papilledema.
3. **Motor System:** The patient had difficulty standing tending to fall to the right. She was unable to walk because of severe ataxia. There was no limb dysmetria.
4. **Reflexes:** Deep tendon stretch reflexes were symmetrical. The right plantar response was equivocal.
5. **Sensory system:** Intact

Clinical diagnosis: Midline cerebellar tumor metastatic from breast.

Laboratory data :

1. **CT scan of brain:** A large (3-4 cm) enhancing tumor was present involving the midline vermis and right paramedian cerebellum and compressing the fourth ventricle.

2. **MRI of brain** (3 days after admission): An enhancing midline mass involved the cerebellar vermis extended into the right cerebellar hemisphere, and produced mass effect upon 4th ventricle (Fig. 20-5).

3. **CT scan of abdomen** demonstrated two solitary possible metastatic lesions in the liver.

Subsequent course: The patient was immediately placed on dexamethasone with significant improvement. Within 12 hours the examination demonstrated only a mild ataxia tandem gait on turns and bilateral extensor plantar responses. The patient strongly insisted on removal of the solitary central nervous system metastases. Histological examination of the tumor resected by Dr. Gerald McGullicuddy demonstrated poorly differentiated adenocarcinoma with extensive necrosis similar to the tumor which previously had been removed from the breast. Following surgery she received 3000cGy(rads) whole brain radiation and was begun on the antitumor agent tamoxifen. She continued to manifest some unsteadiness on gait but had no difficulty in finger to nose or heel to shin tests. Three months after her admission, a repeat CT scan of the abdomen and pelvis demonstrated diffuse hepatic metastases with mesenteric and retroperitoneal lymphadenopathy. She expired at home, four

months after surgery before she was to start additional treatment with the antineoplastic combination of Cytosan, methotrexate and 5-fluorouracil .

Comment : This patient had a highly malignant poorly differentiated adenocarcinoma of the breast and was clearly at risk for the development of distant metastases ,a risk that was likely increased by her unwillingness to receive antitumor medication. Six years after the lumpectomy she presented with vertigo, ataxia headache and nausea and vomiting, without limb dysmetria. These symptoms suggested involvement of those areas of cerebellum related to the vestibular system and the axis of the body: the floccular nodular area and vermis. Certainly ,the best treatment of a solitary metastatic brain tumor where systemic metastases are not present is the combination of total resection of the brain lesion followed by radiotherapy. However at the time of surgery ,this patient already had evidence of two probable metastatic lesions in the liver. Except for the strong insistence of the patient that the tumor in brain be removed ,an alternate course of radiotherapy, dexamethasone and chemotherapy might have been pursued. Never the less the patient had several additional months of life during which she was able to travel to visit various relatives for a last time. Consistent with the highly malignant character of the tumor, this patient succumbed to the non neurologic effects of her disease

The following case history 20-3 illustrates the problem of alcoholic cerebellar degeneration.

Case History 20-3: This 64-year-old, white male was admitted with a chief complaint of a slowly progressive incoordination of gait present for 8 years. The patient and others had noted that his gait was staggering. The patient denied weakness, numbness, diplopia, vertigo, or memory difficulty. The patient admitted to the consumption of one half pint (250cc) of brandy every 4 nights since symptoms had developed. He indicated that he use to drink more in his younger days, at least 6 to 8 beers in addition to brandy or other alcoholic beverages every night.

There was no history of pes cavus or neurological disease.

General physical examination ; Blood pressure 140/80. Liver was enlarged with the inferior edge extending 2 finger breadths beyond the costal margin. Face was red with dilation of vessels.

Neurological examination:

1. *Mental status:* The patient was slightly disoriented for time. He gave the date as September 31. The date was actually October 19. Delayed recall was 0-out-of-5 objects in 5 minutes. He was unable to give the date of his birth, but he knew his phone number. Digit span was 7 forward, 4 in reverse. Calculations: The patient was unable to subtract 7 from 100 or 3 from 30; he could not add 14 and 13, although he had a fourth grade education.

2. *Cranial nerves:* All were intact. No nystagmus was present.

3. *Motor system:* Strength was intact. Gait was broad-based with an ataxia of trunk. The patient was unable to walk a tandem gait. His ataxia was accentuated by rapid walking. Small lateral nodding movements of the head were noted. He was relatively stable when sitting. There was a minimal tremor at rest. In addition, there was, to minor degree, a resistance to passive motion at the wrists and elbows with a suggestion of a cogwheel component. There was a minor tremor on finger-to-nose testing and a minor impairment of alternating hand movements.

There was, however, a very significant heel-to-shin ataxia which was out of proportion to any tremor or ataxia involving the upper extremities.

4. *Reflexes:* Deep tendon reflexes were physiological and symmetrical (2-3+). Plantar responses were flexor bilaterally.

5. *Sensory system:* Position, pain and touch were intact. There was a moderate decrease in vibratory sensation at the toes and ankles.

Clinical diagnosis: 1. Alcoholic cerebellar degeneration. 2. Mild dementia possible residuals of Wernicke's-Korsakoff syndrome.

Laboratory data: Complete blood count, albumin and total protein, sedimentation rate, cerebrospinal fluid, and skull and chest X-rays were normal.

Subsequent course: The patient received multiple B vitamins and was advised to discontinue any intake of alcohol. Neurological re-evaluation over the next 6 years indicated that no essential progression had occurred.

Comment: The major findings of the broad-based, staggering gait with truncal ataxia and heel-to-shin ataxia may be related to the anterior lobe of the cerebellum. In view of the absence of progression after the discontinuation of alcohol, a toxic or nutritional factor may be postulated (The reliability of the history obtained, in terms of the specific amount of alcohol intake is always open to question particularly in a patient

with significant problems in memory. The amount stated by the patient is usually assume to be the minimum amount.). The minor extrapyramidal findings of cogwheel rigidity may have represented unrelated disease. The lack of progression would be evidence against the diagnosis of a cerebellar degeneration of other etiology (see below). The minor degree of dementia may have related to previous nutritional problems with minor Wernicke-Korsakoff's syndrome or may have reflected a minor unrelated dementia or may have related to long standing retardation. At the present time, the diagnosis may be confirmed by CT scan or by MRI (midline sagittal section) (as in Fig. 20-7 or 20-8). As a result, evidence of cerebellar atrophy is now found in many patients presenting with other aspects of chronic alcoholism or other nutritional disease who do not necessarily present with initial symptoms of ataxia.

In the following case, a similar cerebellar gait disorder and heel to shin ataxia occurred o a genetic basis.

Case 20-4: A 45-year-old single white male carpenter presented with a 4 year history of progressive unsteadiness in walking, present during the daytime as well as at night. He had, during this period, noted minimal loss of coordinated movements in his hands, but felt that his greatest deficit was unsteadiness. The patient had noted no actual weakness but reported some numbness at the toes. He had also noted some minor difficulty in swallowing.

The patient lived in a small town in Virginia. Family historical information was incomplete His mother and father were second cousins. Several aunts and uncles had "trouble with their legs" in later life, resulting in a difficulty in walking. The patient admitted to a minimal intake of alcohol in the past. He had recently been under the care of a naturopath and had experienced a 7-pound weight loss.

Neurologic examination:

1. *Mental status:* Intact and consistent with his educational level.
2. *Cranial nerves:* Intact except for minimal dysarthria. Horizontal nystagmus was present on lateral gaze, vertical nystagmus on upward gaze.
3. *Motor system:* Strength was intact. The patient walked on a broad base with an ataxia of trunk, as though intoxicated, reeling from side to side, with marked unsteadiness on turns. He was unable to walk a tandem gait with eyes open. The patient was able to sit without significant ataxia of the trunk. A mild intention tremor was present, and there was minimal disorganization of alternating movements. In contrast a marked ataxia and tremor were evident on heel-to-shin test.
4. *Reflexes:* Deep tendon reflexes were intact, except for a relative decrease in ankle jerks compared to knee jerks. Plantar responses were flexor.
5. *Sensory system:* Intact, except for a minimal decrease in vibration sensation at the toes.

Clinical diagnosis: Hereditary cerebellar degeneration involving predominantly anterior lobe

Laboratory Data: Pneumoencephalogram performed at the University of Virginia Hospital (Doctor Stewart) confirmed the significant atrophy of cerebellum. Cerebrospinal fluid and other laboratory data were normal.

Comment: This patient had onset of ataxia at age 41 and was seen relatively early in his disease course. The most prominent features included the ataxia of gait and the heel to shin dysmetria. The patient also had a minor dysarthria, nystagmus and a mild asymptomatic peripheral neuropathy (decreased Achilles reflexes and decreased vibration at toes). There was a familial background but the information was incomplete. The subject of genetic cerebellar degeneration will be considered in a later section. Using older terminology, this patient would have been classified as olivopontocerebellar atrophy. Using more modern terminology, the patient might be included within the category of autosomal dominant cerebellar ataxia type I, had more genetic information regarding the family been available by history and or actual examination.

The following case history illustrates a focal lesion of the lateral hemisphere

Case 20-5 : This 36-year-old white male attorney was referred with a chief complaint of headaches and vomiting. The patient had frontal and biparietal headaches for approximately one month precipitated by coughing, sneezing, or bending. On at least one occasion, the patient had been awakened by the headache. The patient had nausea and vomiting independent of the headaches, at times, occurring suddenly without preceding nausea. For several weeks prior to admission, the patient had been unsteady on his feet, with a tendency to fall to the right, and had noted intermittent clumsiness of his right hand. For several days prior to admission, the

patient had double vision and had to keep one eye closed. During the week prior to admission, he had been excessively drowsy and constantly tired. The headaches had increased in frequency and were now occurring 3 to 4 times per day.

Neurologic examination:

1. Mental status: Intact.

2. *Cranial nerves:*

- a. On funduscopic examination there was evidence of bilateral papilledema.
- b. A bilateral paralysis of the sixth nerve was present.
- c. Horizontal nystagmus was present on right lateral gaze.

3. *Motor system:*

- a. Strength was everywhere intact.
- b. The patient's gait was wide-based. In walking, the patient tended to veer to the right. The patient was unable to stand independently on his right leg.
- c. There was a significant intention tremor of the right upper extremity on finger-to-nose test and of the right lower extremity on heel-to-shin test. Alternating movements of the right hand were disorganized.

4. *Reflexes:* Deep tendon stretch reflexes were normal and plantar responses were flexor.

5. *Sensory system:* All modalities were intact.

Clinical diagnosis: Tumor of the right cerebellar hemisphere with obstruction of ventricular system producing increased intracranial pressure and resulting in papilledema and bilateral cranial nerve VI palsy.

Laboratory Data:

1. Complete blood count and skull x-rays were normal.
2. *Right brachial arteriogram* revealed, in the late arterial phase, a blush in the right inferior and posterior cerebellar hemisphere consistent with a hemangioblastoma.
3. *Pantopaque ventriculogram* revealed a dilated third ventricle and a dilated aqueduct with obstruction to outflow from the fourth ventricle. The fourth ventricle and to a lesser degree, the aqueduct, were shifted to the left. These findings were consistent with a right cerebellar mass displacing and obstructing the fourth ventricle.

Hospital Course: The patient was placed on high dosage of dexamethasone to relieve increased intracranial pressure. Later that day a suboccipital craniectomy was performed by Doctor Samuel Brendler. When the dura was opened, bulging of the lower portion of the right cerebellar hemisphere was noted, with widening of the cerebellar folia. The widest area of the folia was tapped with a needle and a yellow cystic fluid was removed. A transcortical incision was then made, revealing a large cyst with a small strawberry-shaped hemangioma located within. The stalk of this tumor was ligated, and the hemangioma separated from the cystic capsule. Histologic examination of the tumor revealed a hemangioblastoma.

Postoperatively, the patient did well. His headache and diplopia disappeared. There was then improvement in the patient's tremor and ataxia, although there was a slight slowness on finger-to-nose testing on the right. A minor side-to-side tremor was present on right heel-to-shin testing. There was a tendency to veer to the right in walking, but tandem gait indicated only a minor unsteadiness. Evaluation six months after surgery, indicated only a minimal unsteadiness on tandem walking. Evaluation 9 months after surgery later indicated no significant neurologic findings. Re-evaluation three and one-half years after surgery, again indicated a completely intact neurologic status.

Comment: The headaches experienced by the patient, with pain occurring on coughing, sneezing, or mechanical changes, suggested a space-occupying lesion near the ventricular system or meninges. The tumor had produced a block of the ventricular system relatively early in its course, leading to an increase in intracranial pressure, with headache, vomiting and papilledema. The bilateral sixth-cranial nerve weakness was of moderate degree, and

its occurrence would not be unusual in a situation where intracranial pressure had rapidly increased.

The cerebellar symptoms experienced by the patient were lateralized in the sense that the patient was falling to the right side and had noted clumsiness of his right hand. Lateralized cerebellar disease was confirmed by the examination findings of intention tremor of the right arm and leg and disorganization of alternating movements on the right side.

In this case, the hemangioblastoma was in the lateral cerebellar hemisphere. In other cases of hemangioblastoma, the lesion is much more midline in location, and the symptoms are those of a midline cerebellar tumor. Thus, the patient may complain of an ataxia of gait and truncal ataxia and not display clearly lateralized symptoms involving the appendages, such as intention tremor and/or ataxia on heel-to-shin testing. The nodule of tumor often exists within a non-neoplastic cystic cavity. It is, therefore, possible to remove the tumor without sacrificing a large amount of the cerebellum. In some cases, both the mural nodule and the cyst are removed. In almost all cases a complete cure is obtained; recurrences are unlikely and the patients usually have a relatively complete resolution of symptoms and no residual disability.

In some cases, hemangioblastomas of the cerebellum are associated with angiomatous malformations of the retina (Landau-von-Hippel's disease). In some cases, there is an association with a secondary increase in red blood cell production (polycythemia). In rare cases, there is an association with tumors of the kidney. Other neoplasms may also involve the cerebellar hemispheres: cystic astrocytomas, metastatic tumors, and posterior fossa meningiomas. Meningiomas of the angioblastic type may be difficult to distinguish from hemangioblastomas.

At the present time, the diagnosis of these tumors may be readily made by means of MRI and CT scan (Fig. 20-11). Ventriculograms are no longer required. Arteriograms may still be of value in defining the vascularity and blood supply of the tumor.

The following case history presents a typical example of posterior inferior cerebellar artery infarct, the territory most frequently affected selectively.

Case 20-6: This 64-year-old right-handed married white male postmaster, on the morning prior to admission, awoke at 3:00 a.m. with severe posterior headache and severe vertigo, which was exacerbated by any head movement. Nausea, projectile vomiting and slurred speech soon developed. Shortly afterwards, he noted left facial paresthesias, clumsiness of the left upper extremity, and diplopia. He was admitted to his local hospital with a diagnosis of labyrinthine vertigo and then transferred to the neurology unit at Saint Vincent Hospital when symptoms began to evolve.

Two weeks previously, the patient had been seen for a transient episode of difficulty controlling the right arm, a hissing sensation, and impairment of speech.

Past history: The patient had evidence of significant vascular disease. He had hypertension and had undergone coronary artery bypass surgery. Beginning six years previously he had experienced episodes of transient weakness and numbness of the right arm with transient aphasia. He had normal aortic arch and carotid angiographic studies but EEG had demonstrated focal left frontal/temporal slow wave activity. He had been placed on long term anticoagulation. He had experienced migraine headaches without aura for many years.

Neurologic examination:

1. *Mental status:* Intact.
2. *Cranial nerves:* Conjugate lateral gaze to the left was impaired.
3. *Motor system:* Strength was intact. Significant lateralized cerebellar findings were present with marked dysmetria of left upper extremity on finger-to-nose testing and impairment of alternating hand movements. In attempting to stand, the patient was markedly ataxic.

4. *Reflexes*: Deep tendon stretch reflexes were decreased in both lower extremities. Plantar response was extensor on the right and flexor on the left.
5. *Sensory system*: Intact
- Clinical diagnosis**: Left cerebellar hemisphere infarct or hemorrhage with possible minor involvement of brainstem secondary to mass effect.

Laboratory data:

1. Duplex scans of carotids and vertebrals were normal.
2. *Transcranial Doppler studies* indicated normal flow velocities in the vertebral, basilar, anterior and middle cerebral arteries.
3. *Magnetic-resonance angiography* demonstrated occlusion of the left vertebral artery.
4. *CT scan* demonstrated a large left cerebellar infarct pressing the fourth ventricle to the right.
5. *MRI* (2 months after onset of symptoms): Infarction of the total cerebellar territory of the left posterior inferior cerebellar artery with no actual infarct of the brain stem (Fig. 20-12).

Subsequent course: The patient was somewhat vague with some difficulty in memory during the subsequent 8-day hospital course and remained ataxic. He was then transferred to the Fairlawn Rehabilitation Hospital where, over the next three weeks, he had a significant improvement. When re-evaluated two months after onset of symptoms, he was able to walk well with the use of a cane. A minor intention tremor was present on the left finger-to-nose test. An MRI study was obtained at this point, with results indicated above (because new symptoms suggested possible involvement of upper cervical nerve roots and spinal accessory nerve). Additional improvement was evident on evaluation three months after onset of symptoms. Evaluation 6 months after onset of symptoms demonstrated only a slight slowness of alternating movements of the left hand.

Comment: The acute onset of headache, vertigo, vomiting, ataxia of gait, and dysmetria of the left arm suggested an acute cerebrovascular problem involving the posterior circulation and the posterior fossa. (The syndrome of acute headache, vertigo, ataxia, nausea and vomiting is also seen in cases of acute cerebellar hemorrhage.) Numbness on the left side of the face and diplopia suggested, as well, possible brainstem involvement. The initial diagnosis at the local hospital of acute vestibular disturbance did not explain the headache, the diplopia or the lateralized findings. The presence of the left arm dysmetria suggested lateral hemispheric involvement rather than limited midline involvement.

In the era before CT scan and MRI, the distinction between acute cerebellar hemorrhage and acute cerebellar infarct was often difficult to make. Either lesion could produce block or distortion of the ventricular system and secondary hydrocephalus. Either lesion could be associated with the development of brainstem symptoms. The cerebellar infarct, often in the distribution of the posterior inferior cerebellar artery or the anterior inferior cerebellar artery, could also involve the medullary or pontine territories of these vessels. In addition, either type of lesion could cause significant edema with secondary distortion of the brainstem. Hemorrhage could also extend into the cerebellar peduncle and brainstem.

If significant clinical hydrocephalus or brainstem compromise develops, either type of lesion may require neurosurgical decompression or a shunt procedure.

A final note should be made regarding the considerable ability of the human nervous system to recover from extensive cerebellar lesions. Considerable recovery is possible because the cerebellum does not have a direct line role in the control of motor activity but instead, acts as a modulator of the motor control and motor planning circuits.

The following case history provides an example of a cerebellar hemorrhage secondary to an arteriovenous malformation.

Case 20-7: This 57-year-old right-handed married white female had the sudden onset of a severe left-sided pounding headache one afternoon. There was some stuffiness of the nose and tearing of the left eye. She had had a similar, but less severe, headache 20 years previously when taking birth-control pills. No headaches had occurred in the interim. As the current headache began to decrease, she noted that hearing in the left ear had decreased to a minor degree, and an echo sensation was present in the left ear. She also had the sensation that the environment was off balance, particularly if she was in a moving automobile. She subsequently reported a sense of unsteadiness. There was some sense of nausea when the symptoms first occurred. A vague blurring of vision was also present. She had a vague diplopia at the onset of symptoms but this then disappeared.

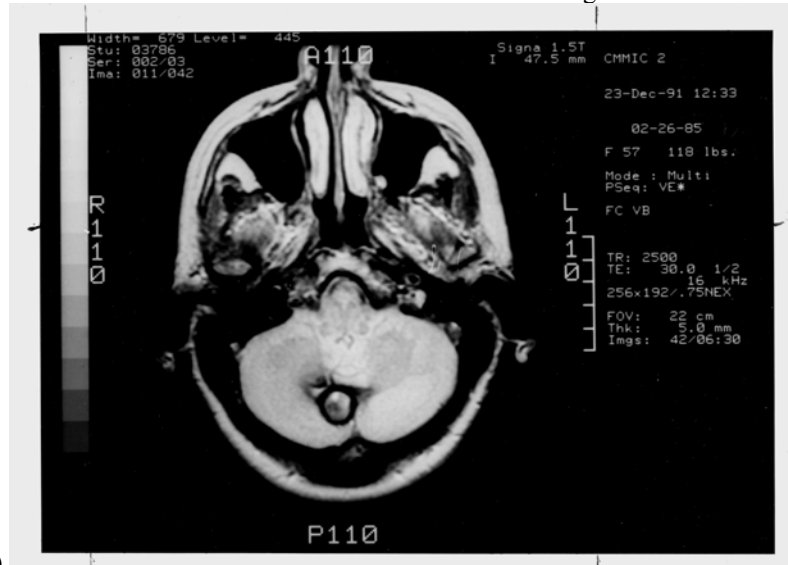
General physical examination: There were multiple pinpoint cavernous angiomas over the arms.

Neurologic examination: Entirely within normal limits.

Clinical diagnosis :Diagnosis unclear: possible migraine headache, or brain stem cerebrovascular event.

Laboratory data: 1. *CT scan of head* indicated hemorrhage in the right paramedian posterior cerebellum.

2. *MRI* showed a rim of hemosiderin stain around the residual hemorrhage in the cerebellar vermis



3. (Figure 20-14).

Subsequent course: The patient had no additional acute episodes. Because two episodes had occurred, she was referred for neurosurgical evaluation. A cavernous hemangioma of the right cerebellum was removed by Doctor Bernard Stone. Post-operatively, she had some right-sided clumsiness and ataxia, which gradually improved.

Evaluation by Doctor Stone one month following surgery, indicated minimal, if any, cerebellar signs. Finger-to-nose test showed no tremor. Gait demonstrated a minimal unsteadiness. Evaluation one year after surgery demonstrated no neurological findings, although some episodic symptoms of imbalance persisted.

CHAPTER 21: SENSORY FUNCTION AND PARIETAL LOBE

The following case demonstrates the localizing significance of focal sensory seizures beginning in the face of a 40 year old patient without prior neurological disease. As predicted, the etiology was neoplastic: a glioblastoma.

Case 21 -1:One week prior to evaluation, this 40-year old right-handed married white male had the onset of repeated 15-21 minute duration episodes of focal numbness (tingling or paresthesias) involving the left side of the face, head, ear, and posterior neck and occasionally spreading into the left hand and fingers, and rarely subsequently spreading into the left leg. There was no associated pain or headache or weakness or associated focal motor phenomena. Biting or eating would trigger the episodes. Past history was not remarkable.

Initial neurological examination: This was completely within normal limits as regards mental status, cranial nerves, motor system, reflexes, and sensory system.

Clinical diagnosis: Focal seizures originating lower third post central gyrus. In view of patient's age, a brain tumor must remain the prime consideration

Laboratory data:

- (1) *EEG*: no focal abnormalities were present. (The record, however, was abnormal because of bilateral bursts of spikes and slow waves - triggered by photic stimulation accompanied by myoclonic jerks - suggesting a predisposition to primary generalized epilepsy (refer to epilepsy chapter for the significance of this finding which was not relevant to this case).
- (2) *CT Scan* (Fig 21-2): The non-enhanced study was normal. The enhanced study demonstrated a small enhancing lesion just above the right Sylvian fissure.
- (3) *MRI* (Fig. 21 - 3): Demonstrated the more extensive nature of this process involving the operculum - above the right sylvian fissure including the lower end of the post central gyrus, the area of representation of the face. A probable infiltrating tumor was suggested as the most likely diagnosis.
- (4) *Arteriogram* - demonstrated a tumor blush at the right sylvian area, consistent with a glioblastoma, a rapidly growing infiltrating tumor - originating from astrocytic glia.

Subsequent Course: Treatment with an anticonvulsant reduced the frequency of the episodes. Neurosurgical consultation suggested an additional observation period and periodic CT scans in view of the normal neurological examination. Three months after onset of symptoms, the patient developed a numbness of the left arm and difficulty in coordination of left arm. Exam now demonstrated left central facial weakness, mild weakness of the left hand. A loss of stereognosis and graphesthesia with a relative alteration in pinprick perception was present in the left hand. The CT scan showed significant enlargement of the previous lesion. EEG now indicated focal 2-3 Hz Delta slow waves in the right frontal central Rolandic area. Subtotal resection of a glioblastoma - in the right temporal parietal area was performed by Dr. Bernard Stone. Radiation therapy was administered following surgery, 4000 rads total whole brain and 5210 rad total to the tumor area. Reevaluation 3 months after surgery, indicated only rare focal seizures involving the face. The neurological examination was normal. Repeat CT scans, however, continued to demonstrate a large area of enhancing tumor in the right temporal-frontal-parietal area. Despite the use of dexamethasone and arterial chemotherapy with cis-Platinum, he continued to progress. At the time of neurological follow-up, 29 months after onset of symptoms, he had developed a left field defect, left hemiparesis and a loss of all modalities of sensation on the left side. He subsequently developed significant changes in memory and cognition, as well as a complete left hemiplegia. CT scan demonstrated progression with extensive involvement of the right side of the brain and spread to the left hemisphere. Death occurred 33 months after onset of symptoms. **Postmortem examination of the brain:** almost the entire right hemisphere was replaced by necrotic infiltrating tumor. The tumor now had spread into the corpus callosum and temporal and occipital lobes. The internal capsule, thalamus, hypothalamus and basal ganglia were destroyed.

Comment: The initial occurrence of the limited focal sensory seizures involving the face and head in a patient of age 40 with no history of trauma or of vascular disease or hypertension clearly predicted the following conclusions (1) The location of the discharging lesion: the sensory cortex

just above the sylvian fissure. (Note that the actual extent of the pathology was more extensive but that is almost always the case in an infiltrating glioma). (2) The nature of the underlying pathology. The most common cause of focal seizures beginning at age 40 in a patient with no significant head trauma, vascular disease, hypertension or other medical disease is a tumor. Among tumors involving the cerebral hemispheres, an infiltrating glioma is by far the most common and on a statistical basis, a glioblastoma is by far the most likely histologic type. 3) The subsequent course was consistent with the natural history of a malignant glioma of the astrocytic series, a glioblastoma. The 33 month survival (30 months after surgery is beyond the median survival for this type of tumor.

The following patient (case 21-2) had a metastatic nodule in the post central gyrus producing a pseudo thalamic pain syndrome.

Case 21-2: This 62-year-old white, right-handed housewife, six years prior to admission

had undergone a left radical mastectomy for carcinoma of the breast. Five months prior to admission, the patient developed a persistent cough, left pleuritic pain and a collection of fluid in the left pleural space (pleural effusion) as well as daily headaches in the right orbit, occasionally awakening the patient from sleep. Four months prior to admission, over a 3 to 4 week period, the patient developed progressive "weakness" and difficulty in control of the right lower extremity. Several weeks later, the patient now experienced, aching pain in the right index finger in addition to a progressive deficit in the use of the right hand. This was more a "stiffness and incoordination" than any actual weakness. One month prior to admission the patient noted episodes of pain in the toes of the right foot and numbness of right foot occurred, lasting 2 to 3 days at a time. She subsequently developed, difficulty in memory and some minor language deficit, suggesting a nominal aphasia, prompting hospital admission.

Neurological examination:

1. *Mental status:* The patient was oriented for time, place, and person. Delayed recall was slightly reduced to 3-out-of-five in 5 minutes. A slowness in naming objects was present although she missed only one item of 6. Calculations, reading, and attention were normal. There was no left-right confusion.

2. Cranial nerves:

a. Nerve II: early papilledema was noted: absence of venous pulsations, indistinctness

of disc margins, and minimal elevation of vessels as they passed over the disc margin.

b. Nerve VII: right central facial weakness was present.

3. **Motor system:**

- a. Mild weakness of the right upper limb was present. A more marked weakness was present in the lower limb (most marked distally).
- b. Spasticity was present at the right elbow and knee.
- c. Gait: The right leg was circumducted; the right arm was held in a flexed posture.

4. **Reflexes:**

- a. Deep tendon reflexes were increased on the right.
- b. A right Babinski response was present.

5. **Sensory system:**

- a. Touch intact.
- b. An ill-defined alteration in pain perception was present in the right arm and leg - more of a relative difference in quality of the pain than any actual deficit.
- c. Repeated stimulation of the right lower extremity (pain or touch) produced dysesthesias (painful sensation).
- d. Vibratory sensation was decreased to a minor degree at the toes bilaterally but intact in the upper extremities.
- e. Position sense was markedly defective in the right fingers with errors in perception of fine and medium amplitude movement in the right toes.
- f. Simultaneous stimulation resulted in extinction in the right lower extremity.
- g. Graphesthesia (identification of numbers, e.g., 8, 5, 4 drawn on cutaneous surface) was absent in the right hand and fingers and poor in the right leg.
- h. Tactile localization and two-point discrimination were decreased on the right side.

Clinical diagnosis: Metastatic tumor to the left post central and precentral gyri with a cortical pain syndrome (pseudo thalamic pain syndrome).

Laboratory data:

1. *Skull x-rays:* the pineal was shifted from left to right. Demineralization of the dorsum sellae also had occurred: consistent with the increase in intracranial pressure.

2. *Chest x-ray:* Several metastatic nodules were present in the left lung.

3. *Electroencephalogram:* A focal disturbance, having the quality of damage, was present in the left posterior frontal central and parietal areas (almost continuous focal 4 to 7 cps slow wave activity).

4. *Left carotid arteriogram:* A left posterior frontal lobe lesion was suggested by a shift of the posterior portion of the anterior cerebral artery from the left to the right. The middle cerebral artery in the sylvian fissure was also depressed downwards.

5. *Brain scan:* The findings were consistent with a focal metastatic lesion with a focal uptake of radioisotope (Hg^{197}) in the left parietal area: high and close to the midline with uptake in the adjacent subcortical white matter.

6. **Erythrocyte sedimentation rate** was elevated to 90 mm., consistent with metastatic disease.

Subsequent course: There was evidence in this case that the disease had spread to multiple organs: brain (findings as noted), lung (chest x-rays and biopsy), and liver (abnormal laboratory tests of liver function). Radiation and hormonal therapy were, therefore, administered rather than any attempt at surgical removal of the left parietal metastatic lesion. Follow-up examination one month later indicated that a significant improvement had occurred in motor function in the arm. Sensory deficits persisted. Speech was slow but relatively intact. The patient eventually expired five months after admission.

Post mortem findings: Autopsy was performed by Dr. Humphrey Lloyd of the Beverly Hospital and disclosed extensive metastatic disease in the lungs, liver, and lymph nodes. A single necrotic metastatic lesion was present in

the brain. This was located in the upper postcentral gyrus of the left parietal area, 1.0 cm. below the pial surface and measuring 1.2 x 1.0 x 0.6 cm.

Comment: This patient had a progressive neurological deficit with headache and papilledema, a clinical course that clearly indicates the presence of a neoplasm. This case predated the era of CT and MRI scan. Today contrast-enhanced scans would be performed. This diagnosis was supported by the ancillary laboratory studies that were available at that time. Moreover this diagnosis however was clear based on the history and clinical-laboratory findings. The fact that motor findings in the arm relevant to the precentral gyrus improved with treatment might suggest that these findings were due to edema. In contrast the findings relevant to the area of the necrotic tumor, the post central gyrus, showed little improvement. In general, one should assume that a patient with a past history of carcinoma of the breast, carcinoma of the lung, malignant melanoma, or renal cell carcinoma, who develops symptoms of central nervous system disease, has metastatic disease until proven otherwise. Such symptoms at their onset may be minor and nonfocal and appear trivial: headache, subjective weakness, and a change in personality. On the other hand more focal symptoms and signs may be present: focal weakness, focal seizure. The metastatic lesions may be single or multiple.

A diagnosis of metastatic disease does not imply that no treatment of central nervous system lesions is possible. Surgical resection of single lesions may be successfully performed. Often the apparent deficits are far out of proportion to the actual size of the tumor because of the surrounding swelling (edema) in the adjacent tissues.

The pattern of sensory involvement in this case clearly localized this lesion to the cortex (or white matter close to cortical surface) rather than to the thalamus. The relative intactness of pain, touch, and vibration sensation should be contrasted to the significant deficits in position sense,

graphesthesia, tactile localization, and two-point discrimination with extinction on simultaneous stimulation. The occurrence of episodic pain in the involved arms and legs along with the production of an experienced painful sensation on repetitive tactile stimulation (dysesthesias) in patients with sensory pathway lesions is sometimes referred to as a "thalamic" or "pseudo thalamic" syndrome. (Refer to discussion of Wilkins and Brody, 1969). In this case, the anatomical locus for the pseudo thalamic syndrome is apparent.

The effects of deficits in cortical sensation on the total sensory motor function of a limb are apparent in this case. The actual disability and disuse of the right arm and leg were far out of proportion to any actual weakness. Such an extremity is often referred to as a "useless limb." The actual weakness that was present undoubtedly reflected pressure effects on the precentral gyrus and the descending motor fibers in adjacent white matter.

The following case (21-3) demonstrates many of the features of a non dominant parietal lobe lesion.

Case 21-3: This 70-year-old, single, white female, right-handed, retired candy maker underwent a left radical mastectomy for carcinoma of the breast, three years prior to admission. Four months prior to evaluation, the patient became unsteady with a sensation of rocking as though on a boat. She no longer attended to her housekeeping and to dressing. Over a three-week period, prior to evaluation, a relatively rapid progression occurred with deterioration of recent memory. A perseveration occurred in motor activities and speech. The patient was incontinent but was no longer concerned with urinary and fecal incontinence. For 2 weeks, right temporal headaches had been present. During this time, her sister noted the patient to be neglecting the left side of her body. She would fail to put on the left shoe when dressing. In undressing, the stocking on the left would be only half removed.

Family History: The patient's mother died of metastatic carcinoma of the breast.

Neurological examination:

1. Mental status:

- a. The patient was oriented for time, place and person.
- b. Delayed recall was 5-out-of-5 objects in 5 minutes.
- c. There was no evidence of aphasia.
 - d. The patient often wandered in her conversation. She often asked irrelevant questions and was often impersistent in motor activities.
- e. There was marked disorganization in the drawing of a house or of a clock. A similar marked disorganization was noted in attempts at copying the picture of a railroad engine (Fig 21-4).
- f. There was a marked neglect of the left side of space and of the left side of the body. The patient failed to read the left half of a page. When she put her glasses on, she did not put the left bow over the ear. When getting into bed, she did not move the left leg into bed. She had slipped off her dress on the right side, but was lying in bed with the dress still covering the left side.

- g. The patient had been reluctant to come for neurological consultation. Although she complained of headache and nausea, she denied any other deficits. Her relatives provided information concerning these problems. Much additional persuasion over a two-week period was required before the patient would agree to be hospitalized.

(2) *Cranial nerves:*

- a. Nerve II: A dense left homonymous hemianopsia was present. When reading, the patient left off the left side of a page. She bisected a line markedly off center. Disc margins were blurred and venous pulsations were absent, indicating papilledema.
- b. Nerve III: The right pupil was slightly larger than the left.
- c. Nerve VII: A minimal left central facial weakness was present.
3. *Motor system:* Strength was intact. There was, however, little spontaneous movement of the left arm and leg. Tone was normal.
4. *Reflexes:* deep tendon reflexes were symmetrical and physiologic and plantar responses, flexor.
5. *Gait:* The patient was ataxic on a narrow base with eyes open with a tendency to fall to the left, and was unable to stand with eyes closed even on a broad base.
6. *Sensory system:*
- a. Pain, touch and vibration were intact. At times, however, there was a decreased awareness of stimuli on the left side.
 - b. Errors were made in position sense at toes and fingers on the left.
 - c. With double simultaneous stimulation, the patient neglected stimuli on the left face, arm and leg.
 - d. Tactile localization was poor over the left arm and leg.

Clinical diagnosis: Metastatic tumor from breast to right non-dominant parietal cortex.

Laboratory data:

1. *Skull X-rays* were negative.
2. *Chest X-ray* indicated a possible metastatic lesion at the right hilum.
3. *Erythrocyte sedimentation rate* was elevated to 72 mm/hr, consistent with metastatic disease.
4. *Electroencephalogram* (Fig 21-5) was abnormal because of frequent focal 3 to 4 cps slow waves in the right temporal and parietal areas, suggesting focal damage in these areas.
5. *Brain scan (radioisotope)* (Fig 21-6) indicated that a large but well-defined area of increased uptake of isotope (Hg197) was present in the right parietal area extending from the midline to the lateral surface, measuring 7 x 5 x 7 cm. The most likely diagnosis was that of a solitary large metastatic lesion
6. *Right carotid arteriogram* showed that a large vascular tumor mass, probably metastatic, was present in the posterior section of the right temporal inferior parietal area. There was displacement of the middle cerebral artery upward and to the left.

Subsequent course: Treatment with steroids (dexamethasone and estrogens) resulted in temporary improvement. The patient refused surgery. Her condition soon deteriorated with increasing obtundation of consciousness. She expired two months following her initial neurological consultation.

Comment: This patient certainly presented a syndrome characterized by disturbance in concept of body image with a marked neglect of the left side, a denial of illness, and marked constructional apraxia. The various laboratory studies indicated a large lesion in the right posterior temporal parietal area. A CT scan from a more recent case demonstrating many aspects of this syndrome is illustrated in Figure 21-7. In many cases, the location of lesion may appear to be predominantly posterior temporal. Such large posterior temporal lesions would certainly compromise the cortex and subcortical white matter of the adjacent inferior parietal area.

In this case, marked deficits in perception of the cortical modalities of sensation were present. In other cases, as in the case demonstrated in Fig 21-7, such involvement is much less marked.

In some cases, involvement of the motor cortex is evident with an actual left hemiparesis accompanied by an increase in deep tendon reflexes and an extensor plantar response. At times in patients with neglect syndromes, there may be several indications in the clinical examination and in the laboratory studies that the involvement of the frontal lobe areas is more prominent than the parietal involvement. We have already indicated that the neglect components of this syndrome may also be noted in lesions of the anterior premotor

area (area 8). The premotor area as discussed above and in chapter 18, receives projection fibers from the multimodal area of the posterior parietal area. It is possible that in some cases the posterior temporal - inferior parietal location of the lesion may also be critical in interrupting these association fibers. For these several reasons, it is perhaps more appropriate to use the term, *syndrome of the non-dominant hemisphere*, rather than the more localized designation, non-dominant inferior parietal syndrome. Duffner et al, 1990 have presented the concept of a network for directed attention - with right frontal lesions leading to left hemi spatial neglect only for tasks that emphasize exploratory-motor components of directed attention whereas parietal lesions emphasize the perceptual-sensory aspects of neglect.

With lesions of the non-dominant hemisphere, there is a significant alteration of the patient's awareness of his environment. The behavior of an individual is in part determined by his or her own particular perception of the environment. If that perception is altered or disorganized, the behavioral responses of the patient may appear inappropriate to others. Obviously, not all individuals will respond in the same manner to a given environmental situation; part of the response will be determined by the past experience and personality of the individual. Thus, given the same lesion, one individual may be unaware of a hemiparesis, another may deny the hemiparesis but agree an illness is present, a third may claim to be healthy and claim that people are conspiring to keep him in the hospital.

CHAPTER 22: THE LIMBIC SYSTEM

In general, as we have indicated, there is mixed symptomatology during partial seizures of temporal lobe origin. The following case history (22-1) illustrates many of the points just discussed regarding seizures of temporal lobe origin.

Case 22-1: This 56-year-old white right-handed male baker was referred for evaluation of a seizure disorder. Three months before admission the patient had the onset of episodes of vertigo and tinnitus, each episode lasting 4 minutes and unrelated to position. The patient then noted increasing forgetfulness. Later that month he had a generalized convulsive seizure that occurred without any warning. The patient then developed episodes of confusion and unresponsiveness, followed by a left frontal headache. Several studies; EEG, pneumoencephalogram, and carotid arteriogram—were all negative at that point in time. One month before admission, the patient began to have minor episodes, characterized by lip smacking and a vertiginous sensation, during which he reported seeing several well-formed, colorful scenes. At times, he had hallucinations of “loaves of bread being laid out on the wall.” In addition, he would have a perceptual disturbance at the same time (e.g., objects would appear larger than normal) and “terrifying dreams.”

General physical examination: unremarkable.

Neurological examination: The essential neurological findings were as follows:

1. *General observations of seizures:* The patient was observed to have frequent transient episodes of distress characterized by saying, “Oh, oh, oh, my”. On occasion, these were accompanied by automatisms: fluttering of the eyelids, smacking of the lips, and repetitive picking at bedclothes with his right hand. Consciousness was not completely impaired during these episodes, which lasted from 30 seconds to 3 minutes, and the patient reported afterward that at the onset of the seizure he had seen loaves of bread on the wall and smelled a poorly described unpleasant odor. At other times, the olfactory hallucination was described as pleasant, resembling the aroma of baked bread.
2. *Mental status:* The patient was oriented to person but not dates. He could not recall his street address. He was unable to pronounce the name of the hospital correctly. Calculations were correctly performed.
3. *Cranial nerves:* Possible deficit in the periphery of the right visual field and a minor right central facial weakness.
4. *Motor system:* intact
5. *Reflexes:* Deep tendon reflexes were symmetrical and physiologic. A right Babinski sign was present.
6. *Sensory system:* intact.

Clinical diagnosis: Simple and complex partial seizures originating left temporal lobe probably involving at various times left lateral superior temporal gyrus, uncus, amygdala and hippocampus with tumor the most likely etiology in view of age and the focal neurological findings.

Laboratory data:

1. The *initial electroencephalographic recording* indicated frequent focal spike discharge throughout the left temporal and parietal areas, consistent with a focal seizure disorder originating in the left temporal/parietal areas (Fig. 29-1). A recording 6 days later indicated a decrease of focal spikes (i.e., a decrease in seizure activity) but the presence of frequent focal slow-wave activity in the left temporal area (almost continuous, 3 to 5 cps (Hz) slow-wave activity) suggesting that focal damage was present in the left temporal area .
2. *Brain scan* (H_g197) normal
3. *Left carotid arteriogram* indicated a possible avascular mass lesion left posterior frontal (the only abnormality was a 4-mm shift of the anterior cerebral artery).

Subsequent course: The patient continued to have multiple short episodes characterized by the sensation of odor and a sensation that he was looking at objects upon the wall. These episodes were eventually controlled with anticonvulsant medication: phenytoin (Dilantin) and primidone (Mysoline). However, 2 months later the patient had a day with several episodes with “crazy things occurring “ (colorful visions and terrifying nightmares).

The patient was readmitted to the hospital 7 months after onset of symptoms because of the recurrence of seizures. An aura of unpleasant odor was followed by a generalized convulsion followed by four or five

subsequent seizures of a somewhat different character (deviation of the head and eyes to the right, then tonic and clonic movements of the right hand spreading to the arm, foot, and leg lasting approximately 1 to 2 minutes, followed by a post-ictal right hemiparesis).

Neurologic examination now indicated a marked expressive aphasia, with little spontaneous speech and difficulty in naming objects. There was a dense right homonymous hemianopia, a flattening of the right nasolabial fold, and a right hemiparesis, with a right Babinski sign.

During a 2-week hospital period the patient continued to have minor seizures characterized by sensory phenomena on the right side of the body. A moderate degree of expressive aphasia persisted throughout the hospital course, although the right homonymous hemianopia largely disappeared. The symptoms and findings suggested that the basic disease process might well have spread to involve the adjacent areas across the sylvian fissure—the speech areas of the inferior frontal convolution, premotor areas, and sensory motor cortex.

The patient developed increasing expressive aphasia and right hemiparesis, with increasingly severe headache. An arteriogram indicated a large space-occupying tumor of the left temporal lobe, and surgery was undertaken by Dr. Robert Yuan 16 months after the onset of symptoms. The anterior and middle portions of the superior temporal gyrus appeared to be widened, and the anterior temporal area (the temporal tip) had an abnormal and discolored appearance. At a depth of 1 to 2 cm within the superior temporal gyrus and involving all of the deeper temporal areas, obvious necrotic glial tissue was found. The process had extended superficially under the Sylvian fissure to involve the adjacent posterior portion of the inferior frontal gyrus.

A temporal lobectomy was performed (from the anterior temporal pole posteriorly for a distance of 6 cm). The operative impression of a malignant glial tumor (glioblastoma) was confirmed by histologic examination.

Comment: This patient presented, at one time or another during his seizures, most of the phenomena associated with temporal lobe lesions: vertigo, tinnitus, visual distortions and hallucinations, olfactory hallucinations, fear, automatisms involving the lips and hands, and episodes of confusion. The visual and olfactory hallucinations are of interest in that both reflected the patient's occupation as a baker. As Halgren and colleagues (1978) note, the experiential phenomena of temporal-lobe seizures are often specific to the individual's experience and personality. The later progression clearly indicated spread across the sylvian fissure to involve the motor cortex and Broca's area in the inferior frontal gyrus areas. This patient had a highly malignant tumor, which clearly involved the cortex of the lateral surface, the deeper white matter, and presumably the medial temporal areas, including the amygdaloid-hippocampal regions. His clinical picture is highly reminiscent of the case described in 1887 by Hughlings Jackson of Emily M., a cook who experienced visual and olfactory hallucinations and who had a tumor arising in the "temporosphenoidal lobe" (the uncus). Such seizures have subsequently been referred to as uncinate epilepsy, but as we have indicated, the disease invariably involves more than just the uncus.

Today, CT scan and MRI would be employed for early diagnosis (see Figs. 22-17 and 22-18). Cases 22-2 and 22-3 which follow demonstrate the correlation of partial seizures with temporal lobe pathology.

Case 22-2. This 17-year-old right-handed male, at age 4 years began to have "staring spells and bizarre behavior". Some episodes had been preceded by the "sound of a musical rhythm". EEG at that time indicated a right temporal spike discharge. Seizures were controlled for ten years with anticonvulsants but then recurred and were poorly controlled occurring several times per day.

Neurological examination: The findings were limited to the following features:

1. *Observed 3 minute seizure:* The seizure began with loss of contact and a stare and then automatisms of the hands. He stood up, walked around the room, went to the physician's desk and attempted to pull open a nonexistent middle drawer. He answered questions vaguely with one or two word answers. Confusion was present for 1-2 minutes after the end of the episode.
2. *Cranial nerves:* a left central facial weakness was present.

Clinical diagnosis: Focal seizures originating right temporal lobe. Observed seizure was complex partial. The seizures beginning with the musical sound might be classified as simple partial with secondary complex partial.

Laboratory data:

1. *EEG*: Intermittent focal spike discharge anterior-middle temporal area.
2. *CT scan*: (Fig. 22-17) An area of focal atrophy was present in the right anterior temporal lobe with possible enhancement at the border.
3. *MRI*: At the Yale Epilepsy Center was more consistent with a tumor in the right anterior temporal lobe.

Subsequent course: Dr. Dennis Spencer at the Yale Epilepsy Center performed a temporal lobectomy. This demonstrated a cystic glial tumor with components of astrocytes and oligodendrocytes. Cerebral cortex also demonstrated abnormal lamination and dysplastic features. Seizures were fully controlled over the next three years.

Case 22-3. This 47-year-old ambidextrous male experienced his first seizure one month prior to admission. He felt light-headed and warm. Then he was observed to walk 100 feet down a hallway, appearing “dazed” and not recognizing people. He fell to the floor, with a loss of consciousness, bit his tongue and was confused afterwards for several minutes.

Neurological examination at 2, 16 and 48 hours after the episode: A persistent right Babinski sign, and slight right hyperreflexia were present. Otherwise the examinations were not remarkable.

Clinical diagnosis: Complex partial seizures. In view of age of onset and persistent focal signs a brain tumor was suspected as the etiology.

Laboratory diagnosis:

1. Sleep deprived EEG :normal.
2. *CT and MRI scans* (Fig. 22-18) demonstrated an extensive infiltrating tumor of the left temporal lobe most likely a glioblastoma.

Subsequent course: Despite Anticonvulsant therapy (phenytoin) additional episodes occurred over the next month: loss of train of thought while talking and several minutes of loss of memory. A subtotal resection by Dr. Bernard Stone (St. Vincent Hospital) demonstrated a Grade III-IV astrocytoma (glioblastoma). Despite radiotherapy and chemotherapy, the disease pursued a relentless course producing early and severe disability prior to death, approximately one year after onset of symptoms.

The following case histories illustrate many of the features of focal disease involving the prefrontal areas.

Case 22-4: This 69-year-old right handed white housewife; two years prior to neurological evaluation visited a relative (a physician) in Israel whom she had not seen in a number of years. The relative then wrote to the patient’s physician, (an old family friend) indicating concern over a change in the patient’s personality. The patient was described as apathetic with silly immature reactions. In retrospect, the patient’s husband felt that these alternations had begun insidiously a number of years previously. A year later, the same relative again wrote indicating that letters received from the patient had become incoherent. Letters became less frequent and then the patient no longer wrote letters. Ten months prior to evaluation, a left central facial weakness was first noted followed two months later by a decreased left arm swing. Six months prior to evaluation, her husband noted, she was purchasing items for which she had no need: 24 pairs of shoes, 15 brassieres. Subsequently she became careless in her housework. On occasions she lost her purse. Her ability to play bridge had decreased over the last year, although her golf game was unchanged.

Neurological examination:**1. Mental status**

- a. She was oriented x3
- b. There was a marked impersistence in motor activities. She was often inattentive. Her answers were often irrelevant. (According to her husband this had been present for many years.
- c. There was inappropriate joking.
- d. Delayed recall without assistance was 2/5 objects in 5 minutes. But 5/5 with assistance.
- e. Digit span was decreased to 5 forward and 3 in reverses.

- f. There were marked deficits in serial 7 subtractions. At times she began to subtract other numbers, at times she added rather than subtracted.
- g. There was a significant spatial disorientation. There was a marked impairment in the ability to copy a cube and deficits in drawing a house. There was disorientation in locating cities on a map.

2.Cranial nerves:

- a. There was a significant neglect of single stimulus objects in the left visual field; this was greater when bilateral simultaneous stimuli were utilized.
- b. At times there was a limitation of voluntary gaze to the left.
- c. A left central facial weakness was present.

3.Motor system:

- a. There was minimal weakness of the left arm and leg.
- b. Variable resistance was present on passive motion at left wrist and elbow suggesting the "gegenhalten" of frontal lobe disease.
- c. There was a decreased swing of the left arm in walking. The gait was initially apraxic but improved as the patient picked up speed.

4.Reflexes

- a. Deep tendon stretch reflexes were increased on the left.
- b. A left Babinski sign was present.
- c. There was a bilateral release of the grasp reflex.

5. Sensory system: intact.

Clinical diagnosis: Right frontal lobe tumor: probable meningioma based on the long history.

Laboratory data:

1.*Skull x-rays* there was a 5mm shift to the left of the calcified pineal gland. Long standing increased intracranial pressure was suggested by the demineralization of the sella turcica.

2.*EEG* demonstrated focal 2-5 Hz slow waves in the right frontal area most prominent in the parasagittal recording area

3.*Imaging study: radioactive brain scan (Hgl97):* there was a heavy uptake in the right frontal towards the midline measuring 5x5x4 cm (Fig.22-21).

4.*Arteriograms:* A parasagittal tumor was present in the right frontal area, with vascular supply derived from the left and right middle meningeal and left anterior meningeal arteries.

Hospital course: Following the arteriogram, the patient developed signs of increased intracranial pressure (vomiting, lethargy and papilledema). The patient received dexamethasone glucocorticoid used to reduce cerebral edema, with improvement in these symptoms. The right external carotid artery was ligated since the meningioma derived considerable blood supply from this source. Dr. Samuel Brendler performed a bilateral frontal craniotomy. Bulging of the dura was present requiring the administration of hyperosmotic agent (20% mannitol) with reduction of the swelling. When the dura was opened a large right posterior frontal meningioma was revealed measuring 8x8cm and attached to the right side of the superior sagittal sinus. On histological section this was a fibrous, meningothelial meningioma. During the course of removal of the tumor, it was necessary to ligate several bridging veins entering the superior sagittal sinus as well as the arteries feeding the tumor. At the conclusion of the procedure, it was noted that the right pupil was enlarged and neither responded to light. The patient failed to regain consciousness, remaining in a state of coma with bilateral extensor plantar responses, decerebrate postures on stimulation and bilateral fixed dilated pupils. The patient expired 2 weeks after surgery.

Comment: It is difficult to decide even in retrospect when the symptoms in this case began. It is clear that the initial symptoms involved an insidious change in personality. She was apathetic, her reactions were "silly" and judgment was impaired. Purchases were inappropriate. It would have been of interest to explore which aspects of her bridge playing were impaired in terms of planning and strategy etc. Her motor function was impaired only to a minor degree even late at the time of neurological evaluation, with minimal left-sided weakness and more prominent premotor release. The visual neglect syndrome may have reflected involvement of the premotor area or compromise of the parietal cortex by this large tumor. The fact that there was only minor evidence of involvement of motor cortex would make the premotor/SMA location more likely. While the spatial disorientation and deficits in drawing might

favor a nondominant parietal syndrome, such findings also could be consistent with a nondominant premotor/SMA location based on the close interaction between the posterior parietal and the premotor location. The impairment of voluntary gaze to the left would be consistent with area 8 involvement. There is little doubt that this patient required surgical intervention. The removal of large "benign" tumors of this type is not without risk. Hemorrhagic infarction with massive edema and tentorial herniation is a complication of ligation of bridging veins entering the superior sagittal sinus. In this case, serious brain swelling was already evident even before the dura was opened.

The following case history 22-3 provides an example of a patient with a slowly progressive subfrontal meningioma manifested by symptoms of apathy, loss of ambition, "depression" of mood, emotional lability, with a tendency to introspection and a slowness of mental processes. All of these symptoms were initially attributed to depression and a hypothyroid state. As gait and memory problems developed, these symptoms were attributed to Alzheimer's type senile dementia. When increased intracranial pressure and coma suddenly developed, neurological and neurosurgical intervention occurred.

Case 22-5: This white housewife and fashion designer was first admitted to the hospital at age 60 with a history of several years (?2 to 5) of fatigue, loss of ambition, lack of enthusiasm, and a tendency to readily cry over minor problems. A depression of mood and a tendency to introspection had developed. The patient also reported loss of her taste for food with a subsequent decrease in appetite and weight loss. These symptoms had progressed despite an adequate dosage of thyroid medication (60 mg., t.i.d.). Neurological examination was recorded as negative except for a slowness of speech and of thought processes. She was described by the psychiatric consultant as indecisive in her answers. Cerebrospinal fluid examination revealed no significant findings. Tests of thyroid function indicated hypothyroidism with protein bound iodine of 3.2 micrograms/100 ml. (normal; 4 to 8 micrograms/100 mg.) and a radioactive iodine uptake of 2.3 percent in 24 hours (normal 20 to 50 percent). Discharge diagnosis was chronic depression and hypothyroidism.

These symptoms continued to progress despite treatment with thyroid. The patient had increasing difficulty in walking. This had actually been first noted at age 57, 3 years prior to her initial hospital admission as a "phobia for heights". The patient would "freeze" at the top of a high flight of stairs. She then developed progressive difficulty in climbing stairs. Her husband reported that she would have marked difficulty in getting out of chairs. She would appear unsteady in gait after rising from a chair but would soon recover her equilibrium and would be able to walk in relatively normal manner. Increasingly, the patient's motor and mental activities became slower. She "procrastinated in making decisions". Occasional urinary incontinence developed at age 66 and was attributed to her neurological disease (apparent senile dementia). Although her husband reported her memory as initially well preserved, other observers at that point reported a progressive deficit in memory. At age 67, the patient began to complain of episodic fogging or blurring of vision.

Initial Neurological examination on re-admission to the hospital at age 67 was recorded as demonstrating the following features:

(a), slight disorientation for date and year, (b) slowness of speech and gait (c) deep tendon reflexes 2+, plantar responses flexor, and (d) no significant sensory finding except a slight decrease in position sense at the toes. No details as to the patient's gait were recorded. The sense of smell was apparently not tested and no notes as to the presence or absence of a grasp reflex were recorded.

On the day after admission, the patient developed headache and vomiting. She had difficulty walking unsupported and became increasingly more somnolent but could be roused by painful stimulation. Deep tendon reflexes were increased bilaterally with bilateral extensor plantar responses (bilateral Babinski signs). Grasp response was absent. Pupils responded to light but were sluggish.

Fundusoscopic examination was negative but lumbar puncture indicated a markedly increased pressure, greater than 400 mm. of csf. Cerebrospinal fluid protein was elevated to 125 mg/100 ml. The patient became unresponsive and emergency neurological and neurosurgical consultations were obtained.

Neurological examination:

1. *Mental Status:* The patient was semicomatose with periodic Cheyne-Stokes respirations.
2. *Cranial Nerves:* Pupils were fixed, the left dilated, the right constricted.
3. *Motor System:*
 - a. The patient moved all limbs in response to painful

stimulation, right more than left.

- b. There was a spastic resistance in the upper and lower left extremities.
4. Reflexes:
- a. A generalized hyperreflexia was present with bilateral ankle clonus.
 - b. Bilateral Babinski signs were present.
 - c. A bilateral grasp reflex was present. Note, however, that in a semicomatose patient this may have little localizing significance.
5. *Sensation*: Pain sensation was intact.

Clinical diagnosis: Subfrontal or parasagittal frontal tumor most likely a meningioma in view of the over 10 year course. Tentorial herniation had occurred possibly related to the lumbar puncture.

Laboratory data: An emergency bilateral carotid arteriograms revealed that a large subfrontal butterfly-shaped mass (probably meningioma) was present in the anterior cranial fossa bilaterally. The anterior cerebral arteries as well as the frontal polar, pericallosal and callosal marginal branches and the middle cerebral arteries were displaced backwards. The anterior cerebral arteries were also displaced upwards. The tumor mass derived blood supply from the ophthalmic arteries.

Hospital course:

A bifrontal craniotomy was immediately performed by Doctor Robert Yuan with total removal of a large bifrontal meningioma arising from the falx and olfactory groove. On the right side the tumor was estimated to occupy 75 percent of the anterior cranial fossa, measuring 7 x 5 x 6 cm. On the left the tumor was of approximately half this size, measuring 5 cm. in diameter. The thickness of the cerebral hemisphere covering the tumor in the right prefrontal area was reduced to 0.5 cm. Histological examination of the tumor indicated a benign meningioma (meningotheliomatous type).

The patient showed some immediate improvement at the conclusion of surgery, in the sense that both pupils were equal in size and reacted to light. By the time of discharge from the hospital, two months after surgery, considerable improvement had occurred. She could recognize the doctor by name but did not know the place, the season, or the month; she could, however, describe a picture she had just seen. A bilateral deficit in olfaction was present (anosmia). Assistance was required in walking. A bilateral grasp reflex was present.

Follow-up evaluation two years after surgery indicated continued improvement although the patient still had complaint relevant to impairment of recent memory and slight unsteadiness of gait. Deep tendon reflexes were symmetrical with plantar responses flexor. A bilateral grasp reflex was present and the patient was slow in walking and fell occasionally. Urinary incontinence occurred with wetting of the bed.

Comment: In retrospect, the evolution of symptoms in this patient clearly indicates a tumor initially compression both prefrontal areas and producing alterations in mood and personality. With continued growth of the tumor, compromise of the premotor areas with resultant apraxia of gait and release of grasp reflex began to occur, either as a result of direct compression or secondary to the distortion and compression of the anterior cerebral arteries. It is not unusual to witness the development of a dementia (deficit in recent memory) in large tumors in a subfrontal midline location. A similar dementia may occur in large aneurysms of the anterior communicating artery.

The problem of dementia will be considered in greater detail in the chapter on memory.

The development of headache, vomiting and increasing somnolence indicated the development of increasing intracranial pressure. The sudden unresponsiveness following the lumbar puncture with the development of periodic Cheyne-Stokes respirations, pupillary changes, and bilateral corticospinal tract signs all indicated an additional acute exacerbation of the already compromised brain stem functions, a compromise which had already resulted from the backward displacement of the intracranial contents with distortion of the brain stem. In retrospect, one might hypothesize that the patient's complaint of a loss of taste for her food at the time of her initial hospitalization might well have indicated some loss of olfactory sensation since much of our appreciation of food is dependent on olfaction. Specific tests for olfaction were not recorded.

CHAPTER 23: VISUAL SYSTEM

The following case is an example of a lesion involving the optic nerve, anterior to the optic chiasm.

Case History 23-1 (Fig 23-8).

This 53-year-old white right-handed housewife was referred for evaluation of progressive right-sided supraorbital headache of 23 years duration and decreasing acuity in the right eye. The loss of acuity had progressed to the point of almost total unilateral blindness. During the 3 years before admission, intermittent tingling paresthesia had been noted in the left face, arm, or leg. About 1 year before admission the patient had a sudden loss of consciousness and was amnesic for the events of the next 48

hours. She was hospitalized, but no explanation for the episode was clearly established, although cerebrospinal fluid protein was reported to be elevated (230 mg/dl).

The patient and her family reported some personality changes over a period of several years, including a loss of spontaneity and increasing apathy.

General Physical Examination: Unremarkable except for a minor degree of proptosis (downward protrusion of the right eye).

Neurologic Examination:

1. *Mental Status:* The patient was, in general, alert but at times would become lethargic. Her affect was flat. At times, she would laugh or joke in an inappropriate manner.
2. *Cranial Nerves:* There was anosmia for odors, such as cloves, on the right and a reduced sensitivity on the left.

Marked papilledema (increased intracranial pressure with protrusion of the optic disk and venous engorgement due to obstruction of the normal flow of CSF) was present in the left eye.

Pallor of the right optic disc was present, indicating optic atrophy. Visual acuity in the right eye was markedly reduced. The patient had only a small crescent of vision in the temporal field of the right eye, where only vague outlines of objects could be seen. A slight left central facial weakness was present.

3. *Motor Systems:* Intact although movements on the left side were slow.

4. *Reflexes:* A release of grasp reflex was present on the left side.

5. *Sensory system:* Intact

Clinical diagnosis: Subfrontal meningioma arising from olfactory groove or inner third sphenoid wing.

Laboratory data:

1. *Skull* x-rays demonstrated erosion of the dorsum sellae. Special lamniograms demonstrated hyperostosis of the sphenoid bone (planum sphenoidale) suggesting a meningioma originating from the sphenoid bone.

2. *EEG* demonstrated focal 2-4 Hz slow waves in the right anterior temporal and anterior lateral frontal area.

3. *Brain scan (H_g 197)* revealed a heavy uptake of isotope in the right posterior subfrontal area.

4. *Arteriograms* indicated that the anterior cerebral arteries were shifted backwards, posteriorly and the left. A tumor blush was present on the venous phase in the right subfrontal area extending back to the optic nerve groove (Fig 23-8). These findings were felt to be most consistent with an olfactory groove meningioma.

Hospital course: Dr. Samuel Brendler performed a bifrontal craniotomy which exposed a well-encapsulated smooth tumor attached to the medial third of the sphenoid wing. After intracapsular removal of 90 to 95% of the tumor, the right optic nerve could be visualized. The small portion of the tumor attached to the bone could not be removed because of considerable bleeding from the bone. Examination 4 months after surgery, indicated right anosmia and right optic atrophy were present.

Comment

If one considered only the patient's primary complaint, decreasing vision in the right eye, and the findings of right optic atrophy and left-sided papilledema (Foster-Kennedy syndrome), then the most probable diagnosis was inner-third sphenoid meningioma. The preservation of a small crescent of vision in the temporal field is consistent with compression of the optic nerve on its lateral surface. By the time of hospitalization, the lesion was quite large and had extended into the subfrontal area, producing anosmia on the right and some changes in personality. At this point, the various diagnostic studies suggested only a subfrontal mass and did not clearly differentiate between an olfactory-groove meningioma and a sphenoid-wing meningioma. One might suggest, in retrospect, that the degree of involvement of the right optic nerve was much more pronounced than the changes in prefrontal functions, and therefore, the inner-third sphenoid-wing location was more likely.

The surgical approach in any case was the same. The eventual recovery of vision in such cases is uncertain because the effects of compression often are not reversible

COMPLETE CASE HISTORIES FROM TEXTBOOK: *INTEGRATED NEUROSCIENCES*

PART III. CASES – CEREBRAL HEMISPHERE MOTOR SYSTEM, CEREBELLUM, BASAL GANGLIA

CHAPTER 18: MOTOR SYSTEM I:

The following case 18-1 presents an example of focal seizures beginning in the motor cortex.

Case 18-1. This 29-year-old, right-handed, white woman was in her usual state of good health until three months prior to admission when she developed an intermittent “pulling sensation” over the anterior aspect of the left thigh, lasting a few minutes. This recurred without other symptoms about twice a week. On the evening of admission, while sitting on a couch, she again had the onset of this same sensation in her left. She stood up, noted that her left leg felt “numb” and then started to have “jerky movements” in her left foot which progressed to involve the whole left lower extremity. She sat down, pressed on her left thigh in an attempt to stop the movement. At this point, her husband and a friend came to her (the patient is amnesic for these events), and saw her have tonic extension then clonus of all four limbs associated with grunting respiration, clenched jaw, and rolling of the eyes. She was placed on the floor and after a few seconds she regained consciousness, though she still appeared dazed and slightly confused for the next 5 minutes.

Past history and family history: noncontributory.

Physical Exam: Normal except for bite marks on the left lateral aspect of the tongue.

Neurological Exam: Significant only a slight asymmetry of deep tendon reflexes: left > right.

Clinical Diagnosis: Focal seizures originating right parasagittal motor cortex (foot area), with ? of parasagittal meningioma.

Laboratory Data:

(1) *Electroencephalogram* (Fig.29-1B) demonstrated rare focal spikes, right Rolandic parasagittal consistent with the focal source of the secondarily generalized seizure and rare focal slow waves in the right Rolandic and mid temporal area - consistent with minor damage in this area

2) *CT scan* (Fig.18-13) demonstrated an enhancing lesion in the right parasagittal region just anterior to the central sulcus.

- (3) *Arteriograms* (Fig.18-14) demonstrated a circumscribed vascular tumor in the right parasagittal rolandic area which was supplied by the right anterior cerebral artery (A,B) and the right middle meningeal branch of the external carotid artery©. The venous phase of the study demonstrated a significant draining vein from this area of tumor blush(D). All of these findings were consistent with a right parasagittal meningioma.

Hospital Course: A well-circumscribed right parasagittal meningioma was removed by Doctor Bernard Stone. A distal weakness of the left lower extremity was present in the immediate postoperative period but this improved rapidly so that by two months after surgery, a foot drop brace was no longer required and strength had returned to normal. During all of the pre and post operative period, the patient received diphenylhydantoin (Phenytoin) to prevent additional seizures. A possible sensory seizure involving the hand occurred 2 years later. Four years after surgery, the patient attempted to reduce her dosage of anticonvulsant and experienced a recurrence of focal motor seizure activity beginning in the left leg with subsequent secondary generalization. When evaluated 6 years after surgery, she had experienced no additional seizure activity. Her neurological examination continued to demonstrate an increase in deep tendon reflexes on the left and a left sign of Babinski. Her CT scan demonstrated no recurrence of tumor, there was very minor atrophy at the site of the previous meningioma. The EEG continued to demonstrate bursts of blunt spikes and slow waves in the right parasagittal Rolandic and parietal areas. Follow-up 10.5 years after surgery in indicated no additional seizures.

Comment: The onset of focal seizure activity should always raise the question of focal pathology. When these seizures begin at age 29, without a prior medical history, there is always a strong possibility of a primary brain tumor. In general gliomas are much more common than meningiomas but the odds of a meningioma are increased by the parasagittal location and the gender of the patient. In this case, there was a very close correlation of the clinical phenomena with the laboratory data regarding the anatomical location of the lesion. Surgical therapy eliminated the underlying benign tumor - the parasagittal meningioma, but the predisposition to focal seizures remained. Thus, the tumor in compression of cerebral cortex had produced alterations in neuronal excitability which persisted following the removal of the tumor.

Case 18-2 provides an example of a slow growing tumor involving the premotor and supplementary motor cortex from the standpoint of focal seizure activity. The motor effects of frontal lesions are presented in case histories 22-2 and 22-3 which follows the discussion of the prefrontal areas.

Case 18-2: This 57-year-old right-handed single nun and occupational therapist, had the onset of her first generalized convulsive seizure at age 47, ten years prior to consultation. This occurred without warning with sudden loss of consciousness and an observed generalized tonic clonic seizure. Both an EEG and CT scan were reported to have been normal. Approximately 4 additional generalized convulsive seizures occurred over the next 4 years. Shortly after the onset of the grand mal seizures, the patient began to have focal seizures. She described these as beginning with the abduction and raising of the right arm at the side, over her head, then a jerking of the right arm, and then she would fall to the ground. She would remain fully conscious but she would be unable to talk. She would have an awareness that something strange was occurring. She had a sinking sensation. She denied any impairment of memory after the episode. But, she would be aware that her right arm and leg were tingling and weak for perhaps 5 minutes afterwards and she would be unable to speak for 10-30 minutes afterwards. These focal seizures occurred once a month, but for the last 2 years, they had been occurring once a week. The patient indicated that over the last 10 years she has had problems with her memory.

She was reported to have had three “negative” CT scans over the years, and yearly EEG’s which did not reveal focal features or electrical seizure discharges although some bilateral slow wave activity was present. The patient has been treated with a variety of medications over the years without attaining seizure control. Her initial evaluation 4 years after onset of seizures at another neurological center indicated some increased activity in the finger jerks on the right with withdrawal of both plantar responses, and a diminished swing of the right arm.

Past history and family history were negative: she was the product of a full-term delivery weighing 9 pounds and had excellent developmental and educational milestones.

Neurological examination :The following abnormalities were present:

1. *Mental Status*: Although orientation and language functions were all intact, delayed recall without assistance, was 0 out of 5; and with assistance 2 out of 5. Proverb interpretation was abstract for 1/3 proverbs, but similarity testing was abstract.
2. *Cranial Nerves* II through XII were intact.
3. *Motor System* was intact except for a decreased swing of the right arm in walking.
4. *Reflexes*: deep tendon reflexes were increased on the right at biceps and patellar. Plantar response was extensor on the right and equivocally extensor on the left.
5. Sensory system was intact.

Clinical diagnosis: Seizures of focal origin left premotor/supplementary motor cortex possibly secondary to low grade glioma. A meningioma was less likely due to the reports of “normal CT scans”.

Laboratory data:

1. **CT scan** (Fig.18-16),demonstrated an area of calcification with surrounding edema in the left premotor area .

2. **MRI scan** (Fig.18-17),demonstrated extensive involvement of the premotor and supplementary areas by tumor and edema.

Subsequent course: Subtotal resection of this tumor was performed by Doctor Bernard Stone. Histological examination of the tissue confirmed the preoperative impression of an infiltrating glioma - predominantly oligodendroglioma in type. The patient received postoperative radiotherapy, 5000 rads to the left hemisphere and an additional 1000 rads to area of tumor. When last seen in follow-up 4 years after surgery, the patient was still experiencing infrequent (1-2 per month) short focal seizures of the same type involving focal movements of right arm, plus speech arrest. The neurological examination demonstrated some decrease in spontaneous speech and some blunting of affect. However, she was fluent; naming of objects and repetitions was intact. Strength was intact. Reflexes were symmetrical but bilateral extensor plantar responses were present. She had a moderate frontal type apraxia of gait and required a cane to avoid falls.

Comment :This patient presented with seizures of focal origin. The description of the posture adopted by the arm at the very beginning of the seizure, raised the possibility that her seizures were originating in the supplementary motor cortex of the left hemisphere and then spreading into the motor and sensory area. The arrest of speech would be compatible with such an origin since there is a superior speech area located in relationship to supplementary motor cortex. The fact that the patient remembered much of the seizure would also be consistent with such an origin. The post ictal depression of motor and sensory function in right arm and right leg and the depression of speech would all be consistent with post ictal phenomena involving the left hemisphere, particularly its sensory, motor and speech areas. The fact that the EEG's had not been particularly remarkable would also be consistent with such an origin of discharge. Thus, the discharging focus may well be buried on the parasagittal surface and not accessible to recording electrodes at the surface.

As regards the underlying nature of the pathology, when the patient was seen 10 years after onset of symptoms, she now has some focal findings; in terms of a right Babinski sign and increased reflexes in the right arm raising the question of a low grade glioma such as an oligodendroglioma in this area. The previous “negative” CT scans would have ruled out a meningioma or arteriovenous malformation. The long history and the finding of calcification within the tumor all made oligodendroglioma the most likely diagnosis. Low grade gliomas of this type often produce seizures without producing major neurological findings .Thus frontal release signs were minimal.

The following case history provide an example of normal pressure hydrocephalus producing the triad of a gait apraxia, urinary incontinence and problems in memory.

Case 18-3: This 72-year-old retired white handed carpenter was referred for evaluation of progressive impairment of gait, and more recent problems, in memory. The gait problems began insidiously five years previously but had become more significant in the past six months. He described his walking as involving small steps and then “going forward at too fast a rate, with difficulty in stopping”. As a result, he would stumble and tend to fall forward, losing his balance. He had considerable fear of falling and made use of a cane to avoid falling. For the last four to five months, the patient had noted urinary frequency and incontinence. He kept a bucket with him at all times. “Once I have to go, I can’t hold on.” Memory problems had developed during the last two to three months related to the recall of recent events and new material. He would enter a room and be

unable to recall why he had entered the room. Emotional lability had also developed during the past year. It was difficult not to cry when he heard a sad story.

Past history indicated at least three myocardial infarctions.

Neurological examination:

1. Mental Status:

- a. Oriented for time, place and person.
- b. Delayed recall, even with assistance, was limited to 1/3 in five minutes.
- c. The patient often lost track of what he was saying or doing.
- d. Serial 7 subtractions was slowly performed but intact.
- e. Reading, writing, drawing and naming of objects were intact but spelling was poor.
- e. Abstract reasoning was intact.
- g. Affect demonstrated changes: At times, he was tearful; at times, inappropriately jocular.

2. Cranial Nerves: Intact except bilateral decrease in hearing - long standing.

3. Motor System: Intact except for gait. The patient walked on a broad base with small steps. He was slow in starting and then picked up speed. He was unsteady on the turns and tended to turn "en bloc". No rigidity and no tremor were present. Finger to nose and heel to shin tests were normal.

4. Reflexes: Deep tendon reflexes were hyperactive at patellar. Plantar responses were equivocal. No definite frontal release signs were present.

Clinical diagnosis: Frontal lobe syndrome with involvement of premotor and prefrontal areas. The combination of a frontal gait apraxia, memory impairment and urinary incontinence raised the question of normal pressure hydrocephalus.

Laboratory data:

- 1. *CT scan (Fig. 18-21):* Demonstrated markedly dilated lateral; third and fourth ventricles but with no enlargement of the sulci.

Figure 18-21 Normal Pressure Hydrocephalus - CT Scan - Case 18-3 A. Ventricular Enlargement B. Section Through Vertex: Demonstrating No Enlargement of Sulci PART II: Comparison patient with progressive multiple sclerosis involving cerebral hemispheres at relatively comparable levels of section demonstrating A. Ventricular Enlargement B. Accompanied by Enlargement of Cortical Sulci

- 2. Lumbar puncture studies were normal.

- 3. *Radio-isotope cisternogram (Fig 18-22)* demonstrated continued presence of isotope within the ventricular system with no reabsorption over the convexities - subarachnoid space at 24, 48, and 72 hours.

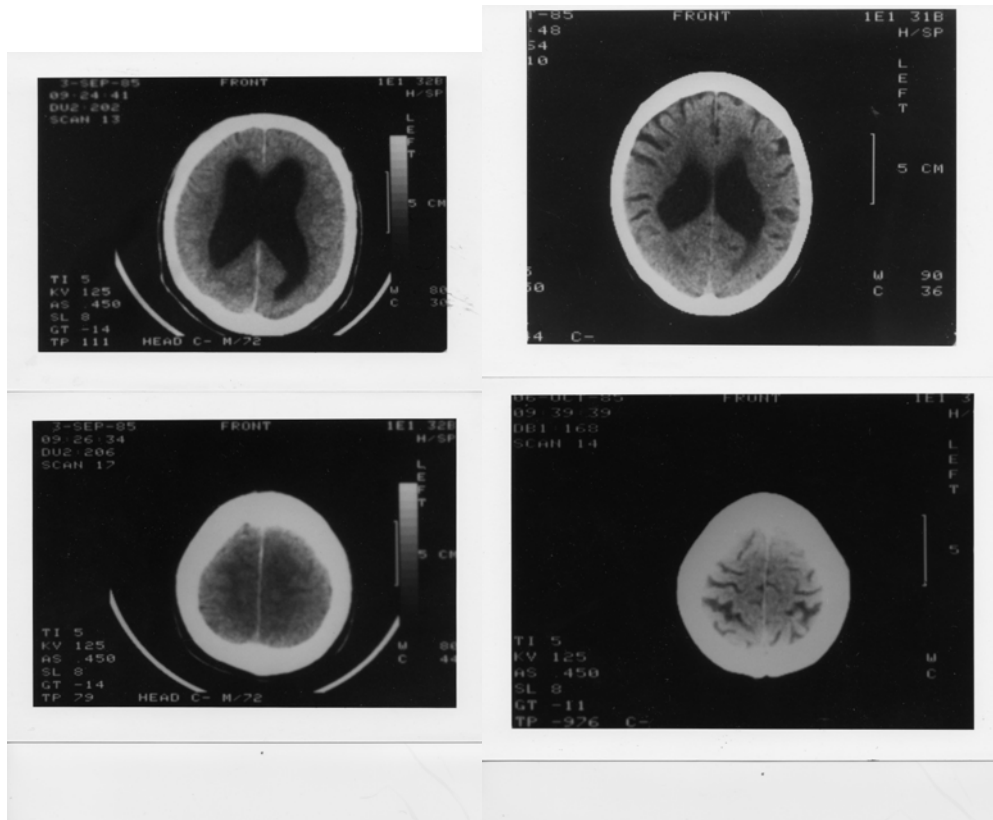
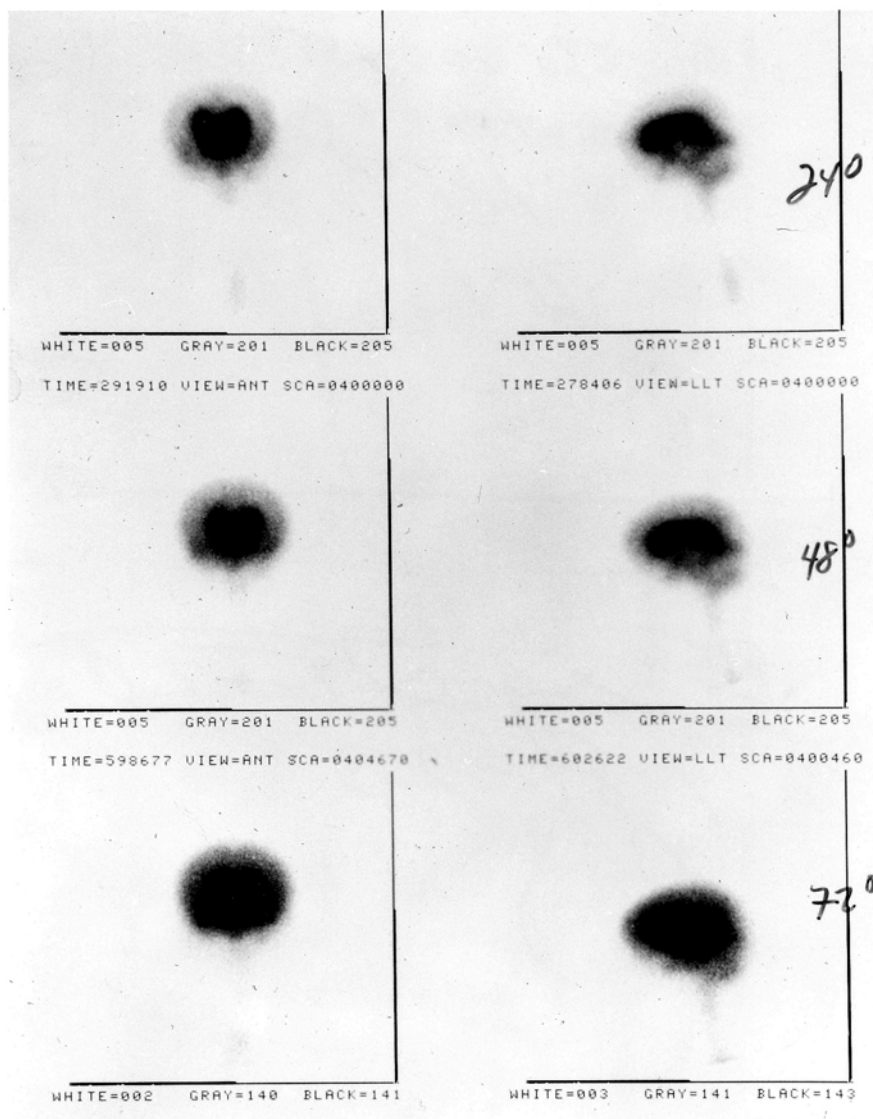


Figure 18-21. Normal Pressure Hydrocephalus Figure 18-21. Comparison Scan.

Figure 18-22: Normal Pressure Hydrocephalus: Isotope Flow Study: Lumbar CSF Injection Case 18-3 Isotope remaining in ventricular system at 24, 48 and 72 hours B. Comparison Case: Progressive multiple sclerosis of

cerebral hemispheres with enlargement of ventricular system but with enlargement of sulci. Isotope has begun to leave ventricles at 24 hours - appearing over the convexity and this is even more apparent at 48 and 72 hours.

Fig 18- 22. Normal Pressure Hydrocephalus; Isotope Flow Study



Subsequent course: Doctor Alex Danylevich performed a ventriculo-peritoneal shunt procedure (right lateral ventricle to peritoneal cavity). The patient did well with clearing of his triad of symptoms: Ataxia, dementia and urinary incontinence and was able to return to work as a carpenter , 12 hours per day. Subsequently , symptoms recurred due to infection of the peritoneal component of the shunt tube. Following revision of the shunt, symptoms improved only to worsen again in 6 months later. The patient had to use a wheelchair at times. A more marked apraxia of gait, frontal release signs, bilateral Babinski signs and urinary incontinence were present on examination 6 months after the revision. CT scan indicated a greater degree of ventricular enlargement. Following removal of 30 cc. of CSF, the patient was more responsive, and better oriented. Myocardial problems prevented additional neurosurgical revision of the shunt at that time. Subsequently, Doctor Robert Ojemann, of the Massachusetts General Hospital, revised the shunt utilizing a valve which allowed greater flow. At last evaluation, two years after admission, gait had improved (he was using a walker). Mentation was clearer (he was still described as showing aspects of a “frontal lobe syndrome”). Urinary incontinence was no longer present.

Comment: This patient presented a premotor/prefrontal syndrome .The imaging studies allowed a more specific delineation of the etiology of the syndrome. In most cases of normal pressure hydrocephalus, the gait disturbance is out of proportion to any change in mental status.

CHAPTER 19: MOTOR SYSTEM II: BASAL GANGLIA AND MOVEMENT DISORDERS

The following case presents an example of a patient with Parkinson's disease followed for 19 years.

Case 19-1 : This 48-year-old married white male, left-handed school master and physics teacher, was referred on 08/16/82 by his orthopedic surgeon for neurological evaluation of problems of control of the left arm and dragging of the left leg. Symptoms had begun 3 months previously with a sense of fatigue, stiffness and lack of control in the left arm. After a period of prolonged writing, he would have to make a conscious effort to continue writing. Approximately one month prior to the evaluation, he first noted a slowing down in movements of the left leg. "I have to remember to lift it."

Past medical history: Negative except for neck pain eight years previously related to cervical spondylosis, which cleared with the use of collar and traction except for occasional tingling in the 4th and 5th fingers of the left arm. Family history was unremarkable.

Neurological examination:

1. Mental Status: intact
2. *Cranial Nerves I-XII:* Intact except for a tremor of the closed eyelids and a positive glabellar sign (he was unable to suppress eye lid blinking on tap of forehead).
3. Motor System:
 - a. Strength : intact
 - b. Gait : There was a tendency to turn en bloc and a decreased swing of the left arm. However he could walk a tandem gait without difficulty.
 - c. There was a slight increase in resistance to passive motion at the left elbow, wrist and knee (rigidity without definite cogwheel component).
 - d. Although the patient was left-handed, there was a slowness of alternating finger movements of the left hand.
 - e. No tremor was present.
 - f. Handwriting was intact with no evidence of micrographia.
4. *Reflexes:* deep tendon stretch reflexes and plantar responses were physiologic
5. *Sensation:* all modalities were intact.

Clinical diagnosis: early Parkinson's disease, predominantly unilateral.

Laboratory data: all studies were normal including CT Scan of the brain, thyroid studies, blood chemistries, erythrocyte sedimentation rate, antinuclear antibody and serologic test for syphilis.

Subsequent course⁴: The patient did not wish to begin any treatment at that point in time. When evaluated 3 months later progression had occurred. He occasionally had the sense of moving slowly. He was now aware that with continuous writing, the writing became smaller, that is, micrographia emerged, evident on examination of handwriting. In addition, a minimal tremor was noted in the Archimedean spiral. A greater, but still minor, degree of cogwheel rigidity was now present at left wrist and elbow. Again, the patient was reluctant to begin therapy. On evaluation 1 year after onset of symptoms, additional progression was evident with significant micrographia (Fig. 19-6) and cogwheel rigidity now evident at left shoulder, elbow and wrist. Therapy with Sinemet (10-100 mg., t.i.d.)⁵ was begun. Re-evaluation one week later demonstrated a marked improvement in handwriting (Fig. 19-6) and decreased cogwheel rigidity.

⁴ This patient was followed for a total of 19 years after disease onset, initially for the first 13 years by the author, subsequently by Dr Paula Ravin at the University of Massachusetts Medical Center, Dr. David Standeart at the Massachusetts General Hospital and Dr. Warren Olanow at the Mount Sinai Hospital in New York.

⁵ This is a combination of 10 mg. of carbidopa (Dopa decarboxylase inhibitor) and 100 mg. of L-Dopa. Higher dosage combinations are a) 25 mg. of carbidopa with 100 mg L-Dopa, and b) 25 mg. carbidopa with 250 mg. L-Dopa. A sustained release form is also available (50 mg. of carbidopa with 200 mg. of L-Dopa), and is marketed as Sinemet CR.

As the dose of Sinemet was increased to (10-100) mg.5x/day over the next week, occasional choreiform movements of the fingers of the left hand and occasional backward flinging (hemi ballistic) movements of the left arm occurred. As the dose reached 10-100 mg. 6x/day, the patient reported that his handwriting now was back to normal. Examination confirmed the significant improvement in handwriting and in gait - with a better movement of the left leg. He no longer turned en bloc. Cogwheel rigidity was still present at left shoulder but to only a minimal degree at left wrist and elbow. The patient did experience 90 minutes after a Sinemet dose - a tremor of the left shoulder and an exaggerated grasp of the left foot toes on lifting the leg (possible form of dyskinetic or dystonic reaction).

The patient did well. When seen one year later, he had only a minimal degree of cogwheel rigidity. No tremor was evident. In walking he had a good swing of the arms and no longer turned en bloc. He was aware that some symptoms of his underlying disease would emerge 3-4 hours after a dose of Sinemet.

He continued to have progression of disease despite the use of all of the known anti Parkinson medications. He eventually underwent a fetal cell transplant in 1997 with apparently little improvement but with a significant increase in dyskinesias.

Re-evaluation, three years after onset of symptoms, indicated a minor progression with decreased swing of the arm and movements of the left leg, which were less smooth. The patient had increased his daily dosage of Sinemet to (10-100 mg) 6 (or) 7 tabs and noted that duration of action was approximately three hours. Re-evaluation, five years after onset of symptoms, indicated that despite having increased his dosage of Sinemet to 25-100 mg. tablets, 7 or 8 x/day, more resting tremor of the left hand had emerged. (In actuality 75-100mg of carbidopa is probably sufficient to saturate the peripheral dopa decarboxylase system). Moreover, choreiform movements of the left arm occurred 60 to 90 minutes after each dose of Sinemet. Examination demonstrated a pill-rolling tremor of the left hand as the patient walked down the hall. The choreiform movements disappeared when the dosage of Sinemet was reduced to 25/100mg 6/day. The increased rigidity and tremor responded to the addition of a DOPA agonist Bromocriptine (Parlodel) - Initial dosage 1.25 mg. 2x/day then increased to a total dose of 5.0 mg., and subsequently to 7.5 mg./day. Despite increasing dosage of the Bromocriptine to 17.5 mg/day - no additional improvement occurred. Additional reduction of Sinemet to (25-100) 5x/day - eliminated sudden myoclonic jerks and dyskinetic movement of the left lower extremity, which would occur - 45 minutes after a dose of Sinemet. Examination 6 years after onset of symptoms, examination and 3.5 hours after last dose of Sinemet demonstrated a coarse pill rolling tremor of the left hand and a shuffling of the left foot in walking. Marked cogwheel rigidity was present at left wrist and elbow. Considerable slowness of alternating finger movements was present. Handwriting was small and slow. Amantadine (an antiviral agent with mild ant parkinsonian effects), 200 mg./day was added at this point with a considerable improvement in symptomatology.

When examined 7 years after onset of symptoms, and 2.5 hours after Sinemet dosage and he now had a prominent tremor of the left hand at rest and a minor tremor of the right hand. Only minor cogwheel rigidity of left wrist and elbow were present. There was mild facial akinesia, tremor of the closed lids and a positive glabellar sign. As he walked he had a problem with sequential movements of the left leg. He reported that initially in the mornings, he had considerable problems in the initiation of movements of his left hand. Because effects of the Sinemet were wearing off in a shorter period of time - the dosing interval was altered to every three hours, in the process increasing total intake to 6 and then 7 tablets per day, with transient improvement. When seen 8 years after onset of symptoms, he was having sudden "kick in of the on effects" at 30-45 minutes and wearing off effects of greater degree at 3 hours after Sinemet dosage. As a result balance had shown some deterioration. Although tremor and cogwheel rigidity were primarily present left arm lesser symptoms were present in the right arm. At this point, a monoamine oxidase B. inhibitor was added: Selegiline (Deprenyl) in a total dose of 10 mg./day (5 mg., b.i.d.). When seen 6months later, the patient was uncertain that any benefit had been achieved. A major symptom was now "freezing" - he would have times in going over the threshold of a door when he would suddenly freeze. This, at times, related to the wearing off of medication (Sinemet) effect but at other times, usually in the afternoon, was unrelated to time of last dose. In the morning, freezing effect was clearly related to time of dosage. He remained relatively stable for the next year and then had a progression of symptoms - increasing tremor, increasing dragging of the left leg and more wearing off of dose effect - usually after 2.5 hours. In addition, "freezing" episodes were occurring more frequently in between dose wear off periods, usually in going through a doorway or even in hallways. At this point, the patient was switched to the sustained release form of Sinemet (50/200 mg carbidopa/L-Dopa) taken three times a day. Amantadine, Bromocriptine and Selegiline were continued unchanged. When evaluated 6 weeks later, there had been a remarkable improvement. He had a smoother day with fewer ups and downs, less dyskinesia and less stiffness. Effects of the medication were lasting 5-6 hours. When seen 3.5 hours after his last Sinemet dosage, he had

very little cogwheel rigidity. He could walk with a good swing of the arms. Handwriting was good with little tremor and little dyskinesia. On the other hand, when seen several weeks later, approximately 5.5 hours after his dose of sustained release Sinemet, he had marked difficulty, walked with small steps, and would arrest going through a doorway. Balance was poor, requiring a cane. There was a marked tremor of the left hand and to a lesser degree, of the right hand. A marked akinesia was present. However, within 20 minutes of his taking an additional tablet of sustained release Sinemet, a marked improvement again occurred. Despite this long course, the patient had been able to continue in his usual occupation. The patient subsequently was treated with a COMT inhibitor and was switched to another dopamine agonist pergolide with little apparent benefit. Eventually, in 1997 he was entered into the NIH sponsored fetal transplant study (subsequent imaging study did indicate that the patient was in the transplant and not the placebo group). It was unclear that this had produced any decrease in his disability. However evaluation 3 years after the transplant did demonstrate a marked increase in the dyskinesias involving head arms and torso. Some improvement in dyskinesias occurred when dopaminergic medications were reduced

Comment: Parkinson's disease is a progressive disorder of motor function, with variable manifestations of tremor, rigidity, akinesia, bradykinesia, and impairment of postural reflexes. Patients vary in the type of major involvement and in the rate of progression. Pharmacological management has rapidly evolved and in the process has provided considerable insights into the nature of basal ganglia function. For the specific patient, therapy must still be individualized. As this case history illustrates the pharmacological effects are time limited. Evaluation of therapy must always record the time of drug intake and the time of examination.

It is important to note that the disease remains progressive, despite the impressive pharmacological achievements. To prevent progression would require arresting or reversing the loss of the nigral cells producing dopamine or of introducing another source of dopamine producing neurons into the basal ganglia as discussed above. The future of fetal transplantation remains uncertain. Surgical procedures particularly deep brain stimulation involving the subthalamic nucleus or the globus pallidus may offer benefit to specific patients.

The following case, 19-2 provides an example of hemichorea.

Case 19-2 : This 88-year-old, right-handed, widowed white female with a past medical history of profound hearing impairment, adult onset diabetes, euthyroid goiter, coronary artery disease, and hypertension was brought by her daughter to Saint Vincent's Hospital because of uncontrollable movements ("twitching") of her left foot and shoulder. The daughter described the insidious onset of involuntary rotary movement in the left foot five days prior to admission, which increased in intensity and progressed to involve the left shoulder. The movements were constantly present, even during sleep. The movement was accompanied by a "shooting" pain on the left side of the body which the patient was not able to further describe. She denied loss of consciousness, dizziness, change in mental status, weakness, sensory impairment, visual changes, aphasia, or dysphagia associated with the movement disorder, but did describe a dull headache greater on the left side than on the right during the last few days prior to admission, not accompanied by nausea or vomiting. There was no history of a past movement disorder. Progression rather than spontaneous resolution of the choreiform movements which had begun to impair the patient's ability to ambulate with her walker prompted her daughter to seek medical attention.

Past history: The patient had been admitted briefly one year previously with confusion. and hyperglycemic state related to diabetes mellitus.

Physical Examination: vital signs were all normal.. Patient was alert and cooperative, though profoundly hard of hearing and exhibited involuntary twisting movements of her left foot and upward jerking movements of her left shoulder.

Neurological examination:

1. *Mental Status:* The patient was oriented x3. Memory and language were grossly intact, questions were answered appropriately, and mental status was consistent with the patient's baseline according to her daughter.
2. *Cranial Nerves:* Intact except: for Left eye blindness (cataracts), and gross impairment of hearing such that shouting was necessary to communicate.
3. *Motor System:*
 - a. Tone and strength in upper and lower extremities were normal except for minimal weakness in the left upper extremity(5-/5) .
 - b. Finger tapping, finger-to-nose and heel-to-shin were grossly intact with only slight left-sided difficulty due to involuntary movements.

- c. There was a persistent hemichorea without flinging motions in the left foot, more marked than the left shoulder. There were rotary, twisting movements at the left ankle and upward and rotary motions at the left shoulder. The movement was exacerbated by motor—tasks but did dissipate with sleep.
- d. Gait was slightly unsteady due to hesitant placement of the left foot. She did quite well with minimal assistance.
- e. Romberg was negative.
4. *Reflexes*: Deep tendon reflexes were symmetrical, and physiologic except for decreased Achilles secondary to diabetes. The right plantar response was flexor, the left ;extensor.
5. *Sensation*: Intact except for symmetrically diminished vibration sense in toes.

Clinical diagnosis: hemichorea

Laboratory data:

1. *Electrolytes creatinine, and CBC* were normal. *Glucose* was elevated to 168; *ESR* - 36 mm/hr. *RPR* non-reactive. *ANA* was 1:80(not significant) .*Urine culture* was positive for group B Streptococcal - infection sensitive to Ampicillin. *EKG and chest X-ray* were unchanged from last admission.
2. *CT scan* on admission revealed bilateral basal ganglia calcification, bifrontal atrophy consistent with age, but no evidence of infarction, hemorrhage, or tumor and revealed no change from previous CT scan of 2 months previously.
3. *MRI scan* 3 days after admission, revealed mild cortical atrophy and a hyperdense area without mass effect or enhancement on gadolinium in the right basal ganglia (particularly the head of caudate and putamen) and external capsule consistent with subacute hemorrhage (Fig.19-7).

Hospital course: The patient was begun on haloperidol 0.5 mg by mouth every morning and advanced to 1 mg., by mouth., t.i.d. with some improvement in the hemichorea, particularly in the upper - extremity. Her hemichorea continued to improve over the next two weeks on haloperidol with only occasional twitching of the left shoulder and diminished but persistent, rotary movement of the left foot, both still exacerbated by motor tasks.

The following case 19-3 provides an example of hemiballismus

Case 19-3: This 79-year-old, right-handed, white housewife had the abrupt onset in the early morning hours, 2 days prior to admission, of almost constant flinging movements of the right arm over which she had no control. At the same time, she noted that her right arm felt numb and heavy. Over the next 2 days, the movements decreased markedly and she regained more control of the arm.

Past history: The patient had been a known diabetic for 21 years, receiving insulin - most recently, lente insulin, 25 units each morning.

Neurological examination:

1. *Mental Status*: intact ,the patient was alert and well oriented and without aphasia.
2. *Cranial Nerves*: All were intact.
3. *Motor System*:
 - a. Minimal weakness was present in the right upper extremity at the elbow, wrist and fingers
 - b. Alternating movements and finger-to-nose testing in the right hand were markedly impaired.
 - c. Gait was intact.
 - d. Occasional involuntary flinging movements occurred at the right shoulder.
4. *Sensory System*: Pain, touch, vibration and position sense were all absent in the right upper extremity to the elbow and decreased in this extremity above the elbow.

Clinical diagnosis: hemiballismus

Laboratory data: Chest and skull X-rays EEG, and cerebrospinal fluid studies were all normal.

Subsequent course: The flinging movements of the right arm subsided spontaneously, shortly after admission. Position sense returned and pain sensation showed a mild improvement. The ataxia on finger-to-nose testing disappeared.

Comment: The loss of pain, touch, vibration and position sense in the right upper extremity at the onset of symptoms in this case, would suggest a lesion involving the ventral posterior lateral nucleus of the thalamus, presumably as a result of occlusion of the penetrating branches of the

posterior cerebral artery. Such a lesion could have damaged the subthalamic nucleus as well. The severe dysmetria in the right upper extremity could well have reflected the severe sensory deficit in the right upper extremity. This would appear to be more likely than postulating a lacunar ataxic hemiplegia, due to involvement of the corona radiata in which the origin of the hemiballistic movements could have been in the adjacent caudate putamen. This however would not explain the severe sensory deficit. Note that the use of antidopaminergic agents will decrease or eliminate hemiballismus or hemichorea; however many patients as in this case resolve spontaneously.

The following case history provides an example of Huntington's disease.

Case 19-4: This 54-year-old right-handed divorced white female was referred for evaluation of a movement disorder. The patient lived alone and it was difficult to obtain much of any history from the patient. So far as she was concerned, she had no neurological problems. She denied any problem with her movements. She did indicate that she had worked for 10 years as a secretary/computer operator but had been fired 10 years ago because "she did not work fast enough". She did indicate that she had experienced problems with memory over the last year. The patient denied that she had never been treated on a psychiatric service. She denied receiving neuroleptics. She had a past history of hypertension but had not been reliable in taking her prescribed medication. The patient's son was aware that changes in emotion, personality, speech, gait and a movement disorder had been present for at least 3 years.

Family history: The patient denied any neurological family history except for a maternal uncle who had the "shakes". By contacting the patient's son age 27 and her mother now age 81 and then obtaining old records we were able to assemble additional information. The patient's father had been hospitalized at age 55 on the psychiatry service of St. Vincent Hospital. A review of that record indicated that for several years he had been showing irritability, had become suspicious and paranoid at work. He gave a history of choreiform movements of 20–30 years duration beginning with twitchings about the shoulders. This had progressed over the several years prior to admission, affecting his gait and the movements of the hands. The examination demonstrated that he was moderately depressed and impatient. As he sat, he had "purposeless" movements of his body particularly of the lower extremities. In walking he had "ballistic" movements. He walked on a broad base. Choreiform movements were noted in the tongue. The diagnosis of the neuropsychiatrist was Huntington's disease. He apparently died of cardiac disease shortly after that hospitalization.

The paternal grandfather had died at age 43 of pneumonia, the paternal grandmother at age 37 of gall bladder disease, neither was known to have Huntington's disease, but information was scanty. The patient's father had two siblings one alive at age 81, the other dead at age 68, both apparently unaffected. The patient's mother had a sister with essential tremor.

The patient had 2 siblings, a brother age 60, a sister age 44; both unaffected according to the patient's mother.

The patient had 4 children ages 34, 32, 30 and 27, and 3 grandchildren ages 13 years, 2 years, and 3 months. The eldest daughter age 34 had been depressed for 5 years and had problems with speech and walking for a number of years.

Neurological examination:

1. *Mental status*: the patient often avoided eye contact. Affect was usually inappropriate with laughter as the response to many questions. The overall mini-mental status score was 27/30. The only deficit related to delayed recall portion of the test (0/3 objects).

2. *Cranial nerves*: the patient had a hyperactive jaw jerk. She had frequent facial grimacing.

3. *Motor system*: the patient had decreased tone at wrists and elbows, but strength was intact.

As she sat she had frequent restless and at times choreiform movements of hands and feet.

Gait was often "bizarre" in terms of occasional sudden movements of a leg as moved down the hall and came to a stop. These same movements occurred as she remained standing. In addition in standing or walking, there were intermittent dystonic postures of either left or right arm.

4. *Reflexes*: Deep tendon stretch reflexes were everywhere hyperactive. Plantar responses were flexor. There was a minimal suggestion of grasp release.

5. *Sensory system*: intact

Clinical diagnosis: Huntington's disease.

Laboratory data:

1. *MRI scans of head* (Fig.19-13): The heads of the caudate nuclei were very atrophic. Cortical sulci were wide consistent with cortical atrophy. The lateral and third ventricles were secondarily dilated.
2. PCR testing for the CAG trinucleotide repeats of the Huntingtin gene.: allele 1=17; allele 2=42.
3. Thyroid studies, sedimentation rate, electrolytes, RPR, and antinuclear antibody were all normal.

Subsequent course: The patient refused any treatment for the movement disorder. The patient's son requested genetic testing and the issues were discussed. He and his siblings finally decided not to have the genetic testing performed. The patient's neurological status according to the son worsened to a moderate degree over the subsequent 3 years as regards speech, unsteadiness of gait, and mood swings but without any additional change in memory. The patient herself always appeared unaccompanied for follow up visits and reported no change in her condition.

Comment: Occasionally patients are encountered where changes in psychological function limit the information that the patient can provide.. In other cases denial of illness has a neurological as well as a psychological basis. In this case it was evident that this patient had not only symptoms relevant to the basal ganglia but also changes in cognitive function relevant to the cerebral cortex particularly the frontal areas. In such cases, information must be sought from other sources. In this case, the patient was willing to provide permission to contact those possible sources.

The clinical presentation in this case was clear-cut. In retrospect, many of the neurological features were similar to her father's findings on his admission 30 years previously. When did the patient's disease begin? This was uncertain, but we may presume that serious problems had been present at least 10 years earlier when she had been fired from her long time employment. Did this relate to motor problems, to changes in personality and interpersonal relations or to cognitive changes? Most likely, there were problems in all of these areas. According to her family, symptoms had been present for 2-3 years suggesting onset at age 51 or 52 years.

Case 19-5 provides an example of a patient with Huntington's disease followed over a longer period of time.

This 32 year old right-handed married white male spray painter at a computer factory, was referred for evaluation of a possible hereditary movement disorder. The patient was unclear about the reasons for his evaluation and much of the history was provided by his wife. She reported that the patient had undergone a personality change in the last several months. He had noticeable mood swings and on one occasion he reported people outside the window when no one actually had been there. He had some problems with remembering incidental matters, but no major problems and his job performance had remained intact. He was described as always having been "fidgety".

Past medical history - Mild hypertension for three years.

Family history - The patient's initial history indicated that the family had "Parkinson's" disease and his father had died in his 40's at the state hospital after a 10-15 year illness. The patient indicated that he was a child at the time and his mother never really told him much about the father or let him visit the father in the hospital but he did recall that perhaps his father had some excessive movements of the hands and face. The records were subsequently obtained and these indicated the father had been admitted to Worcester State Hospital in 1968 at age 37. At that time, he had already had three previous hospitalizations for "nervous breakdowns". At the time of his final admission, he had developed hallucinations, seeing people in his room. He had threatened his wife and other relatives. He had difficulty sleeping and he had also developed a problem with his legs "they are jumping". The father's examination had demonstrated a mumbled speech with repetition of the same phrases. His responses would often be tangential and then incoherent with impairment of memory and judgment. His mood was depressed. He was noted to have involuntary movements of the fingers and occasional facial grimacing. The deep tendon reflexes were hyperactive and the plantar responses were extensor. His gait was ataxic. The subsequent course indicated increasing ataxia, choreiform movements and rigidity with increasing weakness, difficulty swallowing and the final development of bronchial pneumonia with death at age 42. The diagnosis of Huntington's disease was confirmed at autopsy.

The paternal grandfather had expired at age 67 with a diagnosis of Huntington's disease, manifested by "nervous breakdowns, inability to sleep and movement disorder". The father's three siblings apparently did not manifest the disease. The patient had two siblings, brother age 28, a sister age 35, all without known disease. He had two children ages 9 and 5.

Neurological examination

1. *Mental Status* - The patient was anxious, often appeared blunted in emotional expression or in answering questions. He avoided eye contact. He was oriented for time, place and person. He was able to name objects and colors. His delayed recall was 2/5 without assistance and 4/5 with assistance.
2. *Cranial Nerves II-XII* were intact, except for the occurrence of occasional, sudden darting movements of the eyes to either left or right. In addition, occasional facial grimacing was noted occurring in a rather irregular manner.
3. *Motor System* : Strength and gait were intact . There were occasional, sudden, irregular, lateral, tremulous movements of the fingers of a choreiform-type.
4. *Reflexes* : Deep tendon reflexes including the jaw jerk were everywhere hyperactive. Plantar responses were bilaterally extensor (bilateral Babinski signs).
5. *Sensory system* : intact

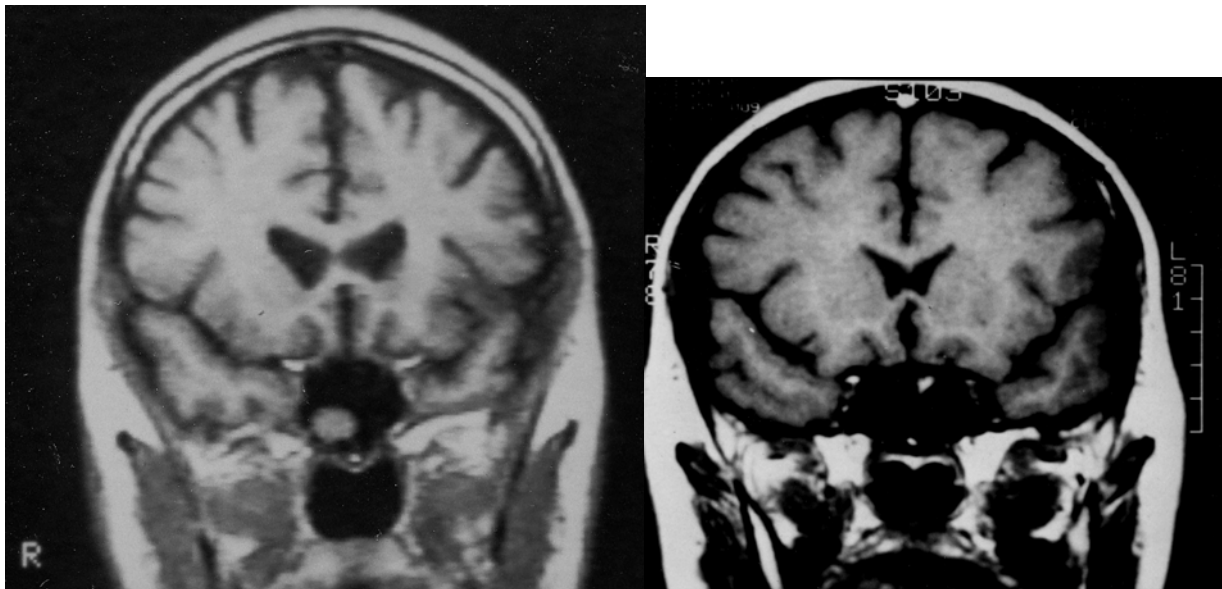
Clinical diagnosis: Huntington's disease

Laboratory Data :

1. All blood chemistries, including glucose; BUN, calcium, electrolytes, liver function studies, ceruloplasmin level, thyroid studies and serological test for syphilis were within normal limits. Ceruloplasmin levels are low in Wilson's disease but normal in Huntington's disease.
2. *Electroencephalogram* was normal with a dominant awake background activity of 10 Hz alpha rhythm.
3. *CT scan of the head* demonstrated enlargement of the ventricles with particular atrophy of the caudate. In addition the sulci were prominent for the age, suggesting some degree of cortical atrophy. The study was considered consistent with the clinical diagnosis of Huntington's disease.
4. The *MRI scan* (fig 19-11A) demonstrated mild enlargement of the ventricles and deepening of the cortical sulci, as well as a very significant atrophy of the head of the caudate nucleus. The MRI from this patient is compared to a similar section from a patient without signs of neurological disease (Figure 19-B)..

Figure 19-11A ;Case 19-5. Huntington's Disease

Figure 19-11B. Normal, age matched



Subsequent course :The patient subsequently developed increased paranoid ideation, increasing dependency with regard to his wife. He was treated with Haloperidol (a neuroleptic, tranquilizer) with considerable improvement with regard to personality. When evaluated, 3 years after onset of disease, it was evident that in the interim, the patient's personality problems had decreased. Attacks of anger and paranoid features had subsided. Mood swings were less. Memory problems, however, were worse and choreiform movements were worse. Dysarthria was now present. The patient had been divorced in the interim and he was on social security disability and no longer working. The examination now showed an exacerbation of many of those features noted at the time of his initial evaluation. He had occasional, sporadic movements of head or eyes of a

choreiform nature. He had frequent choreiform movements involving the fingers as he was sitting, also a similar type of movement appeared to involve the abdominal musculature. He had a moderate degree of dysarthria. He could walk a tandem gait but as he did so, the left arm came up in an somewhat flexed position. When last seen 4 years after onset of disease, he had more dysarthria and his speech was more difficult to interpret. There had been some increase in degree of rigidity but this had decreased when the dose of haloperidol had been decreased. The decrease in this medication, however, then resulted in a greater prominence of the choreiform movements. He could still handle a deck of cards, although he was dropping objects more often than previously. His neurological examination showed a significant degree of dysarthria, a greater degree of facial akinesia, more frequent choreiform movements of hands and face. He had difficulty in mimicking facial expression. As before, all of his deep tendon reflexes were hyperactive and the plantar responses were extensor. The patient walked in a flexed position and tended to turn en bloc. He had a mild degree of cogwheel rigidity at wrist and elbows. His memory remained remarkably good for delayed recall. Final telephone follow-up with his primary physician (approximately 7 years after apparent clinical onset of disease) indicated that the patient was no longer able to drive. He had continued weight loss. He had a marked dysarthria so that his speech was barely intelligible. Choreiform movements had increased. His gait was ataxic, but he could still walk without stumbling. He was relatively stable from a psychiatric standpoint. He was now living with his mother and brother.

Comment: This patient and his family demonstrate the relatively typical course of most patients with Huntington's disease. Patients and families do vary as to whether it is the psychiatric features or the movement disorder features that first bring the patient to medical attention. In this case, the psychiatric features, that is, the change in personality and the increasing paranoid ideation were the first features noted. Subsequently, involvement of the motor system became the most prominent feature. As in the previous case, the patient was unclear as to why he had come for neurological evaluation. Was this a neurological or a psychological denial of illness? Most likely both factors were operational. It was of considerable interest that this patient when first seen, although he was aware of some neurological problem that had occurred in the family, was unclear as to the specific diagnosis. It was also evident that almost no genetic counseling had been done in a disorder that was very clearly an autosomal dominant disorder. The significant family impact, social and economic impact of the disease are clearly evident in this patient. The implications of presymptomatic detection are discussed by Meisser et al (1988), and Klawans (1972).

The following Case 19-6 illustrates the clinical problem of hepatolenticular degeneration in a 21 year old female with a brother who had died at age 16 with hepatic disease, a Kayser Fleischer ring and choreoathetosis. The patient had serum elevation of free copper and a decrease in protein bound copper. She was successfully treated with penicillamine.

Case 19-6 (Patient of Doctor Huntington Porter) :This 21-year-old, single, white female shoe worker in January 1954 had the onset of a "shaking", or trembling of the fingers and hands which progressed to involve both arms and legs. The degree of involvement increased sufficiently to force her to give up her work. Nine months after onset of symptoms, she began to note increasing difficulty with balance and coordination and a slurring of speech. She had also noted increasing weakness and difficulty in doing repetitive tasks. One year after onset, the patient noted blurring of vision, occasional diplopia, and periods of "staring". She also had experienced increasing urgency and occasional urinary incontinence.

Family history: A brother of the patient had died in 1952, at age 16, of a disease with manifestations similar to this patient's. Evaluation of the sibling 2 years before his death by Drs. John Sullivan, Raymond Adams and D. Denny-Brown, had indicated the presence of choreoathetosis with lapses in posture of the hands. In addition, a brownish green ring at the corneal -

scleral junction was noted. Liver disease was present in this sibling and possibly other members of the family.

Neurological examination:

1. Mental status:

- a. The patient was anxious, at times crying, at other times, euphoric.
- b. Digit span was limited to 6 forward, 3 in reverse.
- c. Serial 7 subtractions were poorly performed.

2. Cranial Nerves:

- a. A brown rim was present at the limbus of the cornea, more evidence inferiorly and superiorly.
- b. Extraocular movements were impaired by involuntary jerk movements, The patient was unable to track a moving finger.
- c. Facial expression was mask-like.
- d. Speech was dysarthric and of a nasal quality with slurring and slowness of articulation.

3. Motor System:

- a. No actual weakness was present. However, this patient had difficulty maintaining the limbs in a fixed posture.
- b. There was a rigidity to passive movement of the limbs.
- c. A coarse arrhythmic tremor was present which was most marked proximally and more marked on sustained posture and on movement than at rest.
- d. Alternating movements were poorly performed.
- e. Gait was ataxic. Romberg test was negative.

4. Reflexes: Deep tendon stretch reflexes were hyperactive but plantar responses were flexor

5. Sensation: Intact

Clinical diagnosis: Wilson's disease: hepatolenticular degeneration.

Laboratory data:

- 1. Liver function tests were normal.
- 2. *Glucose tolerance test* was normal, but glycosuria occurred.
- 3. *Total plasma copper* 52 ug/100 ml. (normal range in a young adult is 65 to 150 ug/100 ml).
Direct reacting copper (unbound to ceruloplasmin) 31 ug/100 ml (normal 10 ug/100 ml).
Indirect copper (ceruloplasmin bound) 21 ug/100 ml, normal 105 ug/ ml).

Subsequent course: The patient did relatively well following the use of the chelating agents, BAL and calcium versenate and the institution of a copper free diet. A liver biopsy performed at the time of a cesarean section 18 months after beginning treatment was compatible with perihepatitis with a question of post-necrotic cirrhosis.

Re-evaluation 6 years after onset revealed, in addition to the earlier findings, the presence of "continual spontaneous involuntary movements of the limbs; at the feet, characterized by alternating flexion and extension at the ankle and a waving of the toes". A broad amplitude coarse tremor was noted when the patient was asked to abduct arms, flex elbows, and hold hands just before her nose (wing beating position). A side-to-side tremor of the head was also present. The gait was slightly wide-based and associated with continual dystonic movements of the hands and arms. Treatment with d-penicillamine (which had just become available) was begun at that time.

Urine copper excretion increased from 700 ug per 24 hours to 3240 ug per 24 hours. Normal 24-hour urinary copper in the adult is less than 40 ug. Neurological symptoms soon demonstrated improvement from the previously noted status. The patient was now able to do her house work and take care of her children.

Follow-up 2 years later, indicated significant improvement as regards the findings noted in 1960; dystonic facies and dysarthria was less marked. No tremor was present in the left hand; that in the right hand was evident only when under tension. Dystonic posturing of the hands was present only to a minimal degree. At last report 4 years later, and 12 years after onset of the disease, the patient continued to do well. She had remarried and was expecting another child.

Comment:

This patient presents a typical case of Wilson's disease with onset in the young adult years and with a definite familial background. The copper levels were consistent with the diagnosis (an increased unbound fraction and a decreased bound fraction). At the time that this patient was seen in the mid 1950's and early 1960's, ceruloplasmin levels were not available. Early establishment of a specific diagnosis in this case allowed for specific therapy with improvement of neurological symptoms and the prevention of progression of hepatic disease. With a specific diagnosis established in the patient, periodic blood tests were performed on her offspring to determine whether they also had inherited this genetic disease. (The child born 18 months after onset of the disease had not the disorder.)

An acquired form of non-Wilsonian hepatic and cerebral degeneration occurs in patients who have had multiple episodes of hepatic coma. Degenerative changes occur in the astrocytes and neurons of the basal ganglia. This disorder which was first described by Adams and Victor is discussed in greater detail above.

CHAPTER 20. MOTOR SYSTEMS III: CEREBELLUM

The following case provides an example of a child with a medulloblastoma.

Case 20-1: This 27-month old white female was referred for evaluation of ataxia. The mother had noted that the child had been unsteady in gait, with poor balance, falling frequently since the age of 13 months, when she began to walk. Three months prior to admission, in relation to a viral infection manifested by fever and diarrhea, the patient developed increasing anorexia and lethargy. One-month prior to admission, vomiting increased, and the patient also became more irritable. Perinatal history had been normal, and head circumference had remained normal.

Neurologic examination:

1. *Mental Status:* The child was irritable but cooperative.
2. *Cranial Nerves:* The fundi could not be visualized. Bobbing of the head was present in the sitting position.
3. *Motor System:* A significant ataxia of the trunk was present when sitting or standing. Gait was broad-based and ataxic, requiring assistance. No ataxia or tremor of the extremities was present. Strength and tone were normal.
4. *Reflexes:* Deep tendon reflexes were symmetric and plantar responses were flexor.
5. *Sensory System:* All modalities were intact.

Clinical diagnosis: Probable midline cerebellar tumor, most likely based on age a medulloblastoma

Laboratory data:

1. *Left brachial arteriogram* indicated an avascular area in the posterior fossa. The superior cerebellar artery was elevated. The inferior cerebellar arteries were depressed.
2. *Air-contrast ventriculogram* demonstrated enlargement of the lateral and third ventricles. The cerebral aqueduct was displaced forward to a marked degree. The fourth ventricle was deformed by a mass overlying the posterior wall (essentially located in the nodulus).

Hospital Course: Doctor Peter Carney performed a suboccipital craniotomy. The dura was bulging. The cerebellar tonsils were herniated to a minor degree. On gentle retraction of the inferior posterior vermis, a pinkish gray tumor, originating from a higher point in the fourth ventricle, was visualized at the obex. Limited biopsies of this tumor were taken, revealing a medulloblastoma. Samples of cerebrospinal fluid obtained at surgery revealed the presence of many malignant cells. A permanent shunt from the lateral ventricle to the jugular vein was not installed because of the possibility of spread of tumor cells into systemic circulation. Instead, a catheter was connected from the lateral ventricle to a small reservoir inserted under the skin of the scalp to allow daily drainage. Radiation therapy to the entire central nervous axis was begun one week after surgery. By the time of hospital discharge two weeks after the operation, the patient was able to walk unassisted, with only a moderate degree of ataxia. Three months after the operation, the patient was readmitted because of recurrent irritability and vomiting. A mild degree of papilledema was present. Horizontal nystagmus was present on lateral gaze bilaterally. A wide-base ataxic gait was still present. Various antineoplastic agents were employed (methotrexate into the cerebrospinal fluid and vincristine intravenously) without significant improvement. One month later, respirations became slow, deep, and irregular and death occurred. The findings at autopsy are demonstrated in Fig. 20-4.

In the following case a metastatic tumor in the midline cerebellum produced vertigo, ataxia of gait and headaches.

Case 20-2: This 67 year old white female 6 weeks prior to admission developed intermittent vertigo. Two weeks prior to admission she developed an ataxia of gait. Two days later headaches and true vertigo developed, ataxia increased and vomiting occurred. On the day of admission severe vertigo, headache and nausea and vomiting resulted in her visit to the emergency room

Past history: The patient had a lumpectomy 6 years prior to admission for carcinoma of the left breast. She had undergone a radical mastectomy followed by radiation therapy 3 years prior to admission for a recurrence of malignancy. Histologic examination of the excised tissue indicated a very poorly differentiated (high grade of malignancy) infiltrating ductal tumor which was negative for estrogen and progesterone receptors. On both occasions, the patient refused chemotherapy. The patient had multiple other medical problems including non insulin dependent diabetes mellitus, coronary artery disease, mild hypertension, and prior hip replacement surgery.

Neurological examination (in the emergency room)

1. **Mental Status:** Intact
2. **Cranial Nerves:** Intact except for an absence of venous pulsations on funduscopic examination suggesting a mild increase in intracranial pressure without frank papilledema.
3. **Motor System:** The patient had difficulty standing tending to fall to the right. She was unable to walk because of severe ataxia. There was no limb dysmetria.
4. **Reflexes:** Deep tendon stretch reflexes were symmetrical. The right plantar response was equivocal.
5. **Sensory system:** Intact

Clinical diagnosis: Midline cerebellar tumor metastatic from breast.

Laboratory data :

1. **CT scan of brain:** A large (3-4 cm) enhancing tumor was present involving the midline vermis and right paramedian cerebellum and compressing the fourth ventricle.

2. **MRI of brain** (3 days after admission): An enhancing midline mass involved the cerebellar vermis extended into the right cerebellar hemisphere, and produced mass effect upon 4th ventricle (Fig. 20-5).

3. **CT scan of abdomen** demonstrated two solitary possible metastatic lesions in the liver.

Subsequent course: The patient was immediately placed on dexamethasone with significant improvement. Within 12 hours the examination demonstrated only a mild ataxia tandem gait on turns and bilateral extensor plantar responses. The patient strongly insisted on removal of the solitary central nervous system metastases. Histological examination of the tumor resected by Dr. Gerald McGullicuddy demonstrated poorly differentiated adenocarcinoma with extensive necrosis similar to the tumor which previously had been removed from the breast. Following surgery she received 3000cGy(rads) whole brain radiation and was begun on the antitumor agent tamoxifen. She continued to manifest some unsteadiness on gait but had no difficulty in finger to nose or heel to shin tests. Three months after her admission, a repeat CT scan of the abdomen and pelvis demonstrated diffuse hepatic metastases with mesenteric and retroperitoneal lymphadenopathy. She expired at home, four

months after surgery before she was to start additional treatment with the antineoplastic combination of Cytosan, methotrexate and 5-fluorouracil.

Comment: This patient had a highly malignant poorly differentiated adenocarcinoma of the breast and was clearly at risk for the development of distant metastases, a risk that was likely increased by her unwillingness to receive antitumor medication. Six years after the lumpectomy she presented with vertigo, ataxia headache and nausea and vomiting, without limb dysmetria. These symptoms suggested involvement of those areas of cerebellum related to the vestibular system and the axis of the body: the floccular nodular area and vermis. Certainly, the best treatment of a solitary metastatic brain tumor where systemic metastases are not present is the combination of total resection of the brain lesion followed by radiotherapy. However at the time of surgery, this patient already had evidence of two probable metastatic lesions in the liver. Except for the strong insistence of the patient that the tumor in brain be removed, an alternate course of radiotherapy, dexamethasone and chemotherapy might have been pursued. Nevertheless the patient had several additional months of life during which she was able to travel to visit various relatives for a last time. Consistent with the highly malignant character of the tumor, this patient succumbed to the non neurologic effects of her disease.

The following case history 20-3 illustrates the problem of alcoholic cerebellar degeneration.

Case History 20-3: This 64-year-old, white male was admitted with a chief complaint of a slowly progressive incoordination of gait present for 8 years. The patient and others had noted that his gait was staggering. The patient denied weakness, numbness, diplopia, vertigo, or memory difficulty. The patient admitted to the consumption of one half pint (250cc) of brandy every 4 nights since symptoms had developed. He indicated that he used to drink more in his younger days, at least 6 to 8 beers in addition to brandy or other alcoholic beverages every night.

There was no history of pes cavus or neurological disease.

General physical examination: Blood pressure 140/80. Liver was enlarged with the inferior edge extending 2 finger breadths beyond the costal margin. Face was red with dilation of vessels.

Neurological examination:

1. *Mental status:* The patient was slightly disoriented for time. He gave the date as September 31. The date was actually October 19. Delayed recall was 0-out-of-5 objects in 5 minutes. He was unable to give the date of his birth, but he knew his phone number. Digit span was 7 forward, 4 in reverse. Calculations: The patient was unable to subtract 7 from 100 or 3 from 30; he could not add 14 and 13, although he had a fourth grade education.

2. *Cranial nerves:* All were intact. No nystagmus was present.

3. *Motor system:* Strength was intact. Gait was broad-based with an ataxia of trunk. The patient was unable to walk a tandem gait. His ataxia was accentuated by rapid walking. Small lateral nodding movements of the head were noted. He was relatively stable when sitting. There was a minimal tremor at rest. In addition, there was, to minor degree, a resistance to passive motion at the wrists and elbows with a suggestion of a cogwheel component. There was a minor tremor on finger-to-nose testing and a minor impairment of alternating hand movements.

There was, however, a very significant heel-to-shin ataxia which was out of proportion to any tremor or ataxia involving the upper extremities.

4. *Reflexes:* Deep tendon reflexes were physiological and symmetrical (2-3+). Plantar responses were flexor bilaterally.

5. *Sensory system:* Position, pain and touch were intact. There was a moderate decrease in vibratory sensation at the toes and ankles.

Clinical diagnosis: 1. Alcoholic cerebellar degeneration. 2. Mild dementia possible residuals of Wernicke's-Korsakoff syndrome.

Laboratory data: Complete blood count, albumin and total protein, sedimentation rate, cerebrospinal fluid, and skull and chest X-rays were normal.

Subsequent course: The patient received multiple B vitamins and was advised to discontinue any intake of alcohol. Neurological re-evaluation over the next 6 years indicated that no essential progression had occurred.

Comment: The major findings of the broad-based, staggering gait with truncal ataxia and heel-to-shin ataxia may be related to the anterior lobe of the cerebellum. In view of the absence of progression after the discontinuation of alcohol, a toxic or nutritional factor may be postulated (The reliability of the history obtained, in terms of the specific amount of alcohol intake is always open to question particularly in a patient

with significant problems in memory. The amount stated by the patient is usually assume to be the minimum amount.). The minor extrapyramidal findings of cogwheel rigidity may have represented unrelated disease. The lack of progression would be evidence against the diagnosis of a cerebellar degeneration of other etiology (see below). The minor degree of dementia may have related to previous nutritional problems with minor Wernicke-Korsakoff's syndrome or may have reflected a minor unrelated dementia or may have related to long standing retardation. At the present time, the diagnosis may be confirmed by CT scan or by MRI (midline sagittal section) (as in Fig. 20-7 or 20-8). As a result, evidence of cerebellar atrophy is now found in many patients presenting with other aspects of chronic alcoholism or other nutritional disease who do not necessarily present with initial symptoms of ataxia.

In the following case, a similar cerebellar gait disorder and heel to shin ataxia occurred o a genetic basis.

Case 20-4: A 45-year-old single white male carpenter presented with a 4 year history of progressive unsteadiness in walking, present during the daytime as well as at night. He had, during this period, noted minimal loss of coordinated movements in his hands, but felt that his greatest deficit was unsteadiness. The patient had noted no actual weakness but reported some numbness at the toes. He had also noted some minor difficulty in swallowing.

The patient lived in a small town in Virginia. Family historical information was incomplete His mother and father were second cousins. Several aunts and uncles had "trouble with their legs" in later life, resulting in a difficulty in walking. The patient admitted to a minimal intake of alcohol in the past. He had recently been under the care of a naturopath and had experienced a 7-pound weight loss.

Neurologic examination:

1. *Mental status:* Intact and consistent with his educational level.
2. *Cranial nerves:* Intact except for minimal dysarthria. Horizontal nystagmus was present on lateral gaze, vertical nystagmus on upward gaze.
3. *Motor system:* Strength was intact. The patient walked on a broad base with an ataxia of trunk, as though intoxicated, reeling from side to side, with marked unsteadiness on turns. He was unable to walk a tandem gait with eyes open. The patient was able to sit without significant ataxia of the trunk. A mild intention tremor was present, and there was minimal disorganization of alternating movements. In contrast a marked ataxia and tremor were evident on heel-to-shin test.
4. *Reflexes:* Deep tendon reflexes were intact, except for a relative decrease in ankle jerks compared to knee jerks. Plantar responses were flexor.
5. *Sensory system:* Intact, except for a minimal decrease in vibration sensation at the toes.

Clinical diagnosis: Hereditary cerebellar degeneration involving predominantly anterior lobe

Laboratory Data: Pneumoencephalogram performed at the University of Virginia Hospital (Doctor Stewart) confirmed the significant atrophy of cerebellum. Cerebrospinal fluid and other laboratory data were normal.

Comment: This patient had onset of ataxia at age 41 and was seen relatively early in his disease course. The most prominent features included the ataxia of gait and the heel to shin dysmetria. The patient also had a minor dysarthria, nystagmus and a mild asymptomatic peripheral neuropathy (decreased Achilles reflexes and decreased vibration at toes). There was a familial background but the information was incomplete. The subject of genetic cerebellar degeneration will be considered in a later section. Using older terminology, this patient would have been classified as olivopontocerebellar atrophy. Using more modern terminology, the patient might be included within the category of autosomal dominant cerebellar ataxia type I, had more genetic information regarding the family been available by history and or actual examination.

The following case history illustrates a focal lesion of the lateral hemisphere

Case 20-5 : This 36-year-old white male attorney was referred with a chief complaint of headaches and vomiting. The patient had frontal and biparietal headaches for approximately one month precipitated by coughing, sneezing, or bending. On at least one occasion, the patient had been awakened by the headache. The patient had nausea and vomiting independent of the headaches, at times, occurring suddenly without preceding nausea. For several weeks prior to admission, the patient had been unsteady on his feet, with a tendency to fall to the right, and had noted intermittent clumsiness of his right hand. For several days prior to admission, the

patient had double vision and had to keep one eye closed. During the week prior to admission, he had been excessively drowsy and constantly tired. The headaches had increased in frequency and were now occurring 3 to 4 times per day.

Neurologic examination:

1. Mental status: Intact.

2. *Cranial nerves:*

- a. On funduscopic examination there was evidence of bilateral papilledema.
- b. A bilateral paralysis of the sixth nerve was present.
- c. Horizontal nystagmus was present on right lateral gaze.

3. *Motor system:*

- a. Strength was everywhere intact.
- b. The patient's gait was wide-based. In walking, the patient tended to veer to the right. The patient was unable to stand independently on his right leg.
- c. There was a significant intention tremor of the right upper extremity on finger-to-nose test and of the right lower extremity on heel-to-shin test. Alternating movements of the right hand were disorganized.

4. *Reflexes:* Deep tendon stretch reflexes were normal and plantar responses were flexor.

5. *Sensory system:* All modalities were intact.

Clinical diagnosis: Tumor of the right cerebellar hemisphere with obstruction of ventricular system producing increased intracranial pressure and resulting in papilledema and bilateral cranial nerve VI palsy.

Laboratory Data:

1. Complete blood count and skull x-rays were normal.
2. *Right brachial arteriogram* revealed, in the late arterial phase, a blush in the right inferior and posterior cerebellar hemisphere consistent with a hemangioblastoma.
3. *Pantopaque ventriculogram* revealed a dilated third ventricle and a dilated aqueduct with obstruction to outflow from the fourth ventricle. The fourth ventricle and to a lesser degree, the aqueduct, were shifted to the left. These findings were consistent with a right cerebellar mass displacing and obstructing the fourth ventricle.

Hospital Course: The patient was placed on high dosage of dexamethasone to relieve increased intracranial pressure. Later that day a suboccipital craniectomy was performed by Doctor Samuel Brendler. When the dura was opened, bulging of the lower portion of the right cerebellar hemisphere was noted, with widening of the cerebellar folia. The widest area of the folia was tapped with a needle and a yellow cystic fluid was removed. A transcortical incision was then made, revealing a large cyst with a small strawberry-shaped hemangioma located within. The stalk of this tumor was ligated, and the hemangioma separated from the cystic capsule. Histologic examination of the tumor revealed a hemangioblastoma.

Postoperatively, the patient did well. His headache and diplopia disappeared. There was then improvement in the patient's tremor and ataxia, although there was a slight slowness on finger-to-nose testing on the right. A minor side-to-side tremor was present on right heel-to-shin testing. There was a tendency to veer to the right in walking, but tandem gait indicated only a minor unsteadiness. Evaluation six months after surgery, indicated only a minimal unsteadiness on tandem walking. Evaluation 9 months after surgery later indicated no significant neurologic findings. Re-evaluation three and one-half years after surgery, again indicated a completely intact neurologic status.

Comment: The headaches experienced by the patient, with pain occurring on coughing, sneezing, or mechanical changes, suggested a space-occupying lesion near the ventricular system or meninges. The tumor had produced a block of the ventricular system relatively early in its course, leading to an increase in intracranial pressure, with headache, vomiting and papilledema. The bilateral sixth-cranial nerve weakness was of moderate degree, and

its occurrence would not be unusual in a situation where intracranial pressure had rapidly increased.

The cerebellar symptoms experienced by the patient were lateralized in the sense that the patient was falling to the right side and had noted clumsiness of his right hand. Lateralized cerebellar disease was confirmed by the examination findings of intention tremor of the right arm and leg and disorganization of alternating movements on the right side.

In this case, the hemangioblastoma was in the lateral cerebellar hemisphere. In other cases of hemangioblastoma, the lesion is much more midline in location, and the symptoms are those of a midline cerebellar tumor. Thus, the patient may complain of an ataxia of gait and truncal ataxia and not display clearly lateralized symptoms involving the appendages, such as intention tremor and/or ataxia on heel-to-shin testing. The nodule of tumor often exists within a non-neoplastic cystic cavity. It is, therefore, possible to remove the tumor without sacrificing a large amount of the cerebellum. In some cases, both the mural nodule and the cyst are removed. In almost all cases a complete cure is obtained; recurrences are unlikely and the patients usually have a relatively complete resolution of symptoms and no residual disability.

In some cases, hemangioblastomas of the cerebellum are associated with angiomatous malformations of the retina (Landau-von-Hippel's disease). In some cases, there is an association with a secondary increase in red blood cell production (polycythemia). In rare cases, there is an association with tumors of the kidney. Other neoplasms may also involve the cerebellar hemispheres: cystic astrocytomas, metastatic tumors, and posterior fossa meningiomas. Meningiomas of the angioblastic type may be difficult to distinguish from hemangioblastomas.

At the present time, the diagnosis of these tumors may be readily made by means of MRI and CT scan (Fig. 20-11). Ventriculograms are no longer required. Arteriograms may still be of value in defining the vascularity and blood supply of the tumor.

The following case history presents a typical example of posterior inferior cerebellar artery infarct, the territory most frequently affected selectively.

Case 20-6: This 64-year-old right-handed married white male postmaster, on the morning prior to admission, awoke at 3:00 a.m. with severe posterior headache and severe vertigo, which was exacerbated by any head movement. Nausea, projectile vomiting and slurred speech soon developed. Shortly afterwards, he noted left facial paresthesias, clumsiness of the left upper extremity, and diplopia. He was admitted to his local hospital with a diagnosis of labyrinthine vertigo and then transferred to the neurology unit at Saint Vincent Hospital when symptoms began to evolve.

Two weeks previously, the patient had been seen for a transient episode of difficulty controlling the right arm, a hissing sensation, and impairment of speech.

Past history: The patient had evidence of significant vascular disease. He had hypertension and had undergone coronary artery bypass surgery. Beginning six years previously he had experienced episodes of transient weakness and numbness of the right arm with transient aphasia. He had normal aortic arch and carotid angiographic studies but EEG had demonstrated focal left frontal/temporal slow wave activity. He had been placed on long term anticoagulation. He had experienced migraine headaches without aura for many years.

Neurologic examination:

1. *Mental status:* Intact.
2. *Cranial nerves:* Conjugate lateral gaze to the left was impaired.
3. *Motor system:* Strength was intact. Significant lateralized cerebellar findings were present with marked dysmetria of left upper extremity on finger-to-nose testing and impairment of alternating hand movements. In attempting to stand, the patient was markedly ataxic.

4. *Reflexes*: Deep tendon stretch reflexes were decreased in both lower extremities. Plantar response was extensor on the right and flexor on the left.
5. *Sensory system*: Intact
- Clinical diagnosis**: Left cerebellar hemisphere infarct or hemorrhage with possible minor involvement of brainstem secondary to mass effect.

Laboratory data:

1. Duplex scans of carotids and vertebrals were normal.
2. *Transcranial Doppler studies* indicated normal flow velocities in the vertebral, basilar, anterior and middle cerebral arteries.
3. *Magnetic-resonance angiography* demonstrated occlusion of the left vertebral artery.
4. *CT scan* demonstrated a large left cerebellar infarct pressing the fourth ventricle to the right.
5. *MRI* (2 months after onset of symptoms): Infarction of the total cerebellar territory of the left posterior inferior cerebellar artery with no actual infarct of the brain stem (Fig. 20-12).

Subsequent course: The patient was somewhat vague with some difficulty in memory during the subsequent 8-day hospital course and remained ataxic. He was then transferred to the Fairlawn Rehabilitation Hospital where, over the next three weeks, he had a significant improvement. When re-evaluated two months after onset of symptoms, he was able to walk well with the use of a cane. A minor intention tremor was present on the left finger-to-nose test. An MRI study was obtained at this point, with results indicated above (because new symptoms suggested possible involvement of upper cervical nerve roots and spinal accessory nerve). Additional improvement was evident on evaluation three months after onset of symptoms. Evaluation 6 months after onset of symptoms demonstrated only a slight slowness of alternating movements of the left hand.

Comment: The acute onset of headache, vertigo, vomiting, ataxia of gait, and dysmetria of the left arm suggested an acute cerebrovascular problem involving the posterior circulation and the posterior fossa. (The syndrome of acute headache, vertigo, ataxia, nausea and vomiting is also seen in cases of acute cerebellar hemorrhage.) Numbness on the left side of the face and diplopia suggested, as well, possible brainstem involvement. The initial diagnosis at the local hospital of acute vestibular disturbance did not explain the headache, the diplopia or the lateralized findings. The presence of the left arm dysmetria suggested lateral hemispheric involvement rather than limited midline involvement.

In the era before CT scan and MRI, the distinction between acute cerebellar hemorrhage and acute cerebellar infarct was often difficult to make. Either lesion could produce block or distortion of the ventricular system and secondary hydrocephalus. Either lesion could be associated with the development of brainstem symptoms. The cerebellar infarct, often in the distribution of the posterior inferior cerebellar artery or the anterior inferior cerebellar artery, could also involve the medullary or pontine territories of these vessels. In addition, either type of lesion could cause significant edema with secondary distortion of the brainstem. Hemorrhage could also extend into the cerebellar peduncle and brainstem.

If significant clinical hydrocephalus or brainstem compromise develops, either type of lesion may require neurosurgical decompression or a shunt procedure.

A final note should be made regarding the considerable ability of the human nervous system to recover from extensive cerebellar lesions. Considerable recovery is possible because the cerebellum does not have a direct line role in the control of motor activity but instead, acts as a modulator of the motor control and motor planning circuits.

The following case history provides an example of a cerebellar hemorrhage secondary to an arteriovenous malformation.

Case 20-7: This 57-year-old right-handed married white female had the sudden onset of a severe left-sided pounding headache one afternoon. There was some stuffiness of the nose and tearing of the left eye. She had had a similar, but less severe, headache 20 years previously when taking birth-control pills. No headaches had occurred in the interim. As the current headache began to decrease, she noted that hearing in the left ear had decreased to a minor degree, and an echo sensation was present in the left ear. She also had the sensation that the environment was off balance, particularly if she was in a moving automobile. She subsequently reported a sense of unsteadiness. There was some sense of nausea when the symptoms first occurred. A vague blurring of vision was also present. She had a vague diplopia at the onset of symptoms but this then disappeared.

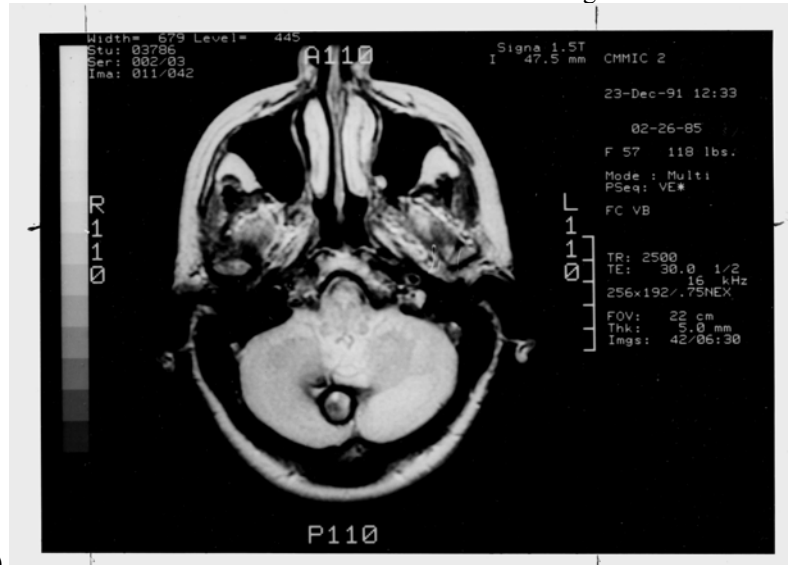
General physical examination: There were multiple pinpoint cavernous angiomas over the arms.

Neurologic examination: Entirely within normal limits.

Clinical diagnosis :Diagnosis unclear: possible migraine headache, or brain stem cerebrovascular event.

Laboratory data: 1. *CT scan of head* indicated hemorrhage in the right paramedian posterior cerebellum.

2. *MRI* showed a rim of hemosiderin stain around the residual hemorrhage in the cerebellar vermis



3. (Figure 20-14).

Subsequent course: The patient had no additional acute episodes. Because two episodes had occurred, she was referred for neurosurgical evaluation. A cavernous hemangioma of the right cerebellum was removed by Doctor Bernard Stone. Post-operatively, she had some right-sided clumsiness and ataxia, which gradually improved.

Evaluation by Doctor Stone one month following surgery, indicated minimal, if any, cerebellar signs. Finger-to-nose test showed no tremor. Gait demonstrated a minimal unsteadiness. Evaluation one year after surgery demonstrated no neurological findings, although some episodic symptoms of imbalance persisted.

CHAPTER 21: SENSORY FUNCTION AND PARIETAL LOBE

The following case demonstrates the localizing significance of focal sensory seizures beginning in the face of a 40 year old patient without prior neurological disease. As predicted, the etiology was neoplastic: a glioblastoma.

Case 21 -1:One week prior to evaluation, this 40-year old right-handed married white male had the onset of repeated 15-21 minute duration episodes of focal numbness (tingling or paresthesias) involving the left side of the face, head, ear, and posterior neck and occasionally spreading into the left hand and fingers, and rarely subsequently spreading into the left leg. There was no associated pain or headache or weakness or associated focal motor phenomena. Biting or eating would trigger the episodes. Past history was not remarkable.

Initial neurological examination: This was completely within normal limits as regards mental status, cranial nerves, motor system, reflexes, and sensory system.

Clinical diagnosis: Focal seizures originating lower third post central gyrus. In view of patient's age, a brain tumor must remain the prime consideration

Laboratory data:

- (1) *EEG*: no focal abnormalities were present. (The record, however, was abnormal because of bilateral bursts of spikes and slow waves - triggered by photic stimulation accompanied by myoclonic jerks - suggesting a predisposition to primary generalized epilepsy (refer to epilepsy chapter for the significance of this finding which was not relevant to this case).
- (2) *CT Scan* (Fig 21-2): The non-enhanced study was normal. The enhanced study demonstrated a small enhancing lesion just above the right Sylvian fissure.
- (3) *MRI* (Fig. 21 - 3): Demonstrated the more extensive nature of this process involving the operculum - above the right sylvian fissure including the lower end of the post central gyrus, the area of representation of the face. A probable infiltrating tumor was suggested as the most likely diagnosis.
- (4) *Arteriogram* - demonstrated a tumor blush at the right sylvian area, consistent with a glioblastoma, a rapidly growing infiltrating tumor - originating from astrocytic glia.

Subsequent Course: Treatment with an anticonvulsant reduced the frequency of the episodes. Neurosurgical consultation suggested an additional observation period and periodic CT scans in view of the normal neurological examination. Three months after onset of symptoms, the patient developed a numbness of the left arm and difficulty in coordination of left arm. Exam now demonstrated left central facial weakness, mild weakness of the left hand. A loss of stereognosis and graphesthesia with a relative alteration in pinprick perception was present in the left hand. The CT scan showed significant enlargement of the previous lesion. EEG now indicated focal 2-3 Hz Delta slow waves in the right frontal central Rolandic area. Subtotal resection of a glioblastoma - in the right temporal parietal area was performed by Dr. Bernard Stone. Radiation therapy was administered following surgery, 4000 rads total whole brain and 5210 rad total to the tumor area. Reevaluation 3 months after surgery, indicated only rare focal seizures involving the face. The neurological examination was normal. Repeat CT scans, however, continued to demonstrate a large area of enhancing tumor in the right temporal-frontal-parietal area. Despite the use of dexamethasone and arterial chemotherapy with cis-Platinum, he continued to progress. At the time of neurological follow-up, 29 months after onset of symptoms, he had developed a left field defect, left hemiparesis and a loss of all modalities of sensation on the left side. He subsequently developed significant changes in memory and cognition, as well as a complete left hemiplegia. CT scan demonstrated progression with extensive involvement of the right side of the brain and spread to the left hemisphere. Death occurred 33 months after onset of symptoms. **Postmortem examination of the brain:** almost the entire right hemisphere was replaced by necrotic infiltrating tumor. The tumor now had spread into the corpus callosum and temporal and occipital lobes. The internal capsule, thalamus, hypothalamus and basal ganglia were destroyed.

Comment: The initial occurrence of the limited focal sensory seizures involving the face and head in a patient of age 40 with no history of trauma or of vascular disease or hypertension clearly predicted the following conclusions (1) The location of the discharging lesion: the sensory cortex

just above the sylvian fissure. (Note that the actual extent of the pathology was more extensive but that is almost always the case in an infiltrating glioma). (2) The nature of the underlying pathology. The most common cause of focal seizures beginning at age 40 in a patient with no significant head trauma, vascular disease, hypertension or other medical disease is a tumor. Among tumors involving the cerebral hemispheres, an infiltrating glioma is by far the most common and on a statistical basis, a glioblastoma is by far the most likely histologic type. 3) The subsequent course was consistent with the natural history of a malignant glioma of the astrocytic series, a glioblastoma. The 33 month survival (30 months after surgery is beyond the median survival for this type of tumor.

The following patient (case 21-2) had a metastatic nodule in the post central gyrus producing a pseudo thalamic pain syndrome.

Case 21-2: This 62-year-old white, right-handed housewife, six years prior to admission

had undergone a left radical mastectomy for carcinoma of the breast. Five months prior to admission, the patient developed a persistent cough, left pleuritic pain and a collection of fluid in the left pleural space (pleural effusion) as well as daily headaches in the right orbit, occasionally awakening the patient from sleep. Four months prior to admission, over a 3 to 4 week period, the patient developed progressive "weakness" and difficulty in control of the right lower extremity. Several weeks later, the patient now experienced, aching pain in the right index finger in addition to a progressive deficit in the use of the right hand. This was more a "stiffness and incoordination" than any actual weakness. One month prior to admission the patient noted episodes of pain in the toes of the right foot and numbness of right foot occurred, lasting 2 to 3 days at a time. She subsequently developed, difficulty in memory and some minor language deficit, suggesting a nominal aphasia, prompting hospital admission.

Neurological examination:

1. *Mental status:* The patient was oriented for time, place, and person. Delayed recall was slightly reduced to 3-out-of-five in 5 minutes. A slowness in naming objects was present although she missed only one item of 6. Calculations, reading, and attention were normal. There was no left-right confusion.

2. Cranial nerves:

a. Nerve II: early papilledema was noted: absence of venous pulsations, indistinctness

of disc margins, and minimal elevation of vessels as they passed over the disc margin.

b. Nerve VII: right central facial weakness was present.

3. **Motor system:**

- a. Mild weakness of the right upper limb was present. A more marked weakness was present in the lower limb (most marked distally).
- b. Spasticity was present at the right elbow and knee.
- c. Gait: The right leg was circumducted; the right arm was held in a flexed posture.

4. **Reflexes:**

- a. Deep tendon reflexes were increased on the right.
- b. A right Babinski response was present.

5. **Sensory system:**

- a. Touch intact.
- b. An ill-defined alteration in pain perception was present in the right arm and leg - more of a relative difference in quality of the pain than any actual deficit.
- c. Repeated stimulation of the right lower extremity (pain or touch) produced dysesthesias (painful sensation).
- d. Vibratory sensation was decreased to a minor degree at the toes bilaterally but intact in the upper extremities.
- e. Position sense was markedly defective in the right fingers with errors in perception of fine and medium amplitude movement in the right toes.
- f. Simultaneous stimulation resulted in extinction in the right lower extremity.
- g. Graphesthesia (identification of numbers, e.g., 8, 5, 4 drawn on cutaneous surface) was absent in the right hand and fingers and poor in the right leg.
- h. Tactile localization and two-point discrimination were decreased on the right side.

Clinical diagnosis: Metastatic tumor to the left post central and precentral gyri with a cortical pain syndrome (pseudo thalamic pain syndrome).

Laboratory data:

1. *Skull x-rays:* the pineal was shifted from left to right. Demineralization of the dorsum sellae also had occurred: consistent with the increase in intracranial pressure.

2. *Chest x-ray:* Several metastatic nodules were present in the left lung.

3. *Electroencephalogram:* A focal disturbance, having the quality of damage, was present in the left posterior frontal central and parietal areas (almost continuous focal 4 to 7 cps slow wave activity).

4. *Left carotid arteriogram:* A left posterior frontal lobe lesion was suggested by a shift of the posterior portion of the anterior cerebral artery from the left to the right. The middle cerebral artery in the sylvian fissure was also depressed downwards.

5. *Brain scan:* The findings were consistent with a focal metastatic lesion with a focal uptake of radioisotope (Hg^{197}) in the left parietal area: high and close to the midline with uptake in the adjacent subcortical white matter.

6. **Erythrocyte sedimentation rate** was elevated to 90 mm., consistent with metastatic disease.

Subsequent course: There was evidence in this case that the disease had spread to multiple organs: brain (findings as noted), lung (chest x-rays and biopsy), and liver (abnormal laboratory tests of liver function). Radiation and hormonal therapy were, therefore, administered rather than any attempt at surgical removal of the left parietal metastatic lesion. Follow-up examination one month later indicated that a significant improvement had occurred in motor function in the arm. Sensory deficits persisted. Speech was slow but relatively intact. The patient eventually expired five months after admission.

Post mortem findings: Autopsy was performed by Dr. Humphrey Lloyd of the Beverly Hospital and disclosed extensive metastatic disease in the lungs, liver, and lymph nodes. A single necrotic metastatic lesion was present in

the brain. This was located in the upper postcentral gyrus of the left parietal area, 1.0 cm. below the pial surface and measuring 1.2 x 1.0 x 0.6 cm.

Comment: This patient had a progressive neurological deficit with headache and papilledema, a clinical course that clearly indicates the presence of a neoplasm. This case predated the era of CT and MRI scan. Today contrast-enhanced scans would be performed. This diagnosis was supported by the ancillary laboratory studies that were available at that time. Moreover this diagnosis however was clear based on the history and clinical-laboratory findings. The fact that motor findings in the arm relevant to the precentral gyrus improved with treatment might suggest that these findings were due to edema. In contrast the findings relevant to the area of the necrotic tumor, the post central gyrus, showed little improvement. In general, one should assume that a patient with a past history of carcinoma of the breast, carcinoma of the lung, malignant melanoma, or renal cell carcinoma, who develops symptoms of central nervous system disease, has metastatic disease until proven otherwise. Such symptoms at their onset may be minor and nonfocal and appear trivial: headache, subjective weakness, and a change in personality. On the other hand more focal symptoms and signs may be present: focal weakness, focal seizure. The metastatic lesions may be single or multiple.

A diagnosis of metastatic disease does not imply that no treatment of central nervous system lesions is possible. Surgical resection of single lesions may be successfully performed. Often the apparent deficits are far out of proportion to the actual size of the tumor because of the surrounding swelling (edema) in the adjacent tissues.

The pattern of sensory involvement in this case clearly localized this lesion to the cortex (or white matter close to cortical surface) rather than to the thalamus. The relative intactness of pain, touch, and vibration sensation should be contrasted to the significant deficits in position sense,

graphesthesia, tactile localization, and two-point discrimination with extinction on simultaneous stimulation. The occurrence of episodic pain in the involved arms and legs along with the production of an experienced painful sensation on repetitive tactile stimulation (dysesthesias) in patients with sensory pathway lesions is sometimes referred to as a "thalamic" or "pseudo thalamic" syndrome. (Refer to discussion of Wilkins and Brody, 1969). In this case, the anatomical locus for the pseudo thalamic syndrome is apparent.

The effects of deficits in cortical sensation on the total sensory motor function of a limb are apparent in this case. The actual disability and disuse of the right arm and leg were far out of proportion to any actual weakness. Such an extremity is often referred to as a "useless limb." The actual weakness that was present undoubtedly reflected pressure effects on the precentral gyrus and the descending motor fibers in adjacent white matter.

The following case (21-3) demonstrates many of the features of a non dominant parietal lobe lesion.

Case 21-3: This 70-year-old, single, white female, right-handed, retired candy maker underwent a left radical mastectomy for carcinoma of the breast, three years prior to admission. Four months prior to evaluation, the patient became unsteady with a sensation of rocking as though on a boat. She no longer attended to her housekeeping and to dressing. Over a three-week period, prior to evaluation, a relatively rapid progression occurred with deterioration of recent memory. A perseveration occurred in motor activities and speech. The patient was incontinent but was no longer concerned with urinary and fecal incontinence. For 2 weeks, right temporal headaches had been present. During this time, her sister noted the patient to be neglecting the left side of her body. She would fail to put on the left shoe when dressing. In undressing, the stocking on the left would be only half removed.

Family History: The patient's mother died of metastatic carcinoma of the breast.

Neurological examination:

1. Mental status:

- a. The patient was oriented for time, place and person.
- b. Delayed recall was 5-out-of-5 objects in 5 minutes.
- c. There was no evidence of aphasia.
 - d. The patient often wandered in her conversation. She often asked irrelevant questions and was often impersistent in motor activities.
- e. There was marked disorganization in the drawing of a house or of a clock. A similar marked disorganization was noted in attempts at copying the picture of a railroad engine (Fig 21-4).
- f. There was a marked neglect of the left side of space and of the left side of the body. The patient failed to read the left half of a page. When she put her glasses on, she did not put the left bow over the ear. When getting into bed, she did not move the left leg into bed. She had slipped off her dress on the right side, but was lying in bed with the dress still covering the left side.

- g. The patient had been reluctant to come for neurological consultation. Although she complained of headache and nausea, she denied any other deficits. Her relatives provided information concerning these problems. Much additional persuasion over a two-week period was required before the patient would agree to be hospitalized.

(2) *Cranial nerves:*

- a. Nerve II: A dense left homonymous hemianopsia was present. When reading, the patient left off the left side of a page. She bisected a line markedly off center. Disc margins were blurred and venous pulsations were absent, indicating papilledema.
- b. Nerve III: The right pupil was slightly larger than the left.
- c. Nerve VII: A minimal left central facial weakness was present.
3. *Motor system:* Strength was intact. There was, however, little spontaneous movement of the left arm and leg. Tone was normal.
4. *Reflexes:* deep tendon reflexes were symmetrical and physiologic and plantar responses, flexor.
5. *Gait:* The patient was ataxic on a narrow base with eyes open with a tendency to fall to the left, and was unable to stand with eyes closed even on a broad base.
6. *Sensory system:*
- a. Pain, touch and vibration were intact. At times, however, there was a decreased awareness of stimuli on the left side.
 - b. Errors were made in position sense at toes and fingers on the left.
 - c. With double simultaneous stimulation, the patient neglected stimuli on the left face, arm and leg.
 - d. Tactile localization was poor over the left arm and leg.

Clinical diagnosis: Metastatic tumor from breast to right non-dominant parietal cortex.

Laboratory data:

1. *Skull X-rays* were negative.
2. *Chest X-ray* indicated a possible metastatic lesion at the right hilum.
3. *Erythrocyte sedimentation rate* was elevated to 72 mm/hr, consistent with metastatic disease.
4. *Electroencephalogram* (Fig 21-5) was abnormal because of frequent focal 3 to 4 cps slow waves in the right temporal and parietal areas, suggesting focal damage in these areas.
5. *Brain scan (radioisotope)* (Fig 21-6) indicated that a large but well-defined area of increased uptake of isotope (Hg197) was present in the right parietal area extending from the midline to the lateral surface, measuring 7 x 5 x 7 cm. The most likely diagnosis was that of a solitary large metastatic lesion
6. *Right carotid arteriogram* showed that a large vascular tumor mass, probably metastatic, was present in the posterior section of the right temporal inferior parietal area. There was displacement of the middle cerebral artery upward and to the left.

Subsequent course: Treatment with steroids (dexamethasone and estrogens) resulted in temporary improvement. The patient refused surgery. Her condition soon deteriorated with increasing obtundation of consciousness. She expired two months following her initial neurological consultation.

Comment: This patient certainly presented a syndrome characterized by disturbance in concept of body image with a marked neglect of the left side, a denial of illness, and marked constructional apraxia. The various laboratory studies indicated a large lesion in the right posterior temporal parietal area. A CT scan from a more recent case demonstrating many aspects of this syndrome is illustrated in Figure 21-7. In many cases, the location of lesion may appear to be predominantly posterior temporal. Such large posterior temporal lesions would certainly compromise the cortex and subcortical white matter of the adjacent inferior parietal area.

In this case, marked deficits in perception of the cortical modalities of sensation were present. In other cases, as in the case demonstrated in Fig 21-7, such involvement is much less marked.

In some cases, involvement of the motor cortex is evident with an actual left hemiparesis accompanied by an increase in deep tendon reflexes and an extensor plantar response. At times in patients with neglect syndromes, there may be several indications in the clinical examination and in the laboratory studies that the involvement of the frontal lobe areas is more prominent than the parietal involvement. We have already indicated that the neglect components of this syndrome may also be noted in lesions of the anterior premotor

area (area 8). The premotor area as discussed above and in chapter 18, receives projection fibers from the multimodal area of the posterior parietal area. It is possible that in some cases the posterior temporal - inferior parietal location of the lesion may also be critical in interrupting these association fibers. For these several reasons, it is perhaps more appropriate to use the term, *syndrome of the non-dominant hemisphere*, rather than the more localized designation, non-dominant inferior parietal syndrome. Duffner et al, 1990 have presented the concept of a network for directed attention - with right frontal lesions leading to left hemi spatial neglect only for tasks that emphasize exploratory-motor components of directed attention whereas parietal lesions emphasize the perceptual-sensory aspects of neglect.

With lesions of the non-dominant hemisphere, there is a significant alteration of the patient's awareness of his environment. The behavior of an individual is in part determined by his or her own particular perception of the environment. If that perception is altered or disorganized, the behavioral responses of the patient may appear inappropriate to others. Obviously, not all individuals will respond in the same manner to a given environmental situation; part of the response will be determined by the past experience and personality of the individual. Thus, given the same lesion, one individual may be unaware of a hemiparesis, another may deny the hemiparesis but agree an illness is present, a third may claim to be healthy and claim that people are conspiring to keep him in the hospital.

CHAPTER 22: THE LIMBIC SYSTEM

In general, as we have indicated, there is mixed symptomatology during partial seizures of temporal lobe origin. The following case history (22-1) illustrates many of the points just discussed regarding seizures of temporal lobe origin.

Case 22-1: This 56-year-old white right-handed male baker was referred for evaluation of a seizure disorder. Three months before admission the patient had the onset of episodes of vertigo and tinnitus, each episode lasting 4 minutes and unrelated to position. The patient then noted increasing forgetfulness. Later that month he had a generalized convulsive seizure that occurred without any warning. The patient then developed episodes of confusion and unresponsiveness, followed by a left frontal headache. Several studies; EEG, pneumoencephalogram, and carotid arteriogram—were all negative at that point in time. One month before admission, the patient began to have minor episodes, characterized by lip smacking and a vertiginous sensation, during which he reported seeing several well-formed, colorful scenes. At times, he had hallucinations of “loaves of bread being laid out on the wall.” In addition, he would have a perceptual disturbance at the same time (e.g., objects would appear larger than normal) and “terrifying dreams.”

General physical examination: unremarkable.

Neurological examination: The essential neurological findings were as follows:

1. *General observations of seizures:* The patient was observed to have frequent transient episodes of distress characterized by saying, “Oh, oh, oh, my”. On occasion, these were accompanied by automatisms: fluttering of the eyelids, smacking of the lips, and repetitive picking at bedclothes with his right hand. Consciousness was not completely impaired during these episodes, which lasted from 30 seconds to 3 minutes, and the patient reported afterward that at the onset of the seizure he had seen loaves of bread on the wall and smelled a poorly described unpleasant odor. At other times, the olfactory hallucination was described as pleasant, resembling the aroma of baked bread.
2. *Mental status:* The patient was oriented to person but not dates. He could not recall his street address. He was unable to pronounce the name of the hospital correctly. Calculations were correctly performed.
3. *Cranial nerves:* Possible deficit in the periphery of the right visual field and a minor right central facial weakness.
4. *Motor system:* intact
5. *Reflexes:* Deep tendon reflexes were symmetrical and physiologic. A right Babinski sign was present.
6. *Sensory system:* intact.

Clinical diagnosis: Simple and complex partial seizures originating left temporal lobe probably involving at various times left lateral superior temporal gyrus, uncus, amygdala and hippocampus with tumor the most likely etiology in view of age and the focal neurological findings.

Laboratory data:

1. The *initial electroencephalographic recording* indicated frequent focal spike discharge throughout the left temporal and parietal areas, consistent with a focal seizure disorder originating in the left temporal/parietal areas (Fig. 29-1). A recording 6 days later indicated a decrease of focal spikes (i.e., a decrease in seizure activity) but the presence of frequent focal slow-wave activity in the left temporal area (almost continuous, 3 to 5 cps (Hz) slow-wave activity) suggesting that focal damage was present in the left temporal area .
2. *Brain scan* (H_g197) normal
3. *Left carotid arteriogram* indicated a possible avascular mass lesion left posterior frontal (the only abnormality was a 4-mm shift of the anterior cerebral artery).

Subsequent course: The patient continued to have multiple short episodes characterized by the sensation of odor and a sensation that he was looking at objects upon the wall. These episodes were eventually controlled with anticonvulsant medication: phenytoin (Dilantin) and primidone (Mysoline). However, 2 months later the patient had a day with several episodes with “crazy things occurring “ (colorful visions and terrifying nightmares).

The patient was readmitted to the hospital 7 months after onset of symptoms because of the recurrence of seizures. An aura of unpleasant odor was followed by a generalized convulsion followed by four or five

subsequent seizures of a somewhat different character (deviation of the head and eyes to the right, then tonic and clonic movements of the right hand spreading to the arm, foot, and leg lasting approximately 1 to 2 minutes, followed by a post-ictal right hemiparesis).

Neurologic examination now indicated a marked expressive aphasia, with little spontaneous speech and difficulty in naming objects. There was a dense right homonymous hemianopia, a flattening of the right nasolabial fold, and a right hemiparesis, with a right Babinski sign.

During a 2-week hospital period the patient continued to have minor seizures characterized by sensory phenomena on the right side of the body. A moderate degree of expressive aphasia persisted throughout the hospital course, although the right homonymous hemianopia largely disappeared. The symptoms and findings suggested that the basic disease process might well have spread to involve the adjacent areas across the sylvian fissure—the speech areas of the inferior frontal convolution, premotor areas, and sensory motor cortex.

The patient developed increasing expressive aphasia and right hemiparesis, with increasingly severe headache. An arteriogram indicated a large space-occupying tumor of the left temporal lobe, and surgery was undertaken by Dr. Robert Yuan 16 months after the onset of symptoms. The anterior and middle portions of the superior temporal gyrus appeared to be widened, and the anterior temporal area (the temporal tip) had an abnormal and discolored appearance. At a depth of 1 to 2 cm within the superior temporal gyrus and involving all of the deeper temporal areas, obvious necrotic glial tissue was found. The process had extended superficially under the Sylvian fissure to involve the adjacent posterior portion of the inferior frontal gyrus.

A temporal lobectomy was performed (from the anterior temporal pole posteriorly for a distance of 6 cm). The operative impression of a malignant glial tumor (glioblastoma) was confirmed by histologic examination.

Comment: This patient presented, at one time or another during his seizures, most of the phenomena associated with temporal lobe lesions: vertigo, tinnitus, visual distortions and hallucinations, olfactory hallucinations, fear, automatisms involving the lips and hands, and episodes of confusion. The visual and olfactory hallucinations are of interest in that both reflected the patient's occupation as a baker. As Halgren and colleagues (1978) note, the experiential phenomena of temporal-lobe seizures are often specific to the individual's experience and personality. The later progression clearly indicated spread across the sylvian fissure to involve the motor cortex and Broca's area in the inferior frontal gyrus areas. This patient had a highly malignant tumor, which clearly involved the cortex of the lateral surface, the deeper white matter, and presumably the medial temporal areas, including the amygdaloid-hippocampal regions. His clinical picture is highly reminiscent of the case described in 1887 by Hughlings Jackson of Emily M., a cook who experienced visual and olfactory hallucinations and who had a tumor arising in the "temporosphenoidal lobe" (the uncus). Such seizures have subsequently been referred to as uncinate epilepsy, but as we have indicated, the disease invariably involves more than just the uncus.

Today, CT scan and MRI would be employed for early diagnosis (see Figs. 22-17 and 22-18). Cases 22-2 and 22-3 which follow demonstrate the correlation of partial seizures with temporal lobe pathology.

Case 22-2. This 17-year-old right-handed male, at age 4 years began to have "staring spells and bizarre behavior". Some episodes had been preceded by the "sound of a musical rhythm". EEG at that time indicated a right temporal spike discharge. Seizures were controlled for ten years with anticonvulsants but then recurred and were poorly controlled occurring several times per day.

Neurological examination: The findings were limited to the following features:

1. *Observed 3 minute seizure:* The seizure began with loss of contact and a stare and then automatisms of the hands. He stood up, walked around the room, went to the physician's desk and attempted to pull open a nonexistent middle drawer. He answered questions vaguely with one or two word answers. Confusion was present for 1-2 minutes after the end of the episode.
2. *Cranial nerves:* a left central facial weakness was present.

Clinical diagnosis: Focal seizures originating right temporal lobe. Observed seizure was complex partial. The seizures beginning with the musical sound might be classified as simple partial with secondary complex partial.

Laboratory data:

1. *EEG*: Intermittent focal spike discharge anterior-middle temporal area.
2. *CT scan*: (Fig. 22-17) An area of focal atrophy was present in the right anterior temporal lobe with possible enhancement at the border.
3. *MRI*: At the Yale Epilepsy Center was more consistent with a tumor in the right anterior temporal lobe.

Subsequent course: Dr. Dennis Spencer at the Yale Epilepsy Center performed a temporal lobectomy. This demonstrated a cystic glial tumor with components of astrocytes and oligodendrocytes. Cerebral cortex also demonstrated abnormal lamination and dysplastic features. Seizures were fully controlled over the next three years.

Case 22-3. This 47-year-old ambidextrous male experienced his first seizure one month prior to admission. He felt light-headed and warm. Then he was observed to walk 100 feet down a hallway, appearing “dazed” and not recognizing people. He fell to the floor, with a loss of consciousness, bit his tongue and was confused afterwards for several minutes.

Neurological examination at 2, 16 and 48 hours after the episode: A persistent right Babinski sign, and slight right hyperreflexia were present. Otherwise the examinations were not remarkable.

Clinical diagnosis: Complex partial seizures. In view of age of onset and persistent focal signs a brain tumor was suspected as the etiology.

Laboratory diagnosis:

1. Sleep deprived EEG :normal.
2. *CT and MRI scans* (Fig. 22-18) demonstrated an extensive infiltrating tumor of the left temporal lobe most likely a glioblastoma.

Subsequent course: Despite Anticonvulsant therapy (phenytoin) additional episodes occurred over the next month: loss of train of thought while talking and several minutes of loss of memory. A subtotal resection by Dr. Bernard Stone (St. Vincent Hospital) demonstrated a Grade III-IV astrocytoma (glioblastoma). Despite radiotherapy and chemotherapy, the disease pursued a relentless course producing early and severe disability prior to death, approximately one year after onset of symptoms.

The following case histories illustrate many of the features of focal disease involving the prefrontal areas.

Case 22-4: This 69-year-old right handed white housewife; two years prior to neurological evaluation visited a relative (a physician) in Israel whom she had not seen in a number of years. The relative then wrote to the patient’s physician, (an old family friend) indicating concern over a change in the patient’s personality. The patient was described as apathetic with silly immature reactions. In retrospect, the patient’s husband felt that these alternations had begun insidiously a number of years previously. A year later, the same relative again wrote indicating that letters received from the patient had become incoherent. Letters became less frequent and then the patient no longer wrote letters. Ten months prior to evaluation, a left central facial weakness was first noted followed two months later by a decreased left arm swing. Six months prior to evaluation, her husband noted, she was purchasing items for which she had no need: 24 pairs of shoes, 15 brassieres. Subsequently she became careless in her housework. On occasions she lost her purse. Her ability to play bridge had decreased over the last year, although her golf game was unchanged.

Neurological examination:**1. Mental status**

- a. She was oriented x3
- b. There was a marked impersistence in motor activities. She was often inattentive. Her answers were often irrelevant. (According to her husband this had been present for many years.
- c. There was inappropriate joking.
- d. Delayed recall without assistance was 2/5 objects in 5 minutes. But 5/5 with assistance.
- e. Digit span was decreased to 5 forward and 3 in reverses.

- f. There were marked deficits in serial 7 subtractions. At times she began to subtract other numbers, at times she added rather than subtracted.
- g. There was a significant spatial disorientation. There was a marked impairment in the ability to copy a cube and deficits in drawing a house. There was disorientation in locating cities on a map.

2.Cranial nerves:

- a. There was a significant neglect of single stimulus objects in the left visual field; this was greater when bilateral simultaneous stimuli were utilized.
- b. At times there was a limitation of voluntary gaze to the left.
- c. A left central facial weakness was present.

3.Motor system:

- a. There was minimal weakness of the left arm and leg.
- b. Variable resistance was present on passive motion at left wrist and elbow suggesting the "gegenhalten" of frontal lobe disease.
- c. There was a decreased swing of the left arm in walking. The gait was initially apraxic but improved as the patient picked up speed.

4.Reflexes

- a. Deep tendon stretch reflexes were increased on the left.
- b. A left Babinski sign was present.
- c. There was a bilateral release of the grasp reflex.

5. Sensory system: intact.

Clinical diagnosis: Right frontal lobe tumor: probable meningioma based on the long history.

Laboratory data:

1.*Skull x-rays* there was a 5mm shift to the left of the calcified pineal gland. Long standing increased intracranial pressure was suggested by the demineralization of the sella turcica.

2.*EEG* demonstrated focal 2-5 Hz slow waves in the right frontal area most prominent in the parasagittal recording area

3.*Imaging study: radioactive brain scan (Hgl97):* there was a heavy uptake in the right frontal towards the midline measuring 5x5x4 cm (Fig.22-21).

4.*Arteriograms:* A parasagittal tumor was present in the right frontal area, with vascular supply derived from the left and right middle meningeal and left anterior meningeal arteries.

Hospital course: Following the arteriogram, the patient developed signs of increased intracranial pressure (vomiting, lethargy and papilledema). The patient received dexamethasone glucocorticoid used to reduce cerebral edema, with improvement in these symptoms. The right external carotid artery was ligated since the meningioma derived considerable blood supply from this source. Dr. Samuel Brendler performed a bilateral frontal craniotomy. Bulging of the dura was present requiring the administration of hyperosmotic agent (20% mannitol) with reduction of the swelling. When the dura was opened a large right posterior frontal meningioma was revealed measuring 8x8cm and attached to the right side of the superior sagittal sinus. On histological section this was a fibrous, meningothelial meningioma. During the course of removal of the tumor, it was necessary to ligate several bridging veins entering the superior sagittal sinus as well as the arteries feeding the tumor. At the conclusion of the procedure, it was noted that the right pupil was enlarged and neither responded to light. The patient failed to regain consciousness, remaining in a state of coma with bilateral extensor plantar responses, decerebrate postures on stimulation and bilateral fixed dilated pupils. The patient expired 2 weeks after surgery.

Comment: It is difficult to decide even in retrospect when the symptoms in this case began. It is clear that the initial symptoms involved an insidious change in personality. She was apathetic, her reactions were "silly" and judgment was impaired. Purchases were inappropriate. It would have been of interest to explore which aspects of her bridge playing were impaired in terms of planning and strategy etc. Her motor function was impaired only to a minor degree even late at the time of neurological evaluation, with minimal left-sided weakness and more prominent premotor release. The visual neglect syndrome may have reflected involvement of the premotor area or compromise of the parietal cortex by this large tumor. The fact that there was only minor evidence of involvement of motor cortex would make the premotor/SMA location more likely. While the spatial disorientation and deficits in drawing might

favor a nondominant parietal syndrome, such findings also could be consistent with a nondominant premotor/SMA location based on the close interaction between the posterior parietal and the premotor location. The impairment of voluntary gaze to the left would be consistent with area 8 involvement. There is little doubt that this patient required surgical intervention. The removal of large "benign" tumors of this type is not without risk. Hemorrhagic infarction with massive edema and tentorial herniation is a complication of ligation of bridging veins entering the superior sagittal sinus. In this case, serious brain swelling was already evident even before the dura was opened.

The following case history 22-3 provides an example of a patient with a slowly progressive subfrontal meningioma manifested by symptoms of apathy, loss of ambition, "depression" of mood, emotional lability, with a tendency to introspection and a slowness of mental processes. All of these symptoms were initially attributed to depression and a hypothyroid state. As gait and memory problems developed, these symptoms were attributed to Alzheimer's type senile dementia. When increased intracranial pressure and coma suddenly developed, neurological and neurosurgical intervention occurred.

Case 22-5: This white housewife and fashion designer was first admitted to the hospital at age 60 with a history of several years (?2 to 5) of fatigue, loss of ambition, lack of enthusiasm, and a tendency to readily cry over minor problems. A depression of mood and a tendency to introspection had developed. The patient also reported loss of her taste for food with a subsequent decrease in appetite and weight loss. These symptoms had progressed despite an adequate dosage of thyroid medication (60 mg., t.i.d.). Neurological examination was recorded as negative except for a slowness of speech and of thought processes. She was described by the psychiatric consultant as indecisive in her answers. Cerebrospinal fluid examination revealed no significant findings. Tests of thyroid function indicated hypothyroidism with protein bound iodine of 3.2 micrograms/100 ml. (normal; 4 to 8 micrograms/100 mg.) and a radioactive iodine uptake of 2.3 percent in 24 hours (normal 20 to 50 percent). Discharge diagnosis was chronic depression and hypothyroidism.

These symptoms continued to progress despite treatment with thyroid. The patient had increasing difficulty in walking. This had actually been first noted at age 57, 3 years prior to her initial hospital admission as a "phobia for heights". The patient would "freeze" at the top of a high flight of stairs. She then developed progressive difficulty in climbing stairs. Her husband reported that she would have marked difficulty in getting out of chairs. She would appear unsteady in gait after rising from a chair but would soon recover her equilibrium and would be able to walk in relatively normal manner. Increasingly, the patient's motor and mental activities became slower. She "procrastinated in making decisions". Occasional urinary incontinence developed at age 66 and was attributed to her neurological disease (apparent senile dementia). Although her husband reported her memory as initially well preserved, other observers at that point reported a progressive deficit in memory. At age 67, the patient began to complain of episodic fogging or blurring of vision.

Initial Neurological examination on re-admission to the hospital at age 67 was recorded as demonstrating the following features:

(a), slight disorientation for date and year, (b) slowness of speech and gait (c) deep tendon reflexes 2+, plantar responses flexor, and (d) no significant sensory finding except a slight decrease in position sense at the toes. No details as to the patient's gait were recorded. The sense of smell was apparently not tested and no notes as to the presence or absence of a grasp reflex were recorded.

On the day after admission, the patient developed headache and vomiting. She had difficulty walking unsupported and became increasingly more somnolent but could be roused by painful stimulation. Deep tendon reflexes were increased bilaterally with bilateral extensor plantar responses (bilateral Babinski signs). Grasp response was absent. Pupils responded to light but were sluggish.

Fundusoscopic examination was negative but lumbar puncture indicated a markedly increased pressure, greater than 400 mm. of csf. Cerebrospinal fluid protein was elevated to 125 mg/100 ml. The patient became unresponsive and emergency neurological and neurosurgical consultations were obtained.

Neurological examination:

1. *Mental Status:* The patient was semicomatose with periodic Cheyne-Stokes respirations.
2. *Cranial Nerves:* Pupils were fixed, the left dilated, the right constricted.
3. *Motor System:*
 - a. The patient moved all limbs in response to painful

stimulation, right more than left.

- b. There was a spastic resistance in the upper and lower left extremities.
4. Reflexes:
- a. A generalized hyperreflexia was present with bilateral ankle clonus.
 - b. Bilateral Babinski signs were present.
 - c. A bilateral grasp reflex was present. Note, however, that in a semicomatose patient this may have little localizing significance.
5. *Sensation*: Pain sensation was intact.

Clinical diagnosis: Subfrontal or parasagittal frontal tumor most likely a meningioma in view of the over 10 year course. Tentorial herniation had occurred possibly related to the lumbar puncture.

Laboratory data: An emergency bilateral carotid arteriograms revealed that a large subfrontal butterfly-shaped mass (probably meningioma) was present in the anterior cranial fossa bilaterally. The anterior cerebral arteries as well as the frontal polar, pericallosal and callosal marginal branches and the middle cerebral arteries were displaced backwards. The anterior cerebral arteries were also displaced upwards. The tumor mass derived blood supply from the ophthalmic arteries.

Hospital course:

A bifrontal craniotomy was immediately performed by Doctor Robert Yuan with total removal of a large bifrontal meningioma arising from the falx and olfactory groove. On the right side the tumor was estimated to occupy 75 percent of the anterior cranial fossa, measuring 7 x 5 x 6 cm. On the left the tumor was of approximately half this size, measuring 5 cm. in diameter. The thickness of the cerebral hemisphere covering the tumor in the right prefrontal area was reduced to 0.5 cm. Histological examination of the tumor indicated a benign meningioma (meningotheliomatous type).

The patient showed some immediate improvement at the conclusion of surgery, in the sense that both pupils were equal in size and reacted to light. By the time of discharge from the hospital, two months after surgery, considerable improvement had occurred. She could recognize the doctor by name but did not know the place, the season, or the month; she could, however, describe a picture she had just seen. A bilateral deficit in olfaction was present (anosmia). Assistance was required in walking. A bilateral grasp reflex was present.

Follow-up evaluation two years after surgery indicated continued improvement although the patient still had complaint relevant to impairment of recent memory and slight unsteadiness of gait. Deep tendon reflexes were symmetrical with plantar responses flexor. A bilateral grasp reflex was present and the patient was slow in walking and fell occasionally. Urinary incontinence occurred with wetting of the bed.

Comment: In retrospect, the evolution of symptoms in this patient clearly indicates a tumor initially compression both prefrontal areas and producing alterations in mood and personality. With continued growth of the tumor, compromise of the premotor areas with resultant apraxia of gait and release of grasp reflex began to occur, either as a result of direct compression or secondary to the distortion and compression of the anterior cerebral arteries. It is not unusual to witness the development of a dementia (deficit in recent memory) in large tumors in a subfrontal midline location. A similar dementia may occur in large aneurysms of the anterior communicating artery.

The problem of dementia will be considered in greater detail in the chapter on memory.

The development of headache, vomiting and increasing somnolence indicated the development of increasing intracranial pressure. The sudden unresponsiveness following the lumbar puncture with the development of periodic Cheyne-Stokes respirations, pupillary changes, and bilateral corticospinal tract signs all indicated an additional acute exacerbation of the already compromised brain stem functions, a compromise which had already resulted from the backward displacement of the intracranial contents with distortion of the brain stem. In retrospect, one might hypothesize that the patient's complaint of a loss of taste for her food at the time of her initial hospitalization might well have indicated some loss of olfactory sensation since much of our appreciation of food is dependent on olfaction. Specific tests for olfaction were not recorded.

CHAPTER 23: VISUAL SYSTEM

The following case is an example of a lesion involving the optic nerve, anterior to the optic chiasm.

Case History 23-1 (Fig 23-8).

This 53-year-old white right-handed housewife was referred for evaluation of progressive right-sided supraorbital headache of 23 years duration and decreasing acuity in the right eye. The loss of acuity had progressed to the point of almost total unilateral blindness. During the 3 years before admission, intermittent tingling paresthesia had been noted in the left face, arm, or leg. About 1 year before admission the patient had a sudden loss of consciousness and was amnesic for the events of the next 48

hours. She was hospitalized, but no explanation for the episode was clearly established, although cerebrospinal fluid protein was reported to be elevated (230 mg/dl).

The patient and her family reported some personality changes over a period of several years, including a loss of spontaneity and increasing apathy.

General Physical Examination: Unremarkable except for a minor degree of proptosis (downward protrusion of the right eye).

Neurologic Examination:

1. *Mental Status:* The patient was, in general, alert but at times would become lethargic. Her affect was flat. At times, she would laugh or joke in an inappropriate manner.
2. *Cranial Nerves:* There was anosmia for odors, such as cloves, on the right and a reduced sensitivity on the left.

Marked papilledema (increased intracranial pressure with protrusion of the optic disk and venous engorgement due to obstruction of the normal flow of CSF) was present in the left eye.

Pallor of the right optic disc was present, indicating optic atrophy. Visual acuity in the right eye was markedly reduced. The patient had only a small crescent of vision in the temporal field of the right eye, where only vague outlines of objects could be seen. A slight left central facial weakness was present.

3. *Motor Systems:* Intact although movements on the left side were slow.

4. *Reflexes:* A release of grasp reflex was present on the left side.

5. *Sensory system:* Intact

Clinical diagnosis: Subfrontal meningioma arising from olfactory groove or inner third sphenoid wing.

Laboratory data:

1. *Skull* x-rays demonstrated erosion of the dorsum sellae. Special lamniograms demonstrated hyperostosis of the sphenoid bone (planum sphenoidale) suggesting a meningioma originating from the sphenoid bone.

2. *EEG* demonstrated focal 2-4 Hz slow waves in the right anterior temporal and anterior lateral frontal area.

3. *Brain scan (H_g 197)* revealed a heavy uptake of isotope in the right posterior subfrontal area.

4. *Arteriograms* indicated that the anterior cerebral arteries were shifted backwards, posteriorly and the left. A tumor blush was present on the venous phase in the right subfrontal area extending back to the optic nerve groove (Fig 23-8). These findings were felt to be most consistent with an olfactory groove meningioma.

Hospital course: Dr. Samuel Brendler performed a bifrontal craniotomy which exposed a well-encapsulated smooth tumor attached to the medial third of the sphenoid wing. After intracapsular removal of 90 to 95% of the tumor, the right optic nerve could be visualized. The small portion of the tumor attached to the bone could not be removed because of considerable bleeding from the bone. Examination 4 months after surgery, indicated right anosmia and right optic atrophy were present.

Comment

If one considered only the patient's primary complaint, decreasing vision in the right eye, and the findings of right optic atrophy and left-sided papilledema (Foster-Kennedy syndrome), then the most probable diagnosis was inner-third sphenoid meningioma. The preservation of a small crescent of vision in the temporal field is consistent with compression of the optic nerve on its lateral surface. By the time of hospitalization, the lesion was quite large and had extended into the subfrontal area, producing anosmia on the right and some changes in personality. At this point, the various diagnostic studies suggested only a subfrontal mass and did not clearly differentiate between an olfactory-groove meningioma and a sphenoid-wing meningioma. One might suggest, in retrospect, that the degree of involvement of the right optic nerve was much more pronounced than the changes in prefrontal functions, and therefore, the inner-third sphenoid-wing location was more likely.

The surgical approach in any case was the same. The eventual recovery of vision in such cases is uncertain because the effects of compression often are not reversible

COMPLETE CASE HISTORIES FROM TEXTBOOK: *INTEGRATED NEUROSCIENCES*

PART III. CASES – CEREBRAL HEMISPHERE MOTOR SYSTEM, CEREBELLUM, BASAL GANGLIA

CHAPTER 18: MOTOR SYSTEM I:

The following case 18-1 presents an example of focal seizures beginning in the motor cortex.

Case 18-1. This 29-year-old, right-handed, white woman was in her usual state of good health until three months prior to admission when she developed an intermittent “pulling sensation” over the anterior aspect of the left thigh, lasting a few minutes. This recurred without other symptoms about twice a week. On the evening of admission, while sitting on a couch, she again had the onset of this same sensation in her left. She stood up, noted that her left leg felt “numb” and then started to have “jerky movements” in her left foot which progressed to involve the whole left lower extremity. She sat down, pressed on her left thigh in an attempt to stop the movement. At this point, her husband and a friend came to her (the patient is amnesic for these events), and saw her have tonic extension then clonus of all four limbs associated with grunting respiration, clenched jaw, and rolling of the eyes. She was placed on the floor and after a few seconds she regained consciousness, though she still appeared dazed and slightly confused for the next 5 minutes.

Past history and family history: noncontributory.

Physical Exam: Normal except for bite marks on the left lateral aspect of the tongue.

Neurological Exam: Significant only a slight asymmetry of deep tendon reflexes: left > right.

Clinical Diagnosis: Focal seizures originating right parasagittal motor cortex (foot area), with ? of parasagittal meningioma.

Laboratory Data:

(1) *Electroencephalogram* (Fig.29-1B) demonstrated rare focal spikes, right Rolandic parasagittal consistent with the focal source of the secondarily generalized seizure and rare focal slow waves in the right Rolandic and mid temporal area - consistent with minor damage in this area

2) *CT scan* (Fig.18-13) demonstrated an enhancing lesion in the right parasagittal region just anterior to the central sulcus.

- (3) *Arteriograms* (Fig.18-14) demonstrated a circumscribed vascular tumor in the right parasagittal rolandic area which was supplied by the right anterior cerebral artery (A,B) and the right middle meningeal branch of the external carotid artery©. The venous phase of the study demonstrated a significant draining vein from this area of tumor blush(D). All of these findings were consistent with a right parasagittal meningioma.

Hospital Course: A well-circumscribed right parasagittal meningioma was removed by Doctor Bernard Stone. A distal weakness of the left lower extremity was present in the immediate postoperative period but this improved rapidly so that by two months after surgery, a foot drop brace was no longer required and strength had returned to normal. During all of the pre and post operative period, the patient received diphenylhydantoin (Phenytoin) to prevent additional seizures. A possible sensory seizure involving the hand occurred 2 years later. Four years after surgery, the patient attempted to reduce her dosage of anticonvulsant and experienced a recurrence of focal motor seizure activity beginning in the left leg with subsequent secondary generalization. When evaluated 6 years after surgery, she had experienced no additional seizure activity. Her neurological examination continued to demonstrate an increase in deep tendon reflexes on the left and a left sign of Babinski. Her CT scan demonstrated no recurrence of tumor, there was very minor atrophy at the site of the previous meningioma. The EEG continued to demonstrate bursts of blunt spikes and slow waves in the right parasagittal Rolandic and parietal areas. Follow-up 10.5 years after surgery in indicated no additional seizures.

Comment: The onset of focal seizure activity should always raise the question of focal pathology. When these seizures begin at age 29, without a prior medical history, there is always a strong possibility of a primary brain tumor. In general gliomas are much more common than meningiomas but the odds of a meningioma are increased by the parasagittal location and the gender of the patient. In this case, there was a very close correlation of the clinical phenomena with the laboratory data regarding the anatomical location of the lesion. Surgical therapy eliminated the underlying benign tumor - the parasagittal meningioma, but the predisposition to focal seizures remained. Thus, the tumor in compression of cerebral cortex had produced alterations in neuronal excitability which persisted following the removal of the tumor.

Case 18-2 provides an example of a slow growing tumor involving the premotor and supplementary motor cortex from the standpoint of focal seizure activity. The motor effects of frontal lesions are presented in case histories 22-2 and 22-3 which follows the discussion of the prefrontal areas.

Case 18-2: This 57-year-old right-handed single nun and occupational therapist, had the onset of her first generalized convulsive seizure at age 47, ten years prior to consultation. This occurred without warning with sudden loss of consciousness and an observed generalized tonic clonic seizure. Both an EEG and CT scan were reported to have been normal. Approximately 4 additional generalized convulsive seizures occurred over the next 4 years. Shortly after the onset of the grand mal seizures, the patient began to have focal seizures. She described these as beginning with the abduction and raising of the right arm at the side, over her head, then a jerking of the right arm, and then she would fall to the ground. She would remain fully conscious but she would be unable to talk. She would have an awareness that something strange was occurring. She had a sinking sensation. She denied any impairment of memory after the episode. But, she would be aware that her right arm and leg were tingling and weak for perhaps 5 minutes afterwards and she would be unable to speak for 10-30 minutes afterwards. These focal seizures occurred once a month, but for the last 2 years, they had been occurring once a week. The patient indicated that over the last 10 years she has had problems with her memory.

She was reported to have had three “negative” CT scans over the years, and yearly EEG’s which did not reveal focal features or electrical seizure discharges although some bilateral slow wave activity was present. The patient has been treated with a variety of medications over the years without attaining seizure control. Her initial evaluation 4 years after onset of seizures at another neurological center indicated some increased activity in the finger jerks on the right with withdrawal of both plantar responses, and a diminished swing of the right arm.

Past history and family history were negative: she was the product of a full-term delivery weighing 9 pounds and had excellent developmental and educational milestones.

Neurological examination :The following abnormalities were present:

1. *Mental Status*: Although orientation and language functions were all intact, delayed recall without assistance, was 0 out of 5; and with assistance 2 out of 5. Proverb interpretation was abstract for 1/3 proverbs, but similarity testing was abstract.
2. *Cranial Nerves* II through XII were intact.
3. *Motor System* was intact except for a decreased swing of the right arm in walking.
4. *Reflexes*: deep tendon reflexes were increased on the right at biceps and patellar. Plantar response was extensor on the right and equivocally extensor on the left.
5. Sensory system was intact.

Clinical diagnosis: Seizures of focal origin left premotor/supplementary motor cortex possibly secondary to low grade glioma. A meningioma was less likely due to the reports of “normal CT scans”.

Laboratory data:

1. **CT scan** (Fig.18-16),demonstrated an area of calcification with surrounding edema in the left premotor area .

2. **MRI scan** (Fig.18-17),demonstrated extensive involvement of the premotor and supplementary areas by tumor and edema.

Subsequent course: Subtotal resection of this tumor was performed by Doctor Bernard Stone. Histological examination of the tissue confirmed the preoperative impression of an infiltrating glioma - predominantly oligodendroglioma in type. The patient received postoperative radiotherapy, 5000 rads to the left hemisphere and an additional 1000 rads to area of tumor. When last seen in follow-up 4 years after surgery, the patient was still experiencing infrequent (1-2 per month) short focal seizures of the same type involving focal movements of right arm, plus speech arrest. The neurological examination demonstrated some decrease in spontaneous speech and some blunting of affect. However, she was fluent; naming of objects and repetitions was intact. Strength was intact. Reflexes were symmetrical but bilateral extensor plantar responses were present. She had a moderate frontal type apraxia of gait and required a cane to avoid falls.

Comment :This patient presented with seizures of focal origin. The description of the posture adopted by the arm at the very beginning of the seizure, raised the possibility that her seizures were originating in the supplementary motor cortex of the left hemisphere and then spreading into the motor and sensory area. The arrest of speech would be compatible with such an origin since there is a superior speech area located in relationship to supplementary motor cortex. The fact that the patient remembered much of the seizure would also be consistent with such an origin. The post ictal depression of motor and sensory function in right arm and right leg and the depression of speech would all be consistent with post ictal phenomena involving the left hemisphere, particularly its sensory, motor and speech areas. The fact that the EEG's had not been particularly remarkable would also be consistent with such an origin of discharge. Thus, the discharging focus may well be buried on the parasagittal surface and not accessible to recording electrodes at the surface.

As regards the underlying nature of the pathology, when the patient was seen 10 years after onset of symptoms, she now has some focal findings; in terms of a right Babinski sign and increased reflexes in the right arm raising the question of a low grade glioma such as an oligodendroglioma in this area. The previous “negative” CT scans would have ruled out a meningioma or arteriovenous malformation. The long history and the finding of calcification within the tumor all made oligodendroglioma the most likely diagnosis. Low grade gliomas of this type often produce seizures without producing major neurological findings .Thus frontal release signs were minimal.

The following case history provide an example of normal pressure hydrocephalus producing the triad of a gait apraxia, urinary incontinence and problems in memory.

Case 18-3: This 72-year-old retired white handed carpenter was referred for evaluation of progressive impairment of gait, and more recent problems, in memory. The gait problems began insidiously five years previously but had become more significant in the past six months. He described his walking as involving small steps and then “going forward at too fast a rate, with difficulty in stopping”. As a result, he would stumble and tend to fall forward, losing his balance. He had considerable fear of falling and made use of a cane to avoid falling. For the last four to five months, the patient had noted urinary frequency and incontinence. He kept a bucket with him at all times. “Once I have to go, I can’t hold on.” Memory problems had developed during the last two to three months related to the recall of recent events and new material. He would enter a room and be

unable to recall why he had entered the room. Emotional lability had also developed during the past year. It was difficult not to cry when he heard a sad story.

Past history indicated at least three myocardial infarctions.

Neurological examination:

1. Mental Status:

- a. Oriented for time, place and person.
- b. Delayed recall, even with assistance, was limited to 1/3 in five minutes.
- c. The patient often lost track of what he was saying or doing.
- d. Serial 7 subtractions was slowly performed but intact.
- e. Reading, writing, drawing and naming of objects were intact but spelling was poor.
- e. Abstract reasoning was intact.
- g. Affect demonstrated changes: At times, he was tearful; at times, inappropriately jocular.

2. Cranial Nerves: Intact except bilateral decrease in hearing - long standing.

3. Motor System: Intact except for gait. The patient walked on a broad base with small steps. He was slow in starting and then picked up speed. He was unsteady on the turns and tended to turn "en bloc". No rigidity and no tremor were present. Finger to nose and heel to shin tests were normal.

4. Reflexes: Deep tendon reflexes were hyperactive at patellar. Plantar responses were equivocal. No definite frontal release signs were present.

Clinical diagnosis: Frontal lobe syndrome with involvement of premotor and prefrontal areas. The combination of a frontal gait apraxia, memory impairment and urinary incontinence raised the question of normal pressure hydrocephalus.

Laboratory data:

- 1. *CT scan (Fig. 18-21):* Demonstrated markedly dilated lateral; third and fourth ventricles but with no enlargement of the sulci.

Figure 18-21 Normal Pressure Hydrocephalus - CT Scan - Case 18-3 A. Ventricular Enlargement B. Section Through Vertex: Demonstrating No Enlargement of Sulci PART II: Comparison patient with progressive multiple sclerosis involving cerebral hemispheres at relatively comparable levels of section demonstrating A. Ventricular Enlargement B. Accompanied by Enlargement of Cortical Sulci

- 2. Lumbar puncture studies were normal.

- 3. *Radio-isotope cisternogram (Fig 18-22)* demonstrated continued presence of isotope within the ventricular system with no reabsorption over the convexities - subarachnoid space at 24, 48, and 72 hours.

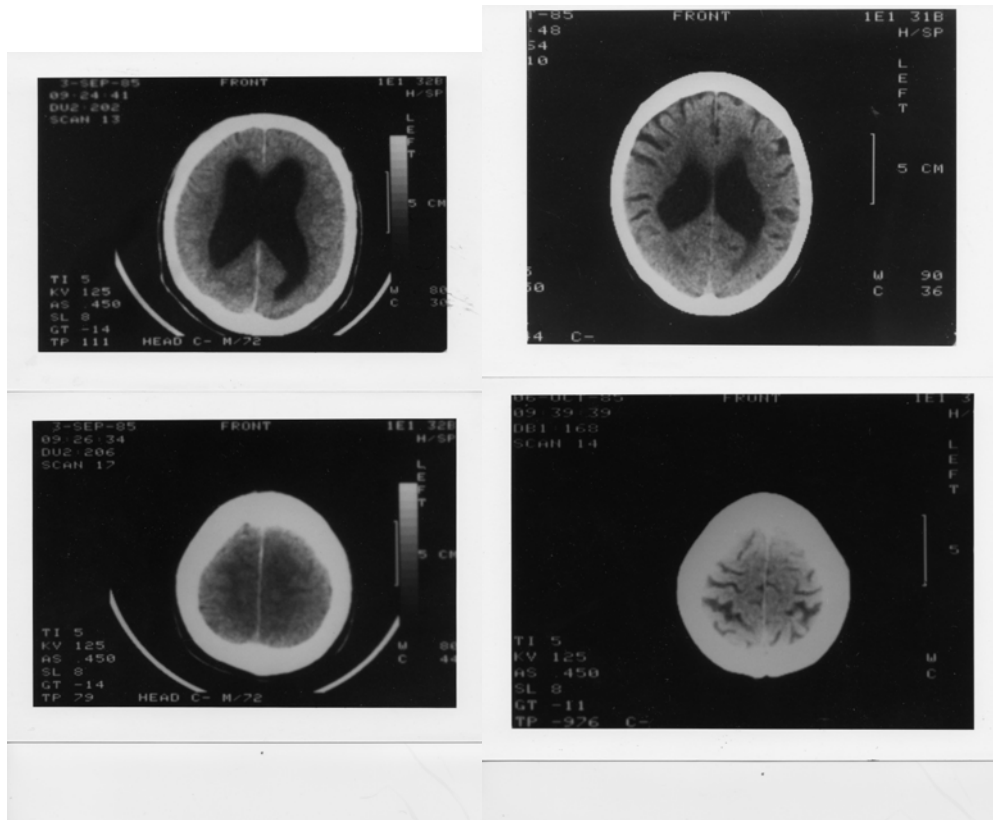
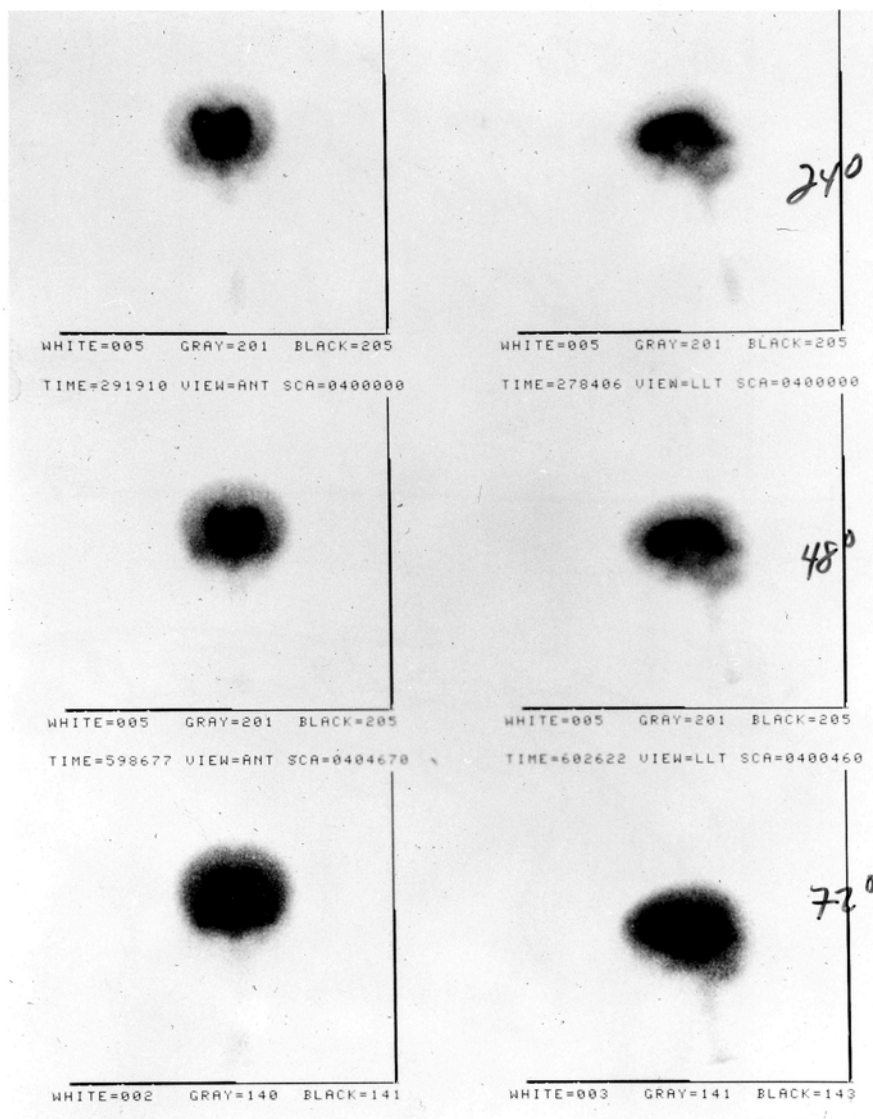


Figure 18-21. Normal Pressure Hydrocephalus Figure 18-21. Comparison Scan.

Figure 18-22: Normal Pressure Hydrocephalus: Isotope Flow Study: Lumbar CSF Injection Case 18-3 Isotope remaining in ventricular system at 24, 48 and 72 hours B. Comparison Case: Progressive multiple sclerosis of

cerebral hemispheres with enlargement of ventricular system but with enlargement of sulci. Isotope has begun to leave ventricles at 24 hours - appearing over the convexity and this is even more apparent at 48 and 72 hours.

Fig 18- 22. Normal Pressure Hydrocephalus; Isotope Flow Study



Subsequent course: Doctor Alex Danylevich performed a ventriculo-peritoneal shunt procedure (right lateral ventricle to peritoneal cavity). The patient did well with clearing of his triad of symptoms: Ataxia, dementia and urinary incontinence and was able to return to work as a carpenter , 12 hours per day. Subsequently , symptoms recurred due to infection of the peritoneal component of the shunt tube. Following revision of the shunt, symptoms improved only to worsen again in 6 months later. The patient had to use a wheelchair at times. A more marked apraxia of gait, frontal release signs, bilateral Babinski signs and urinary incontinence were present on examination 6 months after the revision. CT scan indicated a greater degree of ventricular enlargement. Following removal of 30 cc. of CSF, the patient was more responsive, and better oriented. Myocardial problems prevented additional neurosurgical revision of the shunt at that time. Subsequently, Doctor Robert Ojemann, of the Massachusetts General Hospital, revised the shunt utilizing a valve which allowed greater flow. At last evaluation, two years after admission, gait had improved (he was using a walker). Mentation was clearer (he was still described as showing aspects of a “frontal lobe syndrome”). Urinary incontinence was no longer present.

Comment: This patient presented a premotor/prefrontal syndrome .The imaging studies allowed a more specific delineation of the etiology of the syndrome. In most cases of normal pressure hydrocephalus, the gait disturbance is out of proportion to any change in mental status.

CHAPTER 19: MOTOR SYSTEM II: BASAL GANGLIA AND MOVEMENT DISORDERS

The following case presents an example of a patient with Parkinson's disease followed for 19 years.

Case 19-1 : This 48-year-old married white male, left-handed school master and physics teacher, was referred on 08/16/82 by his orthopedic surgeon for neurological evaluation of problems of control of the left arm and dragging of the left leg. Symptoms had begun 3 months previously with a sense of fatigue, stiffness and lack of control in the left arm. After a period of prolonged writing, he would have to make a conscious effort to continue writing. Approximately one month prior to the evaluation, he first noted a slowing down in movements of the left leg. "I have to remember to lift it."

Past medical history: Negative except for neck pain eight years previously related to cervical spondylosis, which cleared with the use of collar and traction except for occasional tingling in the 4th and 5th fingers of the left arm. Family history was unremarkable.

Neurological examination:

1. Mental Status: intact
2. *Cranial Nerves I-XII:* Intact except for a tremor of the closed eyelids and a positive glabellar sign (he was unable to suppress eye lid blinking on tap of forehead).
3. Motor System:
 - a. Strength : intact
 - b. Gait : There was a tendency to turn en bloc and a decreased swing of the left arm. However he could walk a tandem gait without difficulty.
 - c. There was a slight increase in resistance to passive motion at the left elbow, wrist and knee (rigidity without definite cogwheel component).
 - d. Although the patient was left-handed, there was a slowness of alternating finger movements of the left hand.
 - e. No tremor was present.
 - f. Handwriting was intact with no evidence of micrographia.
4. *Reflexes:* deep tendon stretch reflexes and plantar responses were physiologic
5. *Sensation:* all modalities were intact.

Clinical diagnosis: early Parkinson's disease, predominantly unilateral.

Laboratory data: all studies were normal including CT Scan of the brain, thyroid studies, blood chemistries, erythrocyte sedimentation rate, antinuclear antibody and serologic test for syphilis.

Subsequent course⁴: The patient did not wish to begin any treatment at that point in time. When evaluated 3 months later progression had occurred. He occasionally had the sense of moving slowly. He was now aware that with continuous writing, the writing became smaller, that is, micrographia emerged, evident on examination of handwriting. In addition, a minimal tremor was noted in the Archimedean spiral. A greater, but still minor, degree of cogwheel rigidity was now present at left wrist and elbow. Again, the patient was reluctant to begin therapy. On evaluation 1 year after onset of symptoms, additional progression was evident with significant micrographia (Fig. 19-6) and cogwheel rigidity now evident at left shoulder, elbow and wrist. Therapy with Sinemet (10-100 mg., t.i.d.)⁵ was begun. Re-evaluation one week later demonstrated a marked improvement in handwriting (Fig. 19-6) and decreased cogwheel rigidity.

⁴ This patient was followed for a total of 19 years after disease onset, initially for the first 13 years by the author, subsequently by Dr Paula Ravin at the University of Massachusetts Medical Center, Dr. David Standeart at the Massachusetts General Hospital and Dr. Warren Olanow at the Mount Sinai Hospital in New York.

⁵ This is a combination of 10 mg. of carbidopa (Dopa decarboxylase inhibitor) and 100 mg. of L-Dopa. Higher dosage combinations are a) 25 mg. of carbidopa with 100 mg L-Dopa, and b) 25 mg. carbidopa with 250 mg. L-Dopa. A sustained release form is also available (50 mg. of carbidopa with 200 mg. of L-Dopa), and is marketed as Sinemet CR.

As the dose of Sinemet was increased to (10-100) mg.5x/day over the next week, occasional choreiform movements of the fingers of the left hand and occasional backward flinging (hemi ballistic) movements of the left arm occurred. As the dose reached 10-100 mg. 6x/day, the patient reported that his handwriting now was back to normal. Examination confirmed the significant improvement in handwriting and in gait - with a better movement of the left leg. He no longer turned en bloc. Cogwheel rigidity was still present at left shoulder but to only a minimal degree at left wrist and elbow. The patient did experience 90 minutes after a Sinemet dose - a tremor of the left shoulder and an exaggerated grasp of the left foot toes on lifting the leg (possible form of dyskinetic or dystonic reaction).

The patient did well. When seen one year later, he had only a minimal degree of cogwheel rigidity. No tremor was evident. In walking he had a good swing of the arms and no longer turned en bloc. He was aware that some symptoms of his underlying disease would emerge 3-4 hours after a dose of Sinemet.

He continued to have progression of disease despite the use of all of the known anti Parkinson medications. He eventually underwent a fetal cell transplant in 1997 with apparently little improvement but with a significant increase in dyskinesias.

Re-evaluation, three years after onset of symptoms, indicated a minor progression with decreased swing of the arm and movements of the left leg, which were less smooth. The patient had increased his daily dosage of Sinemet to (10-100 mg) 6 (or) 7 tabs and noted that duration of action was approximately three hours. Re-evaluation, five years after onset of symptoms, indicated that despite having increased his dosage of Sinemet to 25-100 mg. tablets, 7 or 8 x/day, more resting tremor of the left hand had emerged. (In actuality 75-100mg of carbidopa is probably sufficient to saturate the peripheral dopa decarboxylase system). Moreover, choreiform movements of the left arm occurred 60 to 90 minutes after each dose of Sinemet. Examination demonstrated a pill-rolling tremor of the left hand as the patient walked down the hall. The choreiform movements disappeared when the dosage of Sinemet was reduced to 25/100mg 6/day. The increased rigidity and tremor responded to the addition of a DOPA agonist Bromocriptine (Parlodel) - Initial dosage 1.25 mg. 2x/day then increased to a total dose of 5.0 mg., and subsequently to 7.5 mg./day. Despite increasing dosage of the Bromocriptine to 17.5 mg/day - no additional improvement occurred. Additional reduction of Sinemet to (25-100) 5x/day - eliminated sudden myoclonic jerks and dyskinetic movement of the left lower extremity, which would occur - 45 minutes after a dose of Sinemet. Examination 6 years after onset of symptoms, examination and 3.5 hours after last dose of Sinemet demonstrated a coarse pill rolling tremor of the left hand and a shuffling of the left foot in walking. Marked cogwheel rigidity was present at left wrist and elbow. Considerable slowness of alternating finger movements was present. Handwriting was small and slow. Amantadine (an antiviral agent with mild ant parkinsonian effects), 200 mg./day was added at this point with a considerable improvement in symptomatology.

When examined 7 years after onset of symptoms, and 2.5 hours after Sinemet dosage and he now had a prominent tremor of the left hand at rest and a minor tremor of the right hand. Only minor cogwheel rigidity of left wrist and elbow were present. There was mild facial akinesia, tremor of the closed lids and a positive glabellar sign. As he walked he had a problem with sequential movements of the left leg. He reported that initially in the mornings, he had considerable problems in the initiation of movements of his left hand. Because effects of the Sinemet were wearing off in a shorter period of time - the dosing interval was altered to every three hours, in the process increasing total intake to 6 and then 7 tablets per day, with transient improvement. When seen 8 years after onset of symptoms, he was having sudden "kick in of the on effects" at 30-45 minutes and wearing off effects of greater degree at 3 hours after Sinemet dosage. As a result balance had shown some deterioration. Although tremor and cogwheel rigidity were primarily present left arm lesser symptoms were present in the right arm. At this point, a monoamine oxidase B. inhibitor was added: Selegiline (Deprenyl) in a total dose of 10 mg./day (5 mg., b.i.d.). When seen 6months later, the patient was uncertain that any benefit had been achieved. A major symptom was now "freezing" - he would have times in going over the threshold of a door when he would suddenly freeze. This, at times, related to the wearing off of medication (Sinemet) effect but at other times, usually in the afternoon, was unrelated to time of last dose. In the morning, freezing effect was clearly related to time of dosage. He remained relatively stable for the next year and then had a progression of symptoms - increasing tremor, increasing dragging of the left leg and more wearing off of dose effect - usually after 2.5 hours. In addition, "freezing" episodes were occurring more frequently in between dose wear off periods, usually in going through a doorway or even in hallways. At this point, the patient was switched to the sustained release form of Sinemet (50/200 mg carbidopa/L-Dopa) taken three times a day. Amantadine, Bromocriptine and Selegiline were continued unchanged. When evaluated 6 weeks later, there had been a remarkable improvement. He had a smoother day with fewer ups and downs, less dyskinesia and less stiffness. Effects of the medication were lasting 5-6 hours. When seen 3.5 hours after his last Sinemet dosage, he had

very little cogwheel rigidity. He could walk with a good swing of the arms. Handwriting was good with little tremor and little dyskinesia. On the other hand, when seen several weeks later, approximately 5.5 hours after his dose of sustained release Sinemet, he had marked difficulty, walked with small steps, and would arrest going through a doorway. Balance was poor, requiring a cane. There was a marked tremor of the left hand and to a lesser degree, of the right hand. A marked akinesia was present. However, within 20 minutes of his taking an additional tablet of sustained release Sinemet, a marked improvement again occurred. Despite this long course, the patient had been able to continue in his usual occupation. The patient subsequently was treated with a COMT inhibitor and was switched to another dopamine agonist pergolide with little apparent benefit. Eventually, in 1997 he was entered into the NIH sponsored fetal transplant study (subsequent imaging study did indicate that the patient was in the transplant and not the placebo group). It was unclear that this had produced any decrease in his disability. However evaluation 3 years after the transplant did demonstrate a marked increase in the dyskinesias involving head arms and torso. Some improvement in dyskinesias occurred when dopaminergic medications were reduced

Comment: Parkinson's disease is a progressive disorder of motor function, with variable manifestations of tremor, rigidity, akinesia, bradykinesia, and impairment of postural reflexes. Patients vary in the type of major involvement and in the rate of progression. Pharmacological management has rapidly evolved and in the process has provided considerable insights into the nature of basal ganglia function. For the specific patient, therapy must still be individualized. As this case history illustrates the pharmacological effects are time limited. Evaluation of therapy must always record the time of drug intake and the time of examination.

It is important to note that the disease remains progressive, despite the impressive pharmacological achievements. To prevent progression would require arresting or reversing the loss of the nigral cells producing dopamine or of introducing another source of dopamine producing neurons into the basal ganglia as discussed above. The future of fetal transplantation remains uncertain. Surgical procedures particularly deep brain stimulation involving the subthalamic nucleus or the globus pallidus may offer benefit to specific patients.

The following case, 19-2 provides an example of hemichorea.

Case 19-2 : This 88-year-old, right-handed, widowed white female with a past medical history of profound hearing impairment, adult onset diabetes, euthyroid goiter, coronary artery disease, and hypertension was brought by her daughter to Saint Vincent's Hospital because of uncontrollable movements ("twitching") of her left foot and shoulder. The daughter described the insidious onset of involuntary rotary movement in the left foot five days prior to admission, which increased in intensity and progressed to involve the left shoulder. The movements were constantly present, even during sleep. The movement was accompanied by a "shooting" pain on the left side of the body which the patient was not able to further describe. She denied loss of consciousness, dizziness, change in mental status, weakness, sensory impairment, visual changes, aphasia, or dysphagia associated with the movement disorder, but did describe a dull headache greater on the left side than on the right during the last few days prior to admission, not accompanied by nausea or vomiting. There was no history of a past movement disorder. Progression rather than spontaneous resolution of the choreiform movements which had begun to impair the patient's ability to ambulate with her walker prompted her daughter to seek medical attention.

Past history: The patient had been admitted briefly one year previously with confusion. and hyperglycemic state related to diabetes mellitus.

Physical Examination: vital signs were all normal.. Patient was alert and cooperative, though profoundly hard of hearing and exhibited involuntary twisting movements of her left foot and upward jerking movements of her left shoulder.

Neurological examination:

1. *Mental Status:* The patient was oriented x3. Memory and language were grossly intact, questions were answered appropriately, and mental status was consistent with the patient's baseline according to her daughter.
2. *Cranial Nerves:* Intact except: for Left eye blindness (cataracts), and gross impairment of hearing such that shouting was necessary to communicate.
3. *Motor System:*
 - a. Tone and strength in upper and lower extremities were normal except for minimal weakness in the left upper extremity(5-/5) .
 - b. Finger tapping, finger-to-nose and heel-to-shin were grossly intact with only slight left-sided difficulty due to involuntary movements.

- c. There was a persistent hemichorea without flinging motions in the left foot, more marked than the left shoulder. There were rotary, twisting movements at the left ankle and upward and rotary motions at the left shoulder. The movement was exacerbated by motor—tasks but did dissipate with sleep.
 - d. Gait was slightly unsteady due to hesitant placement of the left foot. She did quite well with minimal assistance.
 - e. Romberg was negative.
4. *Reflexes*: Deep tendon reflexes were symmetrical, and physiologic except for decreased Achilles secondary to diabetes. The right plantar response was flexor, the left ;extensor.
 5. *Sensation*: Intact except for symmetrically diminished vibration sense in toes.

Clinical diagnosis: hemichorea

Laboratory data:

1. *Electrolytes creatinine, and CBC* were normal. *Glucose* was elevated to 168; *ESR* - 36 mm/hr. *RPR* non-reactive. *ANA* was 1:80(not significant) .*Urine culture* was positive for group B Streptococcal - infection sensitive to Ampicillin. *EKG and chest X-ray* were unchanged from last admission.
2. *CT scan* on admission revealed bilateral basal ganglia calcification, bifrontal atrophy consistent with age, but no evidence of infarction, hemorrhage, or tumor and revealed no change from previous CT scan of 2 months previously.
3. *MRI scan* 3 days after admission, revealed mild cortical atrophy and a hyperdense area without mass effect or enhancement on gadolinium in the right basal ganglia (particularly the head of caudate and putamen) and external capsule consistent with subacute hemorrhage (Fig.19-7).

Hospital course: The patient was begun on haloperidol 0.5 mg by mouth every morning and advanced to 1 mg., by mouth., t.i.d. with some improvement in the hemichorea, particularly in the upper - extremity. Her hemichorea continued to improve over the next two weeks on haloperidol with only occasional twitching of the left shoulder and diminished but persistent, rotary movement of the left foot, both still exacerbated by motor tasks.

The following case 19-3 provides an example of hemiballismus

Case 19-3: This 79-year-old, right-handed, white housewife had the abrupt onset in the early morning hours, 2 days prior to admission, of almost constant flinging movements of the right arm over which she had no control. At the same time, she noted that her right arm felt numb and heavy. Over the next 2 days, the movements decreased markedly and she regained more control of the arm.

Past history: The patient had been a known diabetic for 21 years, receiving insulin - most recently, lente insulin, 25 units each morning.

Neurological examination:

1. *Mental Status*: intact ,the patient was alert and well oriented and without aphasia.
2. *Cranial Nerves*: All were intact.
3. *Motor System*:
 - a. Minimal weakness was present in the right upper extremity at the elbow, wrist and fingers
 - b. Alternating movements and finger-to-nose testing in the right hand were markedly impaired.
 - c. Gait was intact.
 - d. Occasional involuntary flinging movements occurred at the right shoulder.
4. *Sensory System*: Pain, touch, vibration and position sense were all absent in the right upper extremity to the elbow and decreased in this extremity above the elbow.

Clinical diagnosis: hemiballismus

Laboratory data: Chest and skull X-rays EEG, and cerebrospinal fluid studies were all normal.

Subsequent course: The flinging movements of the right arm subsided spontaneously, shortly after admission. Position sense returned and pain sensation showed a mild improvement. The ataxia on finger-to-nose testing disappeared.

Comment: The loss of pain, touch, vibration and position sense in the right upper extremity at the onset of symptoms in this case, would suggest a lesion involving the ventral posterior lateral nucleus of the thalamus, presumably as a result of occlusion of the penetrating branches of the

posterior cerebral artery. Such a lesion could have damaged the subthalamic nucleus as well. The severe dysmetria in the right upper extremity could well have reflected the severe sensory deficit in the right upper extremity. This would appear to be more likely than postulating a lacunar ataxic hemiplegia, due to involvement of the corona radiata in which the origin of the hemiballistic movements could have been in the adjacent caudate putamen. This however would not explain the severe sensory deficit. Note that the use of antidopaminergic agents will decrease or eliminate hemiballismus or hemichorea; however many patients as in this case resolve spontaneously.

The following case history provides an example of Huntington's disease.

Case 19-4: This 54-year-old right-handed divorced white female was referred for evaluation of a movement disorder. The patient lived alone and it was difficult to obtain much of any history from the patient. So far as she was concerned, she had no neurological problems. She denied any problem with her movements. She did indicate that she had worked for 10 years as a secretary/computer operator but had been fired 10 years ago because "she did not work fast enough". She did indicate that she had experienced problems with memory over the last year. The patient denied that she had never been treated on a psychiatric service. She denied receiving neuroleptics. She had a past history of hypertension but had not been reliable in taking her prescribed medication. The patient's son was aware that changes in emotion, personality, speech, gait and a movement disorder had been present for at least 3 years.

Family history: The patient denied any neurological family history except for a maternal uncle who had the "shakes". By contacting the patient's son age 27 and her mother now age 81 and then obtaining old records we were able to assemble additional information. The patient's father had been hospitalized at age 55 on the psychiatry service of St. Vincent Hospital. A review of that record indicated that for several years he had been showing irritability, had become suspicious and paranoid at work. He gave a history of choreiform movements of 20–30 years duration beginning with twitchings about the shoulders. This had progressed over the several years prior to admission, affecting his gait and the movements of the hands. The examination demonstrated that he was moderately depressed and impatient. As he sat, he had "purposeless" movements of his body particularly of the lower extremities. In walking he had "ballistic" movements. He walked on a broad base. Choreiform movements were noted in the tongue. The diagnosis of the neuropsychiatrist was Huntington's disease. He apparently died of cardiac disease shortly after that hospitalization.

The paternal grandfather had died at age 43 of pneumonia, the paternal grandmother at age 37 of gall bladder disease, neither was known to have Huntington's disease, but information was scanty. The patient's father had two siblings one alive at age 81, the other dead at age 68, both apparently unaffected. The patient's mother had a sister with essential tremor.

The patient had 2 siblings, a brother age 60, a sister age 44; both unaffected according to the patient's mother.

The patient had 4 children ages 34, 32, 30 and 27, and 3 grandchildren ages 13 years, 2 years, and 3 months. The eldest daughter age 34 had been depressed for 5 years and had problems with speech and walking for a number of years.

Neurological examination:

1. *Mental status*: the patient often avoided eye contact. Affect was usually inappropriate with laughter as the response to many questions. The overall mini-mental status score was 27/30. The only deficit related to delayed recall portion of the test (0/3 objects).

2. *Cranial nerves*: the patient had a hyperactive jaw jerk. She had frequent facial grimacing.

3. *Motor system*: the patient had decreased tone at wrists and elbows, but strength was intact.

As she sat she had frequent restless and at times choreiform movements of hands and feet.

Gait was often "bizarre" in terms of occasional sudden movements of a leg as moved down the hall and came to a stop. These same movements occurred as she remained standing. In addition in standing or walking, there were intermittent dystonic postures of either left or right arm.

4. *Reflexes*: Deep tendon stretch reflexes were everywhere hyperactive. Plantar responses were flexor. There was a minimal suggestion of grasp release.

5. *Sensory system*: intact

Clinical diagnosis: Huntington's disease.

Laboratory data:

1. *MRI scans of head* (Fig.19-13): The heads of the caudate nuclei were very atrophic. Cortical sulci were wide consistent with cortical atrophy. The lateral and third ventricles were secondarily dilated.
2. PCR testing for the CAG trinucleotide repeats of the Huntingtin gene.: allele 1=17; allele 2=42.
3. Thyroid studies, sedimentation rate, electrolytes, RPR, and antinuclear antibody were all normal.

Subsequent course: The patient refused any treatment for the movement disorder. The patient's son requested genetic testing and the issues were discussed. He and his siblings finally decided not to have the genetic testing performed. The patient's neurological status according to the son worsened to a moderate degree over the subsequent 3 years as regards speech, unsteadiness of gait, and mood swings but without any additional change in memory. The patient herself always appeared unaccompanied for follow up visits and reported no change in her condition.

Comment: Occasionally patients are encountered where changes in psychological function limit the information that the patient can provide. In other cases denial of illness has a neurological as well as a psychological basis. In this case it was evident that this patient had not only symptoms relevant to the basal ganglia but also changes in cognitive function relevant to the cerebral cortex particularly the frontal areas. In such cases, information must be sought from other sources. In this case, the patient was willing to provide permission to contact those possible sources.

The clinical presentation in this case was clear-cut. In retrospect, many of the neurological features were similar to her father's findings on his admission 30 years previously. When did the patient's disease begin? This was uncertain, but we may presume that serious problems had been present at least 10 years earlier when she had been fired from her long time employment. Did this relate to motor problems, to changes in personality and interpersonal relations or to cognitive changes? Most likely, there were problems in all of these areas. According to her family, symptoms had been present for 2-3 years suggesting onset at age 51 or 52 years.

Case 19-5 provides an example of a patient with Huntington's disease followed over a longer period of time.

This 32 year old right-handed married white male spray painter at a computer factory, was referred for evaluation of a possible hereditary movement disorder. The patient was unclear about the reasons for his evaluation and much of the history was provided by his wife. She reported that the patient had undergone a personality change in the last several months. He had noticeable mood swings and on one occasion he reported people outside the window when no one actually had been there. He had some problems with remembering incidental matters, but no major problems and his job performance had remained intact. He was described as always having been "fidgety".

Past medical history - Mild hypertension for three years.

Family history - The patient's initial history indicated that the family had "Parkinson's" disease and his father had died in his 40's at the state hospital after a 10-15 year illness. The patient indicated that he was a child at the time and his mother never really told him much about the father or let him visit the father in the hospital but he did recall that perhaps his father had some excessive movements of the hands and face. The records were subsequently obtained and these indicated the father had been admitted to Worcester State Hospital in 1968 at age 37. At that time, he had already had three previous hospitalizations for "nervous breakdowns". At the time of his final admission, he had developed hallucinations, seeing people in his room. He had threatened his wife and other relatives. He had difficulty sleeping and he had also developed a problem with his legs "they are jumping". The father's examination had demonstrated a mumbled speech with repetition of the same phrases. His responses would often be tangential and then incoherent with impairment of memory and judgment. His mood was depressed. He was noted to have involuntary movements of the fingers and occasional facial grimacing. The deep tendon reflexes were hyperactive and the plantar responses were extensor. His gait was ataxic. The subsequent course indicated increasing ataxia, choreiform movements and rigidity with increasing weakness, difficulty swallowing and the final development of bronchial pneumonia with death at age 42. The diagnosis of Huntington's disease was confirmed at autopsy.

The paternal grandfather had expired at age 67 with a diagnosis of Huntington's disease, manifested by "nervous breakdowns, inability to sleep and movement disorder". The father's three siblings apparently did not manifest the disease. The patient had two siblings, brother age 28, a sister age 35, all without known disease. He had two children ages 9 and 5.

Neurological examination

1. *Mental Status* - The patient was anxious, often appeared blunted in emotional expression or in answering questions. He avoided eye contact. He was oriented for time, place and person. He was able to name objects and colors. His delayed recall was 2/5 without assistance and 4/5 with assistance.
2. *Cranial Nerves II-XII* were intact, except for the occurrence of occasional, sudden darting movements of the eyes to either left or right. In addition, occasional facial grimacing was noted occurring in a rather irregular manner.
3. *Motor System* : Strength and gait were intact . There were occasional, sudden, irregular, lateral, tremulous movements of the fingers of a choreiform-type.
4. *Reflexes* : Deep tendon reflexes including the jaw jerk were everywhere hyperactive. Plantar responses were bilaterally extensor (bilateral Babinski signs).
5. *Sensory system* : intact

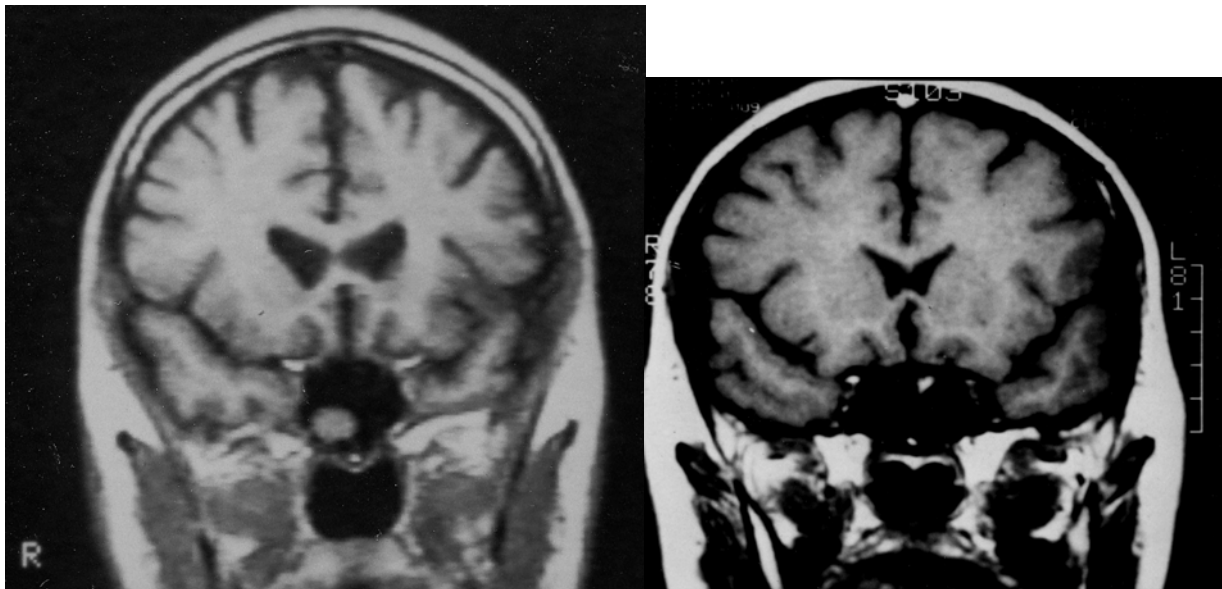
Clinical diagnosis: Huntington's disease

Laboratory Data :

1. All blood chemistries, including glucose; BUN, calcium, electrolytes, liver function studies, ceruloplasmin level, thyroid studies and serological test for syphilis were within normal limits. Ceruloplasmin levels are low in Wilson's disease but normal in Huntington's disease.
2. *Electroencephalogram* was normal with a dominant awake background activity of 10 Hz alpha rhythm.
3. *CT scan of the head* demonstrated enlargement of the ventricles with particular atrophy of the caudate. In addition the sulci were prominent for the age, suggesting some degree of cortical atrophy. The study was considered consistent with the clinical diagnosis of Huntington's disease.
4. The *MRI scan* (fig 19-11A) demonstrated mild enlargement of the ventricles and deepening of the cortical sulci, as well as a very significant atrophy of the head of the caudate nucleus. The MRI from this patient is compared to a similar section from a patient without signs of neurological disease (Figure 19-B)..

Figure 19-11A ;Case 19-5. Huntington's Disease

Figure 19-11B. Normal, age matched



Subsequent course :The patient subsequently developed increased paranoid ideation, increasing dependency with regard to his wife. He was treated with Haloperidol (a neuroleptic, tranquilizer) with considerable improvement with regard to personality. When evaluated, 3 years after onset of disease, it was evident that in the interim, the patient's personality problems had decreased. Attacks of anger and paranoid features had subsided. Mood swings were less. Memory problems, however, were worse and choreiform movements were worse. Dysarthria was now present. The patient had been divorced in the interim and he was on social security disability and no longer working. The examination now showed an exacerbation of many of those features noted at the time of his initial evaluation. He had occasional, sporadic movements of head or eyes of a

choreiform nature. He had frequent choreiform movements involving the fingers as he was sitting, also a similar type of movement appeared to involve the abdominal musculature. He had a moderate degree of dysarthria. He could walk a tandem gait but as he did so, the left arm came up in an somewhat flexed position. When last seen 4 years after onset of disease, he had more dysarthria and his speech was more difficult to interpret. There had been some increase in degree of rigidity but this had decreased when the dose of haloperidol had been decreased. The decrease in this medication, however, then resulted in a greater prominence of the choreiform movements. He could still handle a deck of cards, although he was dropping objects more often than previously. His neurological examination showed a significant degree of dysarthria, a greater degree of facial akinesia, more frequent choreiform movements of hands and face. He had difficulty in mimicking facial expression. As before, all of his deep tendon reflexes were hyperactive and the plantar responses were extensor. The patient walked in a flexed position and tended to turn en bloc. He had a mild degree of cogwheel rigidity at wrist and elbows. His memory remained remarkably good for delayed recall. Final telephone follow-up with his primary physician (approximately 7 years after apparent clinical onset of disease) indicated that the patient was no longer able to drive. He had continued weight loss. He had a marked dysarthria so that his speech was barely intelligible. Choreiform movements had increased. His gait was ataxic, but he could still walk without stumbling. He was relatively stable from a psychiatric standpoint. He was now living with his mother and brother.

Comment: This patient and his family demonstrate the relatively typical course of most patients with Huntington's disease. Patients and families do vary as to whether it is the psychiatric features or the movement disorder features that first bring the patient to medical attention. In this case, the psychiatric features, that is, the change in personality and the increasing paranoid ideation were the first features noted. Subsequently, involvement of the motor system became the most prominent feature. As in the previous case, the patient was unclear as to why he had come for neurological evaluation. Was this a neurological or a psychological denial of illness? Most likely both factors were operational. It was of considerable interest that this patient when first seen, although he was aware of some neurological problem that had occurred in the family, was unclear as to the specific diagnosis. It was also evident that almost no genetic counseling had been done in a disorder that was very clearly an autosomal dominant disorder. The significant family impact, social and economic impact of the disease are clearly evident in this patient. The implications of presymptomatic detection are discussed by Meisser et al (1988), and Klawans (1972).

The following Case 19-6 illustrates the clinical problem of hepatolenticular degeneration in a 21 year old female with a brother who had died at age 16 with hepatic disease, a Kayser Fleischer ring and choreoathetosis. The patient had serum elevation of free copper and a decrease in protein bound copper. She was successfully treated with penicillamine.

Case 19-6 (Patient of Doctor Huntington Porter) :This 21-year-old, single, white female shoe worker in January 1954 had the onset of a "shaking", or trembling of the fingers and hands which progressed to involve both arms and legs. The degree of involvement increased sufficiently to force her to give up her work. Nine months after onset of symptoms, she began to note increasing difficulty with balance and coordination and a slurring of speech. She had also noted increasing weakness and difficulty in doing repetitive tasks. One year after onset, the patient noted blurring of vision, occasional diplopia, and periods of "staring". She also had experienced increasing urgency and occasional urinary incontinence.

Family history: A brother of the patient had died in 1952, at age 16, of a disease with manifestations similar to this patient's. Evaluation of the sibling 2 years before his death by Drs. John Sullivan, Raymond Adams and D. Denny-Brown, had indicated the presence of choreoathetosis with lapses in posture of the hands. In addition, a brownish green ring at the corneal -

scleral junction was noted. Liver disease was present in this sibling and possibly other members of the family.

Neurological examination:

1. Mental status:

- a. The patient was anxious, at times crying, at other times, euphoric.
- b. Digit span was limited to 6 forward, 3 in reverse.
- c. Serial 7 subtractions were poorly performed.

2. Cranial Nerves:

- a. A brown rim was present at the limbus of the cornea, more evidence inferiorly and superiorly.
- b. Extraocular movements were impaired by involuntary jerk movements, The patient was unable to track a moving finger.
- c. Facial expression was mask-like.
- d. Speech was dysarthric and of a nasal quality with slurring and slowness of articulation.

3. Motor System:

- a. No actual weakness was present. However, this patient had difficulty maintaining the limbs in a fixed posture.
- b. There was a rigidity to passive movement of the limbs.
- c. A coarse arrhythmic tremor was present which was most marked proximally and more marked on sustained posture and on movement than at rest.
- d. Alternating movements were poorly performed.
- e. Gait was ataxic. Romberg test was negative.

4. Reflexes: Deep tendon stretch reflexes were hyperactive but plantar responses were flexor

5. Sensation: Intact

Clinical diagnosis: Wilson's disease: hepatolenticular degeneration.

Laboratory data:

1. Liver function tests were normal.
2. *Glucose tolerance test* was normal, but glycosuria occurred.
3. *Total plasma copper* 52 ug/100 ml. (normal range in a young adult is 65 to 150 ug/100 ml).
Direct reacting copper (unbound to ceruloplasmin) 31 ug/100 ml (normal 10 ug/100 ml).
Indirect copper (ceruloplasmin bound) 21 ug/100 ml, normal 105 ug/ ml).

Subsequent course: The patient did relatively well following the use of the chelating agents, BAL and calcium versenate and the institution of a copper free diet. A liver biopsy performed at the time of a cesarean section 18 months after beginning treatment was compatible with perihepatitis with a question of post-necrotic cirrhosis.

Re-evaluation 6 years after onset revealed, in addition to the earlier findings, the presence of "continual spontaneous involuntary movements of the limbs; at the feet, characterized by alternating flexion and extension at the ankle and a waving of the toes". A broad amplitude coarse tremor was noted when the patient was asked to abduct arms, flex elbows, and hold hands just before her nose (wing beating position). A side-to-side tremor of the head was also present. The gait was slightly wide-based and associated with continual dystonic movements of the hands and arms. Treatment with d-penicillamine (which had just become available) was begun at that time.

Urine copper excretion increased from 700 ug per 24 hours to 3240 ug per 24 hours. Normal 24-hour urinary copper in the adult is less than 40 ug. Neurological symptoms soon demonstrated improvement from the previously noted status. The patient was now able to do her house work and take care of her children.

Follow-up 2 years later, indicated significant improvement as regards the findings noted in 1960; dystonic facies and dysarthria was less marked. No tremor was present in the left hand; that in the right hand was evident only when under tension. Dystonic posturing of the hands was present only to a minimal degree. At last report 4 years later, and 12 years after onset of the disease, the patient continued to do well. She had remarried and was expecting another child.

Comment:

This patient presents a typical case of Wilson's disease with onset in the young adult years and with a definite familial background. The copper levels were consistent with the diagnosis (an increased unbound fraction and a decreased bound fraction). At the time that this patient was seen in the mid 1950's and early 1960's, ceruloplasmin levels were not available. Early establishment of a specific diagnosis in this case allowed for specific therapy with improvement of neurological symptoms and the prevention of progression of hepatic disease. With a specific diagnosis established in the patient, periodic blood tests were performed on her offspring to determine whether they also had inherited this genetic disease. (The child born 18 months after onset of the disease had not the disorder.)

An acquired form of non-Wilsonian hepatic and cerebral degeneration occurs in patients who have had multiple episodes of hepatic coma. Degenerative changes occur in the astrocytes and neurons of the basal ganglia. This disorder which was first described by Adams and Victor is discussed in greater detail above.

CHAPTER 20. MOTOR SYSTEMS III: CEREBELLUM

The following case provides an example of a child with a medulloblastoma.

Case 20-1: This 27-month old white female was referred for evaluation of ataxia. The mother had noted that the child had been unsteady in gait, with poor balance, falling frequently since the age of 13 months, when she began to walk. Three months prior to admission, in relation to a viral infection manifested by fever and diarrhea, the patient developed increasing anorexia and lethargy. One-month prior to admission, vomiting increased, and the patient also became more irritable. Perinatal history had been normal, and head circumference had remained normal.

Neurologic examination:

1. *Mental Status:* The child was irritable but cooperative.
2. *Cranial Nerves:* The fundi could not be visualized. Bobbing of the head was present in the sitting position.
3. *Motor System:* A significant ataxia of the trunk was present when sitting or standing. Gait was broad-based and ataxic, requiring assistance. No ataxia or tremor of the extremities was present. Strength and tone were normal.
4. *Reflexes:* Deep tendon reflexes were symmetric and plantar responses were flexor.
5. *Sensory System:* All modalities were intact.

Clinical diagnosis: Probable midline cerebellar tumor, most likely based on age a medulloblastoma

Laboratory data:

1. *Left brachial arteriogram* indicated an avascular area in the posterior fossa. The superior cerebellar artery was elevated. The inferior cerebellar arteries were depressed.
2. *Air-contrast ventriculogram* demonstrated enlargement of the lateral and third ventricles. The cerebral aqueduct was displaced forward to a marked degree. The fourth ventricle was deformed by a mass overlying the posterior wall (essentially located in the nodulus).

Hospital Course: Doctor Peter Carney performed a suboccipital craniotomy. The dura was bulging. The cerebellar tonsils were herniated to a minor degree. On gentle retraction of the inferior posterior vermis, a pinkish gray tumor, originating from a higher point in the fourth ventricle, was visualized at the obex. Limited biopsies of this tumor were taken, revealing a medulloblastoma. Samples of cerebrospinal fluid obtained at surgery revealed the presence of many malignant cells. A permanent shunt from the lateral ventricle to the jugular vein was not installed because of the possibility of spread of tumor cells into systemic circulation. Instead, a catheter was connected from the lateral ventricle to a small reservoir inserted under the skin of the scalp to allow daily drainage. Radiation therapy to the entire central nervous axis was begun one week after surgery. By the time of hospital discharge two weeks after the operation, the patient was able to walk unassisted, with only a moderate degree of ataxia. Three months after the operation, the patient was readmitted because of recurrent irritability and vomiting. A mild degree of papilledema was present. Horizontal nystagmus was present on lateral gaze bilaterally. A wide-base ataxic gait was still present. Various antineoplastic agents were employed (methotrexate into the cerebrospinal fluid and vincristine intravenously) without significant improvement. One month later, respirations became slow, deep, and irregular and death occurred. The findings at autopsy are demonstrated in Fig. 20-4.

In the following case a metastatic tumor in the midline cerebellum produced vertigo, ataxia of gait and headaches.

Case 20-2: This 67 year old white female 6 weeks prior to admission developed intermittent vertigo. Two weeks prior to admission she developed an ataxia of gait. Two days later headaches and true vertigo developed, ataxia increased and vomiting occurred. On the day of admission severe vertigo, headache and nausea and vomiting resulted in her visit to the emergency room

Past history: The patient had a lumpectomy 6 years prior to admission for carcinoma of the left breast. She had undergone a radical mastectomy followed by radiation therapy 3 years prior to admission for a recurrence of malignancy. Histologic examination of the excised tissue indicated a very poorly differentiated (high grade of malignancy) infiltrating ductal tumor which was negative for estrogen and progesterone receptors. On both occasions, the patient refused chemotherapy. The patient had multiple other medical problems including non insulin dependent diabetes mellitus, coronary artery disease, mild hypertension, and prior hip replacement surgery.

Neurological examination (in the emergency room)

1. **Mental Status:** Intact
2. **Cranial Nerves:** Intact except for an absence of venous pulsations on funduscopic examination suggesting a mild increase in intracranial pressure without frank papilledema.
3. **Motor System:** The patient had difficulty standing tending to fall to the right. She was unable to walk because of severe ataxia. There was no limb dysmetria.
4. **Reflexes:** Deep tendon stretch reflexes were symmetrical. The right plantar response was equivocal.
5. **Sensory system:** Intact

Clinical diagnosis: Midline cerebellar tumor metastatic from breast.

Laboratory data :

1. **CT scan of brain:** A large (3-4 cm) enhancing tumor was present involving the midline vermis and right paramedian cerebellum and compressing the fourth ventricle.

2. **MRI of brain** (3 days after admission): An enhancing midline mass involved the cerebellar vermis extended into the right cerebellar hemisphere, and produced mass effect upon 4th ventricle (Fig. 20-5).

3. **CT scan of abdomen** demonstrated two solitary possible metastatic lesions in the liver.

Subsequent course: The patient was immediately placed on dexamethasone with significant improvement. Within 12 hours the examination demonstrated only a mild ataxia tandem gait on turns and bilateral extensor plantar responses. The patient strongly insisted on removal of the solitary central nervous system metastases. Histological examination of the tumor resected by Dr. Gerald McGullicuddy demonstrated poorly differentiated adenocarcinoma with extensive necrosis similar to the tumor which previously had been removed from the breast. Following surgery she received 3000cGy(rads) whole brain radiation and was begun on the antitumor agent tamoxifen. She continued to manifest some unsteadiness on gait but had no difficulty in finger to nose or heel to shin tests. Three months after her admission, a repeat CT scan of the abdomen and pelvis demonstrated diffuse hepatic metastases with mesenteric and retroperitoneal lymphadenopathy. She expired at home, four

months after surgery before she was to start additional treatment with the antineoplastic combination of Cytosan, methotrexate and 5-fluorouracil .

Comment : This patient had a highly malignant poorly differentiated adenocarcinoma of the breast and was clearly at risk for the development of distant metastases ,a risk that was likely increased by her unwillingness to receive antitumor medication. Six years after the lumpectomy she presented with vertigo, ataxia headache and nausea and vomiting, without limb dysmetria. These symptoms suggested involvement of those areas of cerebellum related to the vestibular system and the axis of the body: the floccular nodular area and vermis. Certainly ,the best treatment of a solitary metastatic brain tumor where systemic metastases are not present is the combination of total resection of the brain lesion followed by radiotherapy. However at the time of surgery ,this patient already had evidence of two probable metastatic lesions in the liver. Except for the strong insistence of the patient that the tumor in brain be removed ,an alternate course of radiotherapy, dexamethasone and chemotherapy might have been pursued. Never the less the patient had several additional months of life during which she was able to travel to visit various relatives for a last time. Consistent with the highly malignant character of the tumor, this patient succumbed to the non neurologic effects of her disease

The following case history 20-3 illustrates the problem of alcoholic cerebellar degeneration.

Case History 20-3: This 64-year-old, white male was admitted with a chief complaint of a slowly progressive incoordination of gait present for 8 years. The patient and others had noted that his gait was staggering. The patient denied weakness, numbness, diplopia, vertigo, or memory difficulty. The patient admitted to the consumption of one half pint (250cc) of brandy every 4 nights since symptoms had developed. He indicated that he use to drink more in his younger days, at least 6 to 8 beers in addition to brandy or other alcoholic beverages every night.

There was no history of pes cavus or neurological disease.

General physical examination ; Blood pressure 140/80. Liver was enlarged with the inferior edge extending 2 finger breadths beyond the costal margin. Face was red with dilation of vessels.

Neurological examination:

1. *Mental status:* The patient was slightly disoriented for time. He gave the date as September 31. The date was actually October 19. Delayed recall was 0-out-of-5 objects in 5 minutes. He was unable to give the date of his birth, but he knew his phone number. Digit span was 7 forward, 4 in reverse. Calculations: The patient was unable to subtract 7 from 100 or 3 from 30; he could not add 14 and 13, although he had a fourth grade education.

2. *Cranial nerves:* All were intact. No nystagmus was present.

3. *Motor system:* Strength was intact. Gait was broad-based with an ataxia of trunk. The patient was unable to walk a tandem gait. His ataxia was accentuated by rapid walking. Small lateral nodding movements of the head were noted. He was relatively stable when sitting. There was a minimal tremor at rest. In addition, there was, to minor degree, a resistance to passive motion at the wrists and elbows with a suggestion of a cogwheel component. There was a minor tremor on finger-to-nose testing and a minor impairment of alternating hand movements.

There was, however, a very significant heel-to-shin ataxia which was out of proportion to any tremor or ataxia involving the upper extremities.

4. *Reflexes:* Deep tendon reflexes were physiological and symmetrical (2-3+). Plantar responses were flexor bilaterally.

5. *Sensory system:* Position, pain and touch were intact. There was a moderate decrease in vibratory sensation at the toes and ankles.

Clinical diagnosis: 1. Alcoholic cerebellar degeneration. 2. Mild dementia possible residuals of Wernicke's-Korsakoff syndrome.

Laboratory data: Complete blood count, albumin and total protein, sedimentation rate, cerebrospinal fluid, and skull and chest X-rays were normal.

Subsequent course: The patient received multiple B vitamins and was advised to discontinue any intake of alcohol. Neurological re-evaluation over the next 6 years indicated that no essential progression had occurred.

Comment: The major findings of the broad-based, staggering gait with truncal ataxia and heel-to-shin ataxia may be related to the anterior lobe of the cerebellum. In view of the absence of progression after the discontinuation of alcohol, a toxic or nutritional factor may be postulated (The reliability of the history obtained, in terms of the specific amount of alcohol intake is always open to question particularly in a patient

with significant problems in memory. The amount stated by the patient is usually assume to be the minimum amount.). The minor extrapyramidal findings of cogwheel rigidity may have represented unrelated disease. The lack of progression would be evidence against the diagnosis of a cerebellar degeneration of other etiology (see below). The minor degree of dementia may have related to previous nutritional problems with minor Wernicke-Korsakoff's syndrome or may have reflected a minor unrelated dementia or may have related to long standing retardation. At the present time, the diagnosis may be confirmed by CT scan or by MRI (midline sagittal section) (as in Fig. 20-7 or 20-8). As a result, evidence of cerebellar atrophy is now found in many patients presenting with other aspects of chronic alcoholism or other nutritional disease who do not necessarily present with initial symptoms of ataxia.

In the following case, a similar cerebellar gait disorder and heel to shin ataxia occurred o a genetic basis.

Case 20-4: A 45-year-old single white male carpenter presented with a 4 year history of progressive unsteadiness in walking, present during the daytime as well as at night. He had, during this period, noted minimal loss of coordinated movements in his hands, but felt that his greatest deficit was unsteadiness. The patient had noted no actual weakness but reported some numbness at the toes. He had also noted some minor difficulty in swallowing.

The patient lived in a small town in Virginia. Family historical information was incomplete His mother and father were second cousins. Several aunts and uncles had "trouble with their legs" in later life, resulting in a difficulty in walking. The patient admitted to a minimal intake of alcohol in the past. He had recently been under the care of a naturopath and had experienced a 7-pound weight loss.

Neurologic examination:

1. *Mental status:* Intact and consistent with his educational level.
2. *Cranial nerves:* Intact except for minimal dysarthria. Horizontal nystagmus was present on lateral gaze, vertical nystagmus on upward gaze.
3. *Motor system:* Strength was intact. The patient walked on a broad base with an ataxia of trunk, as though intoxicated, reeling from side to side, with marked unsteadiness on turns. He was unable to walk a tandem gait with eyes open. The patient was able to sit without significant ataxia of the trunk. A mild intention tremor was present, and there was minimal disorganization of alternating movements. In contrast a marked ataxia and tremor were evident on heel-to-shin test.
4. *Reflexes:* Deep tendon reflexes were intact, except for a relative decrease in ankle jerks compared to knee jerks. Plantar responses were flexor.
5. *Sensory system:* Intact, except for a minimal decrease in vibration sensation at the toes.

Clinical diagnosis: Hereditary cerebellar degeneration involving predominantly anterior lobe

Laboratory Data: Pneumoencephalogram performed at the University of Virginia Hospital (Doctor Stewart) confirmed the significant atrophy of cerebellum. Cerebrospinal fluid and other laboratory data were normal.

Comment: This patient had onset of ataxia at age 41 and was seen relatively early in his disease course. The most prominent features included the ataxia of gait and the heel to shin dysmetria. The patient also had a minor dysarthria, nystagmus and a mild asymptomatic peripheral neuropathy (decreased Achilles reflexes and decreased vibration at toes). There was a familial background but the information was incomplete. The subject of genetic cerebellar degeneration will be considered in a later section. Using older terminology, this patient would have been classified as olivopontocerebellar atrophy. Using more modern terminology, the patient might be included within the category of autosomal dominant cerebellar ataxia type I, had more genetic information regarding the family been available by history and or actual examination.

The following case history illustrates a focal lesion of the lateral hemisphere

Case 20-5 : This 36-year-old white male attorney was referred with a chief complaint of headaches and vomiting. The patient had frontal and biparietal headaches for approximately one month precipitated by coughing, sneezing, or bending. On at least one occasion, the patient had been awakened by the headache. The patient had nausea and vomiting independent of the headaches, at times, occurring suddenly without preceding nausea. For several weeks prior to admission, the patient had been unsteady on his feet, with a tendency to fall to the right, and had noted intermittent clumsiness of his right hand. For several days prior to admission, the

patient had double vision and had to keep one eye closed. During the week prior to admission, he had been excessively drowsy and constantly tired. The headaches had increased in frequency and were now occurring 3 to 4 times per day.

Neurologic examination:

1. Mental status: Intact.

2. *Cranial nerves:*

- a. On funduscopic examination there was evidence of bilateral papilledema.
- b. A bilateral paralysis of the sixth nerve was present.
- c. Horizontal nystagmus was present on right lateral gaze.

3. *Motor system:*

- a. Strength was everywhere intact.
- b. The patient's gait was wide-based. In walking, the patient tended to veer to the right. The patient was unable to stand independently on his right leg.
- c. There was a significant intention tremor of the right upper extremity on finger-to-nose test and of the right lower extremity on heel-to-shin test. Alternating movements of the right hand were disorganized.

4. *Reflexes:* Deep tendon stretch reflexes were normal and plantar responses were flexor.

5. *Sensory system:* All modalities were intact.

Clinical diagnosis: Tumor of the right cerebellar hemisphere with obstruction of ventricular system producing increased intracranial pressure and resulting in papilledema and bilateral cranial nerve VI palsy.

Laboratory Data:

1. Complete blood count and skull x-rays were normal.
2. *Right brachial arteriogram* revealed, in the late arterial phase, a blush in the right inferior and posterior cerebellar hemisphere consistent with a hemangioblastoma.
3. *Pantopaque ventriculogram* revealed a dilated third ventricle and a dilated aqueduct with obstruction to outflow from the fourth ventricle. The fourth ventricle and to a lesser degree, the aqueduct, were shifted to the left. These findings were consistent with a right cerebellar mass displacing and obstructing the fourth ventricle.

Hospital Course: The patient was placed on high dosage of dexamethasone to relieve increased intracranial pressure. Later that day a suboccipital craniectomy was performed by Doctor Samuel Brendler. When the dura was opened, bulging of the lower portion of the right cerebellar hemisphere was noted, with widening of the cerebellar folia. The widest area of the folia was tapped with a needle and a yellow cystic fluid was removed. A transcortical incision was then made, revealing a large cyst with a small strawberry-shaped hemangioma located within. The stalk of this tumor was ligated, and the hemangioma separated from the cystic capsule. Histologic examination of the tumor revealed a hemangioblastoma.

Postoperatively, the patient did well. His headache and diplopia disappeared. There was then improvement in the patient's tremor and ataxia, although there was a slight slowness on finger-to-nose testing on the right. A minor side-to-side tremor was present on right heel-to-shin testing. There was a tendency to veer to the right in walking, but tandem gait indicated only a minor unsteadiness. Evaluation six months after surgery, indicated only a minimal unsteadiness on tandem walking. Evaluation 9 months after surgery later indicated no significant neurologic findings. Re-evaluation three and one-half years after surgery, again indicated a completely intact neurologic status.

Comment: The headaches experienced by the patient, with pain occurring on coughing, sneezing, or mechanical changes, suggested a space-occupying lesion near the ventricular system or meninges. The tumor had produced a block of the ventricular system relatively early in its course, leading to an increase in intracranial pressure, with headache, vomiting and papilledema. The bilateral sixth-cranial nerve weakness was of moderate degree, and

its occurrence would not be unusual in a situation where intracranial pressure had rapidly increased.

The cerebellar symptoms experienced by the patient were lateralized in the sense that the patient was falling to the right side and had noted clumsiness of his right hand. Lateralized cerebellar disease was confirmed by the examination findings of intention tremor of the right arm and leg and disorganization of alternating movements on the right side.

In this case, the hemangioblastoma was in the lateral cerebellar hemisphere. In other cases of hemangioblastoma, the lesion is much more midline in location, and the symptoms are those of a midline cerebellar tumor. Thus, the patient may complain of an ataxia of gait and truncal ataxia and not display clearly lateralized symptoms involving the appendages, such as intention tremor and/or ataxia on heel-to-shin testing. The nodule of tumor often exists within a non-neoplastic cystic cavity. It is, therefore, possible to remove the tumor without sacrificing a large amount of the cerebellum. In some cases, both the mural nodule and the cyst are removed. In almost all cases a complete cure is obtained; recurrences are unlikely and the patients usually have a relatively complete resolution of symptoms and no residual disability.

In some cases, hemangioblastomas of the cerebellum are associated with angiomatous malformations of the retina (Landau-von-Hippel's disease). In some cases, there is an association with a secondary increase in red blood cell production (polycythemia). In rare cases, there is an association with tumors of the kidney. Other neoplasms may also involve the cerebellar hemispheres: cystic astrocytomas, metastatic tumors, and posterior fossa meningiomas. Meningiomas of the angioblastic type may be difficult to distinguish from hemangioblastomas.

At the present time, the diagnosis of these tumors may be readily made by means of MRI and CT scan (Fig. 20-11). Ventriculograms are no longer required. Arteriograms may still be of value in defining the vascularity and blood supply of the tumor.

The following case history presents a typical example of posterior inferior cerebellar artery infarct, the territory most frequently affected selectively.

Case 20-6: This 64-year-old right-handed married white male postmaster, on the morning prior to admission, awoke at 3:00 a.m. with severe posterior headache and severe vertigo, which was exacerbated by any head movement. Nausea, projectile vomiting and slurred speech soon developed. Shortly afterwards, he noted left facial paresthesias, clumsiness of the left upper extremity, and diplopia. He was admitted to his local hospital with a diagnosis of labyrinthine vertigo and then transferred to the neurology unit at Saint Vincent Hospital when symptoms began to evolve.

Two weeks previously, the patient had been seen for a transient episode of difficulty controlling the right arm, a hissing sensation, and impairment of speech.

Past history: The patient had evidence of significant vascular disease. He had hypertension and had undergone coronary artery bypass surgery. Beginning six years previously he had experienced episodes of transient weakness and numbness of the right arm with transient aphasia. He had normal aortic arch and carotid angiographic studies but EEG had demonstrated focal left frontal/temporal slow wave activity. He had been placed on long term anticoagulation. He had experienced migraine headaches without aura for many years.

Neurologic examination:

1. *Mental status:* Intact.
2. *Cranial nerves:* Conjugate lateral gaze to the left was impaired.
3. *Motor system:* Strength was intact. Significant lateralized cerebellar findings were present with marked dysmetria of left upper extremity on finger-to-nose testing and impairment of alternating hand movements. In attempting to stand, the patient was markedly ataxic.

4. *Reflexes*: Deep tendon stretch reflexes were decreased in both lower extremities. Plantar response was extensor on the right and flexor on the left.
5. *Sensory system*: Intact
- Clinical diagnosis**: Left cerebellar hemisphere infarct or hemorrhage with possible minor involvement of brainstem secondary to mass effect.

Laboratory data:

1. Duplex scans of carotids and vertebrals were normal.
2. *Transcranial Doppler studies* indicated normal flow velocities in the vertebral, basilar, anterior and middle cerebral arteries.
3. *Magnetic-resonance angiography* demonstrated occlusion of the left vertebral artery.
4. *CT scan* demonstrated a large left cerebellar infarct pressing the fourth ventricle to the right.
5. *MRI* (2 months after onset of symptoms): Infarction of the total cerebellar territory of the left posterior inferior cerebellar artery with no actual infarct of the brain stem (Fig. 20-12).

Subsequent course: The patient was somewhat vague with some difficulty in memory during the subsequent 8-day hospital course and remained ataxic. He was then transferred to the Fairlawn Rehabilitation Hospital where, over the next three weeks, he had a significant improvement. When re-evaluated two months after onset of symptoms, he was able to walk well with the use of a cane. A minor intention tremor was present on the left finger-to-nose test. An MRI study was obtained at this point, with results indicated above (because new symptoms suggested possible involvement of upper cervical nerve roots and spinal accessory nerve). Additional improvement was evident on evaluation three months after onset of symptoms. Evaluation 6 months after onset of symptoms demonstrated only a slight slowness of alternating movements of the left hand.

Comment: The acute onset of headache, vertigo, vomiting, ataxia of gait, and dysmetria of the left arm suggested an acute cerebrovascular problem involving the posterior circulation and the posterior fossa. (The syndrome of acute headache, vertigo, ataxia, nausea and vomiting is also seen in cases of acute cerebellar hemorrhage.) Numbness on the left side of the face and diplopia suggested, as well, possible brainstem involvement. The initial diagnosis at the local hospital of acute vestibular disturbance did not explain the headache, the diplopia or the lateralized findings. The presence of the left arm dysmetria suggested lateral hemispheric involvement rather than limited midline involvement.

In the era before CT scan and MRI, the distinction between acute cerebellar hemorrhage and acute cerebellar infarct was often difficult to make. Either lesion could produce block or distortion of the ventricular system and secondary hydrocephalus. Either lesion could be associated with the development of brainstem symptoms. The cerebellar infarct, often in the distribution of the posterior inferior cerebellar artery or the anterior inferior cerebellar artery, could also involve the medullary or pontine territories of these vessels. In addition, either type of lesion could cause significant edema with secondary distortion of the brainstem. Hemorrhage could also extend into the cerebellar peduncle and brainstem.

If significant clinical hydrocephalus or brainstem compromise develops, either type of lesion may require neurosurgical decompression or a shunt procedure.

A final note should be made regarding the considerable ability of the human nervous system to recover from extensive cerebellar lesions. Considerable recovery is possible because the cerebellum does not have a direct line role in the control of motor activity but instead, acts as a modulator of the motor control and motor planning circuits.

The following case history provides an example of a cerebellar hemorrhage secondary to an arteriovenous malformation.

Case 20-7: This 57-year-old right-handed married white female had the sudden onset of a severe left-sided pounding headache one afternoon. There was some stuffiness of the nose and tearing of the left eye. She had had a similar, but less severe, headache 20 years previously when taking birth-control pills. No headaches had occurred in the interim. As the current headache began to decrease, she noted that hearing in the left ear had decreased to a minor degree, and an echo sensation was present in the left ear. She also had the sensation that the environment was off balance, particularly if she was in a moving automobile. She subsequently reported a sense of unsteadiness. There was some sense of nausea when the symptoms first occurred. A vague blurring of vision was also present. She had a vague diplopia at the onset of symptoms but this then disappeared.

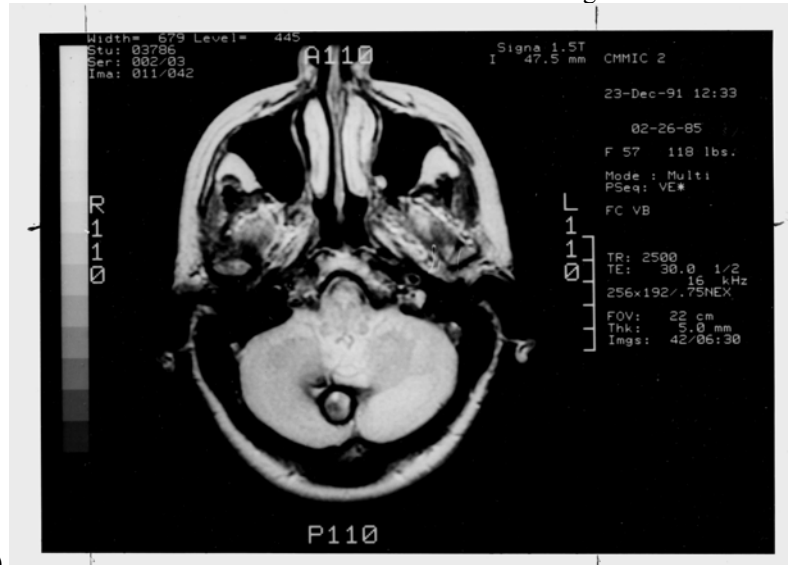
General physical examination: There were multiple pinpoint cavernous angiomas over the arms.

Neurologic examination: Entirely within normal limits.

Clinical diagnosis :Diagnosis unclear: possible migraine headache, or brain stem cerebrovascular event.

Laboratory data: 1. *CT scan of head* indicated hemorrhage in the right paramedian posterior cerebellum.

2. *MRI* showed a rim of hemosiderin stain around the residual hemorrhage in the cerebellar vermis



3. (Figure 20-14).

Subsequent course: The patient had no additional acute episodes. Because two episodes had occurred, she was referred for neurosurgical evaluation. A cavernous hemangioma of the right cerebellum was removed by Doctor Bernard Stone. Post-operatively, she had some right-sided clumsiness and ataxia, which gradually improved.

Evaluation by Doctor Stone one month following surgery, indicated minimal, if any, cerebellar signs. Finger-to-nose test showed no tremor. Gait demonstrated a minimal unsteadiness. Evaluation one year after surgery demonstrated no neurological findings, although some episodic symptoms of imbalance persisted.

CHAPTER 21: SENSORY FUNCTION AND PARIETAL LOBE

The following case demonstrates the localizing significance of focal sensory seizures beginning in the face of a 40 year old patient without prior neurological disease. As predicted, the etiology was neoplastic: a glioblastoma.

Case 21 -1:One week prior to evaluation, this 40-year old right-handed married white male had the onset of repeated 15-21 minute duration episodes of focal numbness (tingling or paresthesias) involving the left side of the face, head, ear, and posterior neck and occasionally spreading into the left hand and fingers, and rarely subsequently spreading into the left leg. There was no associated pain or headache or weakness or associated focal motor phenomena. Biting or eating would trigger the episodes. Past history was not remarkable.

Initial neurological examination: This was completely within normal limits as regards mental status, cranial nerves, motor system, reflexes, and sensory system.

Clinical diagnosis: Focal seizures originating lower third post central gyrus. In view of patient's age, a brain tumor must remain the prime consideration

Laboratory data:

- (1) *EEG*: no focal abnormalities were present. (The record, however, was abnormal because of bilateral bursts of spikes and slow waves - triggered by photic stimulation accompanied by myoclonic jerks - suggesting a predisposition to primary generalized epilepsy (refer to epilepsy chapter for the significance of this finding which was not relevant to this case).
- (2) *CT Scan* (Fig 21-2): The non-enhanced study was normal. The enhanced study demonstrated a small enhancing lesion just above the right Sylvian fissure.
- (3) *MRI* (Fig. 21 - 3): Demonstrated the more extensive nature of this process involving the operculum - above the right sylvian fissure including the lower end of the post central gyrus, the area of representation of the face. A probable infiltrating tumor was suggested as the most likely diagnosis.
- (4) *Arteriogram* - demonstrated a tumor blush at the right sylvian area, consistent with a glioblastoma, a rapidly growing infiltrating tumor - originating from astrocytic glia.

Subsequent Course: Treatment with an anticonvulsant reduced the frequency of the episodes. Neurosurgical consultation suggested an additional observation period and periodic CT scans in view of the normal neurological examination. Three months after onset of symptoms, the patient developed a numbness of the left arm and difficulty in coordination of left arm. Exam now demonstrated left central facial weakness, mild weakness of the left hand. A loss of stereognosis and graphesthesia with a relative alteration in pinprick perception was present in the left hand. The CT scan showed significant enlargement of the previous lesion. EEG now indicated focal 2-3 Hz Delta slow waves in the right frontal central Rolandic area. Subtotal resection of a glioblastoma - in the right temporal parietal area was performed by Dr. Bernard Stone. Radiation therapy was administered following surgery, 4000 rads total whole brain and 5210 rad total to the tumor area. Reevaluation 3 months after surgery, indicated only rare focal seizures involving the face. The neurological examination was normal. Repeat CT scans, however, continued to demonstrate a large area of enhancing tumor in the right temporal-frontal-parietal area. Despite the use of dexamethasone and arterial chemotherapy with cis-Platinum, he continued to progress. At the time of neurological follow-up, 29 months after onset of symptoms, he had developed a left field defect, left hemiparesis and a loss of all modalities of sensation on the left side. He subsequently developed significant changes in memory and cognition, as well as a complete left hemiplegia. CT scan demonstrated progression with extensive involvement of the right side of the brain and spread to the left hemisphere. Death occurred 33 months after onset of symptoms. **Postmortem examination of the brain:** almost the entire right hemisphere was replaced by necrotic infiltrating tumor. The tumor now had spread into the corpus callosum and temporal and occipital lobes. The internal capsule, thalamus, hypothalamus and basal ganglia were destroyed.

Comment: The initial occurrence of the limited focal sensory seizures involving the face and head in a patient of age 40 with no history of trauma or of vascular disease or hypertension clearly predicted the following conclusions (1) The location of the discharging lesion: the sensory cortex

just above the sylvian fissure. (Note that the actual extent of the pathology was more extensive but that is almost always the case in an infiltrating glioma). (2) The nature of the underlying pathology. The most common cause of focal seizures beginning at age 40 in a patient with no significant head trauma, vascular disease, hypertension or other medical disease is a tumor. Among tumors involving the cerebral hemispheres, an infiltrating glioma is by far the most common and on a statistical basis, a glioblastoma is by far the most likely histologic type. 3) The subsequent course was consistent with the natural history of a malignant glioma of the astrocytic series, a glioblastoma. The 33 month survival (30 months after surgery is beyond the median survival for this type of tumor.

The following patient (case 21-2) had a metastatic nodule in the post central gyrus producing a pseudo thalamic pain syndrome.

Case 21-2: This 62-year-old white, right-handed housewife, six years prior to admission

had undergone a left radical mastectomy for carcinoma of the breast. Five months prior to admission, the patient developed a persistent cough, left pleuritic pain and a collection of fluid in the left pleural space (pleural effusion) as well as daily headaches in the right orbit, occasionally awakening the patient from sleep. Four months prior to admission, over a 3 to 4 week period, the patient developed progressive "weakness" and difficulty in control of the right lower extremity. Several weeks later, the patient now experienced, aching pain in the right index finger in addition to a progressive deficit in the use of the right hand. This was more a "stiffness and incoordination" than any actual weakness. One month prior to admission the patient noted episodes of pain in the toes of the right foot and numbness of right foot occurred, lasting 2 to 3 days at a time. She subsequently developed, difficulty in memory and some minor language deficit, suggesting a nominal aphasia, prompting hospital admission.

Neurological examination:

1. *Mental status:* The patient was oriented for time, place, and person. Delayed recall was slightly reduced to 3-out-of-five in 5 minutes. A slowness in naming objects was present although she missed only one item of 6. Calculations, reading, and attention were normal. There was no left-right confusion.

2. Cranial nerves:

a. Nerve II: early papilledema was noted: absence of venous pulsations, indistinctness

of disc margins, and minimal elevation of vessels as they passed over the disc margin.

b. Nerve VII: right central facial weakness was present.

3. **Motor system:**

- a. Mild weakness of the right upper limb was present. A more marked weakness was present in the lower limb (most marked distally).
- b. Spasticity was present at the right elbow and knee.
- c. Gait: The right leg was circumducted; the right arm was held in a flexed posture.

4. **Reflexes:**

- a. Deep tendon reflexes were increased on the right.
- b. A right Babinski response was present.

5. **Sensory system:**

- a. Touch intact.
- b. An ill-defined alteration in pain perception was present in the right arm and leg - more of a relative difference in quality of the pain than any actual deficit.
- c. Repeated stimulation of the right lower extremity (pain or touch) produced dysesthesias (painful sensation).
- d. Vibratory sensation was decreased to a minor degree at the toes bilaterally but intact in the upper extremities.
- e. Position sense was markedly defective in the right fingers with errors in perception of fine and medium amplitude movement in the right toes.
- f. Simultaneous stimulation resulted in extinction in the right lower extremity.
- g. Graphesthesia (identification of numbers, e.g., 8, 5, 4 drawn on cutaneous surface) was absent in the right hand and fingers and poor in the right leg.
- h. Tactile localization and two-point discrimination were decreased on the right side.

Clinical diagnosis: Metastatic tumor to the left post central and precentral gyri with a cortical pain syndrome (pseudo thalamic pain syndrome).

Laboratory data:

1. *Skull x-rays:* the pineal was shifted from left to right. Demineralization of the dorsum sellae also had occurred: consistent with the increase in intracranial pressure.

2. *Chest x-ray:* Several metastatic nodules were present in the left lung.

3. *Electroencephalogram:* A focal disturbance, having the quality of damage, was present in the left posterior frontal central and parietal areas (almost continuous focal 4 to 7 cps slow wave activity).

4. *Left carotid arteriogram:* A left posterior frontal lobe lesion was suggested by a shift of the posterior portion of the anterior cerebral artery from the left to the right. The middle cerebral artery in the sylvian fissure was also depressed downwards.

5. *Brain scan:* The findings were consistent with a focal metastatic lesion with a focal uptake of radioisotope (Hg^{197}) in the left parietal area: high and close to the midline with uptake in the adjacent subcortical white matter.

6. **Erythrocyte sedimentation rate** was elevated to 90 mm., consistent with metastatic disease.

Subsequent course: There was evidence in this case that the disease had spread to multiple organs: brain (findings as noted), lung (chest x-rays and biopsy), and liver (abnormal laboratory tests of liver function). Radiation and hormonal therapy were, therefore, administered rather than any attempt at surgical removal of the left parietal metastatic lesion. Follow-up examination one month later indicated that a significant improvement had occurred in motor function in the arm. Sensory deficits persisted. Speech was slow but relatively intact. The patient eventually expired five months after admission.

Post mortem findings: Autopsy was performed by Dr. Humphrey Lloyd of the Beverly Hospital and disclosed extensive metastatic disease in the lungs, liver, and lymph nodes. A single necrotic metastatic lesion was present in

the brain. This was located in the upper postcentral gyrus of the left parietal area, 1.0 cm. below the pial surface and measuring 1.2 x 1.0 x 0.6 cm.

Comment: This patient had a progressive neurological deficit with headache and papilledema, a clinical course that clearly indicates the presence of a neoplasm. This case predated the era of CT and MRI scan. Today contrast-enhanced scans would be performed. This diagnosis was supported by the ancillary laboratory studies that were available at that time. Moreover this diagnosis however was clear based on the history and clinical-laboratory findings. The fact that motor findings in the arm relevant to the precentral gyrus improved with treatment might suggest that these findings were due to edema. In contrast the findings relevant to the area of the necrotic tumor, the post central gyrus, showed little improvement. In general, one should assume that a patient with a past history of carcinoma of the breast, carcinoma of the lung, malignant melanoma, or renal cell carcinoma, who develops symptoms of central nervous system disease, has metastatic disease until proven otherwise. Such symptoms at their onset may be minor and nonfocal and appear trivial: headache, subjective weakness, and a change in personality. On the other hand more focal symptoms and signs may be present: focal weakness, focal seizure. The metastatic lesions may be single or multiple.

A diagnosis of metastatic disease does not imply that no treatment of central nervous system lesions is possible. Surgical resection of single lesions may be successfully performed. Often the apparent deficits are far out of proportion to the actual size of the tumor because of the surrounding swelling (edema) in the adjacent tissues.

The pattern of sensory involvement in this case clearly localized this lesion to the cortex (or white matter close to cortical surface) rather than to the thalamus. The relative intactness of pain, touch, and vibration sensation should be contrasted to the significant deficits in position sense,

graphesthesia, tactile localization, and two-point discrimination with extinction on simultaneous stimulation. The occurrence of episodic pain in the involved arms and legs along with the production of an experienced painful sensation on repetitive tactile stimulation (dysesthesias) in patients with sensory pathway lesions is sometimes referred to as a "thalamic" or "pseudo thalamic" syndrome. (Refer to discussion of Wilkins and Brody, 1969). In this case, the anatomical locus for the pseudo thalamic syndrome is apparent.

The effects of deficits in cortical sensation on the total sensory motor function of a limb are apparent in this case. The actual disability and disuse of the right arm and leg were far out of proportion to any actual weakness. Such an extremity is often referred to as a "useless limb." The actual weakness that was present undoubtedly reflected pressure effects on the precentral gyrus and the descending motor fibers in adjacent white matter.

The following case (21-3) demonstrates many of the features of a non dominant parietal lobe lesion.

Case 21-3: This 70-year-old, single, white female, right-handed, retired candy maker underwent a left radical mastectomy for carcinoma of the breast, three years prior to admission. Four months prior to evaluation, the patient became unsteady with a sensation of rocking as though on a boat. She no longer attended to her housekeeping and to dressing. Over a three-week period, prior to evaluation, a relatively rapid progression occurred with deterioration of recent memory. A perseveration occurred in motor activities and speech. The patient was incontinent but was no longer concerned with urinary and fecal incontinence. For 2 weeks, right temporal headaches had been present. During this time, her sister noted the patient to be neglecting the left side of her body. She would fail to put on the left shoe when dressing. In undressing, the stocking on the left would be only half removed.

Family History: The patient's mother died of metastatic carcinoma of the breast.

Neurological examination:

1. Mental status:

- a. The patient was oriented for time, place and person.
- b. Delayed recall was 5-out-of-5 objects in 5 minutes.
- c. There was no evidence of aphasia.
 - d. The patient often wandered in her conversation. She often asked irrelevant questions and was often impersistent in motor activities.
- e. There was marked disorganization in the drawing of a house or of a clock. A similar marked disorganization was noted in attempts at copying the picture of a railroad engine (Fig 21-4).
- f. There was a marked neglect of the left side of space and of the left side of the body. The patient failed to read the left half of a page. When she put her glasses on, she did not put the left bow over the ear. When getting into bed, she did not move the left leg into bed. She had slipped off her dress on the right side, but was lying in bed with the dress still covering the left side.

- g. The patient had been reluctant to come for neurological consultation. Although she complained of headache and nausea, she denied any other deficits. Her relatives provided information concerning these problems. Much additional persuasion over a two-week period was required before the patient would agree to be hospitalized.

(2) Cranial nerves:

- a. Nerve II: A dense left homonymous hemianopsia was present. When reading, the patient left off the left side of a page. She bisected a line markedly off center. Disc margins were blurred and venous pulsations were absent, indicating papilledema.
- b. Nerve III: The right pupil was slightly larger than the left.
- c. Nerve VII: A minimal left central facial weakness was present.
3. *Motor system:* Strength was intact. There was, however, little spontaneous movement of the left arm and leg. Tone was normal.
4. *Reflexes:* deep tendon reflexes were symmetrical and physiologic and plantar responses, flexor.
5. *Gait:* The patient was ataxic on a narrow base with eyes open with a tendency to fall to the left, and was unable to stand with eyes closed even on a broad base.
6. *Sensory system:*
- a. Pain, touch and vibration were intact. At times, however, there was a decreased awareness of stimuli on the left side.
 - b. Errors were made in position sense at toes and fingers on the left.
 - c. With double simultaneous stimulation, the patient neglected stimuli on the left face, arm and leg.
 - d. Tactile localization was poor over the left arm and leg.

Clinical diagnosis: Metastatic tumor from breast to right non-dominant parietal cortex.

Laboratory data:

1. *Skull X-rays* were negative.
2. *Chest X-ray* indicated a possible metastatic lesion at the right hilum.
3. *Erythrocyte sedimentation rate* was elevated to 72 mm/hr, consistent with metastatic disease.
4. *Electroencephalogram* (Fig 21-5) was abnormal because of frequent focal 3 to 4 cps slow waves in the right temporal and parietal areas, suggesting focal damage in these areas.
5. *Brain scan (radioisotope)* (Fig 21-6) indicated that a large but well-defined area of increased uptake of isotope (Hg197) was present in the right parietal area extending from the midline to the lateral surface, measuring 7 x 5 x 7 cm. The most likely diagnosis was that of a solitary large metastatic lesion
6. *Right carotid arteriogram* showed that a large vascular tumor mass, probably metastatic, was present in the posterior section of the right temporal inferior parietal area. There was displacement of the middle cerebral artery upward and to the left.

Subsequent course: Treatment with steroids (dexamethasone and estrogens) resulted in temporary improvement. The patient refused surgery. Her condition soon deteriorated with increasing obtundation of consciousness. She expired two months following her initial neurological consultation.

Comment: This patient certainly presented a syndrome characterized by disturbance in concept of body image with a marked neglect of the left side, a denial of illness, and marked constructional apraxia. The various laboratory studies indicated a large lesion in the right posterior temporal parietal area. A CT scan from a more recent case demonstrating many aspects of this syndrome is illustrated in Figure 21-7. In many cases, the location of lesion may appear to be predominantly posterior temporal. Such large posterior temporal lesions would certainly compromise the cortex and subcortical white matter of the adjacent inferior parietal area.

In this case, marked deficits in perception of the cortical modalities of sensation were present. In other cases, as in the case demonstrated in Fig 21-7, such involvement is much less marked.

In some cases, involvement of the motor cortex is evident with an actual left hemiparesis accompanied by an increase in deep tendon reflexes and an extensor plantar response. At times in patients with neglect syndromes, there may be several indications in the clinical examination and in the laboratory studies that the involvement of the frontal lobe areas is more prominent than the parietal involvement. We have already indicated that the neglect components of this syndrome may also be noted in lesions of the anterior premotor

area (area 8). The premotor area as discussed above and in chapter 18, receives projection fibers from the multimodal area of the posterior parietal area. It is possible that in some cases the posterior temporal - inferior parietal location of the lesion may also be critical in interrupting these association fibers. For these several reasons, it is perhaps more appropriate to use the term, *syndrome of the non-dominant hemisphere*, rather than the more localized designation, non-dominant inferior parietal syndrome. Duffner et al, 1990 have presented the concept of a network for directed attention - with right frontal lesions leading to left hemi spatial neglect only for tasks that emphasize exploratory-motor components of directed attention whereas parietal lesions emphasize the perceptual-sensory aspects of neglect.

With lesions of the non-dominant hemisphere, there is a significant alteration of the patient's awareness of his environment. The behavior of an individual is in part determined by his or her own particular perception of the environment. If that perception is altered or disorganized, the behavioral responses of the patient may appear inappropriate to others. Obviously, not all individuals will respond in the same manner to a given environmental situation; part of the response will be determined by the past experience and personality of the individual. Thus, given the same lesion, one individual may be unaware of a hemiparesis, another may deny the hemiparesis but agree an illness is present, a third may claim to be healthy and claim that people are conspiring to keep him in the hospital.

CHAPTER 22: THE LIMBIC SYSTEM

In general, as we have indicated, there is mixed symptomatology during partial seizures of temporal lobe origin. The following case history (22-1) illustrates many of the points just discussed regarding seizures of temporal lobe origin.

Case 22-1: This 56-year-old white right-handed male baker was referred for evaluation of a seizure disorder. Three months before admission the patient had the onset of episodes of vertigo and tinnitus, each episode lasting 4 minutes and unrelated to position. The patient then noted increasing forgetfulness. Later that month he had a generalized convulsive seizure that occurred without any warning. The patient then developed episodes of confusion and unresponsiveness, followed by a left frontal headache. Several studies; EEG, pneumoencephalogram, and carotid arteriogram—were all negative at that point in time. One month before admission, the patient began to have minor episodes, characterized by lip smacking and a vertiginous sensation, during which he reported seeing several well-formed, colorful scenes. At times, he had hallucinations of “loaves of bread being laid out on the wall.” In addition, he would have a perceptual disturbance at the same time (e.g., objects would appear larger than normal) and “terrifying dreams.”

General physical examination: unremarkable.

Neurological examination: The essential neurological findings were as follows:

1. *General observations of seizures:* The patient was observed to have frequent transient episodes of distress characterized by saying, “Oh, oh, oh, my”. On occasion, these were accompanied by automatisms: fluttering of the eyelids, smacking of the lips, and repetitive picking at bedclothes with his right hand. Consciousness was not completely impaired during these episodes, which lasted from 30 seconds to 3 minutes, and the patient reported afterward that at the onset of the seizure he had seen loaves of bread on the wall and smelled a poorly described unpleasant odor. At other times, the olfactory hallucination was described as pleasant, resembling the aroma of baked bread.
2. *Mental status:* The patient was oriented to person but not dates. He could not recall his street address. He was unable to pronounce the name of the hospital correctly. Calculations were correctly performed.
3. *Cranial nerves:* Possible deficit in the periphery of the right visual field and a minor right central facial weakness.
4. *Motor system:* intact
5. *Reflexes:* Deep tendon reflexes were symmetrical and physiologic. A right Babinski sign was present.
6. *Sensory system:* intact.

Clinical diagnosis: Simple and complex partial seizures originating left temporal lobe probably involving at various times left lateral superior temporal gyrus, uncus, amygdala and hippocampus with tumor the most likely etiology in view of age and the focal neurological findings.

Laboratory data:

1. The *initial electroencephalographic recording* indicated frequent focal spike discharge throughout the left temporal and parietal areas, consistent with a focal seizure disorder originating in the left temporal/parietal areas (Fig. 29-1). A recording 6 days later indicated a decrease of focal spikes (i.e., a decrease in seizure activity) but the presence of frequent focal slow-wave activity in the left temporal area (almost continuous, 3 to 5 cps (Hz) slow-wave activity) suggesting that focal damage was present in the left temporal area .
2. *Brain scan* (H_g197) normal
3. *Left carotid arteriogram* indicated a possible avascular mass lesion left posterior frontal (the only abnormality was a 4-mm shift of the anterior cerebral artery).

Subsequent course: The patient continued to have multiple short episodes characterized by the sensation of odor and a sensation that he was looking at objects upon the wall. These episodes were eventually controlled with anticonvulsant medication: phenytoin (Dilantin) and primidone (Mysoline). However, 2 months later the patient had a day with several episodes with “crazy things occurring “ (colorful visions and terrifying nightmares).

The patient was readmitted to the hospital 7 months after onset of symptoms because of the recurrence of seizures. An aura of unpleasant odor was followed by a generalized convulsion followed by four or five

subsequent seizures of a somewhat different character (deviation of the head and eyes to the right, then tonic and clonic movements of the right hand spreading to the arm, foot, and leg lasting approximately 1 to 2 minutes, followed by a post-ictal right hemiparesis).

Neurologic examination now indicated a marked expressive aphasia, with little spontaneous speech and difficulty in naming objects. There was a dense right homonymous hemianopia, a flattening of the right nasolabial fold, and a right hemiparesis, with a right Babinski sign.

During a 2-week hospital period the patient continued to have minor seizures characterized by sensory phenomena on the right side of the body. A moderate degree of expressive aphasia persisted throughout the hospital course, although the right homonymous hemianopia largely disappeared. The symptoms and findings suggested that the basic disease process might well have spread to involve the adjacent areas across the sylvian fissure—the speech areas of the inferior frontal convolution, premotor areas, and sensory motor cortex.

The patient developed increasing expressive aphasia and right hemiparesis, with increasingly severe headache. An arteriogram indicated a large space-occupying tumor of the left temporal lobe, and surgery was undertaken by Dr. Robert Yuan 16 months after the onset of symptoms. The anterior and middle portions of the superior temporal gyrus appeared to be widened, and the anterior temporal area (the temporal tip) had an abnormal and discolored appearance. At a depth of 1 to 2 cm within the superior temporal gyrus and involving all of the deeper temporal areas, obvious necrotic glial tissue was found. The process had extended superficially under the Sylvian fissure to involve the adjacent posterior portion of the inferior frontal gyrus.

A temporal lobectomy was performed (from the anterior temporal pole posteriorly for a distance of 6 cm). The operative impression of a malignant glial tumor (glioblastoma) was confirmed by histologic examination.

Comment: This patient presented, at one time or another during his seizures, most of the phenomena associated with temporal lobe lesions: vertigo, tinnitus, visual distortions and hallucinations, olfactory hallucinations, fear, automatisms involving the lips and hands, and episodes of confusion. The visual and olfactory hallucinations are of interest in that both reflected the patient's occupation as a baker. As Halgren and colleagues (1978) note, the experiential phenomena of temporal-lobe seizures are often specific to the individual's experience and personality. The later progression clearly indicated spread across the sylvian fissure to involve the motor cortex and Broca's area in the inferior frontal gyrus areas. This patient had a highly malignant tumor, which clearly involved the cortex of the lateral surface, the deeper white matter, and presumably the medial temporal areas, including the amygdaloid-hippocampal regions. His clinical picture is highly reminiscent of the case described in 1887 by Hughlings Jackson of Emily M., a cook who experienced visual and olfactory hallucinations and who had a tumor arising in the "temporosphenoidal lobe" (the uncus). Such seizures have subsequently been referred to as uncinate epilepsy, but as we have indicated, the disease invariably involves more than just the uncus.

Today, CT scan and MRI would be employed for early diagnosis (see Figs. 22-17 and 22-18). Cases 22-2 and 22-3 which follow demonstrate the correlation of partial seizures with temporal lobe pathology.

Case 22-2. This 17-year-old right-handed male, at age 4 years began to have "staring spells and bizarre behavior". Some episodes had been preceded by the "sound of a musical rhythm". EEG at that time indicated a right temporal spike discharge. Seizures were controlled for ten years with anticonvulsants but then recurred and were poorly controlled occurring several times per day.

Neurological examination: The findings were limited to the following features:

1. *Observed 3 minute seizure:* The seizure began with loss of contact and a stare and then automatisms of the hands. He stood up, walked around the room, went to the physician's desk and attempted to pull open a nonexistent middle drawer. He answered questions vaguely with one or two word answers. Confusion was present for 1-2 minutes after the end of the episode.
2. *Cranial nerves:* a left central facial weakness was present.

Clinical diagnosis: Focal seizures originating right temporal lobe. Observed seizure was complex partial. The seizures beginning with the musical sound might be classified as simple partial with secondary complex partial.

Laboratory data:

1. *EEG*: Intermittent focal spike discharge anterior-middle temporal area.
2. *CT scan*: (Fig. 22-17) An area of focal atrophy was present in the right anterior temporal lobe with possible enhancement at the border.
3. *MRI*: At the Yale Epilepsy Center was more consistent with a tumor in the right anterior temporal lobe.

Subsequent course: Dr. Dennis Spencer at the Yale Epilepsy Center performed a temporal lobectomy. This demonstrated a cystic glial tumor with components of astrocytes and oligodendrocytes. Cerebral cortex also demonstrated abnormal lamination and dysplastic features. Seizures were fully controlled over the next three years.

Case 22-3. This 47-year-old ambidextrous male experienced his first seizure one month prior to admission. He felt light-headed and warm. Then he was observed to walk 100 feet down a hallway, appearing “dazed” and not recognizing people. He fell to the floor, with a loss of consciousness, bit his tongue and was confused afterwards for several minutes.

Neurological examination at 2, 16 and 48 hours after the episode: A persistent right Babinski sign, and slight right hyperreflexia were present. Otherwise the examinations were not remarkable.

Clinical diagnosis: Complex partial seizures. In view of age of onset and persistent focal signs a brain tumor was suspected as the etiology.

Laboratory diagnosis:

1. Sleep deprived EEG :normal.
2. *CT and MRI scans* (Fig. 22-18) demonstrated an extensive infiltrating tumor of the left temporal lobe most likely a glioblastoma.

Subsequent course: Despite Anticonvulsant therapy (phenytoin) additional episodes occurred over the next month: loss of train of thought while talking and several minutes of loss of memory. A subtotal resection by Dr. Bernard Stone (St. Vincent Hospital) demonstrated a Grade III-IV astrocytoma (glioblastoma). Despite radiotherapy and chemotherapy, the disease pursued a relentless course producing early and severe disability prior to death, approximately one year after onset of symptoms.

The following case histories illustrate many of the features of focal disease involving the prefrontal areas.

Case 22-4: This 69-year-old right handed white housewife; two years prior to neurological evaluation visited a relative (a physician) in Israel whom she had not seen in a number of years. The relative then wrote to the patient’s physician, (an old family friend) indicating concern over a change in the patient’s personality. The patient was described as apathetic with silly immature reactions. In retrospect, the patient’s husband felt that these alternations had begun insidiously a number of years previously. A year later, the same relative again wrote indicating that letters received from the patient had become incoherent. Letters became less frequent and then the patient no longer wrote letters. Ten months prior to evaluation, a left central facial weakness was first noted followed two months later by a decreased left arm swing. Six months prior to evaluation, her husband noted, she was purchasing items for which she had no need: 24 pairs of shoes, 15 brassieres. Subsequently she became careless in her housework. On occasions she lost her purse. Her ability to play bridge had decreased over the last year, although her golf game was unchanged.

Neurological examination:**1. Mental status**

- a. She was oriented x3
- b. There was a marked impersistence in motor activities. She was often inattentive. Her answers were often irrelevant. (According to her husband this had been present for many years.
- c. There was inappropriate joking.
- d. Delayed recall without assistance was 2/5 objects in 5 minutes. But 5/5 with assistance.
- e. Digit span was decreased to 5 forward and 3 in reverses.

- f. There were marked deficits in serial 7 subtractions. At times she began to subtract other numbers, at times she added rather than subtracted.
- g. There was a significant spatial disorientation. There was a marked impairment in the ability to copy a cube and deficits in drawing a house. There was disorientation in locating cities on a map.

2.Cranial nerves:

- a. There was a significant neglect of single stimulus objects in the left visual field; this was greater when bilateral simultaneous stimuli were utilized.
- b. At times there was a limitation of voluntary gaze to the left.
- c. A left central facial weakness was present.

3.Motor system:

- a. There was minimal weakness of the left arm and leg.
- b. Variable resistance was present on passive motion at left wrist and elbow suggesting the "gegenhalten" of frontal lobe disease.
- c. There was a decreased swing of the left arm in walking. The gait was initially apraxic but improved as the patient picked up speed.

4.Reflexes

- a. Deep tendon stretch reflexes were increased on the left.
- b. A left Babinski sign was present.
- c. There was a bilateral release of the grasp reflex.

5. Sensory system: intact.

Clinical diagnosis: Right frontal lobe tumor: probable meningioma based on the long history.

Laboratory data:

1.*Skull x-rays* there was a 5mm shift to the left of the calcified pineal gland. Long standing increased intracranial pressure was suggested by the demineralization of the sella turcica.

2.*EEG* demonstrated focal 2-5 Hz slow waves in the right frontal area most prominent in the parasagittal recording area

3.*Imaging study: radioactive brain scan (Hgl97):* there was a heavy uptake in the right frontal towards the midline measuring 5x5x4 cm (Fig.22-21).

4.*Arteriograms:* A parasagittal tumor was present in the right frontal area, with vascular supply derived from the left and right middle meningeal and left anterior meningeal arteries.

Hospital course: Following the arteriogram, the patient developed signs of increased intracranial pressure (vomiting, lethargy and papilledema). The patient received dexamethasone glucocorticoid used to reduce cerebral edema, with improvement in these symptoms. The right external carotid artery was ligated since the meningioma derived considerable blood supply from this source. Dr. Samuel Brendler performed a bilateral frontal craniotomy. Bulging of the dura was present requiring the administration of hyperosmotic agent (20% mannitol) with reduction of the swelling. When the dura was opened a large right posterior frontal meningioma was revealed measuring 8x8cm and attached to the right side of the superior sagittal sinus. On histological section this was a fibrous, meningothelial meningioma. During the course of removal of the tumor, it was necessary to ligate several bridging veins entering the superior sagittal sinus as well as the arteries feeding the tumor. At the conclusion of the procedure, it was noted that the right pupil was enlarged and neither responded to light. The patient failed to regain consciousness, remaining in a state of coma with bilateral extensor plantar responses, decerebrate postures on stimulation and bilateral fixed dilated pupils. The patient expired 2 weeks after surgery.

Comment: It is difficult to decide even in retrospect when the symptoms in this case began. It is clear that the initial symptoms involved an insidious change in personality. She was apathetic, her reactions were "silly" and judgment was impaired. Purchases were inappropriate. It would have been of interest to explore which aspects of her bridge playing were impaired in terms of planning and strategy etc. Her motor function was impaired only to a minor degree even late at the time of neurological evaluation, with minimal left-sided weakness and more prominent premotor release. The visual neglect syndrome may have reflected involvement of the premotor area or compromise of the parietal cortex by this large tumor. The fact that there was only minor evidence of involvement of motor cortex would make the premotor/SMA location more likely. While the spatial disorientation and deficits in drawing might

favor a nondominant parietal syndrome, such findings also could be consistent with a nondominant premotor/SMA location based on the close interaction between the posterior parietal and the premotor location. The impairment of voluntary gaze to the left would be consistent with area 8 involvement. There is little doubt that this patient required surgical intervention. The removal of large "benign" tumors of this type is not without risk. Hemorrhagic infarction with massive edema and tentorial herniation is a complication of ligation of bridging veins entering the superior sagittal sinus. In this case, serious brain swelling was already evident even before the dura was opened.

The following case history 22-3 provides an example of a patient with a slowly progressive subfrontal meningioma manifested by symptoms of apathy, loss of ambition, "depression" of mood, emotional lability, with a tendency to introspection and a slowness of mental processes. All of these symptoms were initially attributed to depression and a hypothyroid state. As gait and memory problems developed, these symptoms were attributed to Alzheimer's type senile dementia. When increased intracranial pressure and coma suddenly developed, neurological and neurosurgical intervention occurred.

Case 22-5: This white housewife and fashion designer was first admitted to the hospital at age 60 with a history of several years (?2 to 5) of fatigue, loss of ambition, lack of enthusiasm, and a tendency to readily cry over minor problems. A depression of mood and a tendency to introspection had developed. The patient also reported loss of her taste for food with a subsequent decrease in appetite and weight loss. These symptoms had progressed despite an adequate dosage of thyroid medication (60 mg., t.i.d.). Neurological examination was recorded as negative except for a slowness of speech and of thought processes. She was described by the psychiatric consultant as indecisive in her answers. Cerebrospinal fluid examination revealed no significant findings. Tests of thyroid function indicated hypothyroidism with protein bound iodine of 3.2 micrograms/100 ml. (normal; 4 to 8 micrograms/100 mg.) and a radioactive iodine uptake of 2.3 percent in 24 hours (normal 20 to 50 percent). Discharge diagnosis was chronic depression and hypothyroidism.

These symptoms continued to progress despite treatment with thyroid. The patient had increasing difficulty in walking. This had actually been first noted at age 57, 3 years prior to her initial hospital admission as a "phobia for heights". The patient would "freeze" at the top of a high flight of stairs. She then developed progressive difficulty in climbing stairs. Her husband reported that she would have marked difficulty in getting out of chairs. She would appear unsteady in gait after rising from a chair but would soon recover her equilibrium and would be able to walk in relatively normal manner. Increasingly, the patient's motor and mental activities became slower. She "procrastinated in making decisions". Occasional urinary incontinence developed at age 66 and was attributed to her neurological disease (apparent senile dementia). Although her husband reported her memory as initially well preserved, other observers at that point reported a progressive deficit in memory. At age 67, the patient began to complain of episodic fogging or blurring of vision.

Initial Neurological examination on re-admission to the hospital at age 67 was recorded as demonstrating the following features:

(a), slight disorientation for date and year, (b) slowness of speech and gait (c) deep tendon reflexes 2+, plantar responses flexor, and (d) no significant sensory finding except a slight decrease in position sense at the toes. No details as to the patient's gait were recorded. The sense of smell was apparently not tested and no notes as to the presence or absence of a grasp reflex were recorded.

On the day after admission, the patient developed headache and vomiting. She had difficulty walking unsupported and became increasingly more somnolent but could be roused by painful stimulation. Deep tendon reflexes were increased bilaterally with bilateral extensor plantar responses (bilateral Babinski signs). Grasp response was absent. Pupils responded to light but were sluggish.

Fundusoscopic examination was negative but lumbar puncture indicated a markedly increased pressure, greater than 400 mm. of csf. Cerebrospinal fluid protein was elevated to 125 mg/100 ml. The patient became unresponsive and emergency neurological and neurosurgical consultations were obtained.

Neurological examination:

1. *Mental Status:* The patient was semicomatose with periodic Cheyne-Stokes respirations.
2. *Cranial Nerves:* Pupils were fixed, the left dilated, the right constricted.
3. *Motor System:*
 - a. The patient moved all limbs in response to painful

stimulation, right more than left.

- b. There was a spastic resistance in the upper and lower left extremities.
4. Reflexes:
- a. A generalized hyperreflexia was present with bilateral ankle clonus.
 - b. Bilateral Babinski signs were present.
 - c. A bilateral grasp reflex was present. Note, however, that in a semicomatose patient this may have little localizing significance.
5. *Sensation*: Pain sensation was intact.

Clinical diagnosis: Subfrontal or parasagittal frontal tumor most likely a meningioma in view of the over 10 year course. Tentorial herniation had occurred possibly related to the lumbar puncture.

Laboratory data: An emergency bilateral carotid arteriograms revealed that a large subfrontal butterfly-shaped mass (probably meningioma) was present in the anterior cranial fossa bilaterally. The anterior cerebral arteries as well as the frontal polar, pericallosal and callosal marginal branches and the middle cerebral arteries were displaced backwards. The anterior cerebral arteries were also displaced upwards. The tumor mass derived blood supply from the ophthalmic arteries.

Hospital course:

A bifrontal craniotomy was immediately performed by Doctor Robert Yuan with total removal of a large bifrontal meningioma arising from the falx and olfactory groove. On the right side the tumor was estimated to occupy 75 percent of the anterior cranial fossa, measuring 7 x 5 x 6 cm. On the left the tumor was of approximately half this size, measuring 5 cm. in diameter. The thickness of the cerebral hemisphere covering the tumor in the right prefrontal area was reduced to 0.5 cm. Histological examination of the tumor indicated a benign meningioma (meningotheliomatous type).

The patient showed some immediate improvement at the conclusion of surgery, in the sense that both pupils were equal in size and reacted to light. By the time of discharge from the hospital, two months after surgery, considerable improvement had occurred. She could recognize the doctor by name but did not know the place, the season, or the month; she could, however, describe a picture she had just seen. A bilateral deficit in olfaction was present (anosmia). Assistance was required in walking. A bilateral grasp reflex was present.

Follow-up evaluation two years after surgery indicated continued improvement although the patient still had complaint relevant to impairment of recent memory and slight unsteadiness of gait. Deep tendon reflexes were symmetrical with plantar responses flexor. A bilateral grasp reflex was present and the patient was slow in walking and fell occasionally. Urinary incontinence occurred with wetting of the bed.

Comment: In retrospect, the evolution of symptoms in this patient clearly indicates a tumor initially compression both prefrontal areas and producing alterations in mood and personality. With continued growth of the tumor, compromise of the premotor areas with resultant apraxia of gait and release of grasp reflex began to occur, either as a result of direct compression or secondary to the distortion and compression of the anterior cerebral arteries. It is not unusual to witness the development of a dementia (deficit in recent memory) in large tumors in a subfrontal midline location. A similar dementia may occur in large aneurysms of the anterior communicating artery.

The problem of dementia will be considered in greater detail in the chapter on memory.

The development of headache, vomiting and increasing somnolence indicated the development of increasing intracranial pressure. The sudden unresponsiveness following the lumbar puncture with the development of periodic Cheyne-Stokes respirations, pupillary changes, and bilateral corticospinal tract signs all indicated an additional acute exacerbation of the already compromised brain stem functions, a compromise which had already resulted from the backward displacement of the intracranial contents with distortion of the brain stem. In retrospect, one might hypothesize that the patient's complaint of a loss of taste for her food at the time of her initial hospitalization might well have indicated some loss of olfactory sensation since much of our appreciation of food is dependent on olfaction. Specific tests for olfaction were not recorded.

CHAPTER 23: VISUAL SYSTEM

The following case is an example of a lesion involving the optic nerve, anterior to the optic chiasm.

Case History 23-1 (Fig 23-8).

This 53-year-old white right-handed housewife was referred for evaluation of progressive right-sided supraorbital headache of 23 years duration and decreasing acuity in the right eye. The loss of acuity had progressed to the point of almost total unilateral blindness. During the 3 years before admission, intermittent tingling paresthesia had been noted in the left face, arm, or leg. About 1 year before admission the patient had a sudden loss of consciousness and was amnesic for the events of the next 48

hours. She was hospitalized, but no explanation for the episode was clearly established, although cerebrospinal fluid protein was reported to be elevated (230 mg/dl).

The patient and her family reported some personality changes over a period of several years, including a loss of spontaneity and increasing apathy.

General Physical Examination: Unremarkable except for a minor degree of proptosis (downward protrusion of the right eye).

Neurologic Examination:

1. *Mental Status:* The patient was, in general, alert but at times would become lethargic. Her affect was flat. At times, she would laugh or joke in an inappropriate manner.
2. *Cranial Nerves:* There was anosmia for odors, such as cloves, on the right and a reduced sensitivity on the left.

Marked papilledema (increased intracranial pressure with protrusion of the optic disk and venous engorgement due to obstruction of the normal flow of CSF) was present in the left eye.

Pallor of the right optic disc was present, indicating optic atrophy. Visual acuity in the right eye was markedly reduced. The patient had only a small crescent of vision in the temporal field of the right eye, where only vague outlines of objects could be seen. A slight left central facial weakness was present.

3. *Motor Systems:* Intact although movements on the left side were slow.

4. *Reflexes:* A release of grasp reflex was present on the left side.

5. *Sensory system:* Intact

Clinical diagnosis: Subfrontal meningioma arising from olfactory groove or inner third sphenoid wing.

Laboratory data:

1. *Skull x-rays* demonstrated erosion of the dorsum sellae. Special lamniograms demonstrated hyperostosis of the sphenoid bone (planum sphenoidale) suggesting a meningioma originating from the sphenoid bone.

2. *EEG* demonstrated focal 2-4 Hz slow waves in the right anterior temporal and anterior lateral frontal area.

3. *Brain scan (H_g 197)* revealed a heavy uptake of isotope in the right posterior subfrontal area.

4. *Arteriograms* indicated that the anterior cerebral arteries were shifted backwards, posteriorly and the left. A tumor blush was present on the venous phase in the right subfrontal area extending back to the optic nerve groove (Fig 23-8). These findings were felt to be most consistent with an olfactory groove meningioma.

Hospital course: Dr. Samuel Brendler performed a bifrontal craniotomy which exposed a well-encapsulated smooth tumor attached to the medial third of the sphenoid wing. After intracapsular removal of 90 to 95% of the tumor, the right optic nerve could be visualized. The small portion of the tumor attached to the bone could not be removed because of considerable bleeding from the bone. Examination 4 months after surgery, indicated right anosmia and right optic atrophy were present.

Comment

If one considered only the patient's primary complaint, decreasing vision in the right eye, and the findings of right optic atrophy and left-sided papilledema (Foster-Kennedy syndrome), then the most probable diagnosis was inner-third sphenoid meningioma. The preservation of a small crescent of vision in the temporal field is consistent with compression of the optic nerve on its lateral surface. By the time of hospitalization, the lesion was quite large and had extended into the subfrontal area, producing anosmia on the right and some changes in personality. At this point, the various diagnostic studies suggested only a subfrontal mass and did not clearly differentiate between an olfactory-groove meningioma and a sphenoid-wing meningioma. One might suggest, in retrospect, that the degree of involvement of the right optic nerve was much more pronounced than the changes in prefrontal functions, and therefore, the inner-third sphenoid-wing location was more likely.

The surgical approach in any case was the same. The eventual recovery of vision in such cases is uncertain because the effects of compression often are not reversible

COMPLETE CASE HISTORIES FROM TEXTBOOK: *INTEGRATED NEUROSCIENCES*

PART III. CASES – CEREBRAL HEMISPHERE MOTOR SYSTEM, CEREBELLUM, BASAL GANGLIA

CHAPTER 18: MOTOR SYSTEM I:

The following case 18-1 presents an example of focal seizures beginning in the motor cortex.

Case 18-1. This 29-year-old, right-handed, white woman was in her usual state of good health until three months prior to admission when she developed an intermittent “pulling sensation” over the anterior aspect of the left thigh, lasting a few minutes. This recurred without other symptoms about twice a week. On the evening of admission, while sitting on a couch, she again had the onset of this same sensation in her left. She stood up, noted that her left leg felt “numb” and then started to have “jerky movements” in her left foot which progressed to involve the whole left lower extremity. She sat down, pressed on her left thigh in an attempt to stop the movement. At this point, her husband and a friend came to her (the patient is amnesic for these events), and saw her have tonic extension then clonus of all four limbs associated with grunting respiration, clenched jaw, and rolling of the eyes. She was placed on the floor and after a few seconds she regained consciousness, though she still appeared dazed and slightly confused for the next 5 minutes.

Past history and family history: noncontributory.

Physical Exam: Normal except for bite marks on the left lateral aspect of the tongue.

Neurological Exam: Significant only a slight asymmetry of deep tendon reflexes: left > right.

Clinical Diagnosis: Focal seizures originating right parasagittal motor cortex (foot area), with ? of parasagittal meningioma.

Laboratory Data:

(1) *Electroencephalogram* (Fig.29-1B) demonstrated rare focal spikes, right Rolandic parasagittal consistent with the focal source of the secondarily generalized seizure and rare focal slow waves in the right Rolandic and mid temporal area - consistent with minor damage in this area

2) *CT scan* (Fig.18-13) demonstrated an enhancing lesion in the right parasagittal region just anterior to the central sulcus.

- (3) *Arteriograms* (Fig.18-14) demonstrated a circumscribed vascular tumor in the right parasagittal rolandic area which was supplied by the right anterior cerebral artery (A,B) and the right middle meningeal branch of the external carotid artery©. The venous phase of the study demonstrated a significant draining vein from this area of tumor blush(D). All of these findings were consistent with a right parasagittal meningioma.

Hospital Course: A well-circumscribed right parasagittal meningioma was removed by Doctor Bernard Stone. A distal weakness of the left lower extremity was present in the immediate postoperative period but this improved rapidly so that by two months after surgery, a foot drop brace was no longer required and strength had returned to normal. During all of the pre and post operative period, the patient received diphenylhydantoin (Phenytoin) to prevent additional seizures. A possible sensory seizure involving the hand occurred 2 years later. Four years after surgery, the patient attempted to reduce her dosage of anticonvulsant and experienced a recurrence of focal motor seizure activity beginning in the left leg with subsequent secondary generalization. When evaluated 6 years after surgery, she had experienced no additional seizure activity. Her neurological examination continued to demonstrate an increase in deep tendon reflexes on the left and a left sign of Babinski. Her CT scan demonstrated no recurrence of tumor, there was very minor atrophy at the site of the previous meningioma. The EEG continued to demonstrate bursts of blunt spikes and slow waves in the right parasagittal Rolandic and parietal areas. Follow-up 10.5 years after surgery in indicated no additional seizures.

Comment: The onset of focal seizure activity should always raise the question of focal pathology. When these seizures begin at age 29, without a prior medical history, there is always a strong possibility of a primary brain tumor. In general gliomas are much more common than meningiomas but the odds of a meningioma are increased by the parasagittal location and the gender of the patient. In this case, there was a very close correlation of the clinical phenomena with the laboratory data regarding the anatomical location of the lesion. Surgical therapy eliminated the underlying benign tumor - the parasagittal meningioma, but the predisposition to focal seizures remained. Thus, the tumor in compression of cerebral cortex had produced alterations in neuronal excitability which persisted following the removal of the tumor.

Case 18-2 provides an example of a slow growing tumor involving the premotor and supplementary motor cortex from the standpoint of focal seizure activity. The motor effects of frontal lesions are presented in case histories 22-2 and 22-3 which follows the discussion of the prefrontal areas.

Case 18-2: This 57-year-old right-handed single nun and occupational therapist, had the onset of her first generalized convulsive seizure at age 47, ten years prior to consultation. This occurred without warning with sudden loss of consciousness and an observed generalized tonic clonic seizure. Both an EEG and CT scan were reported to have been normal. Approximately 4 additional generalized convulsive seizures occurred over the next 4 years. Shortly after the onset of the grand mal seizures, the patient began to have focal seizures. She described these as beginning with the abduction and raising of the right arm at the side, over her head, then a jerking of the right arm, and then she would fall to the ground. She would remain fully conscious but she would be unable to talk. She would have an awareness that something strange was occurring. She had a sinking sensation. She denied any impairment of memory after the episode. But, she would be aware that her right arm and leg were tingling and weak for perhaps 5 minutes afterwards and she would be unable to speak for 10-30 minutes afterwards. These focal seizures occurred once a month, but for the last 2 years, they had been occurring once a week. The patient indicated that over the last 10 years she has had problems with her memory.

She was reported to have had three “negative” CT scans over the years, and yearly EEG’s which did not reveal focal features or electrical seizure discharges although some bilateral slow wave activity was present. The patient has been treated with a variety of medications over the years without attaining seizure control. Her initial evaluation 4 years after onset of seizures at another neurological center indicated some increased activity in the finger jerks on the right with withdrawal of both plantar responses, and a diminished swing of the right arm.

Past history and family history were negative: she was the product of a full-term delivery weighing 9 pounds and had excellent developmental and educational milestones.

Neurological examination :The following abnormalities were present:

1. *Mental Status*: Although orientation and language functions were all intact, delayed recall without assistance, was 0 out of 5; and with assistance 2 out of 5. Proverb interpretation was abstract for 1/3 proverbs, but similarity testing was abstract.
2. *Cranial Nerves* II through XII were intact.
3. *Motor System* was intact except for a decreased swing of the right arm in walking.
4. *Reflexes*: deep tendon reflexes were increased on the right at biceps and patellar. Plantar response was extensor on the right and equivocally extensor on the left.
5. Sensory system was intact.

Clinical diagnosis: Seizures of focal origin left premotor/supplementary motor cortex possibly secondary to low grade glioma. A meningioma was less likely due to the reports of “normal CT scans”.

Laboratory data:

1. **CT scan** (Fig.18-16),demonstrated an area of calcification with surrounding edema in the left premotor area .

2. **MRI scan** (Fig.18-17),demonstrated extensive involvement of the premotor and supplementary areas by tumor and edema.

Subsequent course: Subtotal resection of this tumor was performed by Doctor Bernard Stone. Histological examination of the tissue confirmed the preoperative impression of an infiltrating glioma - predominantly oligodendroglioma in type. The patient received postoperative radiotherapy, 5000 rads to the left hemisphere and an additional 1000 rads to area of tumor. When last seen in follow-up 4 years after surgery, the patient was still experiencing infrequent (1-2 per month) short focal seizures of the same type involving focal movements of right arm, plus speech arrest. The neurological examination demonstrated some decrease in spontaneous speech and some blunting of affect. However, she was fluent; naming of objects and repetitions was intact. Strength was intact. Reflexes were symmetrical but bilateral extensor plantar responses were present. She had a moderate frontal type apraxia of gait and required a cane to avoid falls.

Comment :This patient presented with seizures of focal origin. The description of the posture adopted by the arm at the very beginning of the seizure, raised the possibility that her seizures were originating in the supplementary motor cortex of the left hemisphere and then spreading into the motor and sensory area. The arrest of speech would be compatible with such an origin since there is a superior speech area located in relationship to supplementary motor cortex. The fact that the patient remembered much of the seizure would also be consistent with such an origin. The post ictal depression of motor and sensory function in right arm and right leg and the depression of speech would all be consistent with post ictal phenomena involving the left hemisphere, particularly its sensory, motor and speech areas. The fact that the EEG's had not been particularly remarkable would also be consistent with such an origin of discharge. Thus, the discharging focus may well be buried on the parasagittal surface and not accessible to recording electrodes at the surface.

As regards the underlying nature of the pathology, when the patient was seen 10 years after onset of symptoms, she now has some focal findings; in terms of a right Babinski sign and increased reflexes in the right arm raising the question of a low grade glioma such as an oligodendroglioma in this area. The previous “negative” CT scans would have ruled out a meningioma or arteriovenous malformation. The long history and the finding of calcification within the tumor all made oligodendroglioma the most likely diagnosis. Low grade gliomas of this type often produce seizures without producing major neurological findings .Thus frontal release signs were minimal.

The following case history provide an example of normal pressure hydrocephalus producing the triad of a gait apraxia, urinary incontinence and problems in memory.

Case 18-3: This 72-year-old retired white handed carpenter was referred for evaluation of progressive impairment of gait, and more recent problems, in memory. The gait problems began insidiously five years previously but had become more significant in the past six months. He described his walking as involving small steps and then “going forward at too fast a rate, with difficulty in stopping”. As a result, he would stumble and tend to fall forward, losing his balance. He had considerable fear of falling and made use of a cane to avoid falling. For the last four to five months, the patient had noted urinary frequency and incontinence. He kept a bucket with him at all times. “Once I have to go, I can’t hold on.” Memory problems had developed during the last two to three months related to the recall of recent events and new material. He would enter a room and be

unable to recall why he had entered the room. Emotional lability had also developed during the past year. It was difficult not to cry when he heard a sad story.

Past history indicated at least three myocardial infarctions.

Neurological examination:

1. Mental Status:

- a. Oriented for time, place and person.
- b. Delayed recall, even with assistance, was limited to 1/3 in five minutes.
- c. The patient often lost track of what he was saying or doing.
- d. Serial 7 subtractions was slowly performed but intact.
- e. Reading, writing, drawing and naming of objects were intact but spelling was poor.
- e. Abstract reasoning was intact.
- g. Affect demonstrated changes: At times, he was tearful; at times, inappropriately jocular.

2. Cranial Nerves: Intact except bilateral decrease in hearing - long standing.

3. Motor System: Intact except for gait. The patient walked on a broad base with small steps. He was slow in starting and then picked up speed. He was unsteady on the turns and tended to turn "en bloc". No rigidity and no tremor were present. Finger to nose and heel to shin tests were normal.

4. Reflexes: Deep tendon reflexes were hyperactive at patellar. Plantar responses were equivocal. No definite frontal release signs were present.

Clinical diagnosis: Frontal lobe syndrome with involvement of premotor and prefrontal areas. The combination of a frontal gait apraxia, memory impairment and urinary incontinence raised the question of normal pressure hydrocephalus.

Laboratory data:

- 1. *CT scan (Fig. 18-21):* Demonstrated markedly dilated lateral; third and fourth ventricles but with no enlargement of the sulci.

Figure 18-21 Normal Pressure Hydrocephalus - CT Scan - Case 18-3 A. Ventricular Enlargement B. Section Through Vertex: Demonstrating No Enlargement of Sulci PART II: Comparison patient with progressive multiple sclerosis involving cerebral hemispheres at relatively comparable levels of section demonstrating A. Ventricular Enlargement B. Accompanied by Enlargement of Cortical Sulci

- 2. Lumbar puncture studies were normal.

- 3. *Radio-isotope cisternogram (Fig 18-22)* demonstrated continued presence of isotope within the ventricular system with no reabsorption over the convexities - subarachnoid space at 24, 48, and 72 hours.

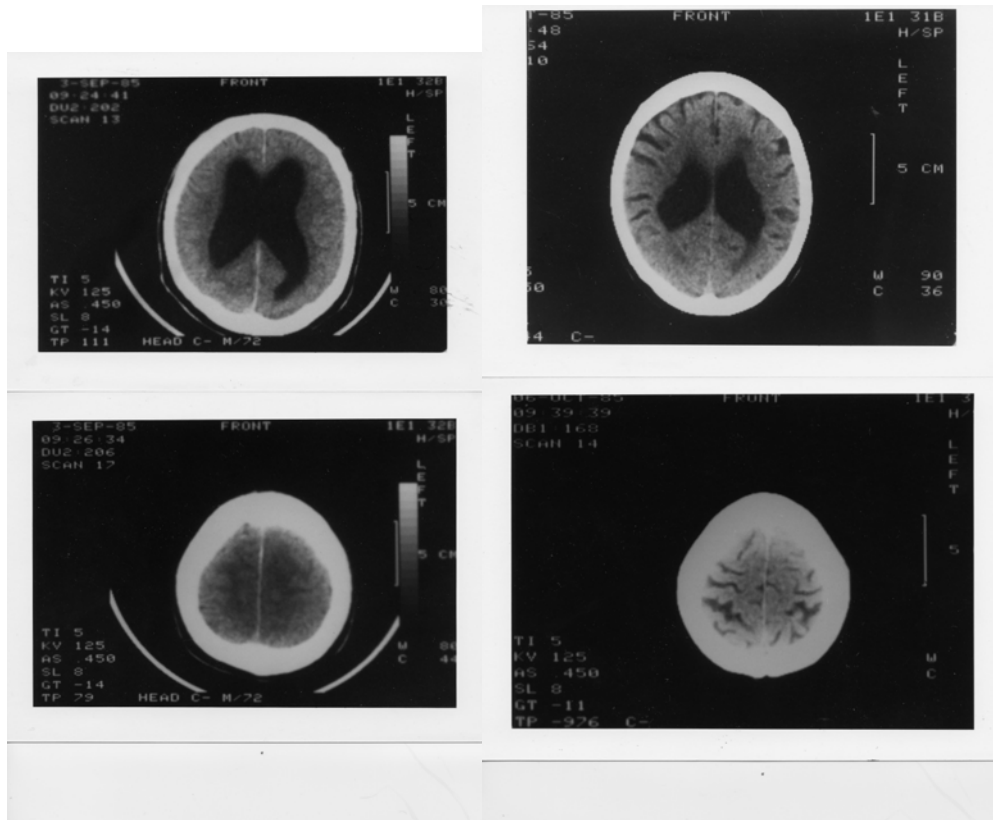
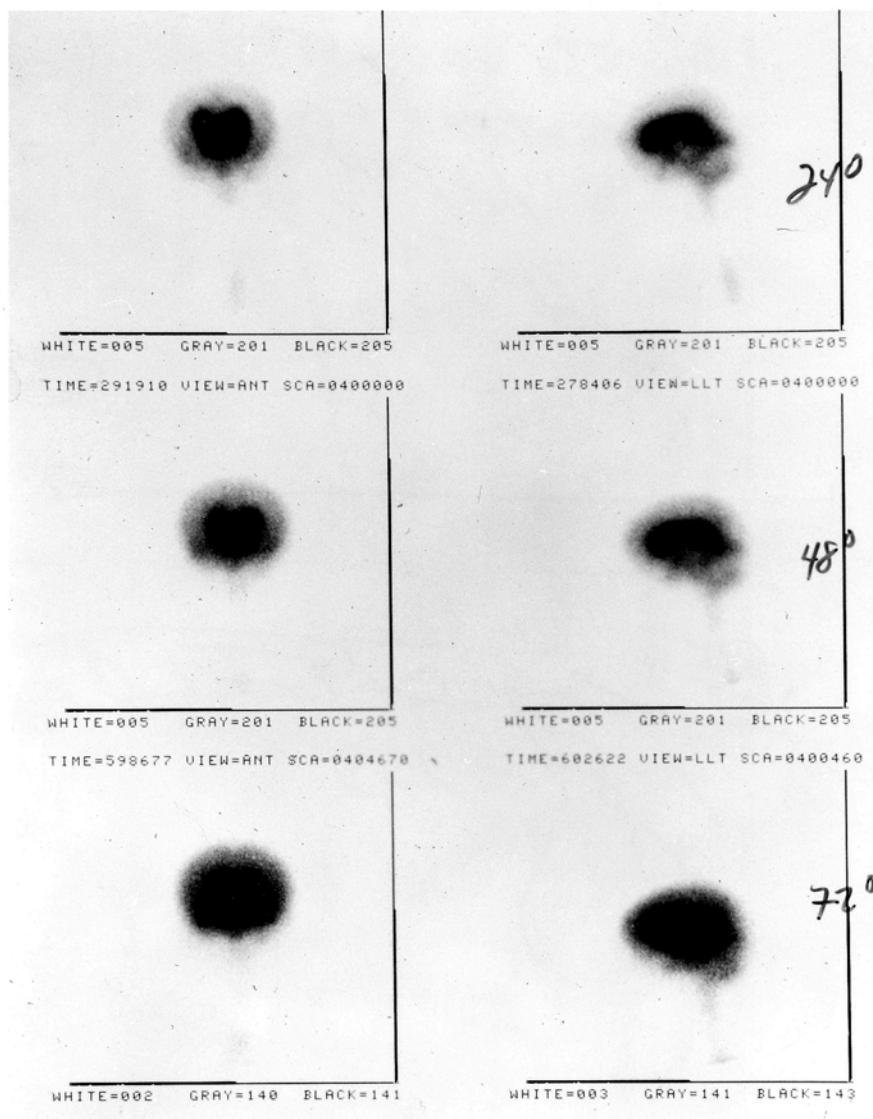


Figure 18-21. Normal Pressure Hydrocephalus Figure 18-21. Comparison Scan.

Figure 18-22: Normal Pressure Hydrocephalus: Isotope Flow Study: Lumbar CSF Injection Case 18-3 Isotope remaining in ventricular system at 24, 48 and 72 hours B. Comparison Case: Progressive multiple sclerosis of

cerebral hemispheres with enlargement of ventricular system but with enlargement of sulci. Isotope has begun to leave ventricles at 24 hours - appearing over the convexity and this is even more apparent at 48 and 72 hours.

Fig 18- 22. Normal Pressure Hydrocephalus; Isotope Flow Study



Subsequent course: Doctor Alex Danylevich performed a ventriculo-peritoneal shunt procedure (right lateral ventricle to peritoneal cavity). The patient did well with clearing of his triad of symptoms: Ataxia, dementia and urinary incontinence and was able to return to work as a carpenter , 12 hours per day. Subsequently , symptoms recurred due to infection of the peritoneal component of the shunt tube. Following revision of the shunt, symptoms improved only to worsen again in 6 months later. The patient had to use a wheelchair at times. A more marked apraxia of gait, frontal release signs, bilateral Babinski signs and urinary incontinence were present on examination 6 months after the revision. CT scan indicated a greater degree of ventricular enlargement. Following removal of 30 cc. of CSF, the patient was more responsive, and better oriented. Myocardial problems prevented additional neurosurgical revision of the shunt at that time. Subsequently, Doctor Robert Ojemann, of the Massachusetts General Hospital, revised the shunt utilizing a valve which allowed greater flow. At last evaluation, two years after admission, gait had improved (he was using a walker). Mentation was clearer (he was still described as showing aspects of a “frontal lobe syndrome”). Urinary incontinence was no longer present.

Comment: This patient presented a premotor/prefrontal syndrome .The imaging studies allowed a more specific delineation of the etiology of the syndrome. In most cases of normal pressure hydrocephalus, the gait disturbance is out of proportion to any change in mental status.

CHAPTER 19: MOTOR SYSTEM II: BASAL GANGLIA AND MOVEMENT DISORDERS

The following case presents an example of a patient with Parkinson's disease followed for 19 years.

Case 19-1 : This 48-year-old married white male, left-handed school master and physics teacher, was referred on 08/16/82 by his orthopedic surgeon for neurological evaluation of problems of control of the left arm and dragging of the left leg. Symptoms had begun 3 months previously with a sense of fatigue, stiffness and lack of control in the left arm. After a period of prolonged writing, he would have to make a conscious effort to continue writing. Approximately one month prior to the evaluation, he first noted a slowing down in movements of the left leg. "I have to remember to lift it."

Past medical history: Negative except for neck pain eight years previously related to cervical spondylosis, which cleared with the use of collar and traction except for occasional tingling in the 4th and 5th fingers of the left arm. Family history was unremarkable.

Neurological examination:

1. Mental Status: intact
2. *Cranial Nerves I-XII:* Intact except for a tremor of the closed eyelids and a positive glabellar sign (he was unable to suppress eye lid blinking on tap of forehead).
3. Motor System:
 - a. Strength : intact
 - b. Gait : There was a tendency to turn en bloc and a decreased swing of the left arm. However he could walk a tandem gait without difficulty.
 - c. There was a slight increase in resistance to passive motion at the left elbow, wrist and knee (rigidity without definite cogwheel component).
 - d. Although the patient was left-handed, there was a slowness of alternating finger movements of the left hand.
 - e. No tremor was present.
 - f. Handwriting was intact with no evidence of micrographia.
4. *Reflexes:* deep tendon stretch reflexes and plantar responses were physiologic
5. *Sensation:* all modalities were intact.

Clinical diagnosis: early Parkinson's disease, predominantly unilateral.

Laboratory data: all studies were normal including CT Scan of the brain, thyroid studies, blood chemistries, erythrocyte sedimentation rate, antinuclear antibody and serologic test for syphilis.

Subsequent course⁴: The patient did not wish to begin any treatment at that point in time. When evaluated 3 months later progression had occurred. He occasionally had the sense of moving slowly. He was now aware that with continuous writing, the writing became smaller, that is, micrographia emerged, evident on examination of handwriting. In addition, a minimal tremor was noted in the Archimedean spiral. A greater, but still minor, degree of cogwheel rigidity was now present at left wrist and elbow. Again, the patient was reluctant to begin therapy. On evaluation 1 year after onset of symptoms, additional progression was evident with significant micrographia (Fig. 19-6) and cogwheel rigidity now evident at left shoulder, elbow and wrist. Therapy with Sinemet (10-100 mg., t.i.d.)⁵ was begun. Re-evaluation one week later demonstrated a marked improvement in handwriting (Fig. 19-6) and decreased cogwheel rigidity.

⁴ This patient was followed for a total of 19 years after disease onset, initially for the first 13 years by the author, subsequently by Dr Paula Ravin at the University of Massachusetts Medical Center, Dr. David Standeart at the Massachusetts General Hospital and Dr. Warren Olanow at the Mount Sinai Hospital in New York.

⁵ This is a combination of 10 mg. of carbidopa (Dopa decarboxylase inhibitor) and 100 mg. of L-Dopa. Higher dosage combinations are a) 25 mg. of carbidopa with 100 mg L-Dopa, and b) 25 mg. carbidopa with 250 mg. L-Dopa. A sustained release form is also available (50 mg. of carbidopa with 200 mg. of L-Dopa), and is marketed as Sinemet CR.

As the dose of Sinemet was increased to (10-100) mg.5x/day over the next week, occasional choreiform movements of the fingers of the left hand and occasional backward flinging (hemi ballistic) movements of the left arm occurred. As the dose reached 10-100 mg. 6x/day, the patient reported that his handwriting now was back to normal. Examination confirmed the significant improvement in handwriting and in gait - with a better movement of the left leg. He no longer turned en bloc. Cogwheel rigidity was still present at left shoulder but to only a minimal degree at left wrist and elbow. The patient did experience 90 minutes after a Sinemet dose - a tremor of the left shoulder and an exaggerated grasp of the left foot toes on lifting the leg (possible form of dyskinetic or dystonic reaction).

The patient did well. When seen one year later, he had only a minimal degree of cogwheel rigidity. No tremor was evident. In walking he had a good swing of the arms and no longer turned en bloc. He was aware that some symptoms of his underlying disease would emerge 3-4 hours after a dose of Sinemet.

He continued to have progression of disease despite the use of all of the known anti Parkinson medications. He eventually underwent a fetal cell transplant in 1997 with apparently little improvement but with a significant increase in dyskinesias.

Re-evaluation, three years after onset of symptoms, indicated a minor progression with decreased swing of the arm and movements of the left leg, which were less smooth. The patient had increased his daily dosage of Sinemet to (10-100 mg) 6 (or) 7 tabs and noted that duration of action was approximately three hours. Re-evaluation, five years after onset of symptoms, indicated that despite having increased his dosage of Sinemet to 25-100 mg. tablets, 7 or 8 x/day, more resting tremor of the left hand had emerged. (In actuality 75-100mg of carbidopa is probably sufficient to saturate the peripheral dopa decarboxylase system). Moreover, choreiform movements of the left arm occurred 60 to 90 minutes after each dose of Sinemet. Examination demonstrated a pill-rolling tremor of the left hand as the patient walked down the hall. The choreiform movements disappeared when the dosage of Sinemet was reduced to 25/100mg 6/day. The increased rigidity and tremor responded to the addition of a DOPA agonist Bromocriptine (Parlodel) - Initial dosage 1.25 mg. 2x/day then increased to a total dose of 5.0 mg., and subsequently to 7.5 mg./day. Despite increasing dosage of the Bromocriptine to 17.5 mg/day - no additional improvement occurred. Additional reduction of Sinemet to (25-100) 5x/day - eliminated sudden myoclonic jerks and dyskinetic movement of the left lower extremity, which would occur - 45 minutes after a dose of Sinemet. Examination 6 years after onset of symptoms, examination and 3.5 hours after last dose of Sinemet demonstrated a coarse pill rolling tremor of the left hand and a shuffling of the left foot in walking. Marked cogwheel rigidity was present at left wrist and elbow. Considerable slowness of alternating finger movements was present. Handwriting was small and slow. Amantadine (an antiviral agent with mild ant parkinsonian effects), 200 mg./day was added at this point with a considerable improvement in symptomatology.

When examined 7 years after onset of symptoms, and 2.5 hours after Sinemet dosage and he now had a prominent tremor of the left hand at rest and a minor tremor of the right hand. Only minor cogwheel rigidity of left wrist and elbow were present. There was mild facial akinesia, tremor of the closed lids and a positive glabellar sign. As he walked he had a problem with sequential movements of the left leg. He reported that initially in the mornings, he had considerable problems in the initiation of movements of his left hand. Because effects of the Sinemet were wearing off in a shorter period of time - the dosing interval was altered to every three hours, in the process increasing total intake to 6 and then 7 tablets per day, with transient improvement. When seen 8 years after onset of symptoms, he was having sudden "kick in of the on effects" at 30-45 minutes and wearing off effects of greater degree at 3 hours after Sinemet dosage. As a result balance had shown some deterioration. Although tremor and cogwheel rigidity were primarily present left arm lesser symptoms were present in the right arm. At this point, a monoamine oxidase B. inhibitor was added: Selegiline (Deprenyl) in a total dose of 10 mg./day (5 mg., b.i.d.). When seen 6months later, the patient was uncertain that any benefit had been achieved. A major symptom was now "freezing" - he would have times in going over the threshold of a door when he would suddenly freeze. This, at times, related to the wearing off of medication (Sinemet) effect but at other times, usually in the afternoon, was unrelated to time of last dose. In the morning, freezing effect was clearly related to time of dosage. He remained relatively stable for the next year and then had a progression of symptoms - increasing tremor, increasing dragging of the left leg and more wearing off of dose effect - usually after 2.5 hours. In addition, "freezing" episodes were occurring more frequently in between dose wear off periods, usually in going through a doorway or even in hallways. At this point, the patient was switched to the sustained release form of Sinemet (50/200 mg carbidopa/L-Dopa) taken three times a day. Amantadine, Bromocriptine and Selegiline were continued unchanged. When evaluated 6 weeks later, there had been a remarkable improvement. He had a smoother day with fewer ups and downs, less dyskinesia and less stiffness. Effects of the medication were lasting 5-6 hours. When seen 3.5 hours after his last Sinemet dosage, he had

very little cogwheel rigidity. He could walk with a good swing of the arms. Handwriting was good with little tremor and little dyskinesia. On the other hand, when seen several weeks later, approximately 5.5 hours after his dose of sustained release Sinemet, he had marked difficulty, walked with small steps, and would arrest going through a doorway. Balance was poor, requiring a cane. There was a marked tremor of the left hand and to a lesser degree, of the right hand. A marked akinesia was present. However, within 20 minutes of his taking an additional tablet of sustained release Sinemet, a marked improvement again occurred. Despite this long course, the patient had been able to continue in his usual occupation. The patient subsequently was treated with a COMT inhibitor and was switched to another dopamine agonist pergolide with little apparent benefit. Eventually, in 1997 he was entered into the NIH sponsored fetal transplant study (subsequent imaging study did indicate that the patient was in the transplant and not the placebo group). It was unclear that this had produced any decrease in his disability. However evaluation 3 years after the transplant did demonstrate a marked increase in the dyskinesias involving head arms and torso. Some improvement in dyskinesias occurred when dopaminergic medications were reduced

Comment: Parkinson's disease is a progressive disorder of motor function, with variable manifestations of tremor, rigidity, akinesia, bradykinesia, and impairment of postural reflexes. Patients vary in the type of major involvement and in the rate of progression. Pharmacological management has rapidly evolved and in the process has provided considerable insights into the nature of basal ganglia function. For the specific patient, therapy must still be individualized. As this case history illustrates the pharmacological effects are time limited. Evaluation of therapy must always record the time of drug intake and the time of examination.

It is important to note that the disease remains progressive, despite the impressive pharmacological achievements. To prevent progression would require arresting or reversing the loss of the nigral cells producing dopamine or of introducing another source of dopamine producing neurons into the basal ganglia as discussed above. The future of fetal transplantation remains uncertain. Surgical procedures particularly deep brain stimulation involving the subthalamic nucleus or the globus pallidus may offer benefit to specific patients.

The following case, 19-2 provides an example of hemichorea.

Case 19-2 : This 88-year-old, right-handed, widowed white female with a past medical history of profound hearing impairment, adult onset diabetes, euthyroid goiter, coronary artery disease, and hypertension was brought by her daughter to Saint Vincent's Hospital because of uncontrollable movements ("twitching") of her left foot and shoulder. The daughter described the insidious onset of involuntary rotary movement in the left foot five days prior to admission, which increased in intensity and progressed to involve the left shoulder. The movements were constantly present, even during sleep. The movement was accompanied by a "shooting" pain on the left side of the body which the patient was not able to further describe. She denied loss of consciousness, dizziness, change in mental status, weakness, sensory impairment, visual changes, aphasia, or dysphagia associated with the movement disorder, but did describe a dull headache greater on the left side than on the right during the last few days prior to admission, not accompanied by nausea or vomiting. There was no history of a past movement disorder. Progression rather than spontaneous resolution of the choreiform movements which had begun to impair the patient's ability to ambulate with her walker prompted her daughter to seek medical attention.

Past history: The patient had been admitted briefly one year previously with confusion. and hyperglycemic state related to diabetes mellitus.

Physical Examination: vital signs were all normal.. Patient was alert and cooperative, though profoundly hard of hearing and exhibited involuntary twisting movements of her left foot and upward jerking movements of her left shoulder.

Neurological examination:

1. *Mental Status:* The patient was oriented x3. Memory and language were grossly intact, questions were answered appropriately, and mental status was consistent with the patient's baseline according to her daughter.
2. *Cranial Nerves:* Intact except: for Left eye blindness (cataracts), and gross impairment of hearing such that shouting was necessary to communicate.
3. *Motor System:*
 - a. Tone and strength in upper and lower extremities were normal except for minimal weakness in the left upper extremity(5-/5) .
 - b. Finger tapping, finger-to-nose and heel-to-shin were grossly intact with only slight left-sided difficulty due to involuntary movements.

- c. There was a persistent hemichorea without flinging motions in the left foot, more marked than the left shoulder. There were rotary, twisting movements at the left ankle and upward and rotary motions at the left shoulder. The movement was exacerbated by motor—tasks but did dissipate with sleep.
 - d. Gait was slightly unsteady due to hesitant placement of the left foot. She did quite well with minimal assistance.
 - e. Romberg was negative.
4. *Reflexes*: Deep tendon reflexes were symmetrical, and physiologic except for decreased Achilles secondary to diabetes. The right plantar response was flexor, the left ;extensor.
 5. *Sensation*: Intact except for symmetrically diminished vibration sense in toes.

Clinical diagnosis: hemichorea

Laboratory data:

1. *Electrolytes creatinine, and CBC* were normal. *Glucose* was elevated to 168; *ESR* - 36 mm/hr. *RPR* non-reactive. *ANA* was 1:80(not significant) .*Urine culture* was positive for group B Streptococcal - infection sensitive to Ampicillin. *EKG and chest X-ray* were unchanged from last admission.
2. *CT scan* on admission revealed bilateral basal ganglia calcification, bifrontal atrophy consistent with age, but no evidence of infarction, hemorrhage, or tumor and revealed no change from previous CT scan of 2 months previously.
3. *MRI scan* 3 days after admission, revealed mild cortical atrophy and a hyperdense area without mass effect or enhancement on gadolinium in the right basal ganglia (particularly the head of caudate and putamen) and external capsule consistent with subacute hemorrhage (Fig.19-7).

Hospital course: The patient was begun on haloperidol 0.5 mg by mouth every morning and advanced to 1 mg., by mouth., t.i.d. with some improvement in the hemichorea, particularly in the upper - extremity. Her hemichorea continued to improve over the next two weeks on haloperidol with only occasional twitching of the left shoulder and diminished but persistent, rotary movement of the left foot, both still exacerbated by motor tasks.

The following case 19-3 provides an example of hemiballismus

Case 19-3: This 79-year-old, right-handed, white housewife had the abrupt onset in the early morning hours, 2 days prior to admission, of almost constant flinging movements of the right arm over which she had no control. At the same time, she noted that her right arm felt numb and heavy. Over the next 2 days, the movements decreased markedly and she regained more control of the arm.

Past history: The patient had been a known diabetic for 21 years, receiving insulin - most recently, lente insulin, 25 units each morning.

Neurological examination:

1. *Mental Status*: intact ,the patient was alert and well oriented and without aphasia.
2. *Cranial Nerves*: All were intact.
3. *Motor System*:
 - a. Minimal weakness was present in the right upper extremity at the elbow, wrist and fingers
 - b. Alternating movements and finger-to-nose testing in the right hand were markedly impaired.
 - c. Gait was intact.
 - d. Occasional involuntary flinging movements occurred at the right shoulder.
4. *Sensory System*: Pain, touch, vibration and position sense were all absent in the right upper extremity to the elbow and decreased in this extremity above the elbow.

Clinical diagnosis: hemiballismus

Laboratory data: Chest and skull X-rays EEG, and cerebrospinal fluid studies were all normal.

Subsequent course: The flinging movements of the right arm subsided spontaneously, shortly after admission. Position sense returned and pain sensation showed a mild improvement. The ataxia on finger-to-nose testing disappeared.

Comment: The loss of pain, touch, vibration and position sense in the right upper extremity at the onset of symptoms in this case, would suggest a lesion involving the ventral posterior lateral nucleus of the thalamus, presumably as a result of occlusion of the penetrating branches of the

posterior cerebral artery. Such a lesion could have damaged the subthalamic nucleus as well. The severe dysmetria in the right upper extremity could well have reflected the severe sensory deficit in the right upper extremity. This would appear to be more likely than postulating a lacunar ataxic hemiplegia, due to involvement of the corona radiata in which the origin of the hemiballistic movements could have been in the adjacent caudate putamen. This however would not explain the severe sensory deficit. Note that the use of antidopaminergic agents will decrease or eliminate hemiballismus or hemichorea; however many patients as in this case resolve spontaneously.

The following case history provides an example of Huntington's disease.

Case 19-4: This 54-year-old right-handed divorced white female was referred for evaluation of a movement disorder. The patient lived alone and it was difficult to obtain much of any history from the patient. So far as she was concerned, she had no neurological problems. She denied any problem with her movements. She did indicate that she had worked for 10 years as a secretary/computer operator but had been fired 10 years ago because "she did not work fast enough". She did indicate that she had experienced problems with memory over the last year. The patient denied that she had never been treated on a psychiatric service. She denied receiving neuroleptics. She had a past history of hypertension but had not been reliable in taking her prescribed medication. The patient's son was aware that changes in emotion, personality, speech, gait and a movement disorder had been present for at least 3 years.

Family history: The patient denied any neurological family history except for a maternal uncle who had the "shakes". By contacting the patient's son age 27 and her mother now age 81 and then obtaining old records we were able to assemble additional information. The patient's father had been hospitalized at age 55 on the psychiatry service of St. Vincent Hospital. A review of that record indicated that for several years he had been showing irritability, had become suspicious and paranoid at work. He gave a history of choreiform movements of 20–30 years duration beginning with twitchings about the shoulders. This had progressed over the several years prior to admission, affecting his gait and the movements of the hands. The examination demonstrated that he was moderately depressed and impatient. As he sat, he had "purposeless" movements of his body particularly of the lower extremities. In walking he had "ballistic" movements. He walked on a broad base. Choreiform movements were noted in the tongue. The diagnosis of the neuropsychiatrist was Huntington's disease. He apparently died of cardiac disease shortly after that hospitalization.

The paternal grandfather had died at age 43 of pneumonia, the paternal grandmother at age 37 of gall bladder disease, neither was known to have Huntington's disease, but information was scanty. The patient's father had two siblings one alive at age 81, the other dead at age 68, both apparently unaffected. The patient's mother had a sister with essential tremor.

The patient had 2 siblings, a brother age 60, a sister age 44; both unaffected according to the patient's mother.

The patient had 4 children ages 34, 32, 30 and 27, and 3 grandchildren ages 13 years, 2 years, and 3 months. The eldest daughter age 34 had been depressed for 5 years and had problems with speech and walking for a number of years.

Neurological examination:

1. *Mental status*: the patient often avoided eye contact. Affect was usually inappropriate with laughter as the response to many questions. The overall mini-mental status score was 27/30. The only deficit related to delayed recall portion of the test (0/3 objects).

2. *Cranial nerves*: the patient had a hyperactive jaw jerk. She had frequent facial grimacing.

3. *Motor system*: the patient had decreased tone at wrists and elbows, but strength was intact.

As she sat she had frequent restless and at times choreiform movements of hands and feet.

Gait was often "bizarre" in terms of occasional sudden movements of a leg as moved down the hall and came to a stop. These same movements occurred as she remained standing. In addition in standing or walking, there were intermittent dystonic postures of either left or right arm.

4. *Reflexes*: Deep tendon stretch reflexes were everywhere hyperactive. Plantar responses were flexor. There was a minimal suggestion of grasp release.

5. *Sensory system*: intact

Clinical diagnosis: Huntington's disease.

Laboratory data:

1. *MRI scans of head* (Fig.19-13): The heads of the caudate nuclei were very atrophic. Cortical sulci were wide consistent with cortical atrophy. The lateral and third ventricles were secondarily dilated.
2. PCR testing for the CAG trinucleotide repeats of the Huntingtin gene.: allele 1=17; allele 2=42.
3. Thyroid studies, sedimentation rate, electrolytes, RPR, and antinuclear antibody were all normal.

Subsequent course: The patient refused any treatment for the movement disorder. The patient's son requested genetic testing and the issues were discussed. He and his siblings finally decided not to have the genetic testing performed. The patient's neurological status according to the son worsened to a moderate degree over the subsequent 3 years as regards speech, unsteadiness of gait, and mood swings but without any additional change in memory. The patient herself always appeared unaccompanied for follow up visits and reported no change in her condition.

Comment: Occasionally patients are encountered where changes in psychological function limit the information that the patient can provide.. In other cases denial of illness has a neurological as well as a psychological basis. In this case it was evident that this patient had not only symptoms relevant to the basal ganglia but also changes in cognitive function relevant to the cerebral cortex particularly the frontal areas. In such cases, information must be sought from other sources. In this case, the patient was willing to provide permission to contact those possible sources.

The clinical presentation in this case was clear-cut. In retrospect, many of the neurological features were similar to her father's findings on his admission 30 years previously. When did the patient's disease begin? This was uncertain, but we may presume that serious problems had been present at least 10 years earlier when she had been fired from her long time employment. Did this relate to motor problems, to changes in personality and interpersonal relations or to cognitive changes? Most likely, there were problems in all of these areas. According to her family, symptoms had been present for 2-3 years suggesting onset at age 51 or 52 years.

Case 19-5 provides an example of a patient with Huntington's disease followed over a longer period of time.

This 32 year old right-handed married white male spray painter at a computer factory, was referred for evaluation of a possible hereditary movement disorder. The patient was unclear about the reasons for his evaluation and much of the history was provided by his wife. She reported that the patient had undergone a personality change in the last several months. He had noticeable mood swings and on one occasion he reported people outside the window when no one actually had been there. He had some problems with remembering incidental matters, but no major problems and his job performance had remained intact. He was described as always having been "fidgety".

Past medical history - Mild hypertension for three years.

Family history - The patient's initial history indicated that the family had "Parkinson's" disease and his father had died in his 40's at the state hospital after a 10-15 year illness. The patient indicated that he was a child at the time and his mother never really told him much about the father or let him visit the father in the hospital but he did recall that perhaps his father had some excessive movements of the hands and face. The records were subsequently obtained and these indicated the father had been admitted to Worcester State Hospital in 1968 at age 37. At that time, he had already had three previous hospitalizations for "nervous breakdowns". At the time of his final admission, he had developed hallucinations, seeing people in his room. He had threatened his wife and other relatives. He had difficulty sleeping and he had also developed a problem with his legs "they are jumping". The father's examination had demonstrated a mumbled speech with repetition of the same phrases. His responses would often be tangential and then incoherent with impairment of memory and judgment. His mood was depressed. He was noted to have involuntary movements of the fingers and occasional facial grimacing. The deep tendon reflexes were hyperactive and the plantar responses were extensor. His gait was ataxic. The subsequent course indicated increasing ataxia, choreiform movements and rigidity with increasing weakness, difficulty swallowing and the final development of bronchial pneumonia with death at age 42. The diagnosis of Huntington's disease was confirmed at autopsy.

The paternal grandfather had expired at age 67 with a diagnosis of Huntington's disease, manifested by "nervous breakdowns, inability to sleep and movement disorder". The father's three siblings apparently did not manifest the disease. The patient had two siblings, brother age 28, a sister age 35, all without known disease. He had two children ages 9 and 5.

Neurological examination

1. *Mental Status* - The patient was anxious, often appeared blunted in emotional expression or in answering questions. He avoided eye contact. He was oriented for time, place and person. He was able to name objects and colors. His delayed recall was 2/5 without assistance and 4/5 with assistance.
2. *Cranial Nerves II-XII* were intact, except for the occurrence of occasional, sudden darting movements of the eyes to either left or right. In addition, occasional facial grimacing was noted occurring in a rather irregular manner.
3. *Motor System* : Strength and gait were intact . There were occasional, sudden, irregular, lateral, tremulous movements of the fingers of a choreiform-type.
4. *Reflexes* : Deep tendon reflexes including the jaw jerk were everywhere hyperactive. Plantar responses were bilaterally extensor (bilateral Babinski signs).
5. *Sensory system* : intact

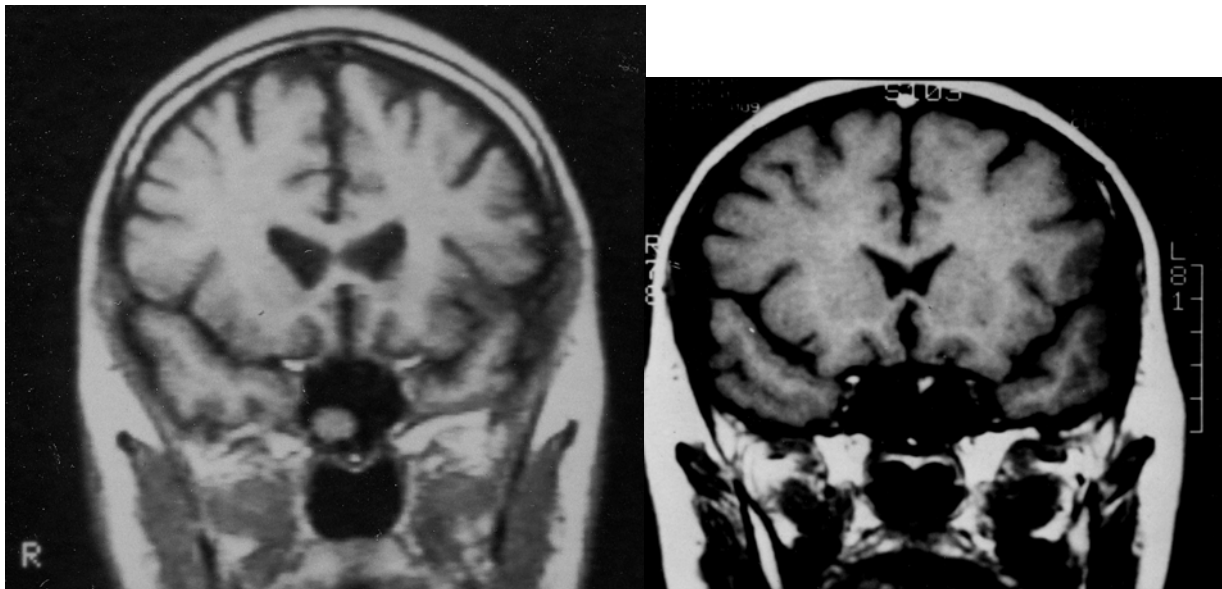
Clinical diagnosis: Huntington's disease

Laboratory Data :

1. All blood chemistries, including glucose; BUN, calcium, electrolytes, liver function studies, ceruloplasmin level, thyroid studies and serological test for syphilis were within normal limits. Ceruloplasmin levels are low in Wilson's disease but normal in Huntington's disease.
2. *Electroencephalogram* was normal with a dominant awake background activity of 10 Hz alpha rhythm.
3. *CT scan of the head* demonstrated enlargement of the ventricles with particular atrophy of the caudate. In addition the sulci were prominent for the age, suggesting some degree of cortical atrophy. The study was considered consistent with the clinical diagnosis of Huntington's disease.
4. The *MRI scan* (fig 19-11A) demonstrated mild enlargement of the ventricles and deepening of the cortical sulci, as well as a very significant atrophy of the head of the caudate nucleus. The MRI from this patient is compared to a similar section from a patient without signs of neurological disease (Figure 19-B)..

Figure 19-11A ;Case 19-5. Huntington's Disease

Figure 19-11B. Normal, age matched



Subsequent course :The patient subsequently developed increased paranoid ideation, increasing dependency with regard to his wife. He was treated with Haloperidol (a neuroleptic, tranquilizer) with considerable improvement with regard to personality. When evaluated, 3 years after onset of disease, it was evident that in the interim, the patient's personality problems had decreased. Attacks of anger and paranoid features had subsided. Mood swings were less. Memory problems, however, were worse and choreiform movements were worse. Dysarthria was now present. The patient had been divorced in the interim and he was on social security disability and no longer working. The examination now showed an exacerbation of many of those features noted at the time of his initial evaluation. He had occasional, sporadic movements of head or eyes of a

choreiform nature. He had frequent choreiform movements involving the fingers as he was sitting, also a similar type of movement appeared to involve the abdominal musculature. He had a moderate degree of dysarthria. He could walk a tandem gait but as he did so, the left arm came up in an somewhat flexed position. When last seen 4 years after onset of disease, he had more dysarthria and his speech was more difficult to interpret. There had been some increase in degree of rigidity but this had decreased when the dose of haloperidol had been decreased. The decrease in this medication, however, then resulted in a greater prominence of the choreiform movements. He could still handle a deck of cards, although he was dropping objects more often than previously. His neurological examination showed a significant degree of dysarthria, a greater degree of facial akinesia, more frequent choreiform movements of hands and face. He had difficulty in mimicking facial expression. As before, all of his deep tendon reflexes were hyperactive and the plantar responses were extensor. The patient walked in a flexed position and tended to turn en bloc. He had a mild degree of cogwheel rigidity at wrist and elbows. His memory remained remarkably good for delayed recall. Final telephone follow-up with his primary physician (approximately 7 years after apparent clinical onset of disease) indicated that the patient was no longer able to drive. He had continued weight loss. He had a marked dysarthria so that his speech was barely intelligible. Choreiform movements had increased. His gait was ataxic, but he could still walk without stumbling. He was relatively stable from a psychiatric standpoint. He was now living with his mother and brother.

Comment: This patient and his family demonstrate the relatively typical course of most patients with Huntington's disease. Patients and families do vary as to whether it is the psychiatric features or the movement disorder features that first bring the patient to medical attention. In this case, the psychiatric features, that is, the change in personality and the increasing paranoid ideation were the first features noted. Subsequently, involvement of the motor system became the most prominent feature. As in the previous case, the patient was unclear as to why he had come for neurological evaluation. Was this a neurological or a psychological denial of illness? Most likely both factors were operational. It was of considerable interest that this patient when first seen, although he was aware of some neurological problem that had occurred in the family, was unclear as to the specific diagnosis. It was also evident that almost no genetic counseling had been done in a disorder that was very clearly an autosomal dominant disorder. The significant family impact, social and economic impact of the disease are clearly evident in this patient. The implications of presymptomatic detection are discussed by Meisser et al (1988), and Klawans (1972).

The following Case 19-6 illustrates the clinical problem of hepatolenticular degeneration in a 21 year old female with a brother who had died at age 16 with hepatic disease, a Kayser Fleischer ring and choreoathetosis. The patient had serum elevation of free copper and a decrease in protein bound copper. She was successfully treated with penicillamine.

Case 19-6 (Patient of Doctor Huntington Porter) :This 21-year-old, single, white female shoe worker in January 1954 had the onset of a "shaking", or trembling of the fingers and hands which progressed to involve both arms and legs. The degree of involvement increased sufficiently to force her to give up her work. Nine months after onset of symptoms, she began to note increasing difficulty with balance and coordination and a slurring of speech. She had also noted increasing weakness and difficulty in doing repetitive tasks. One year after onset, the patient noted blurring of vision, occasional diplopia, and periods of "staring". She also had experienced increasing urgency and occasional urinary incontinence.

Family history: A brother of the patient had died in 1952, at age 16, of a disease with manifestations similar to this patient's. Evaluation of the sibling 2 years before his death by Drs. John Sullivan, Raymond Adams and D. Denny-Brown, had indicated the presence of choreoathetosis with lapses in posture of the hands. In addition, a brownish green ring at the corneal -

scleral junction was noted. Liver disease was present in this sibling and possibly other members of the family.

Neurological examination:

1. Mental status:

- a. The patient was anxious, at times crying, at other times, euphoric.
- b. Digit span was limited to 6 forward, 3 in reverse.
- c. Serial 7 subtractions were poorly performed.

2. Cranial Nerves:

- a. A brown rim was present at the limbus of the cornea, more evidence inferiorly and superiorly.
- b. Extraocular movements were impaired by involuntary jerk movements, The patient was unable to track a moving finger.
- c. Facial expression was mask-like.
- d. Speech was dysarthric and of a nasal quality with slurring and slowness of articulation.

3. Motor System:

- a. No actual weakness was present. However, this patient had difficulty maintaining the limbs in a fixed posture.
- b. There was a rigidity to passive movement of the limbs.
- c. A coarse arrhythmic tremor was present which was most marked proximally and more marked on sustained posture and on movement than at rest.
- d. Alternating movements were poorly performed.
- e. Gait was ataxic. Romberg test was negative.

4. Reflexes: Deep tendon stretch reflexes were hyperactive but plantar responses were flexor

5. Sensation: Intact

Clinical diagnosis: Wilson's disease: hepatolenticular degeneration.

Laboratory data:

- 1. Liver function tests were normal.
- 2. *Glucose tolerance test* was normal, but glycosuria occurred.
- 3. *Total plasma copper* 52 ug/100 ml. (normal range in a young adult is 65 to 150 ug/100 ml).
Direct reacting copper (unbound to ceruloplasmin) 31 ug/100 ml (normal 10 ug/100 ml).
Indirect copper (ceruloplasmin bound) 21 ug/100 ml, normal 105 ug/ ml).

Subsequent course: The patient did relatively well following the use of the chelating agents, BAL and calcium versenate and the institution of a copper free diet. A liver biopsy performed at the time of a cesarean section 18 months after beginning treatment was compatible with perihepatitis with a question of post-necrotic cirrhosis.

Re-evaluation 6 years after onset revealed, in addition to the earlier findings, the presence of "continual spontaneous involuntary movements of the limbs; at the feet, characterized by alternating flexion and extension at the ankle and a waving of the toes". A broad amplitude coarse tremor was noted when the patient was asked to abduct arms, flex elbows, and hold hands just before her nose (wing beating position). A side-to-side tremor of the head was also present. The gait was slightly wide-based and associated with continual dystonic movements of the hands and arms. Treatment with d-penicillamine (which had just become available) was begun at that time.

Urine copper excretion increased from 700 ug per 24 hours to 3240 ug per 24 hours. Normal 24-hour urinary copper in the adult is less than 40 ug. Neurological symptoms soon demonstrated improvement from the previously noted status. The patient was now able to do her house work and take care of her children.

Follow-up 2 years later, indicated significant improvement as regards the findings noted in 1960; dystonic facies and dysarthria was less marked. No tremor was present in the left hand; that in the right hand was evident only when under tension. Dystonic posturing of the hands was present only to a minimal degree. At last report 4 years later, and 12 years after onset of the disease, the patient continued to do well. She had remarried and was expecting another child.

Comment:

This patient presents a typical case of Wilson's disease with onset in the young adult years and with a definite familial background. The copper levels were consistent with the diagnosis (an increased unbound fraction and a decreased bound fraction). At the time that this patient was seen in the mid 1950's and early 1960's, ceruloplasmin levels were not available. Early establishment of a specific diagnosis in this case allowed for specific therapy with improvement of neurological symptoms and the prevention of progression of hepatic disease. With a specific diagnosis established in the patient, periodic blood tests were performed on her offspring to determine whether they also had inherited this genetic disease. (The child born 18 months after onset of the disease had not the disorder.)

An acquired form of non-Wilsonian hepatic and cerebral degeneration occurs in patients who have had multiple episodes of hepatic coma. Degenerative changes occur in the astrocytes and neurons of the basal ganglia. This disorder which was first described by Adams and Victor is discussed in greater detail above.

CHAPTER 20. MOTOR SYSTEMS III: CEREBELLUM

The following case provides an example of a child with a medulloblastoma.

Case 20-1: This 27-month old white female was referred for evaluation of ataxia. The mother had noted that the child had been unsteady in gait, with poor balance, falling frequently since the age of 13 months, when she began to walk. Three months prior to admission, in relation to a viral infection manifested by fever and diarrhea, the patient developed increasing anorexia and lethargy. One-month prior to admission, vomiting increased, and the patient also became more irritable. Perinatal history had been normal, and head circumference had remained normal.

Neurologic examination:

1. *Mental Status:* The child was irritable but cooperative.
2. *Cranial Nerves:* The fundi could not be visualized. Bobbing of the head was present in the sitting position.
3. *Motor System:* A significant ataxia of the trunk was present when sitting or standing. Gait was broad-based and ataxic, requiring assistance. No ataxia or tremor of the extremities was present. Strength and tone were normal.
4. *Reflexes:* Deep tendon reflexes were symmetric and plantar responses were flexor.
5. *Sensory System:* All modalities were intact.

Clinical diagnosis: Probable midline cerebellar tumor, most likely based on age a medulloblastoma

Laboratory data:

1. *Left brachial arteriogram* indicated an avascular area in the posterior fossa. The superior cerebellar artery was elevated. The inferior cerebellar arteries were depressed.
2. *Air-contrast ventriculogram* demonstrated enlargement of the lateral and third ventricles. The cerebral aqueduct was displaced forward to a marked degree. The fourth ventricle was deformed by a mass overlying the posterior wall (essentially located in the nodulus).

Hospital Course: Doctor Peter Carney performed a suboccipital craniotomy. The dura was bulging. The cerebellar tonsils were herniated to a minor degree. On gentle retraction of the inferior posterior vermis, a pinkish gray tumor, originating from a higher point in the fourth ventricle, was visualized at the obex. Limited biopsies of this tumor were taken, revealing a medulloblastoma. Samples of cerebrospinal fluid obtained at surgery revealed the presence of many malignant cells. A permanent shunt from the lateral ventricle to the jugular vein was not installed because of the possibility of spread of tumor cells into systemic circulation. Instead, a catheter was connected from the lateral ventricle to a small reservoir inserted under the skin of the scalp to allow daily drainage. Radiation therapy to the entire central nervous axis was begun one week after surgery. By the time of hospital discharge two weeks after the operation, the patient was able to walk unassisted, with only a moderate degree of ataxia. Three months after the operation, the patient was readmitted because of recurrent irritability and vomiting. A mild degree of papilledema was present. Horizontal nystagmus was present on lateral gaze bilaterally. A wide-base ataxic gait was still present. Various antineoplastic agents were employed (methotrexate into the cerebrospinal fluid and vincristine intravenously) without significant improvement. One month later, respirations became slow, deep, and irregular and death occurred. The findings at autopsy are demonstrated in Fig. 20-4.

In the following case a metastatic tumor in the midline cerebellum produced vertigo, ataxia of gait and headaches.

Case 20-2: This 67 year old white female 6 weeks prior to admission developed intermittent vertigo. Two weeks prior to admission she developed an ataxia of gait. Two days later headaches and true vertigo developed, ataxia increased and vomiting occurred. On the day of admission severe vertigo, headache and nausea and vomiting resulted in her visit to the emergency room

Past history: The patient had a lumpectomy 6 years prior to admission for carcinoma of the left breast. She had undergone a radical mastectomy followed by radiation therapy 3 years prior to admission for a recurrence of malignancy. Histologic examination of the excised tissue indicated a very poorly differentiated (high grade of malignancy) infiltrating ductal tumor which was negative for estrogen and progesterone receptors. On both occasions, the patient refused chemotherapy. The patient had multiple other medical problems including non insulin dependent diabetes mellitus, coronary artery disease, mild hypertension, and prior hip replacement surgery.

Neurological examination (in the emergency room)

1. **Mental Status:** Intact
2. **Cranial Nerves:** Intact except for an absence of venous pulsations on funduscopic examination suggesting a mild increase in intracranial pressure without frank papilledema.
3. **Motor System:** The patient had difficulty standing tending to fall to the right. She was unable to walk because of severe ataxia. There was no limb dysmetria.
4. **Reflexes:** Deep tendon stretch reflexes were symmetrical. The right plantar response was equivocal.
5. **Sensory system:** Intact

Clinical diagnosis: Midline cerebellar tumor metastatic from breast.

Laboratory data :

1. **CT scan of brain:** A large (3-4 cm) enhancing tumor was present involving the midline vermis and right paramedian cerebellum and compressing the fourth ventricle.

2. **MRI of brain** (3 days after admission): An enhancing midline mass involved the cerebellar vermis extended into the right cerebellar hemisphere, and produced mass effect upon 4th ventricle (Fig. 20-5).

3. **CT scan of abdomen** demonstrated two solitary possible metastatic lesions in the liver.

Subsequent course: The patient was immediately placed on dexamethasone with significant improvement. Within 12 hours the examination demonstrated only a mild ataxia tandem gait on turns and bilateral extensor plantar responses. The patient strongly insisted on removal of the solitary central nervous system metastases. Histological examination of the tumor resected by Dr. Gerald McGullicuddy demonstrated poorly differentiated adenocarcinoma with extensive necrosis similar to the tumor which previously had been removed from the breast. Following surgery she received 3000cGy(rads) whole brain radiation and was begun on the antitumor agent tamoxifen. She continued to manifest some unsteadiness on gait but had no difficulty in finger to nose or heel to shin tests. Three months after her admission, a repeat CT scan of the abdomen and pelvis demonstrated diffuse hepatic metastases with mesenteric and retroperitoneal lymphadenopathy. She expired at home, four

months after surgery before she was to start additional treatment with the antineoplastic combination of Cytosan, methotrexate and 5-fluorouracil .

Comment : This patient had a highly malignant poorly differentiated adenocarcinoma of the breast and was clearly at risk for the development of distant metastases ,a risk that was likely increased by her unwillingness to receive antitumor medication. Six years after the lumpectomy she presented with vertigo, ataxia headache and nausea and vomiting, without limb dysmetria. These symptoms suggested involvement of those areas of cerebellum related to the vestibular system and the axis of the body: the floccular nodular area and vermis. Certainly ,the best treatment of a solitary metastatic brain tumor where systemic metastases are not present is the combination of total resection of the brain lesion followed by radiotherapy. However at the time of surgery ,this patient already had evidence of two probable metastatic lesions in the liver. Except for the strong insistence of the patient that the tumor in brain be removed ,an alternate course of radiotherapy, dexamethasone and chemotherapy might have been pursued. Never the less the patient had several additional months of life during which she was able to travel to visit various relatives for a last time. Consistent with the highly malignant character of the tumor, this patient succumbed to the non neurologic effects of her disease

The following case history 20-3 illustrates the problem of alcoholic cerebellar degeneration.

Case History 20-3: This 64-year-old, white male was admitted with a chief complaint of a slowly progressive incoordination of gait present for 8 years. The patient and others had noted that his gait was staggering. The patient denied weakness, numbness, diplopia, vertigo, or memory difficulty. The patient admitted to the consumption of one half pint (250cc) of brandy every 4 nights since symptoms had developed. He indicated that he use to drink more in his younger days, at least 6 to 8 beers in addition to brandy or other alcoholic beverages every night.

There was no history of pes cavus or neurological disease.

General physical examination ; Blood pressure 140/80. Liver was enlarged with the inferior edge extending 2 finger breadths beyond the costal margin. Face was red with dilation of vessels.

Neurological examination:

1. *Mental status:* The patient was slightly disoriented for time. He gave the date as September 31. The date was actually October 19. Delayed recall was 0-out-of-5 objects in 5 minutes. He was unable to give the date of his birth, but he knew his phone number. Digit span was 7 forward, 4 in reverse. Calculations: The patient was unable to subtract 7 from 100 or 3 from 30; he could not add 14 and 13, although he had a fourth grade education.

2. *Cranial nerves:* All were intact. No nystagmus was present.

3. *Motor system:* Strength was intact. Gait was broad-based with an ataxia of trunk. The patient was unable to walk a tandem gait. His ataxia was accentuated by rapid walking. Small lateral nodding movements of the head were noted. He was relatively stable when sitting. There was a minimal tremor at rest. In addition, there was, to minor degree, a resistance to passive motion at the wrists and elbows with a suggestion of a cogwheel component. There was a minor tremor on finger-to-nose testing and a minor impairment of alternating hand movements.

There was, however, a very significant heel-to-shin ataxia which was out of proportion to any tremor or ataxia involving the upper extremities.

4. *Reflexes:* Deep tendon reflexes were physiological and symmetrical (2-3+). Plantar responses were flexor bilaterally.

5. *Sensory system:* Position, pain and touch were intact. There was a moderate decrease in vibratory sensation at the toes and ankles.

Clinical diagnosis: 1. Alcoholic cerebellar degeneration. 2. Mild dementia possible residuals of Wernicke's-Korsakoff syndrome.

Laboratory data: Complete blood count, albumin and total protein, sedimentation rate, cerebrospinal fluid, and skull and chest X-rays were normal.

Subsequent course: The patient received multiple B vitamins and was advised to discontinue any intake of alcohol. Neurological re-evaluation over the next 6 years indicated that no essential progression had occurred.

Comment: The major findings of the broad-based, staggering gait with truncal ataxia and heel-to-shin ataxia may be related to the anterior lobe of the cerebellum. In view of the absence of progression after the discontinuation of alcohol, a toxic or nutritional factor may be postulated (The reliability of the history obtained, in terms of the specific amount of alcohol intake is always open to question particularly in a patient

with significant problems in memory. The amount stated by the patient is usually assume to be the minimum amount.). The minor extrapyramidal findings of cogwheel rigidity may have represented unrelated disease. The lack of progression would be evidence against the diagnosis of a cerebellar degeneration of other etiology (see below). The minor degree of dementia may have related to previous nutritional problems with minor Wernicke-Korsakoff's syndrome or may have reflected a minor unrelated dementia or may have related to long standing retardation. At the present time, the diagnosis may be confirmed by CT scan or by MRI (midline sagittal section) (as in Fig. 20-7 or 20-8). As a result, evidence of cerebellar atrophy is now found in many patients presenting with other aspects of chronic alcoholism or other nutritional disease who do not necessarily present with initial symptoms of ataxia.

In the following case, a similar cerebellar gait disorder and heel to shin ataxia occurred o a genetic basis.

Case 20-4: A 45-year-old single white male carpenter presented with a 4 year history of progressive unsteadiness in walking, present during the daytime as well as at night. He had, during this period, noted minimal loss of coordinated movements in his hands, but felt that his greatest deficit was unsteadiness. The patient had noted no actual weakness but reported some numbness at the toes. He had also noted some minor difficulty in swallowing.

The patient lived in a small town in Virginia. Family historical information was incomplete His mother and father were second cousins. Several aunts and uncles had "trouble with their legs" in later life, resulting in a difficulty in walking. The patient admitted to a minimal intake of alcohol in the past. He had recently been under the care of a naturopath and had experienced a 7-pound weight loss.

Neurologic examination:

1. *Mental status:* Intact and consistent with his educational level.
2. *Cranial nerves:* Intact except for minimal dysarthria. Horizontal nystagmus was present on lateral gaze, vertical nystagmus on upward gaze.
3. *Motor system:* Strength was intact. The patient walked on a broad base with an ataxia of trunk, as though intoxicated, reeling from side to side, with marked unsteadiness on turns. He was unable to walk a tandem gait with eyes open. The patient was able to sit without significant ataxia of the trunk. A mild intention tremor was present, and there was minimal disorganization of alternating movements. In contrast a marked ataxia and tremor were evident on heel-to-shin test.
4. *Reflexes:* Deep tendon reflexes were intact, except for a relative decrease in ankle jerks compared to knee jerks. Plantar responses were flexor.
5. *Sensory system:* Intact, except for a minimal decrease in vibration sensation at the toes.

Clinical diagnosis: Hereditary cerebellar degeneration involving predominantly anterior lobe

Laboratory Data: Pneumoencephalogram performed at the University of Virginia Hospital (Doctor Stewart) confirmed the significant atrophy of cerebellum. Cerebrospinal fluid and other laboratory data were normal.

Comment: This patient had onset of ataxia at age 41 and was seen relatively early in his disease course. The most prominent features included the ataxia of gait and the heel to shin dysmetria. The patient also had a minor dysarthria, nystagmus and a mild asymptomatic peripheral neuropathy (decreased Achilles reflexes and decreased vibration at toes). There was a familial background but the information was incomplete. The subject of genetic cerebellar degeneration will be considered in a later section. Using older terminology, this patient would have been classified as olivopontocerebellar atrophy. Using more modern terminology, the patient might be included within the category of autosomal dominant cerebellar ataxia type I, had more genetic information regarding the family been available by history and or actual examination.

The following case history illustrates a focal lesion of the lateral hemisphere

Case 20-5 : This 36-year-old white male attorney was referred with a chief complaint of headaches and vomiting. The patient had frontal and biparietal headaches for approximately one month precipitated by coughing, sneezing, or bending. On at least one occasion, the patient had been awakened by the headache. The patient had nausea and vomiting independent of the headaches, at times, occurring suddenly without preceding nausea. For several weeks prior to admission, the patient had been unsteady on his feet, with a tendency to fall to the right, and had noted intermittent clumsiness of his right hand. For several days prior to admission, the

patient had double vision and had to keep one eye closed. During the week prior to admission, he had been excessively drowsy and constantly tired. The headaches had increased in frequency and were now occurring 3 to 4 times per day.

Neurologic examination:

1. Mental status: Intact.

2. *Cranial nerves:*

- a. On funduscopic examination there was evidence of bilateral papilledema.
- b. A bilateral paralysis of the sixth nerve was present.
- c. Horizontal nystagmus was present on right lateral gaze.

3. *Motor system:*

- a. Strength was everywhere intact.
- b. The patient's gait was wide-based. In walking, the patient tended to veer to the right. The patient was unable to stand independently on his right leg.
- c. There was a significant intention tremor of the right upper extremity on finger-to-nose test and of the right lower extremity on heel-to-shin test. Alternating movements of the right hand were disorganized.

4. *Reflexes:* Deep tendon stretch reflexes were normal and plantar responses were flexor.

5. *Sensory system:* All modalities were intact.

Clinical diagnosis: Tumor of the right cerebellar hemisphere with obstruction of ventricular system producing increased intracranial pressure and resulting in papilledema and bilateral cranial nerve VI palsy.

Laboratory Data:

1. Complete blood count and skull x-rays were normal.
2. *Right brachial arteriogram* revealed, in the late arterial phase, a blush in the right inferior and posterior cerebellar hemisphere consistent with a hemangioblastoma.
3. *Pantopaque ventriculogram* revealed a dilated third ventricle and a dilated aqueduct with obstruction to outflow from the fourth ventricle. The fourth ventricle and to a lesser degree, the aqueduct, were shifted to the left. These findings were consistent with a right cerebellar mass displacing and obstructing the fourth ventricle.

Hospital Course: The patient was placed on high dosage of dexamethasone to relieve increased intracranial pressure. Later that day a suboccipital craniectomy was performed by Doctor Samuel Brendler. When the dura was opened, bulging of the lower portion of the right cerebellar hemisphere was noted, with widening of the cerebellar folia. The widest area of the folia was tapped with a needle and a yellow cystic fluid was removed. A transcortical incision was then made, revealing a large cyst with a small strawberry-shaped hemangioma located within. The stalk of this tumor was ligated, and the hemangioma separated from the cystic capsule. Histologic examination of the tumor revealed a hemangioblastoma.

Postoperatively, the patient did well. His headache and diplopia disappeared. There was then improvement in the patient's tremor and ataxia, although there was a slight slowness on finger-to-nose testing on the right. A minor side-to-side tremor was present on right heel-to-shin testing. There was a tendency to veer to the right in walking, but tandem gait indicated only a minor unsteadiness. Evaluation six months after surgery, indicated only a minimal unsteadiness on tandem walking. Evaluation 9 months after surgery later indicated no significant neurologic findings. Re-evaluation three and one-half years after surgery, again indicated a completely intact neurologic status.

Comment: The headaches experienced by the patient, with pain occurring on coughing, sneezing, or mechanical changes, suggested a space-occupying lesion near the ventricular system or meninges. The tumor had produced a block of the ventricular system relatively early in its course, leading to an increase in intracranial pressure, with headache, vomiting and papilledema. The bilateral sixth-cranial nerve weakness was of moderate degree, and

its occurrence would not be unusual in a situation where intracranial pressure had rapidly increased.

The cerebellar symptoms experienced by the patient were lateralized in the sense that the patient was falling to the right side and had noted clumsiness of his right hand. Lateralized cerebellar disease was confirmed by the examination findings of intention tremor of the right arm and leg and disorganization of alternating movements on the right side.

In this case, the hemangioblastoma was in the lateral cerebellar hemisphere. In other cases of hemangioblastoma, the lesion is much more midline in location, and the symptoms are those of a midline cerebellar tumor. Thus, the patient may complain of an ataxia of gait and truncal ataxia and not display clearly lateralized symptoms involving the appendages, such as intention tremor and/or ataxia on heel-to-shin testing. The nodule of tumor often exists within a non-neoplastic cystic cavity. It is, therefore, possible to remove the tumor without sacrificing a large amount of the cerebellum. In some cases, both the mural nodule and the cyst are removed. In almost all cases a complete cure is obtained; recurrences are unlikely and the patients usually have a relatively complete resolution of symptoms and no residual disability.

In some cases, hemangioblastomas of the cerebellum are associated with angiomatous malformations of the retina (Landau-von-Hippel's disease). In some cases, there is an association with a secondary increase in red blood cell production (polycythemia). In rare cases, there is an association with tumors of the kidney. Other neoplasms may also involve the cerebellar hemispheres: cystic astrocytomas, metastatic tumors, and posterior fossa meningiomas. Meningiomas of the angioblastic type may be difficult to distinguish from hemangioblastomas.

At the present time, the diagnosis of these tumors may be readily made by means of MRI and CT scan (Fig. 20-11). Ventriculograms are no longer required. Arteriograms may still be of value in defining the vascularity and blood supply of the tumor.

The following case history presents a typical example of posterior inferior cerebellar artery infarct, the territory most frequently affected selectively.

Case 20-6: This 64-year-old right-handed married white male postmaster, on the morning prior to admission, awoke at 3:00 a.m. with severe posterior headache and severe vertigo, which was exacerbated by any head movement. Nausea, projectile vomiting and slurred speech soon developed. Shortly afterwards, he noted left facial paresthesias, clumsiness of the left upper extremity, and diplopia. He was admitted to his local hospital with a diagnosis of labyrinthine vertigo and then transferred to the neurology unit at Saint Vincent Hospital when symptoms began to evolve.

Two weeks previously, the patient had been seen for a transient episode of difficulty controlling the right arm, a hissing sensation, and impairment of speech.

Past history: The patient had evidence of significant vascular disease. He had hypertension and had undergone coronary artery bypass surgery. Beginning six years previously he had experienced episodes of transient weakness and numbness of the right arm with transient aphasia. He had normal aortic arch and carotid angiographic studies but EEG had demonstrated focal left frontal/temporal slow wave activity. He had been placed on long term anticoagulation. He had experienced migraine headaches without aura for many years.

Neurologic examination:

1. *Mental status:* Intact.
2. *Cranial nerves:* Conjugate lateral gaze to the left was impaired.
3. *Motor system:* Strength was intact. Significant lateralized cerebellar findings were present with marked dysmetria of left upper extremity on finger-to-nose testing and impairment of alternating hand movements. In attempting to stand, the patient was markedly ataxic.

4. *Reflexes*: Deep tendon stretch reflexes were decreased in both lower extremities. Plantar response was extensor on the right and flexor on the left.
5. *Sensory system*: Intact
- Clinical diagnosis**: Left cerebellar hemisphere infarct or hemorrhage with possible minor involvement of brainstem secondary to mass effect.

Laboratory data:

1. Duplex scans of carotids and vertebrals were normal.
2. *Transcranial Doppler studies* indicated normal flow velocities in the vertebral, basilar, anterior and middle cerebral arteries.
3. *Magnetic-resonance angiography* demonstrated occlusion of the left vertebral artery.
4. *CT scan* demonstrated a large left cerebellar infarct pressing the fourth ventricle to the right.
5. *MRI* (2 months after onset of symptoms): Infarction of the total cerebellar territory of the left posterior inferior cerebellar artery with no actual infarct of the brain stem (Fig. 20-12).

Subsequent course: The patient was somewhat vague with some difficulty in memory during the subsequent 8-day hospital course and remained ataxic. He was then transferred to the Fairlawn Rehabilitation Hospital where, over the next three weeks, he had a significant improvement. When re-evaluated two months after onset of symptoms, he was able to walk well with the use of a cane. A minor intention tremor was present on the left finger-to-nose test. An MRI study was obtained at this point, with results indicated above (because new symptoms suggested possible involvement of upper cervical nerve roots and spinal accessory nerve). Additional improvement was evident on evaluation three months after onset of symptoms. Evaluation 6 months after onset of symptoms demonstrated only a slight slowness of alternating movements of the left hand.

Comment: The acute onset of headache, vertigo, vomiting, ataxia of gait, and dysmetria of the left arm suggested an acute cerebrovascular problem involving the posterior circulation and the posterior fossa. (The syndrome of acute headache, vertigo, ataxia, nausea and vomiting is also seen in cases of acute cerebellar hemorrhage.) Numbness on the left side of the face and diplopia suggested, as well, possible brainstem involvement. The initial diagnosis at the local hospital of acute vestibular disturbance did not explain the headache, the diplopia or the lateralized findings. The presence of the left arm dysmetria suggested lateral hemispheric involvement rather than limited midline involvement.

In the era before CT scan and MRI, the distinction between acute cerebellar hemorrhage and acute cerebellar infarct was often difficult to make. Either lesion could produce block or distortion of the ventricular system and secondary hydrocephalus. Either lesion could be associated with the development of brainstem symptoms. The cerebellar infarct, often in the distribution of the posterior inferior cerebellar artery or the anterior inferior cerebellar artery, could also involve the medullary or pontine territories of these vessels. In addition, either type of lesion could cause significant edema with secondary distortion of the brainstem. Hemorrhage could also extend into the cerebellar peduncle and brainstem.

If significant clinical hydrocephalus or brainstem compromise develops, either type of lesion may require neurosurgical decompression or a shunt procedure.

A final note should be made regarding the considerable ability of the human nervous system to recover from extensive cerebellar lesions. Considerable recovery is possible because the cerebellum does not have a direct line role in the control of motor activity but instead, acts as a modulator of the motor control and motor planning circuits.

The following case history provides an example of a cerebellar hemorrhage secondary to an arteriovenous malformation.

Case 20-7: This 57-year-old right-handed married white female had the sudden onset of a severe left-sided pounding headache one afternoon. There was some stuffiness of the nose and tearing of the left eye. She had had a similar, but less severe, headache 20 years previously when taking birth-control pills. No headaches had occurred in the interim. As the current headache began to decrease, she noted that hearing in the left ear had decreased to a minor degree, and an echo sensation was present in the left ear. She also had the sensation that the environment was off balance, particularly if she was in a moving automobile. She subsequently reported a sense of unsteadiness. There was some sense of nausea when the symptoms first occurred. A vague blurring of vision was also present. She had a vague diplopia at the onset of symptoms but this then disappeared.

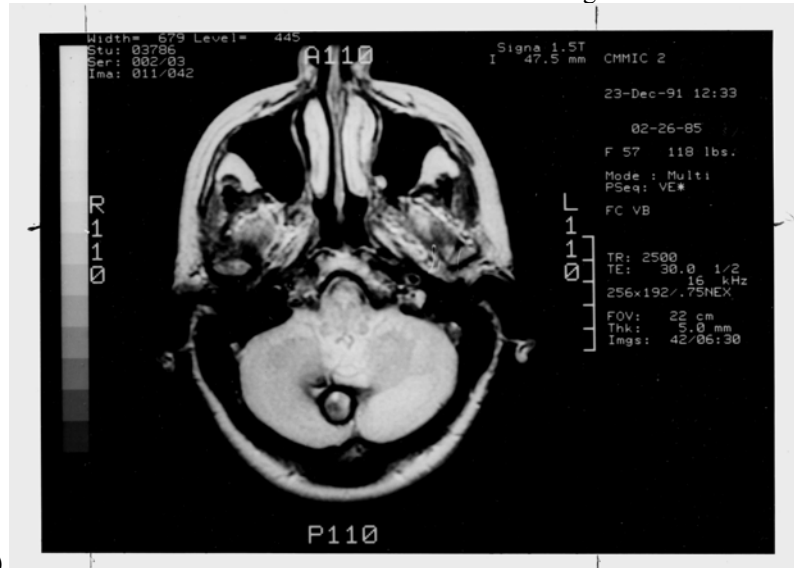
General physical examination: There were multiple pinpoint cavernous angiomas over the arms.

Neurologic examination: Entirely within normal limits.

Clinical diagnosis :Diagnosis unclear: possible migraine headache, or brain stem cerebrovascular event.

Laboratory data: 1. *CT scan of head* indicated hemorrhage in the right paramedian posterior cerebellum.

2. *MRI* showed a rim of hemosiderin stain around the residual hemorrhage in the cerebellar vermis



3. (Figure 20-14).

Subsequent course: The patient had no additional acute episodes. Because two episodes had occurred, she was referred for neurosurgical evaluation. A cavernous hemangioma of the right cerebellum was removed by Doctor Bernard Stone. Post-operatively, she had some right-sided clumsiness and ataxia, which gradually improved.

Evaluation by Doctor Stone one month following surgery, indicated minimal, if any, cerebellar signs. Finger-to-nose test showed no tremor. Gait demonstrated a minimal unsteadiness. Evaluation one year after surgery demonstrated no neurological findings, although some episodic symptoms of imbalance persisted.

CHAPTER 21: SENSORY FUNCTION AND PARIETAL LOBE

The following case demonstrates the localizing significance of focal sensory seizures beginning in the face of a 40 year old patient without prior neurological disease. As predicted, the etiology was neoplastic: a glioblastoma.

Case 21 -1:One week prior to evaluation, this 40-year old right-handed married white male had the onset of repeated 15-21 minute duration episodes of focal numbness (tingling or paresthesias) involving the left side of the face, head, ear, and posterior neck and occasionally spreading into the left hand and fingers, and rarely subsequently spreading into the left leg. There was no associated pain or headache or weakness or associated focal motor phenomena. Biting or eating would trigger the episodes. Past history was not remarkable.

Initial neurological examination: This was completely within normal limits as regards mental status, cranial nerves, motor system, reflexes, and sensory system.

Clinical diagnosis: Focal seizures originating lower third post central gyrus. In view of patient's age, a brain tumor must remain the prime consideration

Laboratory data:

- (1) *EEG*: no focal abnormalities were present. (The record, however, was abnormal because of bilateral bursts of spikes and slow waves - triggered by photic stimulation accompanied by myoclonic jerks - suggesting a predisposition to primary generalized epilepsy (refer to epilepsy chapter for the significance of this finding which was not relevant to this case).
- (2) *CT Scan* (Fig 21-2): The non-enhanced study was normal. The enhanced study demonstrated a small enhancing lesion just above the right Sylvian fissure.
- (3) *MRI* (Fig. 21 - 3): Demonstrated the more extensive nature of this process involving the operculum - above the right sylvian fissure including the lower end of the post central gyrus, the area of representation of the face. A probable infiltrating tumor was suggested as the most likely diagnosis.
- (4) *Arteriogram* - demonstrated a tumor blush at the right sylvian area, consistent with a glioblastoma, a rapidly growing infiltrating tumor - originating from astrocytic glia.

Subsequent Course: Treatment with an anticonvulsant reduced the frequency of the episodes. Neurosurgical consultation suggested an additional observation period and periodic CT scans in view of the normal neurological examination. Three months after onset of symptoms, the patient developed a numbness of the left arm and difficulty in coordination of left arm. Exam now demonstrated left central facial weakness, mild weakness of the left hand. A loss of stereognosis and graphesthesia with a relative alteration in pinprick perception was present in the left hand. The CT scan showed significant enlargement of the previous lesion. EEG now indicated focal 2-3 Hz Delta slow waves in the right frontal central Rolandic area. Subtotal resection of a glioblastoma - in the right temporal parietal area was performed by Dr. Bernard Stone. Radiation therapy was administered following surgery, 4000 rads total whole brain and 5210 rad total to the tumor area. Reevaluation 3 months after surgery, indicated only rare focal seizures involving the face. The neurological examination was normal. Repeat CT scans, however, continued to demonstrate a large area of enhancing tumor in the right temporal-frontal-parietal area. Despite the use of dexamethasone and arterial chemotherapy with cis-Platinum, he continued to progress. At the time of neurological follow-up, 29 months after onset of symptoms, he had developed a left field defect, left hemiparesis and a loss of all modalities of sensation on the left side. He subsequently developed significant changes in memory and cognition, as well as a complete left hemiplegia. CT scan demonstrated progression with extensive involvement of the right side of the brain and spread to the left hemisphere. Death occurred 33 months after onset of symptoms. **Postmortem examination of the brain:** almost the entire right hemisphere was replaced by necrotic infiltrating tumor. The tumor now had spread into the corpus callosum and temporal and occipital lobes. The internal capsule, thalamus, hypothalamus and basal ganglia were destroyed.

Comment: The initial occurrence of the limited focal sensory seizures involving the face and head in a patient of age 40 with no history of trauma or of vascular disease or hypertension clearly predicted the following conclusions (1) The location of the discharging lesion: the sensory cortex

just above the sylvian fissure. (Note that the actual extent of the pathology was more extensive but that is almost always the case in an infiltrating glioma). (2) The nature of the underlying pathology. The most common cause of focal seizures beginning at age 40 in a patient with no significant head trauma, vascular disease, hypertension or other medical disease is a tumor. Among tumors involving the cerebral hemispheres, an infiltrating glioma is by far the most common and on a statistical basis, a glioblastoma is by far the most likely histologic type. 3) The subsequent course was consistent with the natural history of a malignant glioma of the astrocytic series, a glioblastoma. The 33 month survival (30 months after surgery is beyond the median survival for this type of tumor.

The following patient (case 21-2) had a metastatic nodule in the post central gyrus producing a pseudo thalamic pain syndrome.

Case 21-2: This 62-year-old white, right-handed housewife, six years prior to admission

had undergone a left radical mastectomy for carcinoma of the breast. Five months prior to admission, the patient developed a persistent cough, left pleuritic pain and a collection of fluid in the left pleural space (pleural effusion) as well as daily headaches in the right orbit, occasionally awakening the patient from sleep. Four months prior to admission, over a 3 to 4 week period, the patient developed progressive "weakness" and difficulty in control of the right lower extremity. Several weeks later, the patient now experienced, aching pain in the right index finger in addition to a progressive deficit in the use of the right hand. This was more a "stiffness and incoordination" than any actual weakness. One month prior to admission the patient noted episodes of pain in the toes of the right foot and numbness of right foot occurred, lasting 2 to 3 days at a time. She subsequently developed, difficulty in memory and some minor language deficit, suggesting a nominal aphasia, prompting hospital admission.

Neurological examination:

1. *Mental status:* The patient was oriented for time, place, and person. Delayed recall was slightly reduced to 3-out-of-five in 5 minutes. A slowness in naming objects was present although she missed only one item of 6. Calculations, reading, and attention were normal. There was no left-right confusion.

2. Cranial nerves:

a. Nerve II: early papilledema was noted: absence of venous pulsations, indistinctness

of disc margins, and minimal elevation of vessels as they passed over the disc margin.

b. Nerve VII: right central facial weakness was present.

3. **Motor system:**

- a. Mild weakness of the right upper limb was present. A more marked weakness was present in the lower limb (most marked distally).
- b. Spasticity was present at the right elbow and knee.
- c. Gait: The right leg was circumducted; the right arm was held in a flexed posture.

4. **Reflexes:**

- a. Deep tendon reflexes were increased on the right.
- b. A right Babinski response was present.

5. **Sensory system:**

- a. Touch intact.
- b. An ill-defined alteration in pain perception was present in the right arm and leg - more of a relative difference in quality of the pain than any actual deficit.
- c. Repeated stimulation of the right lower extremity (pain or touch) produced dysesthesias (painful sensation).
- d. Vibratory sensation was decreased to a minor degree at the toes bilaterally but intact in the upper extremities.
- e. Position sense was markedly defective in the right fingers with errors in perception of fine and medium amplitude movement in the right toes.
- f. Simultaneous stimulation resulted in extinction in the right lower extremity.
- g. Graphesthesia (identification of numbers, e.g., 8, 5, 4 drawn on cutaneous surface) was absent in the right hand and fingers and poor in the right leg.
- h. Tactile localization and two-point discrimination were decreased on the right side.

Clinical diagnosis: Metastatic tumor to the left post central and precentral gyri with a cortical pain syndrome (pseudo thalamic pain syndrome).

Laboratory data:

1. *Skull x-rays:* the pineal was shifted from left to right. Demineralization of the dorsum sellae also had occurred: consistent with the increase in intracranial pressure.

2. *Chest x-ray:* Several metastatic nodules were present in the left lung.

3. *Electroencephalogram:* A focal disturbance, having the quality of damage, was present in the left posterior frontal central and parietal areas (almost continuous focal 4 to 7 cps slow wave activity).

4. *Left carotid arteriogram:* A left posterior frontal lobe lesion was suggested by a shift of the posterior portion of the anterior cerebral artery from the left to the right. The middle cerebral artery in the sylvian fissure was also depressed downwards.

5. *Brain scan:* The findings were consistent with a focal metastatic lesion with a focal uptake of radioisotope (Hg^{197}) in the left parietal area: high and close to the midline with uptake in the adjacent subcortical white matter.

6. **Erythrocyte sedimentation rate** was elevated to 90 mm., consistent with metastatic disease.

Subsequent course: There was evidence in this case that the disease had spread to multiple organs: brain (findings as noted), lung (chest x-rays and biopsy), and liver (abnormal laboratory tests of liver function). Radiation and hormonal therapy were, therefore, administered rather than any attempt at surgical removal of the left parietal metastatic lesion. Follow-up examination one month later indicated that a significant improvement had occurred in motor function in the arm. Sensory deficits persisted. Speech was slow but relatively intact. The patient eventually expired five months after admission.

Post mortem findings: Autopsy was performed by Dr. Humphrey Lloyd of the Beverly Hospital and disclosed extensive metastatic disease in the lungs, liver, and lymph nodes. A single necrotic metastatic lesion was present in

the brain. This was located in the upper postcentral gyrus of the left parietal area, 1.0 cm. below the pial surface and measuring 1.2 x 1.0 x 0.6 cm.

Comment: This patient had a progressive neurological deficit with headache and papilledema, a clinical course that clearly indicates the presence of a neoplasm. This case predated the era of CT and MRI scan. Today contrast-enhanced scans would be performed. This diagnosis was supported by the ancillary laboratory studies that were available at that time. Moreover this diagnosis however was clear based on the history and clinical-laboratory findings. The fact that motor findings in the arm relevant to the precentral gyrus improved with treatment might suggest that these findings were due to edema. In contrast the findings relevant to the area of the necrotic tumor, the post central gyrus, showed little improvement. In general, one should assume that a patient with a past history of carcinoma of the breast, carcinoma of the lung, malignant melanoma, or renal cell carcinoma, who develops symptoms of central nervous system disease, has metastatic disease until proven otherwise. Such symptoms at their onset may be minor and nonfocal and appear trivial: headache, subjective weakness, and a change in personality. On the other hand more focal symptoms and signs may be present: focal weakness, focal seizure. The metastatic lesions may be single or multiple.

A diagnosis of metastatic disease does not imply that no treatment of central nervous system lesions is possible. Surgical resection of single lesions may be successfully performed. Often the apparent deficits are far out of proportion to the actual size of the tumor because of the surrounding swelling (edema) in the adjacent tissues.

The pattern of sensory involvement in this case clearly localized this lesion to the cortex (or white matter close to cortical surface) rather than to the thalamus. The relative intactness of pain, touch, and vibration sensation should be contrasted to the significant deficits in position sense,

graphesthesia, tactile localization, and two-point discrimination with extinction on simultaneous stimulation. The occurrence of episodic pain in the involved arms and legs along with the production of an experienced painful sensation on repetitive tactile stimulation (dysesthesias) in patients with sensory pathway lesions is sometimes referred to as a "thalamic" or "pseudo thalamic" syndrome. (Refer to discussion of Wilkins and Brody, 1969). In this case, the anatomical locus for the pseudo thalamic syndrome is apparent.

The effects of deficits in cortical sensation on the total sensory motor function of a limb are apparent in this case. The actual disability and disuse of the right arm and leg were far out of proportion to any actual weakness. Such an extremity is often referred to as a "useless limb." The actual weakness that was present undoubtedly reflected pressure effects on the precentral gyrus and the descending motor fibers in adjacent white matter.

The following case (21-3) demonstrates many of the features of a non dominant parietal lobe lesion.

Case 21-3: This 70-year-old, single, white female, right-handed, retired candy maker underwent a left radical mastectomy for carcinoma of the breast, three years prior to admission. Four months prior to evaluation, the patient became unsteady with a sensation of rocking as though on a boat. She no longer attended to her housekeeping and to dressing. Over a three-week period, prior to evaluation, a relatively rapid progression occurred with deterioration of recent memory. A perseveration occurred in motor activities and speech. The patient was incontinent but was no longer concerned with urinary and fecal incontinence. For 2 weeks, right temporal headaches had been present. During this time, her sister noted the patient to be neglecting the left side of her body. She would fail to put on the left shoe when dressing. In undressing, the stocking on the left would be only half removed.

Family History: The patient's mother died of metastatic carcinoma of the breast.

Neurological examination:

1. Mental status:

- a. The patient was oriented for time, place and person.
- b. Delayed recall was 5-out-of-5 objects in 5 minutes.
- c. There was no evidence of aphasia.
 - d. The patient often wandered in her conversation. She often asked irrelevant questions and was often impersistent in motor activities.
- e. There was marked disorganization in the drawing of a house or of a clock. A similar marked disorganization was noted in attempts at copying the picture of a railroad engine (Fig 21-4).
- f. There was a marked neglect of the left side of space and of the left side of the body. The patient failed to read the left half of a page. When she put her glasses on, she did not put the left bow over the ear. When getting into bed, she did not move the left leg into bed. She had slipped off her dress on the right side, but was lying in bed with the dress still covering the left side.

- g. The patient had been reluctant to come for neurological consultation. Although she complained of headache and nausea, she denied any other deficits. Her relatives provided information concerning these problems. Much additional persuasion over a two-week period was required before the patient would agree to be hospitalized.

(2) *Cranial nerves:*

- a. Nerve II: A dense left homonymous hemianopsia was present. When reading, the patient left off the left side of a page. She bisected a line markedly off center. Disc margins were blurred and venous pulsations were absent, indicating papilledema.
- b. Nerve III: The right pupil was slightly larger than the left.
- c. Nerve VII: A minimal left central facial weakness was present.
3. *Motor system:* Strength was intact. There was, however, little spontaneous movement of the left arm and leg. Tone was normal.
4. *Reflexes:* deep tendon reflexes were symmetrical and physiologic and plantar responses, flexor.
5. *Gait:* The patient was ataxic on a narrow base with eyes open with a tendency to fall to the left, and was unable to stand with eyes closed even on a broad base.
6. *Sensory system:*
- a. Pain, touch and vibration were intact. At times, however, there was a decreased awareness of stimuli on the left side.
 - b. Errors were made in position sense at toes and fingers on the left.
 - c. With double simultaneous stimulation, the patient neglected stimuli on the left face, arm and leg.
 - d. Tactile localization was poor over the left arm and leg.

Clinical diagnosis: Metastatic tumor from breast to right non-dominant parietal cortex.

Laboratory data:

1. *Skull X-rays* were negative.
2. *Chest X-ray* indicated a possible metastatic lesion at the right hilum.
3. *Erythrocyte sedimentation rate* was elevated to 72 mm/hr, consistent with metastatic disease.
4. *Electroencephalogram* (Fig 21-5) was abnormal because of frequent focal 3 to 4 cps slow waves in the right temporal and parietal areas, suggesting focal damage in these areas.
5. *Brain scan (radioisotope)* (Fig 21-6) indicated that a large but well-defined area of increased uptake of isotope (Hg197) was present in the right parietal area extending from the midline to the lateral surface, measuring 7 x 5 x 7 cm. The most likely diagnosis was that of a solitary large metastatic lesion
6. *Right carotid arteriogram* showed that a large vascular tumor mass, probably metastatic, was present in the posterior section of the right temporal inferior parietal area. There was displacement of the middle cerebral artery upward and to the left.

Subsequent course: Treatment with steroids (dexamethasone and estrogens) resulted in temporary improvement. The patient refused surgery. Her condition soon deteriorated with increasing obtundation of consciousness. She expired two months following her initial neurological consultation.

Comment: This patient certainly presented a syndrome characterized by disturbance in concept of body image with a marked neglect of the left side, a denial of illness, and marked constructional apraxia. The various laboratory studies indicated a large lesion in the right posterior temporal parietal area. A CT scan from a more recent case demonstrating many aspects of this syndrome is illustrated in Figure 21-7. In many cases, the location of lesion may appear to be predominantly posterior temporal. Such large posterior temporal lesions would certainly compromise the cortex and subcortical white matter of the adjacent inferior parietal area.

In this case, marked deficits in perception of the cortical modalities of sensation were present. In other cases, as in the case demonstrated in Fig 21-7, such involvement is much less marked.

In some cases, involvement of the motor cortex is evident with an actual left hemiparesis accompanied by an increase in deep tendon reflexes and an extensor plantar response. At times in patients with neglect syndromes, there may be several indications in the clinical examination and in the laboratory studies that the involvement of the frontal lobe areas is more prominent than the parietal involvement. We have already indicated that the neglect components of this syndrome may also be noted in lesions of the anterior premotor

area (area 8). The premotor area as discussed above and in chapter 18, receives projection fibers from the multimodal area of the posterior parietal area. It is possible that in some cases the posterior temporal - inferior parietal location of the lesion may also be critical in interrupting these association fibers. For these several reasons, it is perhaps more appropriate to use the term, *syndrome of the non-dominant hemisphere*, rather than the more localized designation, non-dominant inferior parietal syndrome. Duffner et al, 1990 have presented the concept of a network for directed attention - with right frontal lesions leading to left hemi spatial neglect only for tasks that emphasize exploratory-motor components of directed attention whereas parietal lesions emphasize the perceptual-sensory aspects of neglect.

With lesions of the non-dominant hemisphere, there is a significant alteration of the patient's awareness of his environment. The behavior of an individual is in part determined by his or her own particular perception of the environment. If that perception is altered or disorganized, the behavioral responses of the patient may appear inappropriate to others. Obviously, not all individuals will respond in the same manner to a given environmental situation; part of the response will be determined by the past experience and personality of the individual. Thus, given the same lesion, one individual may be unaware of a hemiparesis, another may deny the hemiparesis but agree an illness is present, a third may claim to be healthy and claim that people are conspiring to keep him in the hospital.

CHAPTER 22: THE LIMBIC SYSTEM

In general, as we have indicated, there is mixed symptomatology during partial seizures of temporal lobe origin. The following case history (22-1) illustrates many of the points just discussed regarding seizures of temporal lobe origin.

Case 22-1: This 56-year-old white right-handed male baker was referred for evaluation of a seizure disorder. Three months before admission the patient had the onset of episodes of vertigo and tinnitus, each episode lasting 4 minutes and unrelated to position. The patient then noted increasing forgetfulness. Later that month he had a generalized convulsive seizure that occurred without any warning. The patient then developed episodes of confusion and unresponsiveness, followed by a left frontal headache. Several studies; EEG, pneumoencephalogram, and carotid arteriogram—were all negative at that point in time. One month before admission, the patient began to have minor episodes, characterized by lip smacking and a vertiginous sensation, during which he reported seeing several well-formed, colorful scenes. At times, he had hallucinations of “loaves of bread being laid out on the wall.” In addition, he would have a perceptual disturbance at the same time (e.g., objects would appear larger than normal) and “terrifying dreams.”

General physical examination: unremarkable.

Neurological examination: The essential neurological findings were as follows:

1. *General observations of seizures:* The patient was observed to have frequent transient episodes of distress characterized by saying, “Oh, oh, oh, my”. On occasion, these were accompanied by automatisms: fluttering of the eyelids, smacking of the lips, and repetitive picking at bedclothes with his right hand. Consciousness was not completely impaired during these episodes, which lasted from 30 seconds to 3 minutes, and the patient reported afterward that at the onset of the seizure he had seen loaves of bread on the wall and smelled a poorly described unpleasant odor. At other times, the olfactory hallucination was described as pleasant, resembling the aroma of baked bread.
2. *Mental status:* The patient was oriented to person but not dates. He could not recall his street address. He was unable to pronounce the name of the hospital correctly. Calculations were correctly performed.
3. *Cranial nerves:* Possible deficit in the periphery of the right visual field and a minor right central facial weakness.
4. *Motor system:* intact
5. *Reflexes:* Deep tendon reflexes were symmetrical and physiologic. A right Babinski sign was present.
6. *Sensory system:* intact.

Clinical diagnosis: Simple and complex partial seizures originating left temporal lobe probably involving at various times left lateral superior temporal gyrus, uncus, amygdala and hippocampus with tumor the most likely etiology in view of age and the focal neurological findings.

Laboratory data:

1. The *initial electroencephalographic recording* indicated frequent focal spike discharge throughout the left temporal and parietal areas, consistent with a focal seizure disorder originating in the left temporal/parietal areas (Fig. 29-1). A recording 6 days later indicated a decrease of focal spikes (i.e., a decrease in seizure activity) but the presence of frequent focal slow-wave activity in the left temporal area (almost continuous, 3 to 5 cps (Hz) slow-wave activity) suggesting that focal damage was present in the left temporal area .
2. *Brain scan* (H_g197) normal
3. *Left carotid arteriogram* indicated a possible avascular mass lesion left posterior frontal (the only abnormality was a 4-mm shift of the anterior cerebral artery).

Subsequent course: The patient continued to have multiple short episodes characterized by the sensation of odor and a sensation that he was looking at objects upon the wall. These episodes were eventually controlled with anticonvulsant medication: phenytoin (Dilantin) and primidone (Mysoline). However, 2 months later the patient had a day with several episodes with “crazy things occurring “ (colorful visions and terrifying nightmares).

The patient was readmitted to the hospital 7 months after onset of symptoms because of the recurrence of seizures. An aura of unpleasant odor was followed by a generalized convulsion followed by four or five

subsequent seizures of a somewhat different character (deviation of the head and eyes to the right, then tonic and clonic movements of the right hand spreading to the arm, foot, and leg lasting approximately 1 to 2 minutes, followed by a post-ictal right hemiparesis).

Neurologic examination now indicated a marked expressive aphasia, with little spontaneous speech and difficulty in naming objects. There was a dense right homonymous hemianopia, a flattening of the right nasolabial fold, and a right hemiparesis, with a right Babinski sign.

During a 2-week hospital period the patient continued to have minor seizures characterized by sensory phenomena on the right side of the body. A moderate degree of expressive aphasia persisted throughout the hospital course, although the right homonymous hemianopia largely disappeared. The symptoms and findings suggested that the basic disease process might well have spread to involve the adjacent areas across the sylvian fissure—the speech areas of the inferior frontal convolution, premotor areas, and sensory motor cortex.

The patient developed increasing expressive aphasia and right hemiparesis, with increasingly severe headache. An arteriogram indicated a large space-occupying tumor of the left temporal lobe, and surgery was undertaken by Dr. Robert Yuan 16 months after the onset of symptoms. The anterior and middle portions of the superior temporal gyrus appeared to be widened, and the anterior temporal area (the temporal tip) had an abnormal and discolored appearance. At a depth of 1 to 2 cm within the superior temporal gyrus and involving all of the deeper temporal areas, obvious necrotic glial tissue was found. The process had extended superficially under the Sylvian fissure to involve the adjacent posterior portion of the inferior frontal gyrus.

A temporal lobectomy was performed (from the anterior temporal pole posteriorly for a distance of 6 cm). The operative impression of a malignant glial tumor (glioblastoma) was confirmed by histologic examination.

Comment: This patient presented, at one time or another during his seizures, most of the phenomena associated with temporal lobe lesions: vertigo, tinnitus, visual distortions and hallucinations, olfactory hallucinations, fear, automatisms involving the lips and hands, and episodes of confusion. The visual and olfactory hallucinations are of interest in that both reflected the patient's occupation as a baker. As Halgren and colleagues (1978) note, the experiential phenomena of temporal-lobe seizures are often specific to the individual's experience and personality. The later progression clearly indicated spread across the sylvian fissure to involve the motor cortex and Broca's area in the inferior frontal gyrus areas. This patient had a highly malignant tumor, which clearly involved the cortex of the lateral surface, the deeper white matter, and presumably the medial temporal areas, including the amygdaloid-hippocampal regions. His clinical picture is highly reminiscent of the case described in 1887 by Hughlings Jackson of Emily M., a cook who experienced visual and olfactory hallucinations and who had a tumor arising in the "temporosphenoidal lobe" (the uncus). Such seizures have subsequently been referred to as uncinate epilepsy, but as we have indicated, the disease invariably involves more than just the uncus.

Today, CT scan and MRI would be employed for early diagnosis (see Figs. 22-17 and 22-18). Cases 22-2 and 22-3 which follow demonstrate the correlation of partial seizures with temporal lobe pathology.

Case 22-2. This 17-year-old right-handed male, at age 4 years began to have "staring spells and bizarre behavior". Some episodes had been preceded by the "sound of a musical rhythm". EEG at that time indicated a right temporal spike discharge. Seizures were controlled for ten years with anticonvulsants but then recurred and were poorly controlled occurring several times per day.

Neurological examination: The findings were limited to the following features:

1. *Observed 3 minute seizure:* The seizure began with loss of contact and a stare and then automatisms of the hands. He stood up, walked around the room, went to the physician's desk and attempted to pull open a nonexistent middle drawer. He answered questions vaguely with one or two word answers. Confusion was present for 1-2 minutes after the end of the episode.
2. *Cranial nerves:* a left central facial weakness was present.

Clinical diagnosis: Focal seizures originating right temporal lobe. Observed seizure was complex partial. The seizures beginning with the musical sound might be classified as simple partial with secondary complex partial.

Laboratory data:

1. *EEG*: Intermittent focal spike discharge anterior-middle temporal area.
2. *CT scan*: (Fig. 22-17) An area of focal atrophy was present in the right anterior temporal lobe with possible enhancement at the border.
3. *MRI*: At the Yale Epilepsy Center was more consistent with a tumor in the right anterior temporal lobe.

Subsequent course: Dr. Dennis Spencer at the Yale Epilepsy Center performed a temporal lobectomy. This demonstrated a cystic glial tumor with components of astrocytes and oligodendrocytes. Cerebral cortex also demonstrated abnormal lamination and dysplastic features. Seizures were fully controlled over the next three years.

Case 22-3. This 47-year-old ambidextrous male experienced his first seizure one month prior to admission. He felt light-headed and warm. Then he was observed to walk 100 feet down a hallway, appearing “dazed” and not recognizing people. He fell to the floor, with a loss of consciousness, bit his tongue and was confused afterwards for several minutes.

Neurological examination at 2, 16 and 48 hours after the episode: A persistent right Babinski sign, and slight right hyperreflexia were present. Otherwise the examinations were not remarkable.

Clinical diagnosis: Complex partial seizures. In view of age of onset and persistent focal signs a brain tumor was suspected as the etiology.

Laboratory diagnosis:

1. Sleep deprived EEG :normal.
2. *CT and MRI scans* (Fig. 22-18) demonstrated an extensive infiltrating tumor of the left temporal lobe most likely a glioblastoma.

Subsequent course: Despite Anticonvulsant therapy (phenytoin) additional episodes occurred over the next month: loss of train of thought while talking and several minutes of loss of memory. A subtotal resection by Dr. Bernard Stone (St. Vincent Hospital) demonstrated a Grade III-IV astrocytoma (glioblastoma). Despite radiotherapy and chemotherapy, the disease pursued a relentless course producing early and severe disability prior to death, approximately one year after onset of symptoms.

The following case histories illustrate many of the features of focal disease involving the prefrontal areas.

Case 22-4: This 69-year-old right handed white housewife; two years prior to neurological evaluation visited a relative (a physician) in Israel whom she had not seen in a number of years. The relative then wrote to the patient’s physician, (an old family friend) indicating concern over a change in the patient’s personality. The patient was described as apathetic with silly immature reactions. In retrospect, the patient’s husband felt that these alternations had begun insidiously a number of years previously. A year later, the same relative again wrote indicating that letters received from the patient had become incoherent. Letters became less frequent and then the patient no longer wrote letters. Ten months prior to evaluation, a left central facial weakness was first noted followed two months later by a decreased left arm swing. Six months prior to evaluation, her husband noted, she was purchasing items for which she had no need: 24 pairs of shoes, 15 brassieres. Subsequently she became careless in her housework. On occasions she lost her purse. Her ability to play bridge had decreased over the last year, although her golf game was unchanged.

Neurological examination:**1. Mental status**

- a. She was oriented x3
- b. There was a marked impersistence in motor activities. She was often inattentive. Her answers were often irrelevant. (According to her husband this had been present for many years.
- c. There was inappropriate joking.
- d. Delayed recall without assistance was 2/5 objects in 5 minutes. But 5/5 with assistance.
- e. Digit span was decreased to 5 forward and 3 in reverses.

- f. There were marked deficits in serial 7 subtractions. At times she began to subtract other numbers, at times she added rather than subtracted.
- g. There was a significant spatial disorientation. There was a marked impairment in the ability to copy a cube and deficits in drawing a house. There was disorientation in locating cities on a map.

2.Cranial nerves:

- a. There was a significant neglect of single stimulus objects in the left visual field; this was greater when bilateral simultaneous stimuli were utilized.
- b. At times there was a limitation of voluntary gaze to the left.
- c. A left central facial weakness was present.

3.Motor system:

- a. There was minimal weakness of the left arm and leg.
- b. Variable resistance was present on passive motion at left wrist and elbow suggesting the "gegenhalten" of frontal lobe disease.
- c. There was a decreased swing of the left arm in walking. The gait was initially apraxic but improved as the patient picked up speed.

4.Reflexes

- a. Deep tendon stretch reflexes were increased on the left.
- b. A left Babinski sign was present.
- c. There was a bilateral release of the grasp reflex.

5. Sensory system: intact.

Clinical diagnosis: Right frontal lobe tumor: probable meningioma based on the long history.

Laboratory data:

1.*Skull x-rays* there was a 5mm shift to the left of the calcified pineal gland. Long standing increased intracranial pressure was suggested by the demineralization of the sella turcica.

2.*EEG* demonstrated focal 2-5 Hz slow waves in the right frontal area most prominent in the parasagittal recording area

3.*Imaging study: radioactive brain scan (Hgl97):* there was a heavy uptake in the right frontal towards the midline measuring 5x5x4 cm (Fig.22-21).

4.*Arteriograms:* A parasagittal tumor was present in the right frontal area, with vascular supply derived from the left and right middle meningeal and left anterior meningeal arteries.

Hospital course: Following the arteriogram, the patient developed signs of increased intracranial pressure (vomiting, lethargy and papilledema). The patient received dexamethasone glucocorticoid used to reduce cerebral edema, with improvement in these symptoms. The right external carotid artery was ligated since the meningioma derived considerable blood supply from this source. Dr. Samuel Brendler performed a bilateral frontal craniotomy. Bulging of the dura was present requiring the administration of hyperosmotic agent (20% mannitol) with reduction of the swelling. When the dura was opened a large right posterior frontal meningioma was revealed measuring 8x8cm and attached to the right side of the superior sagittal sinus. On histological section this was a fibrous, meningothelial meningioma. During the course of removal of the tumor, it was necessary to ligate several bridging veins entering the superior sagittal sinus as well as the arteries feeding the tumor. At the conclusion of the procedure, it was noted that the right pupil was enlarged and neither responded to light. The patient failed to regain consciousness, remaining in a state of coma with bilateral extensor plantar responses, decerebrate postures on stimulation and bilateral fixed dilated pupils. The patient expired 2 weeks after surgery.

Comment: It is difficult to decide even in retrospect when the symptoms in this case began. It is clear that the initial symptoms involved an insidious change in personality. She was apathetic, her reactions were "silly" and judgment was impaired. Purchases were inappropriate. It would have been of interest to explore which aspects of her bridge playing were impaired in terms of planning and strategy etc. Her motor function was impaired only to a minor degree even late at the time of neurological evaluation, with minimal left-sided weakness and more prominent premotor release. The visual neglect syndrome may have reflected involvement of the premotor area or compromise of the parietal cortex by this large tumor. The fact that there was only minor evidence of involvement of motor cortex would make the premotor/SMA location more likely. While the spatial disorientation and deficits in drawing might

favor a nondominant parietal syndrome, such findings also could be consistent with a nondominant premotor/SMA location based on the close interaction between the posterior parietal and the premotor location. The impairment of voluntary gaze to the left would be consistent with area 8 involvement. There is little doubt that this patient required surgical intervention. The removal of large "benign" tumors of this type is not without risk. Hemorrhagic infarction with massive edema and tentorial herniation is a complication of ligation of bridging veins entering the superior sagittal sinus. In this case, serious brain swelling was already evident even before the dura was opened.

The following case history 22-3 provides an example of a patient with a slowly progressive subfrontal meningioma manifested by symptoms of apathy, loss of ambition, "depression" of mood, emotional lability, with a tendency to introspection and a slowness of mental processes. All of these symptoms were initially attributed to depression and a hypothyroid state. As gait and memory problems developed, these symptoms were attributed to Alzheimer's type senile dementia. When increased intracranial pressure and coma suddenly developed, neurological and neurosurgical intervention occurred.

Case 22-5: This white housewife and fashion designer was first admitted to the hospital at age 60 with a history of several years (?2 to 5) of fatigue, loss of ambition, lack of enthusiasm, and a tendency to readily cry over minor problems. A depression of mood and a tendency to introspection had developed. The patient also reported loss of her taste for food with a subsequent decrease in appetite and weight loss. These symptoms had progressed despite an adequate dosage of thyroid medication (60 mg., t.i.d.). Neurological examination was recorded as negative except for a slowness of speech and of thought processes. She was described by the psychiatric consultant as indecisive in her answers. Cerebrospinal fluid examination revealed no significant findings. Tests of thyroid function indicated hypothyroidism with protein bound iodine of 3.2 micrograms/100 ml. (normal; 4 to 8 micrograms/100 mg.) and a radioactive iodine uptake of 2.3 percent in 24 hours (normal 20 to 50 percent). Discharge diagnosis was chronic depression and hypothyroidism.

These symptoms continued to progress despite treatment with thyroid. The patient had increasing difficulty in walking. This had actually been first noted at age 57, 3 years prior to her initial hospital admission as a "phobia for heights". The patient would "freeze" at the top of a high flight of stairs. She then developed progressive difficulty in climbing stairs. Her husband reported that she would have marked difficulty in getting out of chairs. She would appear unsteady in gait after rising from a chair but would soon recover her equilibrium and would be able to walk in relatively normal manner. Increasingly, the patient's motor and mental activities became slower. She "procrastinated in making decisions". Occasional urinary incontinence developed at age 66 and was attributed to her neurological disease (apparent senile dementia). Although her husband reported her memory as initially well preserved, other observers at that point reported a progressive deficit in memory. At age 67, the patient began to complain of episodic fogging or blurring of vision.

Initial Neurological examination on re-admission to the hospital at age 67 was recorded as demonstrating the following features:

(a), slight disorientation for date and year, (b) slowness of speech and gait (c) deep tendon reflexes 2+, plantar responses flexor, and (d) no significant sensory finding except a slight decrease in position sense at the toes. No details as to the patient's gait were recorded. The sense of smell was apparently not tested and no notes as to the presence or absence of a grasp reflex were recorded.

On the day after admission, the patient developed headache and vomiting. She had difficulty walking unsupported and became increasingly more somnolent but could be roused by painful stimulation. Deep tendon reflexes were increased bilaterally with bilateral extensor plantar responses (bilateral Babinski signs). Grasp response was absent. Pupils responded to light but were sluggish.

Fundusoscopic examination was negative but lumbar puncture indicated a markedly increased pressure, greater than 400 mm. of csf. Cerebrospinal fluid protein was elevated to 125 mg/100 ml. The patient became unresponsive and emergency neurological and neurosurgical consultations were obtained.

Neurological examination:

1. *Mental Status:* The patient was semicomatose with periodic Cheyne-Stokes respirations.
2. *Cranial Nerves:* Pupils were fixed, the left dilated, the right constricted.
3. *Motor System:*
 - a. The patient moved all limbs in response to painful

stimulation, right more than left.

- b. There was a spastic resistance in the upper and lower left extremities.
4. Reflexes:
- a. A generalized hyperreflexia was present with bilateral ankle clonus.
 - b. Bilateral Babinski signs were present.
 - c. A bilateral grasp reflex was present. Note, however, that in a semicomatose patient this may have little localizing significance.
5. *Sensation*: Pain sensation was intact.

Clinical diagnosis: Subfrontal or parasagittal frontal tumor most likely a meningioma in view of the over 10 year course. Tentorial herniation had occurred possibly related to the lumbar puncture.

Laboratory data: An emergency bilateral carotid arteriograms revealed that a large subfrontal butterfly-shaped mass (probably meningioma) was present in the anterior cranial fossa bilaterally. The anterior cerebral arteries as well as the frontal polar, pericallosal and callosal marginal branches and the middle cerebral arteries were displaced backwards. The anterior cerebral arteries were also displaced upwards. The tumor mass derived blood supply from the ophthalmic arteries.

Hospital course:

A bifrontal craniotomy was immediately performed by Doctor Robert Yuan with total removal of a large bifrontal meningioma arising from the falx and olfactory groove. On the right side the tumor was estimated to occupy 75 percent of the anterior cranial fossa, measuring 7 x 5 x 6 cm. On the left the tumor was of approximately half this size, measuring 5 cm. in diameter. The thickness of the cerebral hemisphere covering the tumor in the right prefrontal area was reduced to 0.5 cm. Histological examination of the tumor indicated a benign meningioma (meningotheliomatous type).

The patient showed some immediate improvement at the conclusion of surgery, in the sense that both pupils were equal in size and reacted to light. By the time of discharge from the hospital, two months after surgery, considerable improvement had occurred. She could recognize the doctor by name but did not know the place, the season, or the month; she could, however, describe a picture she had just seen. A bilateral deficit in olfaction was present (anosmia). Assistance was required in walking. A bilateral grasp reflex was present.

Follow-up evaluation two years after surgery indicated continued improvement although the patient still had complaint relevant to impairment of recent memory and slight unsteadiness of gait. Deep tendon reflexes were symmetrical with plantar responses flexor. A bilateral grasp reflex was present and the patient was slow in walking and fell occasionally. Urinary incontinence occurred with wetting of the bed.

Comment: In retrospect, the evolution of symptoms in this patient clearly indicates a tumor initially compression both prefrontal areas and producing alterations in mood and personality. With continued growth of the tumor, compromise of the premotor areas with resultant apraxia of gait and release of grasp reflex began to occur, either as a result of direct compression or secondary to the distortion and compression of the anterior cerebral arteries. It is not unusual to witness the development of a dementia (deficit in recent memory) in large tumors in a subfrontal midline location. A similar dementia may occur in large aneurysms of the anterior communicating artery.

The problem of dementia will be considered in greater detail in the chapter on memory.

The development of headache, vomiting and increasing somnolence indicated the development of increasing intracranial pressure. The sudden unresponsiveness following the lumbar puncture with the development of periodic Cheyne-Stokes respirations, pupillary changes, and bilateral corticospinal tract signs all indicated an additional acute exacerbation of the already compromised brain stem functions, a compromise which had already resulted from the backward displacement of the intracranial contents with distortion of the brain stem. In retrospect, one might hypothesize that the patient's complaint of a loss of taste for her food at the time of her initial hospitalization might well have indicated some loss of olfactory sensation since much of our appreciation of food is dependent on olfaction. Specific tests for olfaction were not recorded.

CHAPTER 23: VISUAL SYSTEM

The following case is an example of a lesion involving the optic nerve, anterior to the optic chiasm.

Case History 23-1 (Fig 23-8).

This 53-year-old white right-handed housewife was referred for evaluation of progressive right-sided supraorbital headache of 23 years duration and decreasing acuity in the right eye. The loss of acuity had progressed to the point of almost total unilateral blindness. During the 3 years before admission, intermittent tingling paresthesia had been noted in the left face, arm, or leg. About 1 year before admission the patient had a sudden loss of consciousness and was amnesic for the events of the next 48

hours. She was hospitalized, but no explanation for the episode was clearly established, although cerebrospinal fluid protein was reported to be elevated (230 mg/dl).

The patient and her family reported some personality changes over a period of several years, including a loss of spontaneity and increasing apathy.

General Physical Examination: Unremarkable except for a minor degree of proptosis (downward protrusion of the right eye).

Neurologic Examination:

1. *Mental Status:* The patient was, in general, alert but at times would become lethargic. Her affect was flat. At times, she would laugh or joke in an inappropriate manner.
2. *Cranial Nerves:* There was anosmia for odors, such as cloves, on the right and a reduced sensitivity on the left.

Marked papilledema (increased intracranial pressure with protrusion of the optic disk and venous engorgement due to obstruction of the normal flow of CSF) was present in the left eye.

Pallor of the right optic disc was present, indicating optic atrophy. Visual acuity in the right eye was markedly reduced. The patient had only a small crescent of vision in the temporal field of the right eye, where only vague outlines of objects could be seen. A slight left central facial weakness was present.

3. *Motor Systems:* Intact although movements on the left side were slow.

4. *Reflexes:* A release of grasp reflex was present on the left side.

5. *Sensory system:* Intact

Clinical diagnosis: Subfrontal meningioma arising from olfactory groove or inner third sphenoid wing.

Laboratory data:

1. *Skull* x-rays demonstrated erosion of the dorsum sellae. Special lamniograms demonstrated hyperostosis of the sphenoid bone (planum sphenoidale) suggesting a meningioma originating from the sphenoid bone.

2. *EEG* demonstrated focal 2-4 Hz slow waves in the right anterior temporal and anterior lateral frontal area.

3. *Brain scan (H_g 197)* revealed a heavy uptake of isotope in the right posterior subfrontal area.

4. *Arteriograms* indicated that the anterior cerebral arteries were shifted backwards, posteriorly and the left. A tumor blush was present on the venous phase in the right subfrontal area extending back to the optic nerve groove (Fig 23-8). These findings were felt to be most consistent with an olfactory groove meningioma.

Hospital course: Dr. Samuel Brendler performed a bifrontal craniotomy which exposed a well-encapsulated smooth tumor attached to the medial third of the sphenoid wing. After intracapsular removal of 90 to 95% of the tumor, the right optic nerve could be visualized. The small portion of the tumor attached to the bone could not be removed because of considerable bleeding from the bone. Examination 4 months after surgery, indicated right anosmia and right optic atrophy were present.

Comment

If one considered only the patient's primary complaint, decreasing vision in the right eye, and the findings of right optic atrophy and left-sided papilledema (Foster-Kennedy syndrome), then the most probable diagnosis was inner-third sphenoid meningioma. The preservation of a small crescent of vision in the temporal field is consistent with compression of the optic nerve on its lateral surface. By the time of hospitalization, the lesion was quite large and had extended into the subfrontal area, producing anosmia on the right and some changes in personality. At this point, the various diagnostic studies suggested only a subfrontal mass and did not clearly differentiate between an olfactory-groove meningioma and a sphenoid-wing meningioma. One might suggest, in retrospect, that the degree of involvement of the right optic nerve was much more pronounced than the changes in prefrontal functions, and therefore, the inner-third sphenoid-wing location was more likely.

The surgical approach in any case was the same. The eventual recovery of vision in such cases is uncertain because the effects of compression often are not reversible

COMPLETE CASE HISTORIES FROM TEXTBOOK: *INTEGRATED NEUROSCIENCES*

PART III. CASES – CEREBRAL HEMISPHERE MOTOR SYSTEM, CEREBELLUM, BASAL GANGLIA

CHAPTER 18: MOTOR SYSTEM I:

The following case 18-1 presents an example of focal seizures beginning in the motor cortex.

Case 18-1. This 29-year-old, right-handed, white woman was in her usual state of good health until three months prior to admission when she developed an intermittent “pulling sensation” over the anterior aspect of the left thigh, lasting a few minutes. This recurred without other symptoms about twice a week. On the evening of admission, while sitting on a couch, she again had the onset of this same sensation in her left. She stood up, noted that her left leg felt “numb” and then started to have “jerky movements” in her left foot which progressed to involve the whole left lower extremity. She sat down, pressed on her left thigh in an attempt to stop the movement. At this point, her husband and a friend came to her (the patient is amnesic for these events), and saw her have tonic extension then clonus of all four limbs associated with grunting respiration, clenched jaw, and rolling of the eyes. She was placed on the floor and after a few seconds she regained consciousness, though she still appeared dazed and slightly confused for the next 5 minutes.

Past history and family history: noncontributory.

Physical Exam: Normal except for bite marks on the left lateral aspect of the tongue.

Neurological Exam: Significant only a slight asymmetry of deep tendon reflexes: left > right.

Clinical Diagnosis: Focal seizures originating right parasagittal motor cortex (foot area), with ? of parasagittal meningioma.

Laboratory Data:

(1) *Electroencephalogram* (Fig.29-1B) demonstrated rare focal spikes, right Rolandic parasagittal consistent with the focal source of the secondarily generalized seizure and rare focal slow waves in the right Rolandic and mid temporal area - consistent with minor damage in this area

2) *CT scan* (Fig.18-13) demonstrated an enhancing lesion in the right parasagittal region just anterior to the central sulcus.

- (3) *Arteriograms* (Fig.18-14) demonstrated a circumscribed vascular tumor in the right parasagittal rolandic area which was supplied by the right anterior cerebral artery (A,B) and the right middle meningeal branch of the external carotid artery©. The venous phase of the study demonstrated a significant draining vein from this area of tumor blush(D). All of these findings were consistent with a right parasagittal meningioma.

Hospital Course: A well-circumscribed right parasagittal meningioma was removed by Doctor Bernard Stone. A distal weakness of the left lower extremity was present in the immediate postoperative period but this improved rapidly so that by two months after surgery, a foot drop brace was no longer required and strength had returned to normal. During all of the pre and post operative period, the patient received diphenylhydantoin (Phenytoin) to prevent additional seizures. A possible sensory seizure involving the hand occurred 2 years later. Four years after surgery, the patient attempted to reduce her dosage of anticonvulsant and experienced a recurrence of focal motor seizure activity beginning in the left leg with subsequent secondary generalization. When evaluated 6 years after surgery, she had experienced no additional seizure activity. Her neurological examination continued to demonstrate an increase in deep tendon reflexes on the left and a left sign of Babinski. Her CT scan demonstrated no recurrence of tumor, there was very minor atrophy at the site of the previous meningioma. The EEG continued to demonstrate bursts of blunt spikes and slow waves in the right parasagittal Rolandic and parietal areas. Follow-up 10.5 years after surgery indicated no additional seizures.

Comment: The onset of focal seizure activity should always raise the question of focal pathology. When these seizures begin at age 29, without a prior medical history, there is always a strong possibility of a primary brain tumor. In general gliomas are much more common than meningiomas but the odds of a meningioma are increased by the parasagittal location and the gender of the patient. In this case, there was a very close correlation of the clinical phenomena with the laboratory data regarding the anatomical location of the lesion. Surgical therapy eliminated the underlying benign tumor - the parasagittal meningioma, but the predisposition to focal seizures remained. Thus, the tumor in compression of cerebral cortex had produced alterations in neuronal excitability which persisted following the removal of the tumor.

Case 18-2 provides an example of a slow growing tumor involving the premotor and supplementary motor cortex from the standpoint of focal seizure activity. The motor effects of frontal lesions are presented in case histories 22-2 and 22-3 which follows the discussion of the prefrontal areas.

Case 18-2: This 57-year-old right-handed single nun and occupational therapist, had the onset of her first generalized convulsive seizure at age 47, ten years prior to consultation. This occurred without warning with sudden loss of consciousness and an observed generalized tonic clonic seizure. Both an EEG and CT scan were reported to have been normal. Approximately 4 additional generalized convulsive seizures occurred over the next 4 years. Shortly after the onset of the grand mal seizures, the patient began to have focal seizures. She described these as beginning with the abduction and raising of the right arm at the side, over her head, then a jerking of the right arm, and then she would fall to the ground. She would remain fully conscious but she would be unable to talk. She would have an awareness that something strange was occurring. She had a sinking sensation. She denied any impairment of memory after the episode. But, she would be aware that her right arm and leg were tingling and weak for perhaps 5 minutes afterwards and she would be unable to speak for 10-30 minutes afterwards. These focal seizures occurred once a month, but for the last 2 years, they had been occurring once a week. The patient indicated that over the last 10 years she has had problems with her memory.

She was reported to have had three “negative” CT scans over the years, and yearly EEG’s which did not reveal focal features or electrical seizure discharges although some bilateral slow wave activity was present. The patient has been treated with a variety of medications over the years without attaining seizure control. Her initial evaluation 4 years after onset of seizures at another neurological center indicated some increased activity in the finger jerks on the right with withdrawal of both plantar responses, and a diminished swing of the right arm.

Past history and family history were negative: she was the product of a full-term delivery weighing 9 pounds and had excellent developmental and educational milestones.

Neurological examination :The following abnormalities were present:

1. *Mental Status*: Although orientation and language functions were all intact, delayed recall without assistance, was 0 out of 5; and with assistance 2 out of 5. Proverb interpretation was abstract for 1/3 proverbs, but similarity testing was abstract.
2. *Cranial Nerves* II through XII were intact.
3. *Motor System* was intact except for a decreased swing of the right arm in walking.
4. *Reflexes*: deep tendon reflexes were increased on the right at biceps and patellar. Plantar response was extensor on the right and equivocally extensor on the left.
5. Sensory system was intact.

Clinical diagnosis: Seizures of focal origin left premotor/supplementary motor cortex possibly secondary to low grade glioma. A meningioma was less likely due to the reports of “normal CT scans”.

Laboratory data:

1. **CT scan** (Fig.18-16),demonstrated an area of calcification with surrounding edema in the left premotor area .

2. **MRI scan** (Fig.18-17),demonstrated extensive involvement of the premotor and supplementary areas by tumor and edema.

Subsequent course: Subtotal resection of this tumor was performed by Doctor Bernard Stone. Histological examination of the tissue confirmed the preoperative impression of an infiltrating glioma - predominantly oligodendroglioma in type. The patient received postoperative radiotherapy, 5000 rads to the left hemisphere and an additional 1000 rads to area of tumor. When last seen in follow-up 4 years after surgery, the patient was still experiencing infrequent (1-2 per month) short focal seizures of the same type involving focal movements of right arm, plus speech arrest. The neurological examination demonstrated some decrease in spontaneous speech and some blunting of affect. However, she was fluent; naming of objects and repetitions was intact. Strength was intact. Reflexes were symmetrical but bilateral extensor plantar responses were present. She had a moderate frontal type apraxia of gait and required a cane to avoid falls.

Comment :This patient presented with seizures of focal origin. The description of the posture adopted by the arm at the very beginning of the seizure, raised the possibility that her seizures were originating in the supplementary motor cortex of the left hemisphere and then spreading into the motor and sensory area. The arrest of speech would be compatible with such an origin since there is a superior speech area located in relationship to supplementary motor cortex. The fact that the patient remembered much of the seizure would also be consistent with such an origin. The post ictal depression of motor and sensory function in right arm and right leg and the depression of speech would all be consistent with post ictal phenomena involving the left hemisphere, particularly its sensory, motor and speech areas. The fact that the EEG's had not been particularly remarkable would also be consistent with such an origin of discharge. Thus, the discharging focus may well be buried on the parasagittal surface and not accessible to recording electrodes at the surface.

As regards the underlying nature of the pathology, when the patient was seen 10 years after onset of symptoms, she now has some focal findings; in terms of a right Babinski sign and increased reflexes in the right arm raising the question of a low grade glioma such as an oligodendroglioma in this area. The previous “negative” CT scans would have ruled out a meningioma or arteriovenous malformation. The long history and the finding of calcification within the tumor all made oligodendroglioma the most likely diagnosis. Low grade gliomas of this type often produce seizures without producing major neurological findings .Thus frontal release signs were minimal.

The following case history provide an example of normal pressure hydrocephalus producing the triad of a gait apraxia, urinary incontinence and problems in memory.

Case 18-3: This 72-year-old retired white handed carpenter was referred for evaluation of progressive impairment of gait, and more recent problems, in memory. The gait problems began insidiously five years previously but had become more significant in the past six months. He described his walking as involving small steps and then “going forward at too fast a rate, with difficulty in stopping”. As a result, he would stumble and tend to fall forward, losing his balance. He had considerable fear of falling and made use of a cane to avoid falling. For the last four to five months, the patient had noted urinary frequency and incontinence. He kept a bucket with him at all times. “Once I have to go, I can’t hold on.” Memory problems had developed during the last two to three months related to the recall of recent events and new material. He would enter a room and be

unable to recall why he had entered the room. Emotional lability had also developed during the past year. It was difficult not to cry when he heard a sad story.

Past history indicated at least three myocardial infarctions.

Neurological examination:

1. Mental Status:

- a. Oriented for time, place and person.
- b. Delayed recall, even with assistance, was limited to 1/3 in five minutes.
- c. The patient often lost track of what he was saying or doing.
- d. Serial 7 subtractions was slowly performed but intact.
- e. Reading, writing, drawing and naming of objects were intact but spelling was poor.
- e. Abstract reasoning was intact.
- g. Affect demonstrated changes: At times, he was tearful; at times, inappropriately jocular.

2. Cranial Nerves: Intact except bilateral decrease in hearing - long standing.

3. Motor System: Intact except for gait. The patient walked on a broad base with small steps. He was slow in starting and then picked up speed. He was unsteady on the turns and tended to turn "en bloc". No rigidity and no tremor were present. Finger to nose and heel to shin tests were normal.

4. Reflexes: Deep tendon reflexes were hyperactive at patellar. Plantar responses were equivocal. No definite frontal release signs were present.

Clinical diagnosis: Frontal lobe syndrome with involvement of premotor and prefrontal areas. The combination of a frontal gait apraxia, memory impairment and urinary incontinence raised the question of normal pressure hydrocephalus.

Laboratory data:

- 1. *CT scan (Fig. 18-21):* Demonstrated markedly dilated lateral; third and fourth ventricles but with no enlargement of the sulci.

Figure 18-21 Normal Pressure Hydrocephalus - CT Scan - Case 18-3 A. Ventricular Enlargement B. Section Through Vertex: Demonstrating No Enlargement of Sulci PART II: Comparison patient with progressive multiple sclerosis involving cerebral hemispheres at relatively comparable levels of section demonstrating A. Ventricular Enlargement B. Accompanied by Enlargement of Cortical Sulci

- 2. Lumbar puncture studies were normal.

- 3. *Radio-isotope cisternogram (Fig 18-22)* demonstrated continued presence of isotope within the ventricular system with no reabsorption over the convexities - subarachnoid space at 24, 48, and 72 hours.

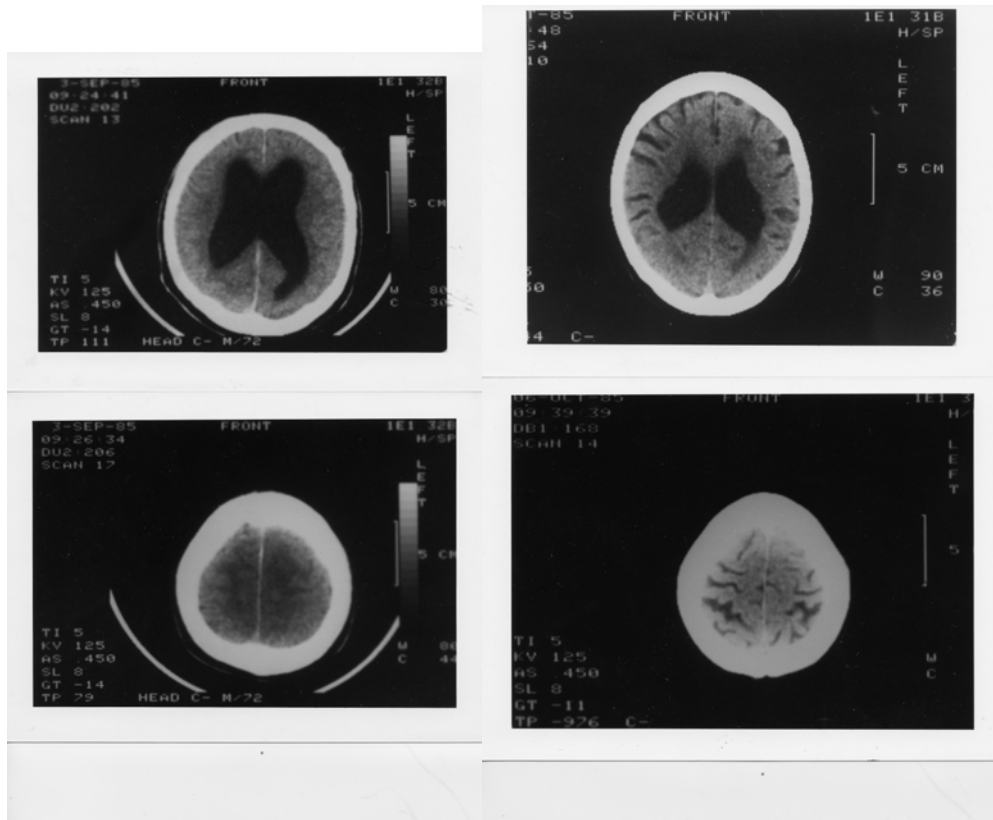
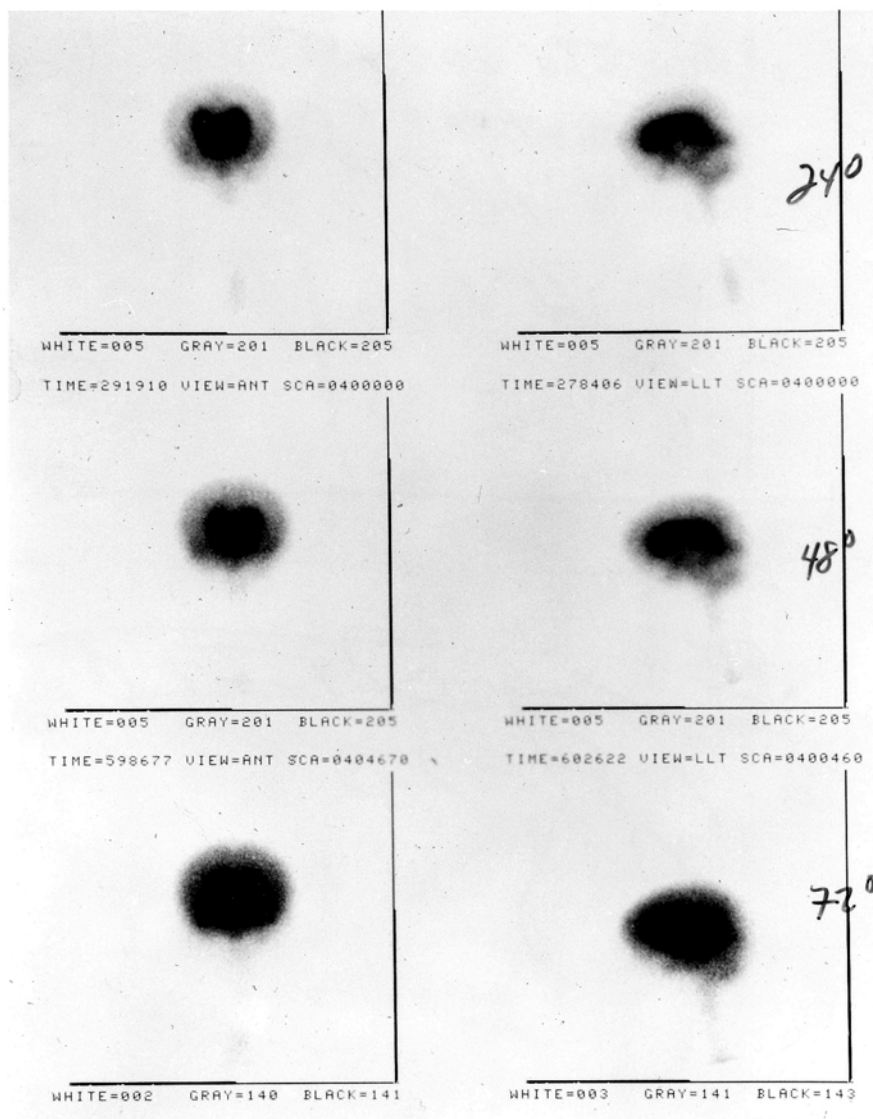


Figure 18-21. Normal Pressure Hydrocephalus Figure 18-21. Comparison Scan.

Figure 18-22: Normal Pressure Hydrocephalus: Isotope Flow Study: Lumbar CSF Injection Case 18-3 Isotope remaining in ventricular system at 24, 48 and 72 hours B. Comparison Case: Progressive multiple sclerosis of

cerebral hemispheres with enlargement of ventricular system but with enlargement of sulci. Isotope has begun to leave ventricles at 24 hours - appearing over the convexity and this is even more apparent at 48 and 72 hours.

Fig 18- 22. Normal Pressure Hydrocephalus; Isotope Flow Study



Subsequent course: Doctor Alex Danylevich performed a ventriculo-peritoneal shunt procedure (right lateral ventricle to peritoneal cavity). The patient did well with clearing of his triad of symptoms: Ataxia, dementia and urinary incontinence and was able to return to work as a carpenter , 12 hours per day. Subsequently , symptoms recurred due to infection of the peritoneal component of the shunt tube. Following revision of the shunt, symptoms improved only to worsen again in 6 months later. The patient had to use a wheelchair at times. A more marked apraxia of gait, frontal release signs, bilateral Babinski signs and urinary incontinence were present on examination 6 months after the revision. CT scan indicated a greater degree of ventricular enlargement. Following removal of 30 cc. of CSF, the patient was more responsive, and better oriented. Myocardial problems prevented additional neurosurgical revision of the shunt at that time. Subsequently, Doctor Robert Ojemann, of the Massachusetts General Hospital, revised the shunt utilizing a valve which allowed greater flow. At last evaluation, two years after admission, gait had improved (he was using a walker). Mentation was clearer (he was still described as showing aspects of a “frontal lobe syndrome”). Urinary incontinence was no longer present.

Comment: This patient presented a premotor/prefrontal syndrome .The imaging studies allowed a more specific delineation of the etiology of the syndrome. In most cases of normal pressure hydrocephalus, the gait disturbance is out of proportion to any change in mental status.

CHAPTER 19: MOTOR SYSTEM II: BASAL GANGLIA AND MOVEMENT DISORDERS

The following case presents an example of a patient with Parkinson's disease followed for 19 years.

Case 19-1 : This 48-year-old married white male, left-handed school master and physics teacher, was referred on 08/16/82 by his orthopedic surgeon for neurological evaluation of problems of control of the left arm and dragging of the left leg. Symptoms had begun 3 months previously with a sense of fatigue, stiffness and lack of control in the left arm. After a period of prolonged writing, he would have to make a conscious effort to continue writing. Approximately one month prior to the evaluation, he first noted a slowing down in movements of the left leg. "I have to remember to lift it."

Past medical history: Negative except for neck pain eight years previously related to cervical spondylosis, which cleared with the use of collar and traction except for occasional tingling in the 4th and 5th fingers of the left arm. Family history was unremarkable.

Neurological examination:

1. Mental Status: intact
2. *Cranial Nerves I-XII:* Intact except for a tremor of the closed eyelids and a positive glabellar sign (he was unable to suppress eye lid blinking on tap of forehead).
3. Motor System:
 - a. Strength : intact
 - b. Gait : There was a tendency to turn en bloc and a decreased swing of the left arm. However he could walk a tandem gait without difficulty.
 - c. There was a slight increase in resistance to passive motion at the left elbow, wrist and knee (rigidity without definite cogwheel component).
 - d. Although the patient was left-handed, there was a slowness of alternating finger movements of the left hand.
 - e. No tremor was present.
 - f. Handwriting was intact with no evidence of micrographia.
4. *Reflexes:* deep tendon stretch reflexes and plantar responses were physiologic
5. *Sensation:* all modalities were intact.

Clinical diagnosis: early Parkinson's disease, predominantly unilateral.

Laboratory data: all studies were normal including CT Scan of the brain, thyroid studies, blood chemistries, erythrocyte sedimentation rate, antinuclear antibody and serologic test for syphilis.

Subsequent course⁴: The patient did not wish to begin any treatment at that point in time. When evaluated 3 months later progression had occurred. He occasionally had the sense of moving slowly. He was now aware that with continuous writing, the writing became smaller, that is, micrographia emerged, evident on examination of handwriting. In addition, a minimal tremor was noted in the Archimedean spiral. A greater, but still minor, degree of cogwheel rigidity was now present at left wrist and elbow. Again, the patient was reluctant to begin therapy. On evaluation 1 year after onset of symptoms, additional progression was evident with significant micrographia (Fig. 19-6) and cogwheel rigidity now evident at left shoulder, elbow and wrist. Therapy with Sinemet (10-100 mg., t.i.d.)⁵ was begun. Re-evaluation one week later demonstrated a marked improvement in handwriting (Fig. 19-6) and decreased cogwheel rigidity.

⁴ This patient was followed for a total of 19 years after disease onset, initially for the first 13 years by the author, subsequently by Dr Paula Ravin at the University of Massachusetts Medical Center, Dr. David Standeart at the Massachusetts General Hospital and Dr. Warren Olanow at the Mount Sinai Hospital in New York.

⁵ This is a combination of 10 mg. of carbidopa (Dopa decarboxylase inhibitor) and 100 mg. of L-Dopa. Higher dosage combinations are a) 25 mg. of carbidopa with 100 mg L-Dopa, and b) 25 mg. carbidopa with 250 mg. L-Dopa. A sustained release form is also available (50 mg. of carbidopa with 200 mg. of L-Dopa), and is marketed as Sinemet CR.

As the dose of Sinemet was increased to (10-100) mg.5x/day over the next week, occasional choreiform movements of the fingers of the left hand and occasional backward flinging (hemi ballistic) movements of the left arm occurred. As the dose reached 10-100 mg. 6x/day, the patient reported that his handwriting now was back to normal. Examination confirmed the significant improvement in handwriting and in gait - with a better movement of the left leg. He no longer turned en bloc. Cogwheel rigidity was still present at left shoulder but to only a minimal degree at left wrist and elbow. The patient did experience 90 minutes after a Sinemet dose - a tremor of the left shoulder and an exaggerated grasp of the left foot toes on lifting the leg (possible form of dyskinetic or dystonic reaction).

The patient did well. When seen one year later, he had only a minimal degree of cogwheel rigidity. No tremor was evident. In walking he had a good swing of the arms and no longer turned en bloc. He was aware that some symptoms of his underlying disease would emerge 3-4 hours after a dose of Sinemet.

He continued to have progression of disease despite the use of all of the known anti Parkinson medications. He eventually underwent a fetal cell transplant in 1997 with apparently little improvement but with a significant increase in dyskinesias.

Re-evaluation, three years after onset of symptoms, indicated a minor progression with decreased swing of the arm and movements of the left leg, which were less smooth. The patient had increased his daily dosage of Sinemet to (10-100 mg) 6 (or) 7 tabs and noted that duration of action was approximately three hours. Re-evaluation, five years after onset of symptoms, indicated that despite having increased his dosage of Sinemet to 25-100 mg. tablets, 7 or 8 x/day, more resting tremor of the left hand had emerged. (In actuality 75-100mg of carbidopa is probably sufficient to saturate the peripheral dopa decarboxylase system). Moreover, choreiform movements of the left arm occurred 60 to 90 minutes after each dose of Sinemet. Examination demonstrated a pill-rolling tremor of the left hand as the patient walked down the hall. The choreiform movements disappeared when the dosage of Sinemet was reduced to 25/100mg 6/day. The increased rigidity and tremor responded to the addition of a DOPA agonist Bromocriptine (Parlodel) - Initial dosage 1.25 mg. 2x/day then increased to a total dose of 5.0 mg., and subsequently to 7.5 mg./day. Despite increasing dosage of the Bromocriptine to 17.5 mg/day - no additional improvement occurred. Additional reduction of Sinemet to (25-100) 5x/day - eliminated sudden myoclonic jerks and dyskinetic movement of the left lower extremity, which would occur - 45 minutes after a dose of Sinemet. Examination 6 years after onset of symptoms, examination and 3.5 hours after last dose of Sinemet demonstrated a coarse pill rolling tremor of the left hand and a shuffling of the left foot in walking. Marked cogwheel rigidity was present at left wrist and elbow. Considerable slowness of alternating finger movements was present. Handwriting was small and slow. Amantadine (an antiviral agent with mild ant parkinsonian effects), 200 mg./day was added at this point with a considerable improvement in symptomatology.

When examined 7 years after onset of symptoms, and 2.5 hours after Sinemet dosage and he now had a prominent tremor of the left hand at rest and a minor tremor of the right hand. Only minor cogwheel rigidity of left wrist and elbow were present. There was mild facial akinesia, tremor of the closed lids and a positive glabellar sign. As he walked he had a problem with sequential movements of the left leg. He reported that initially in the mornings, he had considerable problems in the initiation of movements of his left hand. Because effects of the Sinemet were wearing off in a shorter period of time - the dosing interval was altered to every three hours, in the process increasing total intake to 6 and then 7 tablets per day, with transient improvement. When seen 8 years after onset of symptoms, he was having sudden "kick in of the on effects" at 30-45 minutes and wearing off effects of greater degree at 3 hours after Sinemet dosage. As a result balance had shown some deterioration. Although tremor and cogwheel rigidity were primarily present left arm lesser symptoms were present in the right arm. At this point, a monoamine oxidase B. inhibitor was added: Selegiline (Deprenyl) in a total dose of 10 mg./day (5 mg., b.i.d.). When seen 6months later, the patient was uncertain that any benefit had been achieved. A major symptom was now "freezing" - he would have times in going over the threshold of a door when he would suddenly freeze. This, at times, related to the wearing off of medication (Sinemet) effect but at other times, usually in the afternoon, was unrelated to time of last dose. In the morning, freezing effect was clearly related to time of dosage. He remained relatively stable for the next year and then had a progression of symptoms - increasing tremor, increasing dragging of the left leg and more wearing off of dose effect - usually after 2.5 hours. In addition, "freezing" episodes were occurring more frequently in between dose wear off periods, usually in going through a doorway or even in hallways. At this point, the patient was switched to the sustained release form of Sinemet (50/200 mg carbidopa/L-Dopa) taken three times a day. Amantadine, Bromocriptine and Selegiline were continued unchanged. When evaluated 6 weeks later, there had been a remarkable improvement. He had a smoother day with fewer ups and downs, less dyskinesia and less stiffness. Effects of the medication were lasting 5-6 hours. When seen 3.5 hours after his last Sinemet dosage, he had

very little cogwheel rigidity. He could walk with a good swing of the arms. Handwriting was good with little tremor and little dyskinesia. On the other hand, when seen several weeks later, approximately 5.5 hours after his dose of sustained release Sinemet, he had marked difficulty, walked with small steps, and would arrest going through a doorway. Balance was poor, requiring a cane. There was a marked tremor of the left hand and to a lesser degree, of the right hand. A marked akinesia was present. However, within 20 minutes of his taking an additional tablet of sustained release Sinemet, a marked improvement again occurred. Despite this long course, the patient had been able to continue in his usual occupation. The patient subsequently was treated with a COMT inhibitor and was switched to another dopamine agonist pergolide with little apparent benefit. Eventually, in 1997 he was entered into the NIH sponsored fetal transplant study (subsequent imaging study did indicate that the patient was in the transplant and not the placebo group). It was unclear that this had produced any decrease in his disability. However evaluation 3 years after the transplant did demonstrate a marked increase in the dyskinesias involving head arms and torso. Some improvement in dyskinesias occurred when dopaminergic medications were reduced

Comment: Parkinson's disease is a progressive disorder of motor function, with variable manifestations of tremor, rigidity, akinesia, bradykinesia, and impairment of postural reflexes. Patients vary in the type of major involvement and in the rate of progression. Pharmacological management has rapidly evolved and in the process has provided considerable insights into the nature of basal ganglia function. For the specific patient, therapy must still be individualized. As this case history illustrates the pharmacological effects are time limited. Evaluation of therapy must always record the time of drug intake and the time of examination.

It is important to note that the disease remains progressive, despite the impressive pharmacological achievements. To prevent progression would require arresting or reversing the loss of the nigral cells producing dopamine or of introducing another source of dopamine producing neurons into the basal ganglia as discussed above. The future of fetal transplantation remains uncertain. Surgical procedures particularly deep brain stimulation involving the subthalamic nucleus or the globus pallidus may offer benefit to specific patients.

The following case, 19-2 provides an example of hemichorea.

Case 19-2 : This 88-year-old, right-handed, widowed white female with a past medical history of profound hearing impairment, adult onset diabetes, euthyroid goiter, coronary artery disease, and hypertension was brought by her daughter to Saint Vincent's Hospital because of uncontrollable movements ("twitching") of her left foot and shoulder. The daughter described the insidious onset of involuntary rotary movement in the left foot five days prior to admission, which increased in intensity and progressed to involve the left shoulder. The movements were constantly present, even during sleep. The movement was accompanied by a "shooting" pain on the left side of the body which the patient was not able to further describe. She denied loss of consciousness, dizziness, change in mental status, weakness, sensory impairment, visual changes, aphasia, or dysphagia associated with the movement disorder, but did describe a dull headache greater on the left side than on the right during the last few days prior to admission, not accompanied by nausea or vomiting. There was no history of a past movement disorder. Progression rather than spontaneous resolution of the choreiform movements which had begun to impair the patient's ability to ambulate with her walker prompted her daughter to seek medical attention.

Past history: The patient had been admitted briefly one year previously with confusion. and hyperglycemic state related to diabetes mellitus.

Physical Examination: vital signs were all normal.. Patient was alert and cooperative, though profoundly hard of hearing and exhibited involuntary twisting movements of her left foot and upward jerking movements of her left shoulder.

Neurological examination:

1. *Mental Status:* The patient was oriented x3. Memory and language were grossly intact, questions were answered appropriately, and mental status was consistent with the patient's baseline according to her daughter.
2. *Cranial Nerves:* Intact except: for Left eye blindness (cataracts), and gross impairment of hearing such that shouting was necessary to communicate.
3. *Motor System:*
 - a. Tone and strength in upper and lower extremities were normal except for minimal weakness in the left upper extremity(5-/5) .
 - b. Finger tapping, finger-to-nose and heel-to-shin were grossly intact with only slight left-sided difficulty due to involuntary movements.

- c. There was a persistent hemichorea without flinging motions in the left foot, more marked than the left shoulder. There were rotary, twisting movements at the left ankle and upward and rotary motions at the left shoulder. The movement was exacerbated by motor—tasks but did dissipate with sleep.
 - d. Gait was slightly unsteady due to hesitant placement of the left foot. She did quite well with minimal assistance.
 - e. Romberg was negative.
4. *Reflexes*: Deep tendon reflexes were symmetrical, and physiologic except for decreased Achilles secondary to diabetes. The right plantar response was flexor, the left ;extensor.
 5. *Sensation*: Intact except for symmetrically diminished vibration sense in toes.

Clinical diagnosis: hemichorea

Laboratory data:

1. *Electrolytes creatinine, and CBC* were normal. *Glucose* was elevated to 168; *ESR* - 36 mm/hr. *RPR* non-reactive. *ANA* was 1:80(not significant) .*Urine culture* was positive for group B Streptococcal - infection sensitive to Ampicillin. *EKG and chest X-ray* were unchanged from last admission.
2. *CT scan* on admission revealed bilateral basal ganglia calcification, bifrontal atrophy consistent with age, but no evidence of infarction, hemorrhage, or tumor and revealed no change from previous CT scan of 2 months previously.
3. *MRI scan* 3 days after admission, revealed mild cortical atrophy and a hyperdense area without mass effect or enhancement on gadolinium in the right basal ganglia (particularly the head of caudate and putamen) and external capsule consistent with subacute hemorrhage (Fig.19-7).

Hospital course: The patient was begun on haloperidol 0.5 mg by mouth every morning and advanced to 1 mg., by mouth., t.i.d. with some improvement in the hemichorea, particularly in the upper - extremity. Her hemichorea continued to improve over the next two weeks on haloperidol with only occasional twitching of the left shoulder and diminished but persistent, rotary movement of the left foot, both still exacerbated by motor tasks.

The following case 19-3 provides an example of hemiballismus

Case 19-3: This 79-year-old, right-handed, white housewife had the abrupt onset in the early morning hours, 2 days prior to admission, of almost constant flinging movements of the right arm over which she had no control. At the same time, she noted that her right arm felt numb and heavy. Over the next 2 days, the movements decreased markedly and she regained more control of the arm.

Past history: The patient had been a known diabetic for 21 years, receiving insulin - most recently, lente insulin, 25 units each morning.

Neurological examination:

1. *Mental Status*: intact ,the patient was alert and well oriented and without aphasia.
2. *Cranial Nerves*: All were intact.
3. *Motor System*:
 - a. Minimal weakness was present in the right upper extremity at the elbow, wrist and fingers
 - b. Alternating movements and finger-to-nose testing in the right hand were markedly impaired.
 - c. Gait was intact.
 - d. Occasional involuntary flinging movements occurred at the right shoulder.
4. *Sensory System*: Pain, touch, vibration and position sense were all absent in the right upper extremity to the elbow and decreased in this extremity above the elbow.

Clinical diagnosis: hemiballismus

Laboratory data: Chest and skull X-rays EEG, and cerebrospinal fluid studies were all normal.

Subsequent course: The flinging movements of the right arm subsided spontaneously, shortly after admission. Position sense returned and pain sensation showed a mild improvement. The ataxia on finger-to-nose testing disappeared.

Comment: The loss of pain, touch, vibration and position sense in the right upper extremity at the onset of symptoms in this case, would suggest a lesion involving the ventral posterior lateral nucleus of the thalamus, presumably as a result of occlusion of the penetrating branches of the

posterior cerebral artery. Such a lesion could have damaged the subthalamic nucleus as well. The severe dysmetria in the right upper extremity could well have reflected the severe sensory deficit in the right upper extremity. This would appear to be more likely than postulating a lacunar ataxic hemiplegia, due to involvement of the corona radiata in which the origin of the hemiballistic movements could have been in the adjacent caudate putamen. This however would not explain the severe sensory deficit. Note that the use of antidopaminergic agents will decrease or eliminate hemiballismus or hemichorea; however many patients as in this case resolve spontaneously.

The following case history provides an example of Huntington's disease.

Case 19-4: This 54-year-old right-handed divorced white female was referred for evaluation of a movement disorder. The patient lived alone and it was difficult to obtain much of any history from the patient. So far as she was concerned, she had no neurological problems. She denied any problem with her movements. She did indicate that she had worked for 10 years as a secretary/computer operator but had been fired 10 years ago because "she did not work fast enough". She did indicate that she had experienced problems with memory over the last year. The patient denied that she had never been treated on a psychiatric service. She denied receiving neuroleptics. She had a past history of hypertension but had not been reliable in taking her prescribed medication. The patient's son was aware that changes in emotion, personality, speech, gait and a movement disorder had been present for at least 3 years.

Family history: The patient denied any neurological family history except for a maternal uncle who had the "shakes". By contacting the patient's son age 27 and her mother now age 81 and then obtaining old records we were able to assemble additional information. The patient's father had been hospitalized at age 55 on the psychiatry service of St. Vincent Hospital. A review of that record indicated that for several years he had been showing irritability, had become suspicious and paranoid at work. He gave a history of choreiform movements of 20–30 years duration beginning with twitchings about the shoulders. This had progressed over the several years prior to admission, affecting his gait and the movements of the hands. The examination demonstrated that he was moderately depressed and impatient. As he sat, he had "purposeless" movements of his body particularly of the lower extremities. In walking he had "ballistic" movements. He walked on a broad base. Choreiform movements were noted in the tongue. The diagnosis of the neuropsychiatrist was Huntington's disease. He apparently died of cardiac disease shortly after that hospitalization.

The paternal grandfather had died at age 43 of pneumonia, the paternal grandmother at age 37 of gall bladder disease, neither was known to have Huntington's disease, but information was scanty. The patient's father had two siblings one alive at age 81, the other dead at age 68, both apparently unaffected. The patient's mother had a sister with essential tremor.

The patient had 2 siblings, a brother age 60, a sister age 44; both unaffected according to the patient's mother.

The patient had 4 children ages 34, 32, 30 and 27, and 3 grandchildren ages 13 years, 2 years, and 3 months. The eldest daughter age 34 had been depressed for 5 years and had problems with speech and walking for a number of years.

Neurological examination:

1. *Mental status*: the patient often avoided eye contact. Affect was usually inappropriate with laughter as the response to many questions. The overall mini-mental status score was 27/30. The only deficit related to delayed recall portion of the test (0/3 objects).

2. *Cranial nerves*: the patient had a hyperactive jaw jerk. She had frequent facial grimacing.

3. *Motor system*: the patient had decreased tone at wrists and elbows, but strength was intact.

As she sat she had frequent restless and at times choreiform movements of hands and feet.

Gait was often "bizarre" in terms of occasional sudden movements of a leg as moved down the hall and came to a stop. These same movements occurred as she remained standing. In addition in standing or walking, there were intermittent dystonic postures of either left or right arm.

4. *Reflexes*: Deep tendon stretch reflexes were everywhere hyperactive. Plantar responses were flexor. There was a minimal suggestion of grasp release.

5. *Sensory system*: intact

Clinical diagnosis: Huntington's disease.

Laboratory data:

1. *MRI scans of head* (Fig.19-13): The heads of the caudate nuclei were very atrophic. Cortical sulci were wide consistent with cortical atrophy. The lateral and third ventricles were secondarily dilated.
2. PCR testing for the CAG trinucleotide repeats of the Huntingtin gene.: allele 1=17; allele 2=42.
3. Thyroid studies, sedimentation rate, electrolytes, RPR, and antinuclear antibody were all normal.

Subsequent course: The patient refused any treatment for the movement disorder. The patient's son requested genetic testing and the issues were discussed. He and his siblings finally decided not to have the genetic testing performed. The patient's neurological status according to the son worsened to a moderate degree over the subsequent 3 years as regards speech, unsteadiness of gait, and mood swings but without any additional change in memory. The patient herself always appeared unaccompanied for follow up visits and reported no change in her condition.

Comment: Occasionally patients are encountered where changes in psychological function limit the information that the patient can provide.. In other cases denial of illness has a neurological as well as a psychological basis. In this case it was evident that this patient had not only symptoms relevant to the basal ganglia but also changes in cognitive function relevant to the cerebral cortex particularly the frontal areas. In such cases, information must be sought from other sources. In this case, the patient was willing to provide permission to contact those possible sources.

The clinical presentation in this case was clear-cut. In retrospect, many of the neurological features were similar to her father's findings on his admission 30 years previously. When did the patient's disease begin? This was uncertain, but we may presume that serious problems had been present at least 10 years earlier when she had been fired from her long time employment. Did this relate to motor problems, to changes in personality and interpersonal relations or to cognitive changes? Most likely, there were problems in all of these areas. According to her family, symptoms had been present for 2-3 years suggesting onset at age 51 or 52 years.

Case 19-5 provides an example of a patient with Huntington's disease followed over a longer period of time.

This 32 year old right-handed married white male spray painter at a computer factory, was referred for evaluation of a possible hereditary movement disorder. The patient was unclear about the reasons for his evaluation and much of the history was provided by his wife. She reported that the patient had undergone a personality change in the last several months. He had noticeable mood swings and on one occasion he reported people outside the window when no one actually had been there. He had some problems with remembering incidental matters, but no major problems and his job performance had remained intact. He was described as always having been "fidgety".

Past medical history - Mild hypertension for three years.

Family history - The patient's initial history indicated that the family had "Parkinson's" disease and his father had died in his 40's at the state hospital after a 10-15 year illness. The patient indicated that he was a child at the time and his mother never really told him much about the father or let him visit the father in the hospital but he did recall that perhaps his father had some excessive movements of the hands and face. The records were subsequently obtained and these indicated the father had been admitted to Worcester State Hospital in 1968 at age 37. At that time, he had already had three previous hospitalizations for "nervous breakdowns". At the time of his final admission, he had developed hallucinations, seeing people in his room. He had threatened his wife and other relatives. He had difficulty sleeping and he had also developed a problem with his legs "they are jumping". The father's examination had demonstrated a mumbled speech with repetition of the same phrases. His responses would often be tangential and then incoherent with impairment of memory and judgment. His mood was depressed. He was noted to have involuntary movements of the fingers and occasional facial grimacing. The deep tendon reflexes were hyperactive and the plantar responses were extensor. His gait was ataxic. The subsequent course indicated increasing ataxia, choreiform movements and rigidity with increasing weakness, difficulty swallowing and the final development of bronchial pneumonia with death at age 42. The diagnosis of Huntington's disease was confirmed at autopsy.

The paternal grandfather had expired at age 67 with a diagnosis of Huntington's disease, manifested by "nervous breakdowns, inability to sleep and movement disorder". The father's three siblings apparently did not manifest the disease. The patient had two siblings, brother age 28, a sister age 35, all without known disease. He had two children ages 9 and 5.

Neurological examination

1. *Mental Status* - The patient was anxious, often appeared blunted in emotional expression or in answering questions. He avoided eye contact. He was oriented for time, place and person. He was able to name objects and colors. His delayed recall was 2/5 without assistance and 4/5 with assistance.
2. *Cranial Nerves II-XII* were intact, except for the occurrence of occasional, sudden darting movements of the eyes to either left or right. In addition, occasional facial grimacing was noted occurring in a rather irregular manner.
3. *Motor System* : Strength and gait were intact . There were occasional, sudden, irregular, lateral, tremulous movements of the fingers of a choreiform-type.
4. *Reflexes* : Deep tendon reflexes including the jaw jerk were everywhere hyperactive. Plantar responses were bilaterally extensor (bilateral Babinski signs).
5. *Sensory system* : intact

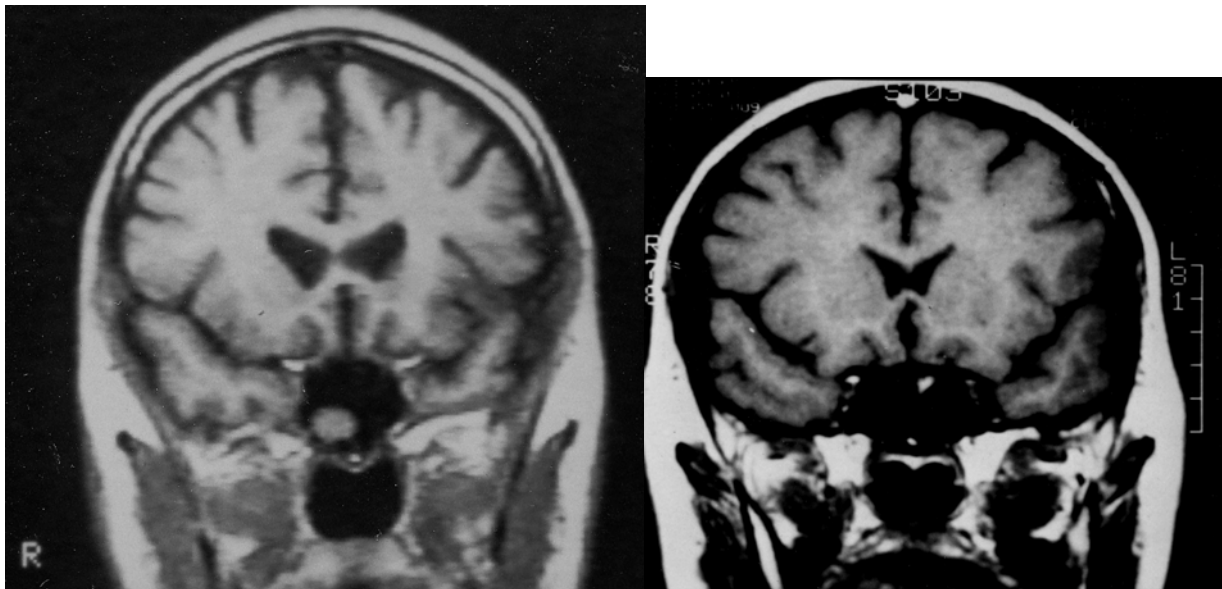
Clinical diagnosis: Huntington's disease

Laboratory Data :

1. All blood chemistries, including glucose; BUN, calcium, electrolytes, liver function studies, ceruloplasmin level, thyroid studies and serological test for syphilis were within normal limits. Ceruloplasmin levels are low in Wilson's disease but normal in Huntington's disease.
2. *Electroencephalogram* was normal with a dominant awake background activity of 10 Hz alpha rhythm.
3. *CT scan of the head* demonstrated enlargement of the ventricles with particular atrophy of the caudate. In addition the sulci were prominent for the age, suggesting some degree of cortical atrophy. The study was considered consistent with the clinical diagnosis of Huntington's disease.
4. The *MRI scan* (fig 19-11A) demonstrated mild enlargement of the ventricles and deepening of the cortical sulci, as well as a very significant atrophy of the head of the caudate nucleus. The MRI from this patient is compared to a similar section from a patient without signs of neurological disease (Figure 19-B)..

Figure 19-11A ;Case 19-5. Huntington's Disease

Figure 19-11B. Normal, age matched



Subsequent course :The patient subsequently developed increased paranoid ideation, increasing dependency with regard to his wife. He was treated with Haloperidol (a neuroleptic, tranquilizer) with considerable improvement with regard to personality. When evaluated, 3 years after onset of disease, it was evident that in the interim, the patient's personality problems had decreased. Attacks of anger and paranoid features had subsided. Mood swings were less. Memory problems, however, were worse and choreiform movements were worse. Dysarthria was now present. The patient had been divorced in the interim and he was on social security disability and no longer working. The examination now showed an exacerbation of many of those features noted at the time of his initial evaluation. He had occasional, sporadic movements of head or eyes of a

choreiform nature. He had frequent choreiform movements involving the fingers as he was sitting, also a similar type of movement appeared to involve the abdominal musculature. He had a moderate degree of dysarthria. He could walk a tandem gait but as he did so, the left arm came up in an somewhat flexed position. When last seen 4 years after onset of disease, he had more dysarthria and his speech was more difficult to interpret. There had been some increase in degree of rigidity but this had decreased when the dose of haloperidol had been decreased. The decrease in this medication, however, then resulted in a greater prominence of the choreiform movements. He could still handle a deck of cards, although he was dropping objects more often than previously. His neurological examination showed a significant degree of dysarthria, a greater degree of facial akinesia, more frequent choreiform movements of hands and face. He had difficulty in mimicking facial expression. As before, all of his deep tendon reflexes were hyperactive and the plantar responses were extensor. The patient walked in a flexed position and tended to turn en bloc. He had a mild degree of cogwheel rigidity at wrist and elbows. His memory remained remarkably good for delayed recall. Final telephone follow-up with his primary physician (approximately 7 years after apparent clinical onset of disease) indicated that the patient was no longer able to drive. He had continued weight loss. He had a marked dysarthria so that his speech was barely intelligible. Choreiform movements had increased. His gait was ataxic, but he could still walk without stumbling. He was relatively stable from a psychiatric standpoint. He was now living with his mother and brother.

Comment: This patient and his family demonstrate the relatively typical course of most patients with Huntington's disease. Patients and families do vary as to whether it is the psychiatric features or the movement disorder features that first bring the patient to medical attention. In this case, the psychiatric features, that is, the change in personality and the increasing paranoid ideation were the first features noted. Subsequently, involvement of the motor system became the most prominent feature. As in the previous case, the patient was unclear as to why he had come for neurological evaluation. Was this a neurological or a psychological denial of illness? Most likely both factors were operational. It was of considerable interest that this patient when first seen, although he was aware of some neurological problem that had occurred in the family, was unclear as to the specific diagnosis. It was also evident that almost no genetic counseling had been done in a disorder that was very clearly an autosomal dominant disorder. The significant family impact, social and economic impact of the disease are clearly evident in this patient. The implications of presymptomatic detection are discussed by Meisser et al (1988), and Klawans (1972).

The following Case 19-6 illustrates the clinical problem of hepatolenticular degeneration in a 21 year old female with a brother who had died at age 16 with hepatic disease, a Kayser Fleischer ring and choreoathetosis. The patient had serum elevation of free copper and a decrease in protein bound copper. She was successfully treated with penicillamine.

Case 19-6 (Patient of Doctor Huntington Porter) :This 21-year-old, single, white female shoe worker in January 1954 had the onset of a "shaking", or trembling of the fingers and hands which progressed to involve both arms and legs. The degree of involvement increased sufficiently to force her to give up her work. Nine months after onset of symptoms, she began to note increasing difficulty with balance and coordination and a slurring of speech. She had also noted increasing weakness and difficulty in doing repetitive tasks. One year after onset, the patient noted blurring of vision, occasional diplopia, and periods of "staring". She also had experienced increasing urgency and occasional urinary incontinence.

Family history: A brother of the patient had died in 1952, at age 16, of a disease with manifestations similar to this patient's. Evaluation of the sibling 2 years before his death by Drs. John Sullivan, Raymond Adams and D. Denny-Brown, had indicated the presence of choreoathetosis with lapses in posture of the hands. In addition, a brownish green ring at the corneal -

scleral junction was noted. Liver disease was present in this sibling and possibly other members of the family.

Neurological examination:

1. Mental status:

- a. The patient was anxious, at times crying, at other times, euphoric.
- b. Digit span was limited to 6 forward, 3 in reverse.
- c. Serial 7 subtractions were poorly performed.

2. Cranial Nerves:

- a. A brown rim was present at the limbus of the cornea, more evidence inferiorly and superiorly.
- b. Extraocular movements were impaired by involuntary jerk movements, The patient was unable to track a moving finger.
- c. Facial expression was mask-like.
- d. Speech was dysarthric and of a nasal quality with slurring and slowness of articulation.

3. Motor System:

- a. No actual weakness was present. However, this patient had difficulty maintaining the limbs in a fixed posture.
- b. There was a rigidity to passive movement of the limbs.
- c. A coarse arrhythmic tremor was present which was most marked proximally and more marked on sustained posture and on movement than at rest.
- d. Alternating movements were poorly performed.
- e. Gait was ataxic. Romberg test was negative.

4. Reflexes: Deep tendon stretch reflexes were hyperactive but plantar responses were flexor

5. Sensation: Intact

Clinical diagnosis: Wilson's disease: hepatolenticular degeneration.

Laboratory data:

1. Liver function tests were normal.
2. *Glucose tolerance test* was normal, but glycosuria occurred.
3. *Total plasma copper* 52 ug/100 ml. (normal range in a young adult is 65 to 150 ug/100 ml).
Direct reacting copper (unbound to ceruloplasmin) 31 ug/100 ml (normal 10 ug/100 ml).
Indirect copper (ceruloplasmin bound) 21 ug/100 ml, normal 105 ug/ ml).

Subsequent course: The patient did relatively well following the use of the chelating agents, BAL and calcium versenate and the institution of a copper free diet. A liver biopsy performed at the time of a cesarean section 18 months after beginning treatment was compatible with perihepatitis with a question of post-necrotic cirrhosis.

Re-evaluation 6 years after onset revealed, in addition to the earlier findings, the presence of "continual spontaneous involuntary movements of the limbs; at the feet, characterized by alternating flexion and extension at the ankle and a waving of the toes". A broad amplitude coarse tremor was noted when the patient was asked to abduct arms, flex elbows, and hold hands just before her nose (wing beating position). A side-to-side tremor of the head was also present. The gait was slightly wide-based and associated with continual dystonic movements of the hands and arms. Treatment with d-penicillamine (which had just become available) was begun at that time.

Urine copper excretion increased from 700 ug per 24 hours to 3240 ug per 24 hours. Normal 24-hour urinary copper in the adult is less than 40 ug. Neurological symptoms soon demonstrated improvement from the previously noted status. The patient was now able to do her house work and take care of her children.

Follow-up 2 years later, indicated significant improvement as regards the findings noted in 1960; dystonic facies and dysarthria was less marked. No tremor was present in the left hand; that in the right hand was evident only when under tension. Dystonic posturing of the hands was present only to a minimal degree. At last report 4 years later, and 12 years after onset of the disease, the patient continued to do well. She had remarried and was expecting another child.

Comment:

This patient presents a typical case of Wilson's disease with onset in the young adult years and with a definite familial background. The copper levels were consistent with the diagnosis (an increased unbound fraction and a decreased bound fraction). At the time that this patient was seen in the mid 1950's and early 1960's, ceruloplasmin levels were not available. Early establishment of a specific diagnosis in this case allowed for specific therapy with improvement of neurological symptoms and the prevention of progression of hepatic disease. With a specific diagnosis established in the patient, periodic blood tests were performed on her offspring to determine whether they also had inherited this genetic disease. (The child born 18 months after onset of the disease had not the disorder.)

An acquired form of non-Wilsonian hepatic and cerebral degeneration occurs in patients who have had multiple episodes of hepatic coma. Degenerative changes occur in the astrocytes and neurons of the basal ganglia. This disorder which was first described by Adams and Victor is discussed in greater detail above.

CHAPTER 20. MOTOR SYSTEMS III: CEREBELLUM

The following case provides an example of a child with a medulloblastoma.

Case 20-1: This 27-month old white female was referred for evaluation of ataxia. The mother had noted that the child had been unsteady in gait, with poor balance, falling frequently since the age of 13 months, when she began to walk. Three months prior to admission, in relation to a viral infection manifested by fever and diarrhea, the patient developed increasing anorexia and lethargy. One-month prior to admission, vomiting increased, and the patient also became more irritable. Perinatal history had been normal, and head circumference had remained normal.

Neurologic examination:

1. *Mental Status:* The child was irritable but cooperative.
2. *Cranial Nerves:* The fundi could not be visualized. Bobbing of the head was present in the sitting position.
3. *Motor System:* A significant ataxia of the trunk was present when sitting or standing. Gait was broad-based and ataxic, requiring assistance. No ataxia or tremor of the extremities was present. Strength and tone were normal.
4. *Reflexes:* Deep tendon reflexes were symmetric and plantar responses were flexor.
5. *Sensory System:* All modalities were intact.

Clinical diagnosis: Probable midline cerebellar tumor, most likely based on age a medulloblastoma

Laboratory data:

1. *Left brachial arteriogram* indicated an avascular area in the posterior fossa. The superior cerebellar artery was elevated. The inferior cerebellar arteries were depressed.
2. *Air-contrast ventriculogram* demonstrated enlargement of the lateral and third ventricles. The cerebral aqueduct was displaced forward to a marked degree. The fourth ventricle was deformed by a mass overlying the posterior wall (essentially located in the nodulus).

Hospital Course: Doctor Peter Carney performed a suboccipital craniotomy. The dura was bulging. The cerebellar tonsils were herniated to a minor degree. On gentle retraction of the inferior posterior vermis, a pinkish gray tumor, originating from a higher point in the fourth ventricle, was visualized at the obex. Limited biopsies of this tumor were taken, revealing a medulloblastoma. Samples of cerebrospinal fluid obtained at surgery revealed the presence of many malignant cells. A permanent shunt from the lateral ventricle to the jugular vein was not installed because of the possibility of spread of tumor cells into systemic circulation. Instead, a catheter was connected from the lateral ventricle to a small reservoir inserted under the skin of the scalp to allow daily drainage. Radiation therapy to the entire central nervous axis was begun one week after surgery. By the time of hospital discharge two weeks after the operation, the patient was able to walk unassisted, with only a moderate degree of ataxia. Three months after the operation, the patient was readmitted because of recurrent irritability and vomiting. A mild degree of papilledema was present. Horizontal nystagmus was present on lateral gaze bilaterally. A wide-base ataxic gait was still present. Various antineoplastic agents were employed (methotrexate into the cerebrospinal fluid and vincristine intravenously) without significant improvement. One month later, respirations became slow, deep, and irregular and death occurred. The findings at autopsy are demonstrated in Fig. 20-4.

In the following case a metastatic tumor in the midline cerebellum produced vertigo, ataxia of gait and headaches.

Case 20-2: This 67 year old white female 6 weeks prior to admission developed intermittent vertigo. Two weeks prior to admission she developed an ataxia of gait. Two days later headaches and true vertigo developed, ataxia increased and vomiting occurred. On the day of admission severe vertigo, headache and nausea and vomiting resulted in her visit to the emergency room

Past history: The patient had a lumpectomy 6 years prior to admission for carcinoma of the left breast. She had undergone a radical mastectomy followed by radiation therapy 3 years prior to admission for a recurrence of malignancy. Histologic examination of the excised tissue indicated a very poorly differentiated (high grade of malignancy) infiltrating ductal tumor which was negative for estrogen and progesterone receptors. On both occasions, the patient refused chemotherapy. The patient had multiple other medical problems including non insulin dependent diabetes mellitus, coronary artery disease, mild hypertension, and prior hip replacement surgery.

Neurological examination (in the emergency room)

1. **Mental Status:** Intact
2. **Cranial Nerves:** Intact except for an absence of venous pulsations on funduscopic examination suggesting a mild increase in intracranial pressure without frank papilledema.
3. **Motor System:** The patient had difficulty standing tending to fall to the right. She was unable to walk because of severe ataxia. There was no limb dysmetria.
4. **Reflexes:** Deep tendon stretch reflexes were symmetrical. The right plantar response was equivocal.
5. **Sensory system:** Intact

Clinical diagnosis: Midline cerebellar tumor metastatic from breast.

Laboratory data :

1. **CT scan of brain:** A large (3-4 cm) enhancing tumor was present involving the midline vermis and right paramedian cerebellum and compressing the fourth ventricle.

2. **MRI of brain** (3 days after admission): An enhancing midline mass involved the cerebellar vermis extended into the right cerebellar hemisphere, and produced mass effect upon 4th ventricle (Fig. 20-5).

3. **CT scan of abdomen** demonstrated two solitary possible metastatic lesions in the liver.

Subsequent course: The patient was immediately placed on dexamethasone with significant improvement. Within 12 hours the examination demonstrated only a mild ataxia tandem gait on turns and bilateral extensor plantar responses. The patient strongly insisted on removal of the solitary central nervous system metastases. Histological examination of the tumor resected by Dr. Gerald McGullicuddy demonstrated poorly differentiated adenocarcinoma with extensive necrosis similar to the tumor which previously had been removed from the breast. Following surgery she received 3000cGy(rads) whole brain radiation and was begun on the antitumor agent tamoxifen. She continued to manifest some unsteadiness on gait but had no difficulty in finger to nose or heel to shin tests. Three months after her admission, a repeat CT scan of the abdomen and pelvis demonstrated diffuse hepatic metastases with mesenteric and retroperitoneal lymphadenopathy. She expired at home, four

months after surgery before she was to start additional treatment with the antineoplastic combination of Cytosan, methotrexate and 5-fluorouracil .

Comment : This patient had a highly malignant poorly differentiated adenocarcinoma of the breast and was clearly at risk for the development of distant metastases ,a risk that was likely increased by her unwillingness to receive antitumor medication. Six years after the lumpectomy she presented with vertigo, ataxia headache and nausea and vomiting, without limb dysmetria. These symptoms suggested involvement of those areas of cerebellum related to the vestibular system and the axis of the body: the floccular nodular area and vermis. Certainly ,the best treatment of a solitary metastatic brain tumor where systemic metastases are not present is the combination of total resection of the brain lesion followed by radiotherapy. However at the time of surgery ,this patient already had evidence of two probable metastatic lesions in the liver. Except for the strong insistence of the patient that the tumor in brain be removed ,an alternate course of radiotherapy, dexamethasone and chemotherapy might have been pursued. Never the less the patient had several additional months of life during which she was able to travel to visit various relatives for a last time. Consistent with the highly malignant character of the tumor, this patient succumbed to the non neurologic effects of her disease

The following case history 20-3 illustrates the problem of alcoholic cerebellar degeneration.

Case History 20-3: This 64-year-old, white male was admitted with a chief complaint of a slowly progressive incoordination of gait present for 8 years. The patient and others had noted that his gait was staggering. The patient denied weakness, numbness, diplopia, vertigo, or memory difficulty. The patient admitted to the consumption of one half pint (250cc) of brandy every 4 nights since symptoms had developed. He indicated that he use to drink more in his younger days, at least 6 to 8 beers in addition to brandy or other alcoholic beverages every night.

There was no history of pes cavus or neurological disease.

General physical examination ; Blood pressure 140/80. Liver was enlarged with the inferior edge extending 2 finger breadths beyond the costal margin. Face was red with dilation of vessels.

Neurological examination:

1. *Mental status:* The patient was slightly disoriented for time. He gave the date as September 31. The date was actually October 19. Delayed recall was 0-out-of-5 objects in 5 minutes. He was unable to give the date of his birth, but he knew his phone number. Digit span was 7 forward, 4 in reverse. Calculations: The patient was unable to subtract 7 from 100 or 3 from 30; he could not add 14 and 13, although he had a fourth grade education.

2. *Cranial nerves:* All were intact. No nystagmus was present.

3. *Motor system:* Strength was intact. Gait was broad-based with an ataxia of trunk. The patient was unable to walk a tandem gait. His ataxia was accentuated by rapid walking. Small lateral nodding movements of the head were noted. He was relatively stable when sitting. There was a minimal tremor at rest. In addition, there was, to minor degree, a resistance to passive motion at the wrists and elbows with a suggestion of a cogwheel component. There was a minor tremor on finger-to-nose testing and a minor impairment of alternating hand movements.

There was, however, a very significant heel-to-shin ataxia which was out of proportion to any tremor or ataxia involving the upper extremities.

4. *Reflexes:* Deep tendon reflexes were physiological and symmetrical (2-3+). Plantar responses were flexor bilaterally.

5. *Sensory system:* Position, pain and touch were intact. There was a moderate decrease in vibratory sensation at the toes and ankles.

Clinical diagnosis: 1. Alcoholic cerebellar degeneration. 2. Mild dementia possible residuals of Wernicke's-Korsakoff syndrome.

Laboratory data: Complete blood count, albumin and total protein, sedimentation rate, cerebrospinal fluid, and skull and chest X-rays were normal.

Subsequent course: The patient received multiple B vitamins and was advised to discontinue any intake of alcohol. Neurological re-evaluation over the next 6 years indicated that no essential progression had occurred.

Comment: The major findings of the broad-based, staggering gait with truncal ataxia and heel-to-shin ataxia may be related to the anterior lobe of the cerebellum. In view of the absence of progression after the discontinuation of alcohol, a toxic or nutritional factor may be postulated (The reliability of the history obtained, in terms of the specific amount of alcohol intake is always open to question particularly in a patient

with significant problems in memory. The amount stated by the patient is usually assume to be the minimum amount.). The minor extrapyramidal findings of cogwheel rigidity may have represented unrelated disease. The lack of progression would be evidence against the diagnosis of a cerebellar degeneration of other etiology (see below). The minor degree of dementia may have related to previous nutritional problems with minor Wernicke-Korsakoff's syndrome or may have reflected a minor unrelated dementia or may have related to long standing retardation. At the present time, the diagnosis may be confirmed by CT scan or by MRI (midline sagittal section) (as in Fig. 20-7 or 20-8). As a result, evidence of cerebellar atrophy is now found in many patients presenting with other aspects of chronic alcoholism or other nutritional disease who do not necessarily present with initial symptoms of ataxia.

In the following case, a similar cerebellar gait disorder and heel to shin ataxia occurred on a genetic basis.

Case 20-4: A 45-year-old single white male carpenter presented with a 4 year history of progressive unsteadiness in walking, present during the daytime as well as at night. He had, during this period, noted minimal loss of coordinated movements in his hands, but felt that his greatest deficit was unsteadiness. The patient had noted no actual weakness but reported some numbness at the toes. He had also noted some minor difficulty in swallowing.

The patient lived in a small town in Virginia. Family historical information was incomplete. His mother and father were second cousins. Several aunts and uncles had "trouble with their legs" in later life, resulting in a difficulty in walking. The patient admitted to a minimal intake of alcohol in the past. He had recently been under the care of a naturopath and had experienced a 7-pound weight loss.

Neurologic examination:

1. *Mental status:* Intact and consistent with his educational level.
2. *Cranial nerves:* Intact except for minimal dysarthria. Horizontal nystagmus was present on lateral gaze, vertical nystagmus on upward gaze.
3. *Motor system:* Strength was intact. The patient walked on a broad base with an ataxia of trunk, as though intoxicated, reeling from side to side, with marked unsteadiness on turns. He was unable to walk a tandem gait with eyes open. The patient was able to sit without significant ataxia of the trunk. A mild intention tremor was present, and there was minimal disorganization of alternating movements. In contrast a marked ataxia and tremor were evident on heel-to-shin test.
4. *Reflexes:* Deep tendon reflexes were intact, except for a relative decrease in ankle jerks compared to knee jerks. Plantar responses were flexor.
5. *Sensory system:* Intact, except for a minimal decrease in vibration sensation at the toes.

Clinical diagnosis: Hereditary cerebellar degeneration involving predominantly anterior lobe

Laboratory Data: Pneumoencephalogram performed at the University of Virginia Hospital (Doctor Stewart) confirmed the significant atrophy of cerebellum. Cerebrospinal fluid and other laboratory data were normal.

Comment: This patient had onset of ataxia at age 41 and was seen relatively early in his disease course. The most prominent features included the ataxia of gait and the heel to shin dysmetria. The patient also had a minor dysarthria, nystagmus and a mild asymptomatic peripheral neuropathy (decreased Achilles reflexes and decreased vibration at toes). There was a familial background but the information was incomplete. The subject of genetic cerebellar degeneration will be considered in a later section. Using older terminology, this patient would have been classified as olivopontocerebellar atrophy. Using more modern terminology, the patient might be included within the category of autosomal dominant cerebellar ataxia type I, had more genetic information regarding the family been available by history and or actual examination.

The following case history illustrates a focal lesion of the lateral hemisphere

Case 20-5 : This 36-year-old white male attorney was referred with a chief complaint of headaches and vomiting. The patient had frontal and biparietal headaches for approximately one month precipitated by coughing, sneezing, or bending. On at least one occasion, the patient had been awakened by the headache. The patient had nausea and vomiting independent of the headaches, at times, occurring suddenly without preceding nausea. For several weeks prior to admission, the patient had been unsteady on his feet, with a tendency to fall to the right, and had noted intermittent clumsiness of his right hand. For several days prior to admission, the

patient had double vision and had to keep one eye closed. During the week prior to admission, he had been excessively drowsy and constantly tired. The headaches had increased in frequency and were now occurring 3 to 4 times per day.

Neurologic examination:

1. Mental status: Intact.

2. *Cranial nerves:*

- a. On funduscopic examination there was evidence of bilateral papilledema.
- b. A bilateral paralysis of the sixth nerve was present.
- c. Horizontal nystagmus was present on right lateral gaze.

3. *Motor system:*

- a. Strength was everywhere intact.
- b. The patient's gait was wide-based. In walking, the patient tended to veer to the right. The patient was unable to stand independently on his right leg.
- c. There was a significant intention tremor of the right upper extremity on finger-to-nose test and of the right lower extremity on heel-to-shin test. Alternating movements of the right hand were disorganized.

4. *Reflexes:* Deep tendon stretch reflexes were normal and plantar responses were flexor.

5. *Sensory system:* All modalities were intact.

Clinical diagnosis: Tumor of the right cerebellar hemisphere with obstruction of ventricular system producing increased intracranial pressure and resulting in papilledema and bilateral cranial nerve VI palsy.

Laboratory Data:

1. Complete blood count and skull x-rays were normal.
2. *Right brachial arteriogram* revealed, in the late arterial phase, a blush in the right inferior and posterior cerebellar hemisphere consistent with a hemangioblastoma.
3. *Pantopaque ventriculogram* revealed a dilated third ventricle and a dilated aqueduct with obstruction to outflow from the fourth ventricle. The fourth ventricle and to a lesser degree, the aqueduct, were shifted to the left. These findings were consistent with a right cerebellar mass displacing and obstructing the fourth ventricle.

Hospital Course: The patient was placed on high dosage of dexamethasone to relieve increased intracranial pressure. Later that day a suboccipital craniectomy was performed by Doctor Samuel Brendler. When the dura was opened, bulging of the lower portion of the right cerebellar hemisphere was noted, with widening of the cerebellar folia. The widest area of the folia was tapped with a needle and a yellow cystic fluid was removed. A transcortical incision was then made, revealing a large cyst with a small strawberry-shaped hemangioma located within. The stalk of this tumor was ligated, and the hemangioma separated from the cystic capsule. Histologic examination of the tumor revealed a hemangioblastoma.

Postoperatively, the patient did well. His headache and diplopia disappeared. There was then improvement in the patient's tremor and ataxia, although there was a slight slowness on finger-to-nose testing on the right. A minor side-to-side tremor was present on right heel-to-shin testing. There was a tendency to veer to the right in walking, but tandem gait indicated only a minor unsteadiness. Evaluation six months after surgery, indicated only a minimal unsteadiness on tandem walking. Evaluation 9 months after surgery later indicated no significant neurologic findings. Re-evaluation three and one-half years after surgery, again indicated a completely intact neurologic status.

Comment: The headaches experienced by the patient, with pain occurring on coughing, sneezing, or mechanical changes, suggested a space-occupying lesion near the ventricular system or meninges. The tumor had produced a block of the ventricular system relatively early in its course, leading to an increase in intracranial pressure, with headache, vomiting and papilledema. The bilateral sixth-cranial nerve weakness was of moderate degree, and

its occurrence would not be unusual in a situation where intracranial pressure had rapidly increased.

The cerebellar symptoms experienced by the patient were lateralized in the sense that the patient was falling to the right side and had noted clumsiness of his right hand. Lateralized cerebellar disease was confirmed by the examination findings of intention tremor of the right arm and leg and disorganization of alternating movements on the right side.

In this case, the hemangioblastoma was in the lateral cerebellar hemisphere. In other cases of hemangioblastoma, the lesion is much more midline in location, and the symptoms are those of a midline cerebellar tumor. Thus, the patient may complain of an ataxia of gait and truncal ataxia and not display clearly lateralized symptoms involving the appendages, such as intention tremor and/or ataxia on heel-to-shin testing. The nodule of tumor often exists within a non-neoplastic cystic cavity. It is, therefore, possible to remove the tumor without sacrificing a large amount of the cerebellum. In some cases, both the mural nodule and the cyst are removed. In almost all cases a complete cure is obtained; recurrences are unlikely and the patients usually have a relatively complete resolution of symptoms and no residual disability.

In some cases, hemangioblastomas of the cerebellum are associated with angiomatous malformations of the retina (Landau-von-Hippel's disease). In some cases, there is an association with a secondary increase in red blood cell production (polycythemia). In rare cases, there is an association with tumors of the kidney. Other neoplasms may also involve the cerebellar hemispheres: cystic astrocytomas, metastatic tumors, and posterior fossa meningiomas. Meningiomas of the angioblastic type may be difficult to distinguish from hemangioblastomas.

At the present time, the diagnosis of these tumors may be readily made by means of MRI and CT scan (Fig. 20-11). Ventriculograms are no longer required. Arteriograms may still be of value in defining the vascularity and blood supply of the tumor.

The following case history presents a typical example of posterior inferior cerebellar artery infarct, the territory most frequently affected selectively.

Case 20-6: This 64-year-old right-handed married white male postmaster, on the morning prior to admission, awoke at 3:00 a.m. with severe posterior headache and severe vertigo, which was exacerbated by any head movement. Nausea, projectile vomiting and slurred speech soon developed. Shortly afterwards, he noted left facial paresthesias, clumsiness of the left upper extremity, and diplopia. He was admitted to his local hospital with a diagnosis of labyrinthine vertigo and then transferred to the neurology unit at Saint Vincent Hospital when symptoms began to evolve.

Two weeks previously, the patient had been seen for a transient episode of difficulty controlling the right arm, a hissing sensation, and impairment of speech.

Past history: The patient had evidence of significant vascular disease. He had hypertension and had undergone coronary artery bypass surgery. Beginning six years previously he had experienced episodes of transient weakness and numbness of the right arm with transient aphasia. He had normal aortic arch and carotid angiographic studies but EEG had demonstrated focal left frontal/temporal slow wave activity. He had been placed on long term anticoagulation. He had experienced migraine headaches without aura for many years.

Neurologic examination:

1. *Mental status:* Intact.
2. *Cranial nerves:* Conjugate lateral gaze to the left was impaired.
3. *Motor system:* Strength was intact. Significant lateralized cerebellar findings were present with marked dysmetria of left upper extremity on finger-to-nose testing and impairment of alternating hand movements. In attempting to stand, the patient was markedly ataxic.

4. *Reflexes*: Deep tendon stretch reflexes were decreased in both lower extremities. Plantar response was extensor on the right and flexor on the left.
5. *Sensory system*: Intact
- Clinical diagnosis**: Left cerebellar hemisphere infarct or hemorrhage with possible minor involvement of brainstem secondary to mass effect.

Laboratory data:

1. Duplex scans of carotids and vertebrals were normal.
2. *Transcranial Doppler studies* indicated normal flow velocities in the vertebral, basilar, anterior and middle cerebral arteries.
3. *Magnetic-resonance angiography* demonstrated occlusion of the left vertebral artery.
4. *CT scan* demonstrated a large left cerebellar infarct pressing the fourth ventricle to the right.
5. *MRI* (2 months after onset of symptoms): Infarction of the total cerebellar territory of the left posterior inferior cerebellar artery with no actual infarct of the brain stem (Fig. 20-12).

Subsequent course: The patient was somewhat vague with some difficulty in memory during the subsequent 8-day hospital course and remained ataxic. He was then transferred to the Fairlawn Rehabilitation Hospital where, over the next three weeks, he had a significant improvement. When re-evaluated two months after onset of symptoms, he was able to walk well with the use of a cane. A minor intention tremor was present on the left finger-to-nose test. An MRI study was obtained at this point, with results indicated above (because new symptoms suggested possible involvement of upper cervical nerve roots and spinal accessory nerve). Additional improvement was evident on evaluation three months after onset of symptoms. Evaluation 6 months after onset of symptoms demonstrated only a slight slowness of alternating movements of the left hand.

Comment: The acute onset of headache, vertigo, vomiting, ataxia of gait, and dysmetria of the left arm suggested an acute cerebrovascular problem involving the posterior circulation and the posterior fossa. (The syndrome of acute headache, vertigo, ataxia, nausea and vomiting is also seen in cases of acute cerebellar hemorrhage.) Numbness on the left side of the face and diplopia suggested, as well, possible brainstem involvement. The initial diagnosis at the local hospital of acute vestibular disturbance did not explain the headache, the diplopia or the lateralized findings. The presence of the left arm dysmetria suggested lateral hemispheric involvement rather than limited midline involvement.

In the era before CT scan and MRI, the distinction between acute cerebellar hemorrhage and acute cerebellar infarct was often difficult to make. Either lesion could produce block or distortion of the ventricular system and secondary hydrocephalus. Either lesion could be associated with the development of brainstem symptoms. The cerebellar infarct, often in the distribution of the posterior inferior cerebellar artery or the anterior inferior cerebellar artery, could also involve the medullary or pontine territories of these vessels. In addition, either type of lesion could cause significant edema with secondary distortion of the brainstem. Hemorrhage could also extend into the cerebellar peduncle and brainstem.

If significant clinical hydrocephalus or brainstem compromise develops, either type of lesion may require neurosurgical decompression or a shunt procedure.

A final note should be made regarding the considerable ability of the human nervous system to recover from extensive cerebellar lesions. Considerable recovery is possible because the cerebellum does not have a direct line role in the control of motor activity but instead, acts as a modulator of the motor control and motor planning circuits.

The following case history provides an example of a cerebellar hemorrhage secondary to an arteriovenous malformation.

Case 20-7: This 57-year-old right-handed married white female had the sudden onset of a severe left-sided pounding headache one afternoon. There was some stuffiness of the nose and tearing of the left eye. She had had a similar, but less severe, headache 20 years previously when taking birth-control pills. No headaches had occurred in the interim. As the current headache began to decrease, she noted that hearing in the left ear had decreased to a minor degree, and an echo sensation was present in the left ear. She also had the sensation that the environment was off balance, particularly if she was in a moving automobile. She subsequently reported a sense of unsteadiness. There was some sense of nausea when the symptoms first occurred. A vague blurring of vision was also present. She had a vague diplopia at the onset of symptoms but this then disappeared.

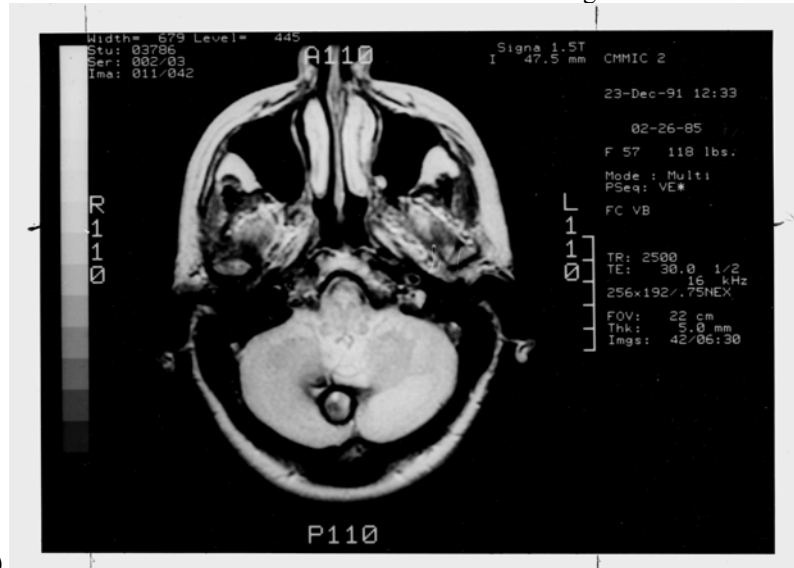
General physical examination: There were multiple pinpoint cavernous angiomas over the arms.

Neurologic examination: Entirely within normal limits.

Clinical diagnosis :Diagnosis unclear: possible migraine headache, or brain stem cerebrovascular event.

Laboratory data: 1. *CT scan of head* indicated hemorrhage in the right paramedian posterior cerebellum.

2. *MRI* showed a rim of hemosiderin stain around the residual hemorrhage in the cerebellar vermis



3. (Figure 20-14).

Subsequent course: The patient had no additional acute episodes. Because two episodes had occurred, she was referred for neurosurgical evaluation. A cavernous hemangioma of the right cerebellum was removed by Doctor Bernard Stone. Post-operatively, she had some right-sided clumsiness and ataxia, which gradually improved.

Evaluation by Doctor Stone one month following surgery, indicated minimal, if any, cerebellar signs. Finger-to-nose test showed no tremor. Gait demonstrated a minimal unsteadiness. Evaluation one year after surgery demonstrated no neurological findings, although some episodic symptoms of imbalance persisted.

CHAPTER 21: SENSORY FUNCTION AND PARIETAL LOBE

The following case demonstrates the localizing significance of focal sensory seizures beginning in the face of a 40 year old patient without prior neurological disease. As predicted, the etiology was neoplastic: a glioblastoma.

Case 21 -1:One week prior to evaluation, this 40-year old right-handed married white male had the onset of repeated 15-21 minute duration episodes of focal numbness (tingling or paresthesias) involving the left side of the face, head, ear, and posterior neck and occasionally spreading into the left hand and fingers, and rarely subsequently spreading into the left leg. There was no associated pain or headache or weakness or associated focal motor phenomena. Biting or eating would trigger the episodes. Past history was not remarkable.

Initial neurological examination: This was completely within normal limits as regards mental status, cranial nerves, motor system, reflexes, and sensory system.

Clinical diagnosis: Focal seizures originating lower third post central gyrus. In view of patient's age, a brain tumor must remain the prime consideration

Laboratory data:

- (1) *EEG*: no focal abnormalities were present. (The record, however, was abnormal because of bilateral bursts of spikes and slow waves - triggered by photic stimulation accompanied by myoclonic jerks - suggesting a predisposition to primary generalized epilepsy (refer to epilepsy chapter for the significance of this finding which was not relevant to this case).
- (2) *CT Scan* (Fig 21-2): The non-enhanced study was normal. The enhanced study demonstrated a small enhancing lesion just above the right Sylvian fissure.
- (3) *MRI* (Fig. 21 - 3): Demonstrated the more extensive nature of this process involving the operculum - above the right sylvian fissure including the lower end of the post central gyrus, the area of representation of the face. A probable infiltrating tumor was suggested as the most likely diagnosis.
- (4) *Arteriogram* - demonstrated a tumor blush at the right sylvian area, consistent with a glioblastoma, a rapidly growing infiltrating tumor - originating from astrocytic glia.

Subsequent Course: Treatment with an anticonvulsant reduced the frequency of the episodes. Neurosurgical consultation suggested an additional observation period and periodic CT scans in view of the normal neurological examination. Three months after onset of symptoms, the patient developed a numbness of the left arm and difficulty in coordination of left arm. Exam now demonstrated left central facial weakness, mild weakness of the left hand. A loss of stereognosis and graphesthesia with a relative alteration in pinprick perception was present in the left hand. The CT scan showed significant enlargement of the previous lesion. EEG now indicated focal 2-3 Hz Delta slow waves in the right frontal central Rolandic area. Subtotal resection of a glioblastoma - in the right temporal parietal area was performed by Dr. Bernard Stone. Radiation therapy was administered following surgery, 4000 rads total whole brain and 5210 rad total to the tumor area. Reevaluation 3 months after surgery, indicated only rare focal seizures involving the face. The neurological examination was normal. Repeat CT scans, however, continued to demonstrate a large area of enhancing tumor in the right temporal-frontal-parietal area. Despite the use of dexamethasone and arterial chemotherapy with cis-Platinum, he continued to progress. At the time of neurological follow-up, 29 months after onset of symptoms, he had developed a left field defect, left hemiparesis and a loss of all modalities of sensation on the left side. He subsequently developed significant changes in memory and cognition, as well as a complete left hemiplegia. CT scan demonstrated progression with extensive involvement of the right side of the brain and spread to the left hemisphere. Death occurred 33 months after onset of symptoms. **Postmortem examination of the brain:** almost the entire right hemisphere was replaced by necrotic infiltrating tumor. The tumor now had spread into the corpus callosum and temporal and occipital lobes. The internal capsule, thalamus, hypothalamus and basal ganglia were destroyed.

Comment: The initial occurrence of the limited focal sensory seizures involving the face and head in a patient of age 40 with no history of trauma or of vascular disease or hypertension clearly predicted the following conclusions (1) The location of the discharging lesion: the sensory cortex

just above the sylvian fissure. (Note that the actual extent of the pathology was more extensive but that is almost always the case in an infiltrating glioma). (2) The nature of the underlying pathology. The most common cause of focal seizures beginning at age 40 in a patient with no significant head trauma, vascular disease, hypertension or other medical disease is a tumor. Among tumors involving the cerebral hemispheres, an infiltrating glioma is by far the most common and on a statistical basis, a glioblastoma is by far the most likely histologic type. 3) The subsequent course was consistent with the natural history of a malignant glioma of the astrocytic series, a glioblastoma. The 33 month survival (30 months after surgery is beyond the median survival for this type of tumor.

The following patient (case 21-2) had a metastatic nodule in the post central gyrus producing a pseudo thalamic pain syndrome.

Case 21-2: This 62-year-old white, right-handed housewife, six years prior to admission

had undergone a left radical mastectomy for carcinoma of the breast. Five months prior to admission, the patient developed a persistent cough, left pleuritic pain and a collection of fluid in the left pleural space (pleural effusion) as well as daily headaches in the right orbit, occasionally awakening the patient from sleep. Four months prior to admission, over a 3 to 4 week period, the patient developed progressive "weakness" and difficulty in control of the right lower extremity. Several weeks later, the patient now experienced, aching pain in the right index finger in addition to a progressive deficit in the use of the right hand. This was more a "stiffness and incoordination" than any actual weakness. One month prior to admission the patient noted episodes of pain in the toes of the right foot and numbness of right foot occurred, lasting 2 to 3 days at a time. She subsequently developed, difficulty in memory and some minor language deficit, suggesting a nominal aphasia, prompting hospital admission.

Neurological examination:

1. *Mental status:* The patient was oriented for time, place, and person. Delayed recall was slightly reduced to 3-out-of-five in 5 minutes. A slowness in naming objects was present although she missed only one item of 6. Calculations, reading, and attention were normal. There was no left-right confusion.

2. Cranial nerves:

a. Nerve II: early papilledema was noted: absence of venous pulsations, indistinctness

of disc margins, and minimal elevation of vessels as they passed over the disc margin.

b. Nerve VII: right central facial weakness was present.

3. **Motor system:**

- a. Mild weakness of the right upper limb was present. A more marked weakness was present in the lower limb (most marked distally).
- b. Spasticity was present at the right elbow and knee.
- c. Gait: The right leg was circumducted; the right arm was held in a flexed posture.

4. **Reflexes:**

- a. Deep tendon reflexes were increased on the right.
- b. A right Babinski response was present.

5. **Sensory system:**

- a. Touch intact.
- b. An ill-defined alteration in pain perception was present in the right arm and leg - more of a relative difference in quality of the pain than any actual deficit.
- c. Repeated stimulation of the right lower extremity (pain or touch) produced dysesthesias (painful sensation).
- d. Vibratory sensation was decreased to a minor degree at the toes bilaterally but intact in the upper extremities.
- e. Position sense was markedly defective in the right fingers with errors in perception of fine and medium amplitude movement in the right toes.
- f. Simultaneous stimulation resulted in extinction in the right lower extremity.
- g. Graphesthesia (identification of numbers, e.g., 8, 5, 4 drawn on cutaneous surface) was absent in the right hand and fingers and poor in the right leg.
- h. Tactile localization and two-point discrimination were decreased on the right side.

Clinical diagnosis: Metastatic tumor to the left post central and precentral gyri with a cortical pain syndrome (pseudo thalamic pain syndrome).

Laboratory data:

1. *Skull x-rays:* the pineal was shifted from left to right. Demineralization of the dorsum sellae also had occurred: consistent with the increase in intracranial pressure.

2. *Chest x-ray:* Several metastatic nodules were present in the left lung.

3. *Electroencephalogram:* A focal disturbance, having the quality of damage, was present in the left posterior frontal central and parietal areas (almost continuous focal 4 to 7 cps slow wave activity).

4. *Left carotid arteriogram:* A left posterior frontal lobe lesion was suggested by a shift of the posterior portion of the anterior cerebral artery from the left to the right. The middle cerebral artery in the sylvian fissure was also depressed downwards.

5. *Brain scan:* The findings were consistent with a focal metastatic lesion with a focal uptake of radioisotope (Hg^{197}) in the left parietal area: high and close to the midline with uptake in the adjacent subcortical white matter.

6. **Erythrocyte sedimentation rate** was elevated to 90 mm., consistent with metastatic disease.

Subsequent course: There was evidence in this case that the disease had spread to multiple organs: brain (findings as noted), lung (chest x-rays and biopsy), and liver (abnormal laboratory tests of liver function). Radiation and hormonal therapy were, therefore, administered rather than any attempt at surgical removal of the left parietal metastatic lesion. Follow-up examination one month later indicated that a significant improvement had occurred in motor function in the arm. Sensory deficits persisted. Speech was slow but relatively intact. The patient eventually expired five months after admission.

Post mortem findings: Autopsy was performed by Dr. Humphrey Lloyd of the Beverly Hospital and disclosed extensive metastatic disease in the lungs, liver, and lymph nodes. A single necrotic metastatic lesion was present in

the brain. This was located in the upper postcentral gyrus of the left parietal area, 1.0 cm. below the pial surface and measuring 1.2 x 1.0 x 0.6 cm.

Comment: This patient had a progressive neurological deficit with headache and papilledema, a clinical course that clearly indicates the presence of a neoplasm. This case predated the era of CT and MRI scan. Today contrast-enhanced scans would be performed. This diagnosis was supported by the ancillary laboratory studies that were available at that time. Moreover this diagnosis however was clear based on the history and clinical-laboratory findings. The fact that motor findings in the arm relevant to the precentral gyrus improved with treatment might suggest that these findings were due to edema. In contrast the findings relevant to the area of the necrotic tumor, the post central gyrus, showed little improvement. In general, one should assume that a patient with a past history of carcinoma of the breast, carcinoma of the lung, malignant melanoma, or renal cell carcinoma, who develops symptoms of central nervous system disease, has metastatic disease until proven otherwise. Such symptoms at their onset may be minor and nonfocal and appear trivial: headache, subjective weakness, and a change in personality. On the other hand more focal symptoms and signs may be present: focal weakness, focal seizure. The metastatic lesions may be single or multiple.

A diagnosis of metastatic disease does not imply that no treatment of central nervous system lesions is possible. Surgical resection of single lesions may be successfully performed. Often the apparent deficits are far out of proportion to the actual size of the tumor because of the surrounding swelling (edema) in the adjacent tissues.

The pattern of sensory involvement in this case clearly localized this lesion to the cortex (or white matter close to cortical surface) rather than to the thalamus. The relative intactness of pain, touch, and vibration sensation should be contrasted to the significant deficits in position sense,

graphesthesia, tactile localization, and two-point discrimination with extinction on simultaneous stimulation. The occurrence of episodic pain in the involved arms and legs along with the production of an experienced painful sensation on repetitive tactile stimulation (dysesthesias) in patients with sensory pathway lesions is sometimes referred to as a "thalamic" or "pseudo thalamic" syndrome. (Refer to discussion of Wilkins and Brody, 1969). In this case, the anatomical locus for the pseudo thalamic syndrome is apparent.

The effects of deficits in cortical sensation on the total sensory motor function of a limb are apparent in this case. The actual disability and disuse of the right arm and leg were far out of proportion to any actual weakness. Such an extremity is often referred to as a "useless limb." The actual weakness that was present undoubtedly reflected pressure effects on the precentral gyrus and the descending motor fibers in adjacent white matter.

The following case (21-3) demonstrates many of the features of a non dominant parietal lobe lesion.

Case 21-3: This 70-year-old, single, white female, right-handed, retired candy maker underwent a left radical mastectomy for carcinoma of the breast, three years prior to admission. Four months prior to evaluation, the patient became unsteady with a sensation of rocking as though on a boat. She no longer attended to her housekeeping and to dressing. Over a three-week period, prior to evaluation, a relatively rapid progression occurred with deterioration of recent memory. A perseveration occurred in motor activities and speech. The patient was incontinent but was no longer concerned with urinary and fecal incontinence. For 2 weeks, right temporal headaches had been present. During this time, her sister noted the patient to be neglecting the left side of her body. She would fail to put on the left shoe when dressing. In undressing, the stocking on the left would be only half removed.

Family History: The patient's mother died of metastatic carcinoma of the breast.

Neurological examination:

1. Mental status:

- a. The patient was oriented for time, place and person.
- b. Delayed recall was 5-out-of-5 objects in 5 minutes.
- c. There was no evidence of aphasia.
 - d. The patient often wandered in her conversation. She often asked irrelevant questions and was often impersistent in motor activities.
- e. There was marked disorganization in the drawing of a house or of a clock. A similar marked disorganization was noted in attempts at copying the picture of a railroad engine (Fig 21-4).
- f. There was a marked neglect of the left side of space and of the left side of the body. The patient failed to read the left half of a page. When she put her glasses on, she did not put the left bow over the ear. When getting into bed, she did not move the left leg into bed. She had slipped off her dress on the right side, but was lying in bed with the dress still covering the left side.

- g. The patient had been reluctant to come for neurological consultation. Although she complained of headache and nausea, she denied any other deficits. Her relatives provided information concerning these problems. Much additional persuasion over a two-week period was required before the patient would agree to be hospitalized.

(2) *Cranial nerves:*

- a. Nerve II: A dense left homonymous hemianopsia was present. When reading, the patient left off the left side of a page. She bisected a line markedly off center. Disc margins were blurred and venous pulsations were absent, indicating papilledema.
- b. Nerve III: The right pupil was slightly larger than the left.
- c. Nerve VII: A minimal left central facial weakness was present.
3. *Motor system:* Strength was intact. There was, however, little spontaneous movement of the left arm and leg. Tone was normal.
4. *Reflexes:* deep tendon reflexes were symmetrical and physiologic and plantar responses, flexor.
5. *Gait:* The patient was ataxic on a narrow base with eyes open with a tendency to fall to the left, and was unable to stand with eyes closed even on a broad base.
6. *Sensory system:*
- a. Pain, touch and vibration were intact. At times, however, there was a decreased awareness of stimuli on the left side.
 - b. Errors were made in position sense at toes and fingers on the left.
 - c. With double simultaneous stimulation, the patient neglected stimuli on the left face, arm and leg.
 - d. Tactile localization was poor over the left arm and leg.

Clinical diagnosis: Metastatic tumor from breast to right non-dominant parietal cortex.

Laboratory data:

1. *Skull X-rays* were negative.
2. *Chest X-ray* indicated a possible metastatic lesion at the right hilum.
3. *Erythrocyte sedimentation rate* was elevated to 72 mm/hr, consistent with metastatic disease.
4. *Electroencephalogram* (Fig 21-5) was abnormal because of frequent focal 3 to 4 cps slow waves in the right temporal and parietal areas, suggesting focal damage in these areas.
5. *Brain scan (radioisotope)* (Fig 21-6) indicated that a large but well-defined area of increased uptake of isotope (Hg197) was present in the right parietal area extending from the midline to the lateral surface, measuring 7 x 5 x 7 cm. The most likely diagnosis was that of a solitary large metastatic lesion
6. *Right carotid arteriogram* showed that a large vascular tumor mass, probably metastatic, was present in the posterior section of the right temporal inferior parietal area. There was displacement of the middle cerebral artery upward and to the left.

Subsequent course: Treatment with steroids (dexamethasone and estrogens) resulted in temporary improvement. The patient refused surgery. Her condition soon deteriorated with increasing obtundation of consciousness. She expired two months following her initial neurological consultation.

Comment: This patient certainly presented a syndrome characterized by disturbance in concept of body image with a marked neglect of the left side, a denial of illness, and marked constructional apraxia. The various laboratory studies indicated a large lesion in the right posterior temporal parietal area. A CT scan from a more recent case demonstrating many aspects of this syndrome is illustrated in Figure 21-7. In many cases, the location of lesion may appear to be predominantly posterior temporal. Such large posterior temporal lesions would certainly compromise the cortex and subcortical white matter of the adjacent inferior parietal area.

In this case, marked deficits in perception of the cortical modalities of sensation were present. In other cases, as in the case demonstrated in Fig 21-7, such involvement is much less marked.

In some cases, involvement of the motor cortex is evident with an actual left hemiparesis accompanied by an increase in deep tendon reflexes and an extensor plantar response. At times in patients with neglect syndromes, there may be several indications in the clinical examination and in the laboratory studies that the involvement of the frontal lobe areas is more prominent than the parietal involvement. We have already indicated that the neglect components of this syndrome may also be noted in lesions of the anterior premotor

area (area 8). The premotor area as discussed above and in chapter 18, receives projection fibers from the multimodal area of the posterior parietal area. It is possible that in some cases the posterior temporal - inferior parietal location of the lesion may also be critical in interrupting these association fibers. For these several reasons, it is perhaps more appropriate to use the term, *syndrome of the non-dominant hemisphere*, rather than the more localized designation, non-dominant inferior parietal syndrome. Duffner et al, 1990 have presented the concept of a network for directed attention - with right frontal lesions leading to left hemi spatial neglect only for tasks that emphasize exploratory-motor components of directed attention whereas parietal lesions emphasize the perceptual-sensory aspects of neglect.

With lesions of the non-dominant hemisphere, there is a significant alteration of the patient's awareness of his environment. The behavior of an individual is in part determined by his or her own particular perception of the environment. If that perception is altered or disorganized, the behavioral responses of the patient may appear inappropriate to others. Obviously, not all individuals will respond in the same manner to a given environmental situation; part of the response will be determined by the past experience and personality of the individual. Thus, given the same lesion, one individual may be unaware of a hemiparesis, another may deny the hemiparesis but agree an illness is present, a third may claim to be healthy and claim that people are conspiring to keep him in the hospital.

CHAPTER 22: THE LIMBIC SYSTEM

In general, as we have indicated, there is mixed symptomatology during partial seizures of temporal lobe origin. The following case history (22-1) illustrates many of the points just discussed regarding seizures of temporal lobe origin.

Case 22-1: This 56-year-old white right-handed male baker was referred for evaluation of a seizure disorder. Three months before admission the patient had the onset of episodes of vertigo and tinnitus, each episode lasting 4 minutes and unrelated to position. The patient then noted increasing forgetfulness. Later that month he had a generalized convulsive seizure that occurred without any warning. The patient then developed episodes of confusion and unresponsiveness, followed by a left frontal headache. Several studies; EEG, pneumoencephalogram, and carotid arteriogram—were all negative at that point in time. One month before admission, the patient began to have minor episodes, characterized by lip smacking and a vertiginous sensation, during which he reported seeing several well-formed, colorful scenes. At times, he had hallucinations of “loaves of bread being laid out on the wall.” In addition, he would have a perceptual disturbance at the same time (e.g., objects would appear larger than normal) and “terrifying dreams.”

General physical examination: unremarkable.

Neurological examination: The essential neurological findings were as follows:

1. *General observations of seizures:* The patient was observed to have frequent transient episodes of distress characterized by saying, “Oh, oh, oh, my”. On occasion, these were accompanied by automatisms: fluttering of the eyelids, smacking of the lips, and repetitive picking at bedclothes with his right hand. Consciousness was not completely impaired during these episodes, which lasted from 30 seconds to 3 minutes, and the patient reported afterward that at the onset of the seizure he had seen loaves of bread on the wall and smelled a poorly described unpleasant odor. At other times, the olfactory hallucination was described as pleasant, resembling the aroma of baked bread.
2. *Mental status:* The patient was oriented to person but not dates. He could not recall his street address. He was unable to pronounce the name of the hospital correctly. Calculations were correctly performed.
3. *Cranial nerves:* Possible deficit in the periphery of the right visual field and a minor right central facial weakness.
4. *Motor system:* intact
5. *Reflexes:* Deep tendon reflexes were symmetrical and physiologic. A right Babinski sign was present.
6. *Sensory system:* intact.

Clinical diagnosis: Simple and complex partial seizures originating left temporal lobe probably involving at various times left lateral superior temporal gyrus, uncus, amygdala and hippocampus with tumor the most likely etiology in view of age and the focal neurological findings.

Laboratory data:

1. The *initial electroencephalographic recording* indicated frequent focal spike discharge throughout the left temporal and parietal areas, consistent with a focal seizure disorder originating in the left temporal/parietal areas (Fig. 29-1). A recording 6 days later indicated a decrease of focal spikes (i.e., a decrease in seizure activity) but the presence of frequent focal slow-wave activity in the left temporal area (almost continuous, 3 to 5 cps (Hz) slow-wave activity) suggesting that focal damage was present in the left temporal area .
2. *Brain scan* (H_g197) normal
3. *Left carotid arteriogram* indicated a possible avascular mass lesion left posterior frontal (the only abnormality was a 4-mm shift of the anterior cerebral artery).

Subsequent course: The patient continued to have multiple short episodes characterized by the sensation of odor and a sensation that he was looking at objects upon the wall. These episodes were eventually controlled with anticonvulsant medication: phenytoin (Dilantin) and primidone (Mysoline). However, 2 months later the patient had a day with several episodes with “crazy things occurring “ (colorful visions and terrifying nightmares).

The patient was readmitted to the hospital 7 months after onset of symptoms because of the recurrence of seizures. An aura of unpleasant odor was followed by a generalized convulsion followed by four or five

subsequent seizures of a somewhat different character (deviation of the head and eyes to the right, then tonic and clonic movements of the right hand spreading to the arm, foot, and leg lasting approximately 1 to 2 minutes, followed by a post-ictal right hemiparesis).

Neurologic examination now indicated a marked expressive aphasia, with little spontaneous speech and difficulty in naming objects. There was a dense right homonymous hemianopia, a flattening of the right nasolabial fold, and a right hemiparesis, with a right Babinski sign.

During a 2-week hospital period the patient continued to have minor seizures characterized by sensory phenomena on the right side of the body. A moderate degree of expressive aphasia persisted throughout the hospital course, although the right homonymous hemianopia largely disappeared. The symptoms and findings suggested that the basic disease process might well have spread to involve the adjacent areas across the sylvian fissure—the speech areas of the inferior frontal convolution, premotor areas, and sensory motor cortex.

The patient developed increasing expressive aphasia and right hemiparesis, with increasingly severe headache. An arteriogram indicated a large space-occupying tumor of the left temporal lobe, and surgery was undertaken by Dr. Robert Yuan 16 months after the onset of symptoms. The anterior and middle portions of the superior temporal gyrus appeared to be widened, and the anterior temporal area (the temporal tip) had an abnormal and discolored appearance. At a depth of 1 to 2 cm within the superior temporal gyrus and involving all of the deeper temporal areas, obvious necrotic glial tissue was found. The process had extended superficially under the Sylvian fissure to involve the adjacent posterior portion of the inferior frontal gyrus.

A temporal lobectomy was performed (from the anterior temporal pole posteriorly for a distance of 6 cm). The operative impression of a malignant glial tumor (glioblastoma) was confirmed by histologic examination.

Comment: This patient presented, at one time or another during his seizures, most of the phenomena associated with temporal lobe lesions: vertigo, tinnitus, visual distortions and hallucinations, olfactory hallucinations, fear, automatisms involving the lips and hands, and episodes of confusion. The visual and olfactory hallucinations are of interest in that both reflected the patient's occupation as a baker. As Halgren and colleagues (1978) note, the experiential phenomena of temporal-lobe seizures are often specific to the individual's experience and personality. The later progression clearly indicated spread across the sylvian fissure to involve the motor cortex and Broca's area in the inferior frontal gyrus areas. This patient had a highly malignant tumor, which clearly involved the cortex of the lateral surface, the deeper white matter, and presumably the medial temporal areas, including the amygdaloid-hippocampal regions. His clinical picture is highly reminiscent of the case described in 1887 by Hughlings Jackson of Emily M., a cook who experienced visual and olfactory hallucinations and who had a tumor arising in the "temporosphenoidal lobe" (the uncus). Such seizures have subsequently been referred to as uncinate epilepsy, but as we have indicated, the disease invariably involves more than just the uncus.

Today, CT scan and MRI would be employed for early diagnosis (see Figs. 22-17 and 22-18). Cases 22-2 and 22-3 which follow demonstrate the correlation of partial seizures with temporal lobe pathology.

Case 22-2. This 17-year-old right-handed male, at age 4 years began to have "staring spells and bizarre behavior". Some episodes had been preceded by the "sound of a musical rhythm". EEG at that time indicated a right temporal spike discharge. Seizures were controlled for ten years with anticonvulsants but then recurred and were poorly controlled occurring several times per day.

Neurological examination: The findings were limited to the following features:

1. *Observed 3 minute seizure:* The seizure began with loss of contact and a stare and then automatisms of the hands. He stood up, walked around the room, went to the physician's desk and attempted to pull open a nonexistent middle drawer. He answered questions vaguely with one or two word answers. Confusion was present for 1-2 minutes after the end of the episode.
2. *Cranial nerves:* a left central facial weakness was present.

Clinical diagnosis: Focal seizures originating right temporal lobe. Observed seizure was complex partial. The seizures beginning with the musical sound might be classified as simple partial with secondary complex partial.

Laboratory data:

1. *EEG*: Intermittent focal spike discharge anterior-middle temporal area.
2. *CT scan*: (Fig. 22-17) An area of focal atrophy was present in the right anterior temporal lobe with possible enhancement at the border.
3. *MRI*: At the Yale Epilepsy Center was more consistent with a tumor in the right anterior temporal lobe.

Subsequent course: Dr. Dennis Spencer at the Yale Epilepsy Center performed a temporal lobectomy. This demonstrated a cystic glial tumor with components of astrocytes and oligodendrocytes. Cerebral cortex also demonstrated abnormal lamination and dysplastic features. Seizures were fully controlled over the next three years.

Case 22-3. This 47-year-old ambidextrous male experienced his first seizure one month prior to admission. He felt light-headed and warm. Then he was observed to walk 100 feet down a hallway, appearing “dazed” and not recognizing people. He fell to the floor, with a loss of consciousness, bit his tongue and was confused afterwards for several minutes.

Neurological examination at 2, 16 and 48 hours after the episode: A persistent right Babinski sign, and slight right hyperreflexia were present. Otherwise the examinations were not remarkable.

Clinical diagnosis: Complex partial seizures. In view of age of onset and persistent focal signs a brain tumor was suspected as the etiology.

Laboratory diagnosis:

1. Sleep deprived EEG :normal.
2. *CT and MRI scans* (Fig. 22-18) demonstrated an extensive infiltrating tumor of the left temporal lobe most likely a glioblastoma.

Subsequent course: Despite Anticonvulsant therapy (phenytoin) additional episodes occurred over the next month: loss of train of thought while talking and several minutes of loss of memory. A subtotal resection by Dr. Bernard Stone (St. Vincent Hospital) demonstrated a Grade III-IV astrocytoma (glioblastoma). Despite radiotherapy and chemotherapy, the disease pursued a relentless course producing early and severe disability prior to death, approximately one year after onset of symptoms.

The following case histories illustrate many of the features of focal disease involving the prefrontal areas.

Case 22-4: This 69-year-old right handed white housewife; two years prior to neurological evaluation visited a relative (a physician) in Israel whom she had not seen in a number of years. The relative then wrote to the patient’s physician, (an old family friend) indicating concern over a change in the patient’s personality. The patient was described as apathetic with silly immature reactions. In retrospect, the patient’s husband felt that these alternations had begun insidiously a number of years previously. A year later, the same relative again wrote indicating that letters received from the patient had become incoherent. Letters became less frequent and then the patient no longer wrote letters. Ten months prior to evaluation, a left central facial weakness was first noted followed two months later by a decreased left arm swing. Six months prior to evaluation, her husband noted, she was purchasing items for which she had no need: 24 pairs of shoes, 15 brassieres. Subsequently she became careless in her housework. On occasions she lost her purse. Her ability to play bridge had decreased over the last year, although her golf game was unchanged.

Neurological examination:**1. Mental status**

- a. She was oriented x3
- b. There was a marked impersistence in motor activities. She was often inattentive. Her answers were often irrelevant. (According to her husband this had been present for many years.
- c. There was inappropriate joking.
- d. Delayed recall without assistance was 2/5 objects in 5 minutes. But 5/5 with assistance.
- e. Digit span was decreased to 5 forward and 3 in reverses.

- f. There were marked deficits in serial 7 subtractions. At times she began to subtract other numbers, at times she added rather than subtracted.
- g. There was a significant spatial disorientation. There was a marked impairment in the ability to copy a cube and deficits in drawing a house. There was disorientation in locating cities on a map.

2.Cranial nerves:

- a. There was a significant neglect of single stimulus objects in the left visual field; this was greater when bilateral simultaneous stimuli were utilized.
- b. At times there was a limitation of voluntary gaze to the left.
- c. A left central facial weakness was present.

3.Motor system:

- a. There was minimal weakness of the left arm and leg.
- b. Variable resistance was present on passive motion at left wrist and elbow suggesting the "gegenhalten" of frontal lobe disease.
- c. There was a decreased swing of the left arm in walking. The gait was initially apraxic but improved as the patient picked up speed.

4.Reflexes

- a. Deep tendon stretch reflexes were increased on the left.
- b. A left Babinski sign was present.
- c. There was a bilateral release of the grasp reflex.

5. Sensory system: intact.

Clinical diagnosis: Right frontal lobe tumor: probable meningioma based on the long history.

Laboratory data:

1.*Skull x-rays* there was a 5mm shift to the left of the calcified pineal gland. Long standing increased intracranial pressure was suggested by the demineralization of the sella turcica.

2.*EEG* demonstrated focal 2-5 Hz slow waves in the right frontal area most prominent in the parasagittal recording area

3.*Imaging study: radioactive brain scan (Hgl97):* there was a heavy uptake in the right frontal towards the midline measuring 5x5x4 cm (Fig.22-21).

4.*Arteriograms:* A parasagittal tumor was present in the right frontal area, with vascular supply derived from the left and right middle meningeal and left anterior meningeal arteries.

Hospital course: Following the arteriogram, the patient developed signs of increased intracranial pressure (vomiting, lethargy and papilledema). The patient received dexamethasone glucocorticoid used to reduce cerebral edema, with improvement in these symptoms. The right external carotid artery was ligated since the meningioma derived considerable blood supply from this source. Dr. Samuel Brendler performed a bilateral frontal craniotomy. Bulging of the dura was present requiring the administration of hyperosmotic agent (20% mannitol) with reduction of the swelling. When the dura was opened a large right posterior frontal meningioma was revealed measuring 8x8cm and attached to the right side of the superior sagittal sinus. On histological section this was a fibrous, meningothelial meningioma. During the course of removal of the tumor, it was necessary to ligate several bridging veins entering the superior sagittal sinus as well as the arteries feeding the tumor. At the conclusion of the procedure, it was noted that the right pupil was enlarged and neither responded to light. The patient failed to regain consciousness, remaining in a state of coma with bilateral extensor plantar responses, decerebrate postures on stimulation and bilateral fixed dilated pupils. The patient expired 2 weeks after surgery.

Comment: It is difficult to decide even in retrospect when the symptoms in this case began. It is clear that the initial symptoms involved an insidious change in personality. She was apathetic, her reactions were "silly" and judgment was impaired. Purchases were inappropriate. It would have been of interest to explore which aspects of her bridge playing were impaired in terms of planning and strategy etc. Her motor function was impaired only to a minor degree even late at the time of neurological evaluation, with minimal left-sided weakness and more prominent premotor release. The visual neglect syndrome may have reflected involvement of the premotor area or compromise of the parietal cortex by this large tumor. The fact that there was only minor evidence of involvement of motor cortex would make the premotor/SMA location more likely. While the spatial disorientation and deficits in drawing might

favor a nondominant parietal syndrome, such findings also could be consistent with a nondominant premotor/SMA location based on the close interaction between the posterior parietal and the premotor location. The impairment of voluntary gaze to the left would be consistent with area 8 involvement. There is little doubt that this patient required surgical intervention. The removal of large "benign" tumors of this type is not without risk. Hemorrhagic infarction with massive edema and tentorial herniation is a complication of ligation of bridging veins entering the superior sagittal sinus. In this case, serious brain swelling was already evident even before the dura was opened.

The following case history 22-3 provides an example of a patient with a slowly progressive subfrontal meningioma manifested by symptoms of apathy, loss of ambition, "depression" of mood, emotional lability, with a tendency to introspection and a slowness of mental processes. All of these symptoms were initially attributed to depression and a hypothyroid state. As gait and memory problems developed, these symptoms were attributed to Alzheimer's type senile dementia. When increased intracranial pressure and coma suddenly developed, neurological and neurosurgical intervention occurred.

Case 22-5: This white housewife and fashion designer was first admitted to the hospital at age 60 with a history of several years (?2 to 5) of fatigue, loss of ambition, lack of enthusiasm, and a tendency to readily cry over minor problems. A depression of mood and a tendency to introspection had developed. The patient also reported loss of her taste for food with a subsequent decrease in appetite and weight loss. These symptoms had progressed despite an adequate dosage of thyroid medication (60 mg., t.i.d.). Neurological examination was recorded as negative except for a slowness of speech and of thought processes. She was described by the psychiatric consultant as indecisive in her answers. Cerebrospinal fluid examination revealed no significant findings. Tests of thyroid function indicated hypothyroidism with protein bound iodine of 3.2 micrograms/100 ml. (normal; 4 to 8 micrograms/100 mg.) and a radioactive iodine uptake of 2.3 percent in 24 hours (normal 20 to 50 percent). Discharge diagnosis was chronic depression and hypothyroidism.

These symptoms continued to progress despite treatment with thyroid. The patient had increasing difficulty in walking. This had actually been first noted at age 57, 3 years prior to her initial hospital admission as a "phobia for heights". The patient would "freeze" at the top of a high flight of stairs. She then developed progressive difficulty in climbing stairs. Her husband reported that she would have marked difficulty in getting out of chairs. She would appear unsteady in gait after rising from a chair but would soon recover her equilibrium and would be able to walk in relatively normal manner. Increasingly, the patient's motor and mental activities became slower. She "procrastinated in making decisions". Occasional urinary incontinence developed at age 66 and was attributed to her neurological disease (apparent senile dementia). Although her husband reported her memory as initially well preserved, other observers at that point reported a progressive deficit in memory. At age 67, the patient began to complain of episodic fogging or blurring of vision.

Initial Neurological examination on re-admission to the hospital at age 67 was recorded as demonstrating the following features:

(a), slight disorientation for date and year, (b) slowness of speech and gait (c) deep tendon reflexes 2+, plantar responses flexor, and (d) no significant sensory finding except a slight decrease in position sense at the toes. No details as to the patient's gait were recorded. The sense of smell was apparently not tested and no notes as to the presence or absence of a grasp reflex were recorded.

On the day after admission, the patient developed headache and vomiting. She had difficulty walking unsupported and became increasingly more somnolent but could be roused by painful stimulation. Deep tendon reflexes were increased bilaterally with bilateral extensor plantar responses (bilateral Babinski signs). Grasp response was absent. Pupils responded to light but were sluggish.

Fundusoscopic examination was negative but lumbar puncture indicated a markedly increased pressure, greater than 400 mm. of csf. Cerebrospinal fluid protein was elevated to 125 mg/100 ml. The patient became unresponsive and emergency neurological and neurosurgical consultations were obtained.

Neurological examination:

1. *Mental Status:* The patient was semicomatose with periodic Cheyne-Stokes respirations.
2. *Cranial Nerves:* Pupils were fixed, the left dilated, the right constricted.
3. *Motor System:*
 - a. The patient moved all limbs in response to painful

stimulation, right more than left.

- b. There was a spastic resistance in the upper and lower left extremities.
4. Reflexes:
- a. A generalized hyperreflexia was present with bilateral ankle clonus.
 - b. Bilateral Babinski signs were present.
 - c. A bilateral grasp reflex was present. Note, however, that in a semicomatose patient this may have little localizing significance.
5. *Sensation*: Pain sensation was intact.

Clinical diagnosis: Subfrontal or parasagittal frontal tumor most likely a meningioma in view of the over 10 year course. Tentorial herniation had occurred possibly related to the lumbar puncture.

Laboratory data: An emergency bilateral carotid arteriograms revealed that a large subfrontal butterfly-shaped mass (probably meningioma) was present in the anterior cranial fossa bilaterally. The anterior cerebral arteries as well as the frontal polar, pericallosal and callosal marginal branches and the middle cerebral arteries were displaced backwards. The anterior cerebral arteries were also displaced upwards. The tumor mass derived blood supply from the ophthalmic arteries.

Hospital course:

A bifrontal craniotomy was immediately performed by Doctor Robert Yuan with total removal of a large bifrontal meningioma arising from the falx and olfactory groove. On the right side the tumor was estimated to occupy 75 percent of the anterior cranial fossa, measuring 7 x 5 x 6 cm. On the left the tumor was of approximately half this size, measuring 5 cm. in diameter. The thickness of the cerebral hemisphere covering the tumor in the right prefrontal area was reduced to 0.5 cm. Histological examination of the tumor indicated a benign meningioma (meningotheliomatous type).

The patient showed some immediate improvement at the conclusion of surgery, in the sense that both pupils were equal in size and reacted to light. By the time of discharge from the hospital, two months after surgery, considerable improvement had occurred. She could recognize the doctor by name but did not know the place, the season, or the month; she could, however, describe a picture she had just seen. A bilateral deficit in olfaction was present (anosmia). Assistance was required in walking. A bilateral grasp reflex was present.

Follow-up evaluation two years after surgery indicated continued improvement although the patient still had complaint relevant to impairment of recent memory and slight unsteadiness of gait. Deep tendon reflexes were symmetrical with plantar responses flexor. A bilateral grasp reflex was present and the patient was slow in walking and fell occasionally. Urinary incontinence occurred with wetting of the bed.

Comment: In retrospect, the evolution of symptoms in this patient clearly indicates a tumor initially compression both prefrontal areas and producing alterations in mood and personality. With continued growth of the tumor, compromise of the premotor areas with resultant apraxia of gait and release of grasp reflex began to occur, either as a result of direct compression or secondary to the distortion and compression of the anterior cerebral arteries. It is not unusual to witness the development of a dementia (deficit in recent memory) in large tumors in a subfrontal midline location. A similar dementia may occur in large aneurysms of the anterior communicating artery.

The problem of dementia will be considered in greater detail in the chapter on memory.

The development of headache, vomiting and increasing somnolence indicated the development of increasing intracranial pressure. The sudden unresponsiveness following the lumbar puncture with the development of periodic Cheyne-Stokes respirations, pupillary changes, and bilateral corticospinal tract signs all indicated an additional acute exacerbation of the already compromised brain stem functions, a compromise which had already resulted from the backward displacement of the intracranial contents with distortion of the brain stem. In retrospect, one might hypothesize that the patient's complaint of a loss of taste for her food at the time of her initial hospitalization might well have indicated some loss of olfactory sensation since much of our appreciation of food is dependent on olfaction. Specific tests for olfaction were not recorded.

CHAPTER 23: VISUAL SYSTEM

The following case is an example of a lesion involving the optic nerve, anterior to the optic chiasm.

Case History 23-1 (Fig 23-8).

This 53-year-old white right-handed housewife was referred for evaluation of progressive right-sided supraorbital headache of 23 years duration and decreasing acuity in the right eye. The loss of acuity had progressed to the point of almost total unilateral blindness. During the 3 years before admission, intermittent tingling paresthesia had been noted in the left face, arm, or leg. About 1 year before admission the patient had a sudden loss of consciousness and was amnesic for the events of the next 48

hours. She was hospitalized, but no explanation for the episode was clearly established, although cerebrospinal fluid protein was reported to be elevated (230 mg/dl).

The patient and her family reported some personality changes over a period of several years, including a loss of spontaneity and increasing apathy.

General Physical Examination: Unremarkable except for a minor degree of proptosis (downward protrusion of the right eye).

Neurologic Examination:

1. *Mental Status:* The patient was, in general, alert but at times would become lethargic. Her affect was flat. At times, she would laugh or joke in an inappropriate manner.
2. *Cranial Nerves:* There was anosmia for odors, such as cloves, on the right and a reduced sensitivity on the left.

Marked papilledema (increased intracranial pressure with protrusion of the optic disk and venous engorgement due to obstruction of the normal flow of CSF) was present in the left eye.

Pallor of the right optic disc was present, indicating optic atrophy. Visual acuity in the right eye was markedly reduced. The patient had only a small crescent of vision in the temporal field of the right eye, where only vague outlines of objects could be seen. A slight left central facial weakness was present.

3. *Motor Systems:* Intact although movements on the left side were slow.

4. *Reflexes:* A release of grasp reflex was present on the left side.

5. *Sensory system:* Intact

Clinical diagnosis: Subfrontal meningioma arising from olfactory groove or inner third sphenoid wing.

Laboratory data:

1. *Skull* x-rays demonstrated erosion of the dorsum sellae. Special lamniograms demonstrated hyperostosis of the sphenoid bone (planum sphenoidale) suggesting a meningioma originating from the sphenoid bone.

2. *EEG* demonstrated focal 2-4 Hz slow waves in the right anterior temporal and anterior lateral frontal area.

3. *Brain scan (H_g 197)* revealed a heavy uptake of isotope in the right posterior subfrontal area.

4. *Arteriograms* indicated that the anterior cerebral arteries were shifted backwards, posteriorly and the left. A tumor blush was present on the venous phase in the right subfrontal area extending back to the optic nerve groove (Fig 23-8). These findings were felt to be most consistent with an olfactory groove meningioma.

Hospital course: Dr. Samuel Brendler performed a bifrontal craniotomy which exposed a well-encapsulated smooth tumor attached to the medial third of the sphenoid wing. After intracapsular removal of 90 to 95% of the tumor, the right optic nerve could be visualized. The small portion of the tumor attached to the bone could not be removed because of considerable bleeding from the bone. Examination 4 months after surgery, indicated right anosmia and right optic atrophy were present.

Comment

If one considered only the patient's primary complaint, decreasing vision in the right eye, and the findings of right optic atrophy and left-sided papilledema (Foster-Kennedy syndrome), then the most probable diagnosis was inner-third sphenoid meningioma. The preservation of a small crescent of vision in the temporal field is consistent with compression of the optic nerve on its lateral surface. By the time of hospitalization, the lesion was quite large and had extended into the subfrontal area, producing anosmia on the right and some changes in personality. At this point, the various diagnostic studies suggested only a subfrontal mass and did not clearly differentiate between an olfactory-groove meningioma and a sphenoid-wing meningioma. One might suggest, in retrospect, that the degree of involvement of the right optic nerve was much more pronounced than the changes in prefrontal functions, and therefore, the inner-third sphenoid-wing location was more likely.

The surgical approach in any case was the same. The eventual recovery of vision in such cases is uncertain because the effects of compression often are not reversible