

COMPLETE CASE HISTORIES FROM TEXTBOOK: *INTEGRATED NEUROSCIENCES*

PART II. CASES – BRAIN STEM

CHAPTER 11 BRAIN STEM :EYE MOVEMENT CASE HISTORIES

Case 11-1. This 75-year-old white male had the onset in March 1984 of diplopia (double vision). Examination in April 1984 revealed only a variable possible lag in movement of the left medial rectus muscle. A Tensilon (edrophonium) test (see Chapter 8) and brain stem auditory evoked potentials were normal. In retrospect, a *CT scan* in April 1984 (**fig 11-1**) revealed a very small enhancing lesion at the level of the facial colliculus. *Chest x-ray* did reveal pleural thickening and a somewhat reticular nodular change of a non-specific type. The erythrocyte sedimentation rate was elevated to 82 mm/hr, a sign of systemic disease.

The diplopia initially improved but the patient then developed weight loss, cough and headache pains.

On readmission in June 1984, there was now a clearly defined left abducens nerve paralysis and nystagmus on right lateral gaze. A left peripheral facial paresis was now also noted.

Cerebrospinal fluid examination was negative.

He was readmitted in July 1989 because of progression of the left facial paralysis. On examination he was unable to close the left eye and he was drooling from the left side of the mouth. He was also complaining of diplopia on gaze to either left or right side.

Neurological examination of eye movements: Several severe problems were now demonstrated:

- 1) on attempted gaze to the left; a total paralysis of left CN VI plus a lesser paresis of conjugate lateral gaze as regards the right eye.
- 2) On gaze to the right a) full abduction of the right eye, b) some adduction of the left eye but this was incomplete, and c) coarse nystagmus of the abducting right eye.
- 3) In primary gaze, the left eye was slightly medial.
- 4) Convergence was intact for both eyes.
- 5) Up gaze was intact but minor vertical nystagmus was present.

Conclusions were:

- 1) Left CN VI paralysis.
- 2) Left lateral gaze center involved
- 3) Left medial longitudinal fasciculus involved.

Except for the left peripheral facial paralysis, the neurological examination was otherwise normal.

The *CT scan* (**Fig 11-1**) now indicated a more prominent enhancing lesion at the level of the facial colliculus.

Despite extensive evaluation of the pulmonary disorder, including bronchoscopy and open lung biopsy (non-specific fibrosis and chronic inflammation)-a specific diagnosis could not be established. The patient was treated both for tuberculosis (chemotherapy) and for possible metastatic tumor to brainstem (radiation therapy). Pulmonary status continued to deteriorate and the patient expired on Nov. 1984.

Post mortem examination: A metastatic tumor nodule was found to have destroyed the left abducens nucleus and part of the adjacent paramedian pontine reticular formation (**Fig 11-2**). Severe degenerative changes were present in the left MLF at the level of rostral pons and midbrain. Sections through the pons at and just below the lesion demonstrated secondary degeneration of the left abducens and left facial nerve.

For a more detailed discussion of this case see Jackal et al (1986).

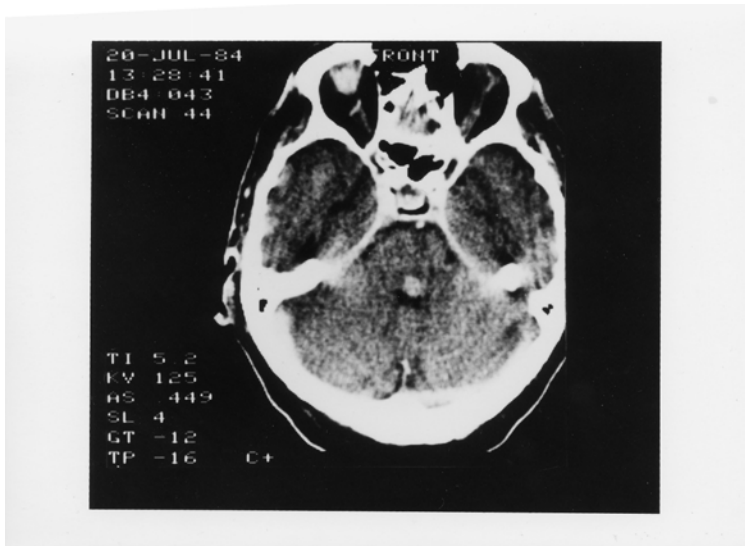


Fig 11-1;Case 11-1. *CT scan* indicating a more prominent enhancing lesion at the level of the facial colliculus

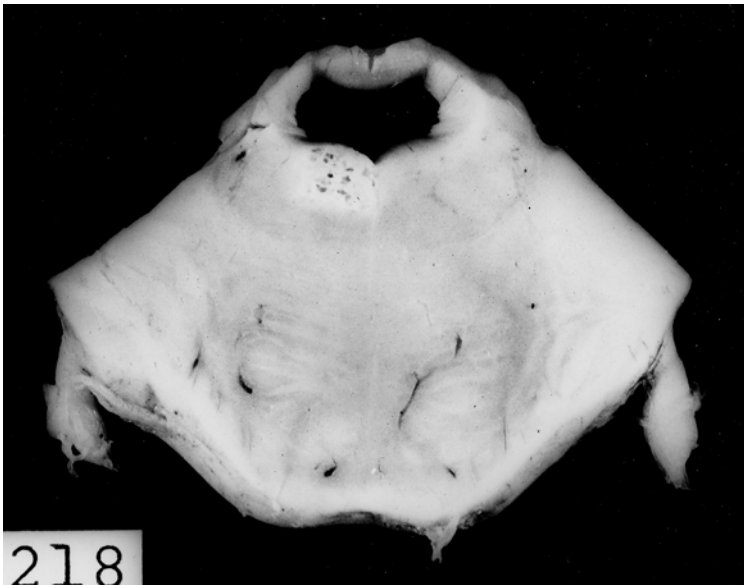


Fig 11-2. Case 11-1 **Post mortem examination:** A metastatic tumor nodule was found to have destroyed the left abducens nucleus and part of the adjacent paramedian pontine reticular formation.

Case history 11-2

This 16-year-old, white male in November 1960 was first noted to be lethargic. Gradually from November 1960 to March 1961 there was a steady decline in school performance with apathy and somnolence. In December 1960 the patient had the onset of diplopia with difficulty in reading. In March 1961 he began to sleep throughout the day and could be awakened only with difficulty. Headaches on arising, with nausea and vomiting, had been noted. In April 1961 evaluation at the Buffalo General Hospital had revealed that the pupils failed to respond to light but did respond to accommodation. Upward gaze was intermittently defective, and conjugate lateral gaze was intact. Findings improved to some degree over a 3-day period.

In August 1961, 2 months prior to admission, he had an onset of a progressive defect in coordination of gait as well as a defect in hearing, predominantly in the right ear with tinnitus. To a lesser degree the left ear was also affected.

In September 1961 there was a 1-day period of hiccoughs. At the same time, there was an onset of a slow, slightly slurred speech.

On the day of admission, an episode of urinary incontinence occurred.

Neurological examination: The relevant findings included:

1. **Mental status:** All areas were relatively intact except for a slowness of response, emotional lability, and immaturity of behavior and questions.
2. **Cranial nerves:**
 - a. The right eye was deviated outward; the patient was unable to converge. There was a paralysis of upward and downward gaze. Bilateral lid ptosis was present. However, spasm of the eyelids was easily stimulated. Pupils were sluggish in response to light. The right pupil was slightly larger than the left. Horizontal nystagmus was present.
 - b. The jaw jerk was hyperactive.
 - c. Guttural and lingual sounds were slurred in a pattern that was consistent with pseudobulbar palsy.
 - d. Hearing was decreased bilaterally.
3. **Motor system:**
 - a. Spasticity was present on passive motion in the lower extremities and possibly in the upper extremities.
 - b. There was slowness in alternating hand movements. A fixed facies was present. A bilateral intention tremor was present on finger-to-nose testing. Gait was broad-based with truncal ataxia.
4. **Reflexes:** a. Deep tendon reflexes were hyperactive bilaterally with ankle clonus.
b. Plantar responses were extensor bilaterally (bilateral sign of Babinski).
5. **Sensory system:** Intact
There were no relevant laboratory data.

Subsequent course: (We are grateful to Dr. Walter Olszewski and Dr. Walter Stafford of the Buffalo General Hospital for information concerning the subsequent course of this case).

The patient was readmitted shortly thereafter to the Buffalo General Hospital where a *pneumoencephalogram* revealed a mass displacing the aqueduct of Sylvius posteriorly. Radiation therapy was begun (a total of 4500 rads over 30 days). Within 10 days improvement in hearing occurred. Tremor of the arms and legs decreased; speech became less slurred, and a few degrees of upward gaze of the eyes returned. Ataxia of gait subsequently decreased so that the patient was able to walk rapidly although on a wide base. His pupils remained fixed to light but responded to accommodation. The eyes were divergent and skewed. Downward gaze never returned and only vertical nystagmus was present on attempted upward gaze. Bilateral Babinski signs remained. This condition remained relatively static for 4 months, when over a two-week period, the patient had a decrease in initiative, gait became more ataxic, headaches returned, and a marked ptosis of the left eyelid developed. Neurological examination on February 7, 1962 now revealed a bilateral ptosis. The pupils were irregular and constricted; the right measured 2.5 mm. in diameter, the left 1.5 mm. Neither reacted to light. The patient could not elevate, depress, or converge the eyes. The patient could look to either side. Nystagmus developed in the left eye on gaze to the right. As previously, intention tremor and bilateral Babinski signs were present. Shortly thereafter, a terminal coma developed with a marked elevation of temperature (104 to 106°) and blood pressure (200/80).

Postmortem examination: A significant degree of ventricular dilatation from infiltration and obstruction of the aqueduct was present. There was an area of apparent necrotic tissue sharply localized to the midbrain tectum and tegmentum, extending from the pretectal area down into the superior and inferior colliculi. The cerebellum and pons were not involved but there was slight bilateral invasion of the thalamus. A small necrotic nodule was also present at the presumed site of the pineal. While some of the necrosis may have been due to radiation, microscopic sections of the necrotic areas of midbrain tegmentum revealed the typical appearance of a pinealoma (a lobulated sinusoidal tumor containing large vesicular cells and a focal cluster of small cells resembling lymphocytes). The most common tumor of the pineal constituting 50% of cases, the germinoma is similar in appearance to the seminoma of the testes. A more complete discussion of the pathological features of pinealomas is presented in Chapter 27.

Comment: The clinical findings in this case clearly suggested a lesion involving the pretectal area (pupillary response to light was defective, but response to accommodation was intact) and the pretectum-superior colliculus (defect in upward and downward gaze). The lethargy, apathy, and somnolence early in the course may have related in part to increased intracranial pressure. Increased intracranial pressure often occurs in these lesions because of the early compression of the aqueduct of Sylvius. However, in view of the early

prominence of the somnolence prior to headache and vomiting, we may presume that there was compromise of tegmental structures including the reticular activating system at the diencephalic-mesencephalic junction. The bilateral impairment of

hearing undoubtedly related to the bilateral involvement of the inferior colliculi. Bilateral involvement of the brachium of the inferior colliculus would also explain this symptom. The bilateral Babinski signs, the signs of pseudobulbar palsy (hyperactive jaw jerk, and slurring of speech sounds) indicated that compression of the corticospinal and corticobulbar pathways had occurred. The bilateral intention tremor and the marked ataxia of gait and trunk may have related to downward pressure on the cerebellum or to involvement of the superior cerebellar peduncles (brachium conjunctivum) and their rostral continuation within the tegmentum. As progression occurred additional involvement of the oculomotor nuclei occurred.

Precocious puberty occasionally develops in preadolescent males with pinealomas. This usually indicates invasion or compromise of the hypothalamus. Cells of the germinoma of the pineal may seed into the structures about the third ventricle.

The usual treatment of pinealomas has been based on shunting procedures to bypass the blockage at the aqueduct and radiation therapy. This patient had a relatively long survival, particularly long in view of the fact that a shunting procedure was not performed. His eventual demise apparently related to the obstruction at the aqueduct of Sylvius and brain stem compression.

More recent diagnostic approaches have involved earlier diagnosis by CT or MRI scan (MRI is the preferred imaging approach). The surgical approach may now include excision via a supracerebellar or transtentorial approach to the tumor utilizing the operating microscope(see Stein 1979).

CHAPTER 12:CRANIAL NERVES

Cranial Nerve III

Case 12-1: This 50-year-old right handed, white male factory foreman was referred for evaluation of ptosis and diplopia involving the left eye. Approximately two weeks prior to admission, the patient developed a bifrontal headache. During the week prior to his evaluation the headache had become a left sided aching pain. It increased in intensity during the two days prior to admission, and was present as a constant pain interfering with sleep. If the patient were to cough he had additional pain in the left eye. On the day of admission the headache became much more severe, it was now the worst headache he had ever experienced.

In retrospect, the patient reported that lights had been brighter in the left eye for approximately one week.

At 3:00 PM on the day of admission the patient noted the sudden onset of diplopia, which was more marked on horizontal gaze to the right and much less marked on horizontal gaze to the left. At approximately the same time he noted the rapid onset of ptosis involving the left lid.

The patient denied any other neurological symptoms.

His past history was not relevant to his present neurological problem.

General physical examination: There was moderate resistance to flexion of the neck.

Neurological examination: The complete neurological examination was within normal limits except for findings relevant to the left 3rd cranial nerve.

1. The left pupil was fully dilated to approximately 7mm. There was no response to light or accommodation.
2. Total ptosis of the left eye lid was present.
3. No medial movement of the left eye was present, there was no upward movement of the left eye possible. The patient had minimal downward gaze of the left eye. He had full lateral movement of the left eye. Movements of the right eye were full.

Clinical diagnosis: Subarachnoid hemorrhage secondary to an aneurysm at the junction of the posterior communicating and internal carotid arteries.

Laboratory data:

1. *Lumbar puncture* demonstrated bloody spinal fluid with no definite clearing from Tube 1 to Tube 3 and approximately 40,000 fresh red blood cells in each tube.

2. *Four vessel angiography* :The left posterior cerebral arose from the left internal carotid artery as a continuation of the posterior communicating artery. At the junction of the posterior communicating and the internal carotid arteries, a 13 mm aneurysm was present directed posteriorly. Other vessels were within normal limits.

Subsequent course: The neck of the aneurysm was clipped by the neurosurgeon Dr. Bernard Stone. Adhesions and clots were present between the aneurysm and the 3rd cranial nerve. The patient did well except that the 3rd nerve paralysis was still present at the time of discharge –3 weeks after surgery.

Comment: Tension and migraine headaches are common ,but generally develop before the age of 50 years. This patient had no prior history of headaches. The initial history of bifrontal headaches ,taken in isolation was nonspecific. The lateralization of the headache with pain in the left eye on coughing and the progression of the headache were all points of concern suggesting a more serious pathology. Finally the occurrence on the day of admission ,of the worst headache ever experienced by the patient suggested the possibility of a subarachnoid hemorrhage. Most (85%) patients with an acute subarachnoid hemorrhage have an underlying saccular aneurysm. There are three major locations for single intracranial aneuysms:1) the junction of the posterior communicating and the internal carotid arteries,2) the junction of the anterior communicating and anterior cerebral arteries and 3) the bifurcation of the middle cerebral artery in the Sylvian fissure. The posterior communicating artery is closely situated and runs parallel to the 3rd cranial nerve. With hemorrhage, compression of (or bleeding into) the nerve, symptoms will develop relevant to cranial nerve 3. Thus in patients with prodromal symptoms ,a third nerve syndrome allows the prediction of this specific location of the aneurysm. Because of the arrangement of the fibers within this nerve ,the initial symptoms of compression often involve the pupillary fibers. In retrospect, the early symptoms of lights being brighter in the left eye ,one week before the ptosis and diplopia developed would be consistent with a pupil that was unable to constrict in response to light. As we will discuss in greater detail in a later chapter, the middle cerebral location can be predicted when symptoms and signs relevant to the middle cerebral artery occur. The anterior communicating location is often difficult to predict because ,weakness in both legs may occur but may be accompanied by loss of consciousness due to bilateral frontal lobe involvement .In many patients, in all locations ,the bleeding may be so massive ,that loss of consciousness, rapidly follows the sudden headache ,and localization is not possible. Management of intracranial aneurysms will be discussed in the chapter 26 on vascular syndromes.

Cranial Nerve V

Case 12-2: This 28 year old single, black, right handed female mother of two children reported approximately 21 days of sudden lancinating jabs of pain plus a duller more steady pain involving the right maxillary and mandibular distribution. She was very aware that she could trigger her pain by touching her nose, or the skin over the maxillary or mandibular area. The pain was so severe that talking ,chewing or eating would all trigger episodes. As a result, she has not been eating a great deal. The was no clear cut extension of pain into the eye, although some of the background pain did spread into the supraorbital area and back towards the interauricular line.

Two years prior to admission, she had a less severe episode in the same distribution that lasted three weeks. She denied any tearing of the eye or nasal stuffiness. She had no tingling of the face, change in hearing, facial paralysis, or diplopia.

Past history indicated :1) treatment for tuberculosis at age 7or 8 years because of a positive skin test after exposure to a relative with the disease ,2) prior treated gonococcal infection.3)Intake of one liter of whiskey on each weekend.

Neurological Examination:

Mental status, motor system (including gait and cerebellar system)and sensory system were intact. There was no L’Hermitte”s sign.

Cranial nerves were not remarkable except for findings relevant to the right fifth cranial nerve .Although touch and pain sensation over the face was normal, there were clearcut exquisite trigger points producing sharp pains on light tactile stimulation of the nose or other maxillary areas as well as the mandibular skin areas and the lower molars.

The reflexes were normal except for an absence of the right patellar and both Achilles deep tendon stretch reflexes.

Clinical Diagnosis: Trigeminal neuralgia :maxillary and mandibular divisions.

Laboratory data:1)*CT scan of the head, sinus x-rays ,and a panoramic dental x-ray series* obtained in the emergency room,11 days prior to evaluation were not remarkable.

2).*White blood count* was normal but the erythrocyte sedimentation rate was significantly elevated to 63mm/hr.

3).*Antinuclear antibody* was positive at 1:1280 (anticentromere pattern) consistent with lupus erythematosus an autoimmune disease.

Subsequent course: Evaluation by a dentist indicated no relevant dental disease .Treatment with phenytoin(Dilantin) produced partial improvement in symptoms so that she was now able to talk without pain. Subsequently the patient received carbamazepine and nerve blocks with greater relief of symptoms. In addition she received treatment of her underlying autoimmune disease.

Comment: This patient had the classical symptoms of trigeminal neuralgia. Patients with onset at this age often have an underlying disorder such as multiple sclerosis or in this case an autoimmune disorder. As regards , the loss of deep tendon reflexes, this may have reflected nutritional causes related to the excessive intake of alcohol or may have related to effects on peripheral nerve of the autoimmune disease.

Patients with onset after age 40 often have compression of the trigeminal nerve by an anomalous loop of artery .Treatment in such cases that fail to respond to medications involves relocating the loop of artery or insulating the nerve from the pulsation of the vessel. Other surgical procedures are designed to alter transmission through the Gasserian ganglion

Case 12-3: This 44-year-old, right handed physician, developed over 24 hours, increasing pain in the right supraorbital and orbital areas. Edema of the eyelid developed within 36 hours. Erythematous, edematous skin lesions developed over the right supraorbital area and the anterior half of the right side of the scalp. Edema of the lid was sufficient to produce closure of the lid. Significant cervical lymphadenopathy, neck pain and low-grade fever developed. The acute pain gradually subsided over two weeks but the skin lesions persisted (**Fig. 12-1**) . The skin lesions crusted and gradually cleared over four weeks. Occasional episodes of right supraorbital pain continued to occur for one year. Faded, depressed scars were still present 24 years after the acute episode.

Clinical diagnosis: Ophthalmic herpes zoster.

Comment: The development of pain followed by the characteristic skin lesions is consistent with the diagnosis of trigeminal neuralgia involving the ophthalmic division of the trigeminal nerve. In some cases the cornea is involved with residual scarring. This complication is more likely to occur when the nasociliary branch of the ophthalmic nerve ,supplying the midline nose ,is involved .This patient did not have this pattern of involvement and did not have corneal involvement. Post herpetic neuralgia (persistence of pain >one year after the acute event) as discussed earlier is more likely to occur in older patients and did not occur in this middle aged individual. As indicated previously this disorder represents a reactivation of the varicella virus residual in sensory ganglia such as the trigeminal. In rare instances, H. zoster ophthalmicus may be complicated by involvement of the intracranial arteries resulting in infarction .

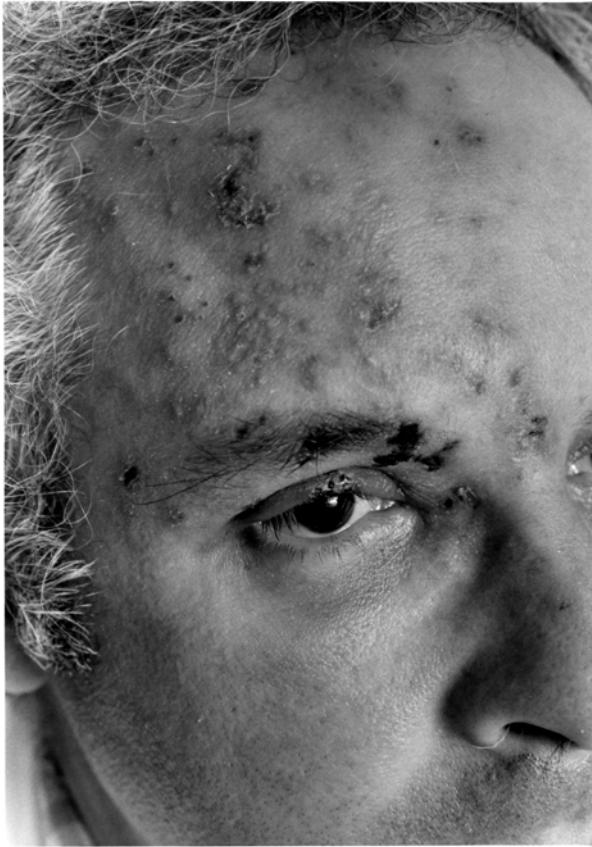


Figure 12-2: Case 12-3. **Ophthalmic herpes zoster.**

Cranial Nerve VII

Case 12-4: This 37-year-old previously healthy right handed, white house wife and registered nurse was referred for emergency consultation regarding left facial paralysis. Three days prior to evaluation the patient had developed a dull pain above and behind the left ear. She then noted occasional muscle twitching about the left lower lip and a vague stiffness of the left side of the face. On the morning of the evaluation, the patient noted that she had difficulty with left eye closure and was drooling from the left side of her mouth. She denied any alteration in taste or in hearing and she had no tinnitus. She had no crusting or any pain within the ear canal.

General physical examination: The external auditory canal and tympanic membrane were normal.

Neurological examination: The complete examination was normal except for findings limited to the left seventh cranial nerve:

The patient had an incomplete paralysis of the entire left side of the face. She had sufficient eye closures sitting or recumbent to cover the cornea. She was able to have minor elevation of the eyebrow in forehead wrinkling. She had minimal elevation of the lower lip in smiling. The patient was unable to wrinkle her forehead.

Taste for sugar was slightly decreased but not absent on left side of the tongue (anterior two-thirds).

Clinical diagnosis: Bell's Palsy: left peripheral 7th cranial nerve palsy.

Laboratory data: Routine blood counts, erythrocyte sedimentation rate, blood chemistries and chest X-ray were all normal.

Subsequent course: The patient was treated with a one week course of prednisone and was seen in follow up at weekly intervals. Over the next 2-3 weeks a complete recovery occurred, related or unrelated to the therapy.

Comment: This patient had an uncomplicated palsy of the 7th cranial nerve, of uncertain etiology. Specific causes such as sarcoid, H. Zoster and immunological disorders were ruled out by the examination and basic laboratory data. An underlying diabetes was not present. No specific tests for Lyme disease were performed, but

there was no exposure to ticks ,no history of tick bites or of skin manifestations. Note that 75% of cases of Bell's palsy recover completely without any specific therapy particularly where the paralysis is incomplete. Patients with insufficient eye closure to cover the cornea in a recumbent position should be provided with an eye patch to protect the cornea.

Cranial Nerve VIII

Case 12-5: This 39 year old left handed married white female medical clinic employee had experienced much of her life symptoms of car, air or seasickness .Three weeks prior to admission while at an amusement park, she had taken a ride on the "Tower of Terror" which involved a free fall of 200feet. Following the vestibular stimulation ,she developed significant but intermittent symptoms of several types of vertigo: rotational or horizontal and the particularly troublesome symptom that the floor was pitching up to meet her .When this latter symptom occurred, she would become diaphoretic, experience tingling in her hands and decreased vision. Loud noises were painful. On the day of admission she had a particularly severe episode and fell to the floor. Examination in the emergency room indicated that she tended to fall to the right when standing on a narrow base. Her symptoms had improved with meclizine –an antivertigo medication. .

Neurological examination : No remarkable features were present except for

1.minimal weakness in the right lower extremity which had been present for 14 years related to a herniated disk at L5-S1.

2.On rotation with the head in the upright position, horizontal and rotational vertigo developed reproducing that aspect of her symptoms. When rotated with the head down on the shoulder-(a maneuver that places the vertical canal in a horizontal position) the "floor pitching up" sensation was reproduced.

Clinical diagnosis: Labyrinthine vertigo

Laboratory data: The *MRI* demonstrated a very minimal (5 mm) non enhancing cyst within the inferior aspect of the right cerebellum located in the cerebellar tonsil.

Comment: This patient had a long history of vertigo and associated nausea and vomiting occurring in relationship to motion cars, airplanes and boats. In relationship to the significant vestibular stimulation, she developed intermittent episodes of severe vertigo. Her symptoms could be reproduced with rotational maneuvers, the type of vertigo and the accompanying nystagmus varying with the head position during the rotation. The *MRI* findings raised the possibility that a minor lesion in that sector of the cerebellum related to the vestibular system may have predisposed the patient to these symptoms. Although the patient had a sense that loud noises were painful, she had no clear cut cochlear symptoms. The acute onset of vestibular symptoms often triggers the occurrence of autonomic symptoms such as diaphoresis. Anxiety and hyperventilation syndrome with manifestations such as blurring of vision and tingling in the hands.

Other disorders of cranial nerve VIII such as vestibular Schwannoma are considered below in relation to combined syndromes.

COMBINED CRANIAL NERVE SYNDROMES:

Cavernous Sinus Syndrome

Case 12-6: This 61 year old right handed white female developed blurring of vision in the left eye 4 days prior to admission. Two days prior to admission, she noted a left eyelid droop, diplopia on forward gaze and numbness of the left side of the face. There was a past history of hypertension and congestive heart failure both treated and under good control. The patient had been a heavy smoker for over 30 years but had quit 14 years previously. There was a family history of lung cancer ,hypertension and congestive heart failure.

Physical examination: 1) Minor proptosis of the left eye 2)minor fullness of the left tonsillar area.

Neurological examination: Findings were limited to *the following left cranial nerves:*

III: incomplete ptosis of the left eyelid, no significant medial ,or upward movement of the left eye was noted . Depression of the left eyeball was possible. Although the left pupil was slightly smaller than the right (2mm vs 3mm) both responded to light.

VI: no lateral movement of the left eye was obtained.

V: pain sensation was decreased over all three divisions over the left side of the face . As regards the mandibular division, the left side of tongue, the oral mucosa ,lip were also involved .However touch sensation was intact and corneal reflex and gag were normal.

Clinical diagnosis: Lesion of skull base involving left cavernous sinus plus possible involvement of foramen ovale region.

Laboratory data:

CT scan of head demonstrated a mass involving the left cavernous sinus extending into the left middle fossa, and as a soft tissue mass within the sphenoid sinus extending through the sphenoid bone into the nasopharynx. There was as well destruction of the vidian canal. Multiple lesions probably metastatic were also present in the calvarium of the skull. of the head demonstrated extensive infiltration of the left skull base with extensive enhancing tumor within the dorsi sphenoid bone with extension into the sphenoid sinus and cavernous sinus

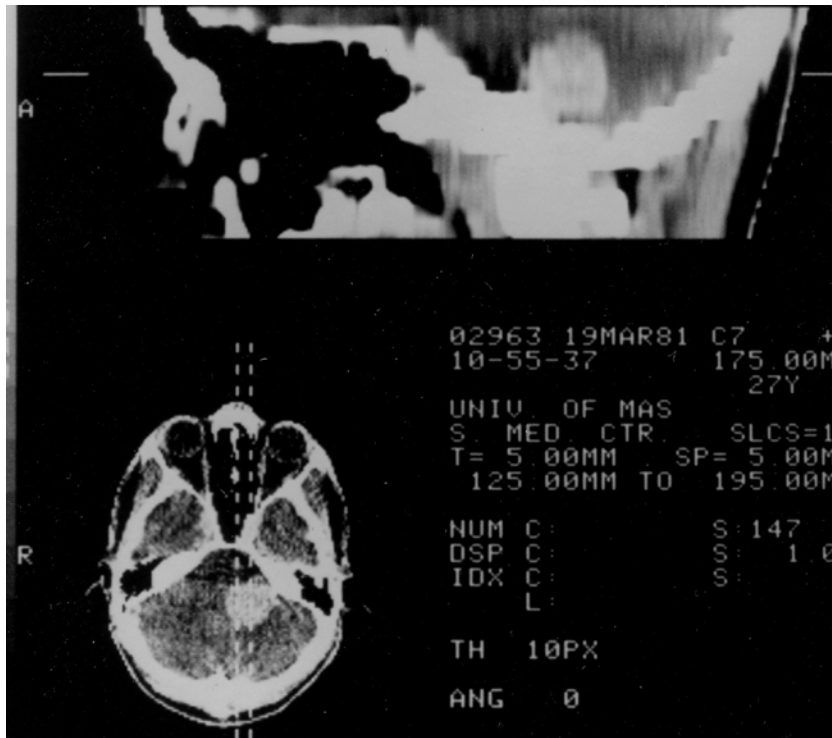


Fig 12-2; Case 12-6. Lesion of skull base involving left cavernous sinus plus possible involvement of foramen ovale region.

There was evidence of the skull lesions involving the parietal bone. There also was apparent thrombosis of the left superior sphenoidal venous sinus.

3. *Chest x-rays and CT scan of the chest* revealed a 3cm nodule in the in the right apical lung area, with enlarged paratracheal and paracarinal nodes.

4. *CT scan of the pelvis* indicated metastatic destruction of the right bony symphysis pubis and a left adnexal cystic mass.

5. *A biopsy of the paratracheal nodes* revealed poorly differentiated small cell carcinoma.

Subsequent course: The patient was begun on radiotherapy and chemotherapy as well as dexamethasone. At the time of hospital discharge-8 days following admission, she had a minor ability to move the left eye medially but had no lateral, upward or downward movement of the eye.

Comment: The simultaneous development of diplopia, and numbness of the left side of the face suggested the possibility of involvement of the cavernous sinus or of multiple cranial nerves at the base of the skull or of the superior orbital fissure. All three of the cranial nerves supplying the motor action of the globe could be involved in these locations. The examination indicated pathology involving at least cranial nerves 3, and 6.

Whether cranial nerve 4 was also involved is not certain. This nerve will act through the action of the superior oblique muscle to depress the eyeball (globe) when the action of the medial rectus has already resulted in adduction of the eye. With the eye in neutral position, the inferior rectus is the main depressor of the globe. In neutral position, the action of the superior oblique is to rotate the globe inward. This specific action was not noted in this patient.

In terms of the trigeminal nerve findings, both divisions V1 and V2 pass through the lateral wall of the cavernous sinus. Only V1 passes through the superior orbital fissure. All 3 divisions could be involved if the trigeminal ganglion were to be involved. A lesion at the base of the skull could involve V2 at the foramen rotundum and V3 at the foramen ovale.

The fact that the extraocular findings developed simultaneously with the trigeminal findings makes the cavernous sinus location the more likely although one would also have to postulate involvement also of the area of the foramen ovale or the trigeminal ganglion to explain the involvement of division 3.

The underlying pathology was a small cell carcinoma arising in the lung. Such a pathology may also produce carcinomatosis of the meninges, with involvement of cranial nerves and this could be complicating the analysis outlined above.

Case 12-7: This 64-year-old, white, right-handed housewife was admitted to the hospital for evaluation of progressive 10-15 year loss of hearing in the right ear with total deafness during the several months prior to admission plus progressive right facial numbness and weakness and increasing headaches. During the two years prior to admission the patient had noted the gradual development of an unsteadiness in walking (ataxia of gait). This had recently worsened, leading to several falls. During this same time a progressive numbness of the right side of the face had developed, and in recent months a weakness of the entire right side of the face had also occurred. During recent months, a bifrontal, or right sided frontal and vertex headache developed, with occasional diplopia. A minor change in hearing in the left ear had also occurred.

Neurological examination: the following limited findings were present

I. Cranial nerves:

II. Fundi—There was evidence of an increase in intracranial pressure with bilateral papilledema (elevation of the discs with old and new retinal hemorrhages).

V. There was a decrease in pain and light touch over the maxillary and mandibular divisions of the right trigeminal nerve. The right corneal reflex was absent and the patient did not feel touch over the cornea.

VII. A moderate right peripheral facial weakness was present with a droop to the right corner of the mouth, a widened right palpebral fissure, and an absence of blinking with the right eye.

VIII. (a)Hearing was markedly decreased in the right ear (both air and bone) compared to the left.

(b)Ice water caloric labyrinthine stimulation indicated no response of the right ear; there was normal response of the left ear.

(c)There was a fine nystagmus on gaze to the left and to the right.

2. *Motor system:* Gait was slightly broad-based with some weaving to the right or left. She was unable to walk a tandem gait (narrow-based heel to toe walking). However no dysmetria was present in the upper extremities.

Clinical diagnosis: Cerebellar pontine angle tumor, most likely a vestibular Schwannoma (acoustic neuroma).

Laboratory data: *Neuroimaging studies* revealed a mass lesion displacing the aqueduct and fourth ventricle posteriorly, slightly upwards and to the left, consistent with a tumor at the right cerebellopontine angle, e.g., a vestibular Schwannoma.

Subsequent course: Dr. Samuel Brendler performed a right suboccipital craniotomy. When the right cerebellar hemisphere was retracted and the right lateral third of the cerebellum amputated, a large neuroma (Schwannoma) was exposed, enveloping cranial nerves VII and VIII and extending into the internal auditory meatus. At its lower end, the capsule of the tumor was also loosely attached to nerves IX, X and XI. At its superior end, the tumor was adherent to nerve V. A portion of the tumor extended superiorly through the hiatus of the tentorium. At several points, the tumor capsule was adherent to the brain stem. In the removal of the tumor, neither cranial nerves VII or VIII could be spared. A small portion of nerve V was also removed with the tumor capsule. As the tumor was being freed from the tentorium and brain stem, there were several episodes of hypotension and cessation of spontaneous respiration. It was therefore necessary to terminate the procedure after 60 per cent of the tumor had been removed.

Follow up evaluation, 10 weeks and 9 months after surgery, revealed the following residual abnormalities:

1.Cranial nerves:

V: Pain and touch were decreased on the right side of the face and the right masseter was weak.

VII: A complete right peripheral facial palsy was present. (The right eyelids had been sutured closed to avoid injury to the right cornea - tarsorrhaphy).

VIII: Hearing was completely absent in the right ear and decreased on the left.

IX,X: There was difficulty in swallowing; gag reflex was depressed and speech indistinct.

2.Motor:The patient was able to walk with assistance. Her gait was unsteady. A slight appendicular ataxia was evident bilaterally on finger-to-nose and heel-to-shin tests.

Comment: The symptoms and findings presented by this patient were those to be expected with a large tumor in the right cerebellar pontine angle. There was a combination of cranial nerves VIII, VII, and V, in addition to cerebellar findings. The tumor, moreover, had displaced brain stem structures, distorting the aqueduct and fourth ventricle. A significant increase in intracranial pressure had been produced. The occasional diplopia reported by the patient may well have suggested some of the bilateral cranial nerve VI dysfunction to be expected when a significant increase in intracranial pressure occurs. As regards the origin of this large tumor, the earliest symptoms were related to cranial nerve VIII, but other cranial nerves had been involved as the tumor progressed and other cranial nerve symptoms therefore developed .Note that in occasional cases, neurofibromas (Schwannomas) may arise from cranial nerves VII, V, IX; the most common site, however, remains nerve VIII.

The patient had been seen relatively late in her disease course. The tumor at operation was certainly very large and presented a formidable problem for the neurosurgeon. The complications of the surgical procedure were not unusual when one considers that nerve VII was completely surrounded by the tumor and that cranial nerve V was also attached to the tumor. In some of these cases, the best result involves a subtotal removal of the tumor, attempting to preserve the continuity of the involved cranial nerves. It should of course be noted that prime indications for neurosurgical intervention were present: increased intracranial pressure and distortion of brain stem structures.

At the present time the use of non-invasive techniques: CT Scan, MRI and brain stem auditory evoked potentials(BAER) allow early diagnosis in almost all patients who present with only mild changes in hearing. The least expensive of these techniques , the BAER, is abnormal in 98% of patients with vestibular Schwannomas (see Martuza et.al 1985) and Chiappa 1989). If the study is abnormal demonstrating a delay between Wave I which is generated in the cochlea and the waves generated in the brain stem, then an MRI with contrast maybe performed. Significant advances have also occurred in operative management related to the use of the operating microscope and intra-operative monitoring of the function of the VIIth and VIIIth cranial nerves. In the recent series from the Mayo Clinic (Harner et.al, 1987)-facial nerve function was intact postoperatively in 81% of 162 cases and in all cases where the tumor was less than 2cm in size. Since the tumor arises primarily from the Schwann cells of the vestibular portion of the nerve, it is theoretically possible in early cases to preserve cochlear function. In the Mayo Clinic Series, the cochlear nerve was preserved in 55 of the 162 cases but only 14 patients had actual preservation of hearing. Thus it is rare to see any longer patients who present the far advanced natural history and complications observed in this patient.

The subject of the relatively rare entity of bilateral acoustic neuromas(Neurofibromatosis 2) has been discussed in chapter 9 (in relationship to the more common neurofibromatosis 1). This disease is usually manifested earlier in life than the more common unilateral acoustic neuroma. Inheritance is autosomal dominant possibly related to a partial deletion in the long arm of the chromosome 22 (see Martuza Eldridge 1988, Wertelecki et. al. 1988).

Vestibular Schwannoma

Case 12-8:This patient was originally evaluated in 1993 at age 71 with a 50 year history of loss of hearing in the right ear. In recent months he had noted an instability of gait .Examination at that time by Dr.Alex Danylevich demonstrated a total loss of hearing in the right ear. He had poor tandem gait ,swaying to the right side. A slight intention tremor and dysdiadochokinesis (disorganization of alternating movements) were present in the right upper extremity. An MRI at that time demonstrated a 4cm diameter mass with heterogenous enhancement arising within the right internal auditory canal and displacing the pons and medulla to the left and also compressing the right cerebellar hemisphere. The 4th ventricle was distorted but no hydrocephalus was present at that time. Surgical resection of this tumor was recommended at that time but refused by the patient. In 1994 .Increasing problems with balance developed ; he tended to fall to the left or right when first standing.

Examination now indicated additional findings of coarse sustained nystagmus on horizontal gaze especially to the right with horizontal and to a lesser degree rotatory components. The patient again refused surgical resection of the tumor. His symptoms were stable until 1997 when increasing gait problems, urinary incontinence and difficulty with memory developed. Imaging studies indicated hydrocephalus and a shunt procedure was performed resulting in improvement. In 2000, increased unsteadiness of gait, right lower extremity weakness, dysarthria of speech, difficulty in gaze to the right and a right peripheral facial weakness developed. *MRI* studies demonstrated severe distortion of the brain stem by the tumor (**Fig. 13-2**). The patient was to undergo surgery but multiple medical problems intervened.

Other Tumors in the Cerebellopontine Angle. Although less frequent, other types of pathology are found in this location: meningiomas (**Fig. 2-10**) arising from arachnoidal cell nests) and cholesteatomas (epidermoids). A recent series from the Mayo Clinic (Laird et al 1985) indicated 20 meningiomas over a six year period compared to 160 acoustic neuromas over a similar period (Harner et al 1985). Specific neurological deficits were as frequent as in patients with acoustic neuromas. Diagnosis may be made with contrast enhanced MRI or if not available contrast enhanced CT Scan.

Jugular Foramen Syndrome

Case 12-9: This 28 year old right handed married white male, junior high school science teacher was referred for evaluation of weakness in movements at the left shoulder which began approximately 5 years ago with a sense of minor soreness in the left shoulder and scapula areas and an inability to abduct above 90 degrees with the left arm. The problem had progressed slowly since that time, with the subsequent development of atrophy in the shoulder area and winging of the scapula. He denied any actual tingling in the arm or any radicular pain etc.

Past history was negative except for problems related to vocal cords. Several months prior to the onset of the shoulder symptoms, he had an upper respiratory infections and developed severe hoarseness. Examination by an ENT specialist (Dr.Fine) at that time indicated a paralysis of the left vocal cord. The left vocal cord was fixed slightly off midline. The right vocal cord moved well but did not fully compensate.

Family history was not remarkable except that his mother died of rheumatic heart disease in her 40's.

General physical examination: there was a café au lait spot on the left forearm 1x2 cm in size, and a large 8x5 cm café au lait spot on the right posterior leg just below the buttock..

Neurological examination:

1. *Mental Status:* intact

2. *Cranial Nerves:*

X: the uvula pulled very slightly to the right on gag. There was only a minimal suggestion of any hoarseness at this time. Gag was intact. Laryngoscopy by the ENT specialist indicated paralysis of the left vocal cord.

XI: There was significant weakness and marked atrophy of the left sternomastoid muscle (**Fig 12-1**). : Minor ridges of atrophy and fasciculations were seen on the left side of the tongue (**Fig.12-2**). There was marked atrophy of the left trapezium seen in both elevation of the shoulder and in abduction of the scapula with involvement of both the middle and lower portions with winging of the medial edge of the scapula (**Fig.12-3**)

XII.

3) *Motor System:* there was questionable minimal weakness of muscles about the left shoulder: supraspinatus, infraspinatus and serratus anterior.

4) *Reflexes:*

a) Deep tendon reflexes were hyperactive except for possible mild depression of finger jerks on the left compared to the right.

b) Plantar response on the right was equivocal ;that on the left was flexor.

5) *Sensory system:* no definite abnormality was present.

Clinical diagnosis: Jugular foramen tumor-probably neurofibroma.

Laboratory data:

1) *Brain stem auditory evoked potential* was normal for the right ear but demonstrated a delay in the I-II interval for the left ear..

- 2) *Tomograms of the petrous bone* showed marked bone destruction in the region of the jugular foramen.
- 3) *CT Scan*. The left skull base demonstrated marked erosion of the left jugular foramen, extending anteriorly to the carotid canal and laterally to the base of the petrous bone. There was a well defined enhancing mass which extended from the jugular foramen superiorly to the height of the left petrous apex. (**Fig. 12-4**). Sagittal and coronal reconstructions demonstrated the continuity of this mass with the jugular foramen. The 4th ventricle was compressed and shifted from left to right. There was a slight effacement of the left CP angle cistern.

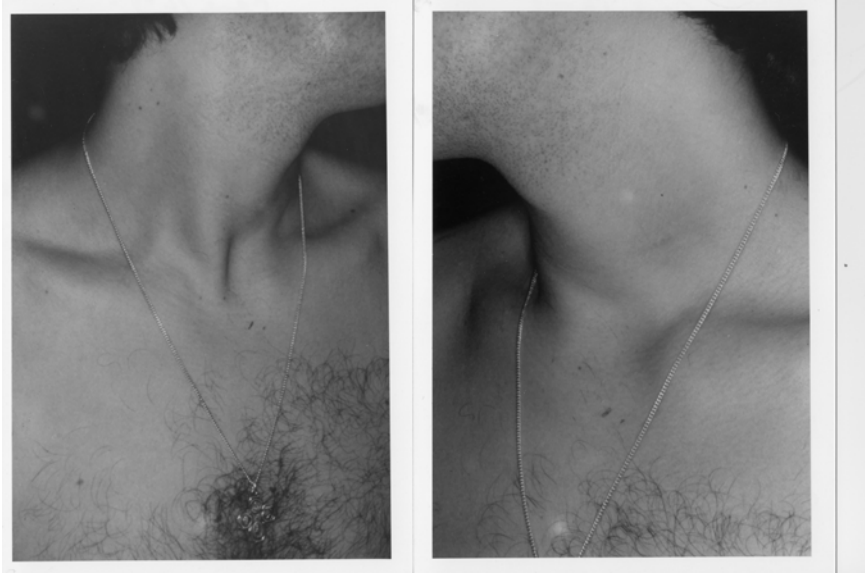
Subsequent course: Dr. Bernard Stone performed a suboccipital craniotomy, revealing a large tumor mass in the lower inferior portion of the left cerebellar-pontine angle originating from the jugular foramen. All of the intracranial extent of the tumor was removed as was most of the tumor within the jugular foramen. However the remainder of the tumor which extended through the foramen into the extracranial space could not be removed by this approach. Histological examination of the tumor confirmed the preoperative impression of a Schwannoma (neurofibroma) of the 9th or 10th cranial nerves which had to be sacrificed during the procedures.

The patient did well and was readmitted four months later for removal of the extracranial portion of this dumbbell tumor at the base of the skull by Dr. Fine. The tumor-mass enmeshed the structures exiting from the jugular foramen.

CT scans 4 years later indicated recurrence of both of the intracranial and the extracranial portion of the tumor (extending again into the parapharyngeal space).

Comment: The Schwannoma in this case presented initial symptoms relevant to cranial nerve 10 that is paralysis of the left vocal cord. Occasionally patients will have a vocal cord paralysis following an upper respiratory infection possibly due to involvement of the recurrent laryngeal nerve. In this case however, within several months, the first signs of involvement of the 11th cranial nerve appeared and progressed over the next 5 years. The CT scan demonstrated a large mass which extended from the jugular foramen into the cerebellar pontine angle. The surgical procedures also indicated the extension of this mass into the extracranial parapharyngeal space. Whether the involvement of cranial nerves 10 and 11 occurred in the extramedullary space proximal to the jugular foramen or within the foramen is unclear. Usually the syndrome of the jugular foramen includes signs relevant to cranial nerve 9 as well but this patient had no involvement of sensation in the posterior pharynx and no clear cut involvement of taste over the posterior 1/3rd of the tongue. As regard the involvement of cranial nerve 12, this could have involvement by this large tumor mass in the intracranial area or the parapharyngeal area. This large tumor mass also produced minor subclinical compromise of cranial nerve 8-evident on the brain stem auditory evoked potential with a delay between the cochlea and the cochlear nucleus. As regards the apparent minor weakness at the left shoulder, these findings may have reflected a failure of stabilization at the left shoulder due to the involvement of the trapezius muscle. The right sided Babinski sign probably reflected the distortion of the left pyramidal tract due to the brain stem distortion produced by the tumor.

As regards the question as to whether this patient had neurofibromatosis type I—the following maybe noted: he had no peripheral neurofibromas, no family history and had only 2 café au lait spots (6 or more over 15 mm in diameter after puberty constitute a significant number).Moreover the patient had none of the other cutaneous or bony abnormalities seen with this disorder.



Atrophy of Sternomastoid muscle

Fig 12-1.Case 12-9.

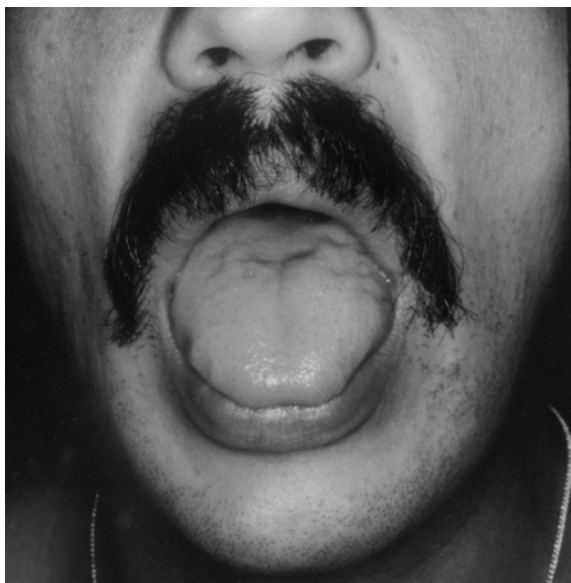


Figure 12-2.Case 12-9. Atrophy of tongue



Figure 12-3. Case 12-9. Atrophy of trapezius.

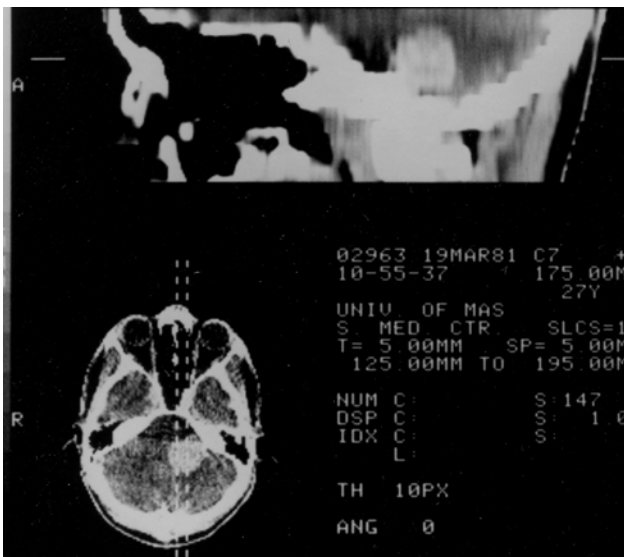


Figure 12-4. Case 12-9. There was a well defined enhancing mass which extended from the jugular foramen superiorly to the height of the left petrous apex

CHAPTER 13: BRAIN STEM CLINICAL CONSIDERATIONS

Case history 13-1 illustrates the effects of platybasia secondary to Paget's disease on cranial nerves, spinal cord and brain stem..

Case 13-1. This 57-year-old, white insurance salesman 5 years prior to admission first noticed difficulty in obtaining a standard-size hat. Two years prior to admission the patient first noted the gradual onset of a steadily progressive difficulty in walking, characterized by a loss of balance. He had experienced increasing difficulty in standing erect and had fallen on several occasions. The patient had noted increasing discomfort at the occipital area of the head. Two months prior to admission the patient had noted a hoarseness of his voice, a weakness or tremor of the tongue, a difficulty in articulating words, and a difficulty in swallowing, and more recently the patient had noted numbness of all fingers, the right more than the left, and a correlated clumsiness in the manipulation of small objects. In the several weeks prior to admission, the patient had noted difficulty in focusing his eyes. He had also noted diplopia particularly when gazing to the right.

Neurological examination: Mental status, strength, deep tendon reflexes, and sensation over limbs and body were intact. Findings were limited to:

1. Cranial nerves:

- a. A right lateral rectus weakness was present with diplopia on right lateral gaze.
- b. Horizontal nystagmus on lateral gaze to either side was present.
- c. Pain and to a lesser degree touch sensation was significantly decreased in the ophthalmic and maxillary divisions of the left fifth nerve, with a decreased left corneal reflex.
- d. Hearing (both bone and air) was decreased bilaterally.
- e. Gag reflex and pharyngeal tactile sensation were bilaterally decreased particularly on the left. The uvula pulled to the right.
- f. Lingual movements and lingual sounds were slowly performed although no definite weakness or atrophy of the tongue was present.

2. Motor system:

- a. Gait was grossly reeling and ataxic.
- b. Ataxia was present on finger-to-nose and heel-to-shin tests of cerebellar function.

3. Head and neck: The head was large. The neck was short. There was limitation of movement on turning the head laterally.

Clinical diagnosis: Paget's disease. Platybasia with involvement of lower cranial nerves and cerebellum.

Laboratory data: The relevant findings included:

1. *Skull x-rays* showed marked thickening of the diploe with the changes characteristic of Paget's disease. Well advanced platybasia was present with the tip of the odontoid of the axis found to be 25 mm. above McGregor's line. (This is a line drawn from the posterior margin of the hard palate to the inferior surface of the basal occipital bone; normally the odontoid should not extend above this line by more than 4 to 5 mm).
2. *Alkaline phosphatase* was significantly elevated (2x the upper limit of normal).

Subsequent course: A suboccipital decompression was performed by Dr. Bertram Silverstone. The bone of the cranium was very thick. There was marked compression of the lower medulla and upper cervical cord by the anterior rim of occipital bone forming the posterior margin of the foramen magnum. The posterior arch of the first cervical vertebra was also compressing the underlying cervical spinal cord. Postoperatively, there was a significant improvement. Follow-up one month later indicated that the patient had regained fine movement skills in the hand. His gait was markedly improved, although still slightly wide-based. Lower cranial nerve findings were no longer present. The sixth and eighth cranial nerve findings were unchanged. Follow-up evaluation one year later indicated continued improvement in gait. Nystagmus was present but the weakness of nerve VI had resolved.

Several years after the surgery patient had increasing ataxia of gait, increasing diplopia, and decreasing vision in the left eye. Within two years bilateral medial rectus weakness was present. Re-evaluation over the next year indicated progression of ataxia. Skull x-rays indicated a progression of the degree of basilar invagination. The patient refused any additional surgical procedures.

Comment: The findings in this case indicated involvement of the cerebellum and lower cranial nerves, particularly the vagus and glossopharyngeal nerves: hoarseness of voice, defect in elevation of the uvula and defective sensation in the posterior pharynx. In addition, there was involvement of the sixth and trigeminal nerves. Whether the fifth nerve involvement related directly to platybasia or whether this reflected occlusion of the ostia of the skull by Paget's disease would not be certain. Involvement of nerve VIII usually reflects narrowing of the internal auditory foramen with compression of the nerve.

Basilar impression occurs in conditions other than Paget's disease. In the majority of cases, the defect reflects a congenital malformation of the basal occipital bone. There are often associated malformations of bone: a fusion of the occipital bone with the atlas, a dislocation of the odontoid³, a fusion of the vertebrae (Klippel-Feil abnormality), cervical spinal bifida, or a small foramen magnum. There may also be associated malformations of the central nervous system, e.g., the Arnold-Chiari malformation—elongation of the inferior portion of the cerebellum through the foramen magnum into the cervical canal or persistence of the embryonal cervical flexure with apparent downward displacement of the medulla and cervical cord. (Refer to the discussion of syringomyelia in the spinal cord chapter for an illustration). Malformations of the meninges (arachnoid cysts) or of the roof of the fourth ventricle, with absence of the foramina of Luschka and Magendie (Dandy-Walker syndrome; see Embryology Chapter) may be present. In occasional cases, syringomyelia or hydrocephalus also will be found. Although many of these malformations will produce their effects in infancy or childhood, not infrequently the first neurological manifestation may be delayed until adult life.

Case 13-2 provides an example of a dorsolateral medullary infarct which also involved the posterior inferior cerebellar artery territory of the cerebellum.

Case 13-2 (Patient of Dr. Steven Donhowe): This 53 year old male customer service representative on the morning of admission (01-07-2001) while seated at his computer, had the sudden onset of vertigo accompanied by nausea and vomiting. He felt better if he was not moving. He also noticed some incoordination of his left arm and leg. When he stood, he leaned and staggered to the left. He also noted numbness of the left side of his face. Initially, he experienced some vaguely defined left ear pain or tinnitus. Several hours later, he noted increasing difficulty in swallowing and his family described a minor dysarthria. He was evaluated at the emergency room of his local hospital where a CT scan of the head was reported as normal. He was then transferred to St Vincent hospital for neurological evaluation. Past history was negative except for a 2 pack per day cigarette smoking history for at least the last 10 years and a possible sinusitis two weeks prior to admission.

Physical examination : Negative except for elevated blood pressure of 166/90.

Neurologic examination:

1. Mental status: Intact
2. Cranial nerves:
 - a. The right pupil was 3mm in diameter, the left was 2mm in diameter. Both were reactive to light. There was partial ptosis of the left eye lid. A horizontal nystagmus was present on left lateral gaze, but extraocular movements were full.
 - b. Pain and temperature sensation was decreased over the left side of the face but touch was intact.
 - c. Speech was mildly dysarthric for lingual and pharyngeal consonants. Secretions pooled in the pharynx. Although the palate and uvula elevated well, the gag reflex was absent. Tongue movements were intact.
3. Motor system:
 - a. Strength was intact except for a minimal left pronator drift.

³ Fractures and dislocations of the odontoid may occur in relationship to trauma and are particularly a frequent occurrence in patients with advanced rheumatoid arthritis.

- b. Cerebellar evaluation: A dysmetria was present on left finger to nose test and heel to shin tests ,When the patient sat up, he tended to drift to the left. When he attempted to stand, he was very unsteady and tended to fall to the left.
4. *Reflexes*: Deep tendon stretch reflexes were symmetrical and physiologic except for ankle jerks which were absent. Plantar responses were flexor.
5. *Sensory system*: Pain and temperature sensation were decreased on the right over the right arm and leg but all other modalities were normal.

Clinical diagnosis: 1.Dorsolateral medullary infarct. 2. Decreased ankle jerks due to possible diabetic peripheral neuropathy

Laboratory data:

1. *Random blood sugar* was elevated to 225 mg%, fasting was elevated to 196 mg%. Hemoglobin a1c was elevated to 9.5 compared to normal of <6.0. *Total cholesterol* was elevated to 340mg% compared to normal of <200mg%. *Low density lipoproteins (LDL)* were elevated to 261 mg%, *High density lipoproteins(HDL)* were 42mg% and triglycerides;183mg%.
2. *MRI* (Fig.13-12): A significant acute or subacute infarct was in the posterior inferior cerebellar artery territory of the left cerebellum and dorsolateral medulla. The *MRA* suggested possible occlusion of the left vertebral artery ,however the vertebral arteries were not well visualized.

Subsequent course: The patient failed his first swallowing test and was still unable to swallow by day 6. A percutaneous endoscopic gastrostomy (PEG) tube was placed. By the time of transfer to a rehabilitation facility ,12 days after admission, gait had improved ,he could walk with a walker. Finger to nose movements had improved. Speech and sensory examination had returned to normal.

Comment: The initial symptoms in this case suggested involvement of the vestibular system (vertigo, nausea and vomiting) and the cerebellum or cerebellar peduncle (incoordination of the left arm and leg). Subsequent symptoms suggested involvement of the trigeminal system on the left side and of the nucleus ambiguus or the 10th cranial nerve (dysarthria and dysphagia).The examination confirmed the involvement of these areas but also provided additional information. The involvement of the trigeminal system was more specific to the descending spinal tract and nucleus of the cranial nerve V, since pain but not touch sensation over the left side of the face was affected. In addition the adjacent left spinal thalamic system was involved since pain and temperature sensation were selectively affected in the right arm and leg. In addition a partial Horner's syndrome was present on the left side(the pupil was smaller and there was partial ptosis) suggesting involvement of the descending sympathetic pathway. Taken all together this constellation of symptoms and signs, suggests an upper medullary location involving the dorsolateral tegmentum. Had cranial nerve 10 not been involved, ,the location of the lesion would have been less precise . A lesion in the lower half of the pons would have produced all of the other findings. However such a lower pontine lesion would have been accompanied by involvement of the auditory nerve or cochlear nucleus and the facial nerve. Such an inferior dorsal lateral lesion of the pontine tegmentum would fall within the territory of the anterior inferior cerebellar artery (discussed below). In the era before CT and MRI scans, this patient would be classified as having only an infarct of the dorsolateral medulla ,the involvement of the posterior inferior cerebellum would be concealed ,since the effects of a lesion of the inferior cerebellar peduncle would be in general similar to a lesion of this area of cerebellum. With these new techniques , we are able to see the full extent of the lesion. Thus occlusion of the posterior inferior cerebellar artery may produce an infarct of the lateral medulla , or of the appropriate cerebellar territory or a combined infarct of both territories. Embolic occlusion is more likely to produce , the limited cerebellar infarction .

Although, this patient had been asymptomatic, multiple predisposing factors were discovered at the time of his hospitalization : heavy tobacco use ,hypertension, diabetes mellitus ,and high cholesterol level. Prevention would have had to address all of these issues.

It is more common to encounter variations of the syndrome rather than the pure syndrome. In some patients a combined lateral and paramedial medullary syndrome could be found Fig.13- 17(A more detailed discussion of course and prognosis will be found in Norrving 1991).

Lateral Medullary Infarct :The following case history provides an additional example of this syndrome

Case 13-3. This 66-year-old, retired white male 10 days prior to admission noted at his evening bath that he was unable to detect the temperature of the water with his left foot and ankle. Several hours later, he awoke from sleep to void and found that his balance was defective; he tended to fall to the right side .He also noted a strange altered sensation over his right ear and face. The following morning, a more marked numbness of the right side of the face was present, in addition to headache, dysarthria, nausea and vomiting. The patient was admitted to his local hospital where skull x-rays and lumbar puncture was essentially normal. His symptoms were beginning to clear at the time of his transfer to the neurological center.

Past history: 6 weeks prior to admission he had been treated for mild symptoms of congestive heart failure.

Neurological examination:

1. Mental status: intact
 2. Cranial nerves:
 - a. there was a partial ptosis of the right eyelid as well as a smaller pupil on the right.
 - b. nystagmus was present on lateral and forward gaze.
 - c. pain but not touch sensation was decreased over the right half of the face. The right corneal reflex was absent.
 - d. the uvula deviated to the left, with right gag reflex depressed.
 - e. the voice was hoarse.
 3. Motor system:
 - a. Strength: intact
 - b. The patient was ataxic standing on a narrow base, tending to fall to the right.
 - c. A side to side intention tremor was present in the right upper extremity on finger to nose testing .A similar dysmetria was apparent in the right lower extremity in heel to shin testing.
 4. Reflexes:
 - a. Deep tendon reflexes were symmetrical and 2+.
 - b. Plantar responses were flexor
5. *Sensory system:* Pain and temperature sensation was decreased over the left lower extremity, an improvement compared to the earlier finding of a decrease over the entire left side below the cervical 2 segment. All other modalities were intact.

Clinical diagnosis: Lateral (dorsolateral) medullary infarct

Subsequent course: Almost all neurological symptoms and signs resolved over the next 15 days.

Comment: This patient presents essentially all the features found in an infarct involving the territory of the posterior inferior cerebellar artery: the dorsolateral medullary syndrome. The initial symptom suggested involvement of the right lateral spinothalamic pathway pain and temperature pathway-unable to detect the temperature of the bath water with the left lower extremity. The subsequent examination confirmed such a deficit in sensation involving the entire left side below the level of cervical 2. Shortly thereafter, sensory symptoms developed on the right side of the face-suggesting possible involvement of the trigeminal system. The subsequent examination demonstrated the specific involvement of pain but not touch sensation on the right side of the face. Thus the more specific involvement of the descending spinal tract/nucleus of the trigeminal system could be deduced. Both the lateral spinothalamic tract and the descending spinal tract are found closely located in the dorsolateral tegmentum of medulla and lower pons. The nausea and vomiting suggested possible involvement of the vestibular nuclei. The presence of nystagmus would be consistent with the involvement of the vestibular system. The vestibular nuclei are located in the lateral tegmentum of lower pons and medulla. The defect in balance could have suggested involvement of either the vestibular or cerebellar system. The findings on examination of lateralized intention tremor in right arm and leg would be consistent with the lateral tegmental location and would more specifically implicate the inferior cerebellar peduncle (conveying the spinocerebellar and cuneocerebellar pathways). The partial Horner's syndrome: partial ptosis of

right eyelid and smaller pupil on the right would implicate the descending sympathetic pathway found in a lateral tegmental location in the medulla or lower pons. The symptom of dysarthria, and the findings of depressed gag reflex on the right with the defect in uvula elevation on the right (so that the uvula pulled to the left) plus the hoarseness all suggested involvement of the right nucleus ambiguus. This nucleus is the source of the vagal innervation of the larynx and pharynx and is located in the dorsolateral tegmental area of the upper medulla supplied by the posterior inferior cerebellar artery. In many cases the actual occlusion is located in the vertebral artery and not in the posterior inferior cerebellar artery.

It is more common to encounter variations of the syndrome rather than the pure syndrome. In some patients a combined lateral and paramedian medullary syndrome could be found Fig.13- 17(A more detailed discussion of course and prognosis will be found in Norrving 1991).

The following case history 13-4 provides an example of ischemia and infarction within the territory of the anterior inferior cerebellar artery.

Case 13-4. This 55-year-old, white, married, machinery salesman, while driving, had the sudden onset of pain on the left side of the head, accompanied by dizziness (counter-clockwise vertigo). The headache soon became generalized and within a short time nausea, projectile vomiting, and anorexia developed. At the same time, the patient noticed that he could not hear sounds in the left ear. Diplopia was present on left lateral gaze. The patient was able to continue driving slowly to his home. When he reached home and walked from the car or sat on the edge of his bed, he noted that he tended to fall to the left.

The symptoms were unrelieved by a night of rest; the patient was brought to the hospital emergency room and subsequently admitted to the hospital.

Past history: Two years previously, the patient had experienced a “dizzy spell” and headache requiring bed rest for 10 days. Elevated blood pressure had required treatment from that time with antihypertensive medication. Obesity of a marked degree had been present for 20 years.

General physical examination:

1. The patient was an obese male who was alert and cooperative.
2. Blood pressure was elevated to 220/110.
3. Skin color was florid.

Neurological examination:

1. Mental status:

- a. Orientation and recent and distant memory were all intact.
- b. Although speech was dysarthric, there was no impairment of higher language functions.
2. Cranial nerves:
 - a. Fundi and visual fields were intact.
 - b. Pupillary responses were intact.
- c. A marked coarse horizontal nystagmus was present at rest on forward gaze and in all directions of gaze but was most marked on left lateral gaze. On upward and downward gaze, vertical nystagmus was also noted. Eye movements were described as “unstable and rolling over” with lack of sustained fixation. One examiner felt that a bilateral weakness of the lateral rectus muscle was present. Convergence and upward gaze were noted to be intact.
- d. Pain sensation was selectively decreased over the left trigeminal distribution, most significantly over the mandibular division. The left corneal reflex was absent and left corneal sensation was reduced. There was a marked weakness of the left masseter muscle.
 - e. An incomplete left peripheral facial palsy was present with greater involvement of the lower half of the face.
 - f. Taste sensation was absent on the anterior two-thirds of the left side of the tongue.
 - g. The left ear was totally deaf.
 - h. The gag reflex was absent on the left. The left half of the uvula and soft palate failed to move on elevation.
 - i. On protrusion, the tongue deviated to the left.
3. Motor system:
 - a. Strength was intact except for very minimal weakness extending the left wrist and elbow.
 - b. Tone was normal.

c. Alternating movements of the left hand and foot were impaired. There was an ataxia and side-to-side intention tremor apparent in the left upper extremity on finger-to-nose test and in the left lower extremity on heel-to-shin test.

d. On attempting to sit or stand, the patient fell to the left.

4. Reflexes:

a. Deep tendon reflexes were questionably more active on the left at the biceps, triceps, and quadriceps. The asymmetry was of minimal degree.

b. Plantar response on the right was extensor, on the left equivocal.

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

6. *Vessels*: The carotid pulses in the neck were strong. The blood pressure in the two arms was equal.

Clinical diagnosis: Basilar artery ischemia and infarction with predominant involvement of the territory of the anterior inferior cerebellar artery

Laboratory data:

1. *Skull x-rays* were negative.

2. Electroencephalogram was normal.

3. *Electrocardiogram* was abnormal and suggested left ventricular hypertrophy (presumed secondary to the patient's hypertension).

4. *Lumbar puncture* demonstrated an elevated cerebrospinal fluid pressure of 275 mm. of water. No cells were present and the protein was normal at 35 mg./100 ml.

5. *Brachial arteriograms* demonstrated an area of relative avascularity in the inferior one-half of the cerebellum. There was a marked tortuosity of the basilar artery secondary to atherosclerosis with an aneurysmal dilatation present at the apex of the basilar artery.

Hospital course: Because of the severe headache and elevated cerebrospinal fluid pressure, arteriograms were performed to rule out an atypical but treatable space-occupying lesion in the posterior fossa (such as an intracerebellar hematoma) with the results as indicated. In actuality both symptoms were most consistent with the edema that accompanies an acute cerebellar infarction (the area of relative avascularity in the inferior cerebellum) which must have been present in addition to the brainstem infarction. Within 6 days, eye movements were described as more stable and a left lateral rectus weakness could now be more clearly defined. The slight reflex asymmetry was no longer present, plantar responses were flexor, and strength was intact. The persistent findings at this time related to nystagmus, left cranial nerves V, VI, VII, and VIII, and to cerebellar findings involving the left arm and leg. Within an additional 10 days, the patient was able to walk with assistance, although he still tended to fall to the left. The patient had continued improvement and was transferred to the rehabilitation division. By the time of his eventual rehabilitation discharge, 9 weeks after the acute admission, the patient was able to walk with a cane. He was described as independent in dressing and shaving. A variable but improving diplopia was still present on lateral gaze to the left or right and at times on superior gaze. On upward gaze, the separation of images was vertical, suggesting an involvement of the superior rectus muscle.

Comment: The combination of vertigo, left-sided deafness, vomiting, left peripheral facial palsy, and left-sided ataxia, suggests a disease process involving the lateral tegmentum of the caudal pons or the cerebellar-pontine angle. Thus, this particular combination of symptoms, accompanied by headache, might also be found in a tumor (a vestibular Schwannoma) at the cerebellar-pontine angle. The suddenness of onset of symptoms, however, is more in favor of a vascular accident, in this case ischemia and infarction within the territory of the anterior inferior cerebellar artery. The vertigo and vomiting may be related to the acute involvement of the vestibular nuclei or nerve. The deafness is due to involvement of the entering auditory division of nerve VIII or of the cochlear nuclei. The left-sided ataxia suggests a lesion involving the inferior or middle cerebellar peduncle or the left half of the cerebellum. The facial palsy suggested damage to the left facial nerve or to the motor nucleus of this nerve. The partial nature of the palsy with greater involvement of the lower face but with some involvement of the upper face is usually more in favor of nuclear rather than peripheral nerve involvement.

The decrease in taste on the anterior two-thirds of the tongue in all likelihood indicates involvement of fibers which have entered the brain stem from the geniculate ganglion in company with the facial nerve to join the tractus solitarius (or involvement of the tractus solitarius per se). These fibers whose bipolar

neurons are located in the geniculate ganglion have traversed in turn the lingual nerve, the chorda tympani, and then the facial nerve to the geniculate ganglion. The taste fibers as they pass from the geniculate ganglion to the brain stem often appear to be grouped in a separate bundle of fibers, the nervus intermedius. Taste sensation from the posterior one-third of the tongue is conveyed by the glossopharyngeal (superior petrosal ganglion); from the epiglottis, by the vagus nerve (nodosa ganglion). These fibers then enter the brain stem to join the tractus solitarius at the medullary level.

It was of course evident at once, from the time of onset, that additional structures outside the distribution of the anterior inferior cerebellar artery were involved by the disease process. It is this more widespread involvement of brain stem structures which makes a vascular process even more likely. Thus, the basic process of stenosis is not in the anterior inferior cerebellar artery per se (although its point of origin may be narrowed or occluded by the process of atherosclerosis) but in the parent basilar artery.

Thus, the patient had diplopia as a prominent symptom. At times early in his hospital course, a bilateral palsy of nerve VI was evident. At times, a palsy of left nerve VI was evident with failure of movement of the left lateral rectus muscle. Such findings suggested some involvement of the paramedian areas in the lower pons (abducens nucleus or more likely abducens nerve fibers), areas usually within the territory of the paramedian branches of the basilar artery in this region. The extraocular findings later in the hospital course suggested a definite vertical separation of images due to dysfunction of the left superior rectus and left inferior oblique muscles. Such findings then would implicate the paramedian branches of the posterior cerebral artery to the midbrain.

The involvement of pain sensation over the left side of the face, most prominent in the mandibular division, is certainly consistent with involvement of a portion of the descending spinal tract and nucleus of the trigeminal nerve in the lateral tegmentum of the caudal pons. The involvement of the masseter muscle, and the motor nucleus of nerve V, suggests involvement of the lateral tegmentum at a midupper pontine level. This area is on the border between supplies of the anterior-inferior and the superior cerebellar arteries.

The deviation of the tongue to the left was of uncertain explanation and might have suggested that the hypoglossal nucleus (perhaps its rostral portion) was involved by the lesion. The deviation, however, was not accompanied by any actual atrophy. Thus a significant lesion of the hypoglossal nucleus was unlikely. Some apparent deviation of the tongue is almost always seen where a significant degree of facial paralysis is present, whether central or peripheral. The patient may also have had involvement of the corticobulbar fibers to the hypoglossal nucleus before or after the decussation of these fibers.

The slight and transient reflex asymmetry with greater activity on the left, accompanied by an equivocal plantar response, suggested a transient involvement of the corticospinal tracts at a pontine location implicating paramedian branches of the basilar artery.

The decreased gag reflex on the left with defect in movement of the uvula and soft palate on the left, indicating involvement of the nucleus ambiguus, suggests some extension of the area of ischemia and infarction into the adjacent lateral tegmentum of the rostral medulla an area usually supplied by the posterior inferior cerebellar artery. This raises additional questions. Was the actual site of disease the vertebral artery? If so this was not demonstrated by the arteriogram. Did the posterior inferior cerebellar artery originate as a branch of the basilar or anterior inferior cerebellar artery? If so this was not demonstrated by the arteriogram. More likely, is the possibility that the nucleus ambiguus may constitute a border zone with supply from both the anterior and posterior inferior cerebellar arteries.

As regards treatment of the cerebrovascular disease in this particular case, there was little specific or definitive therapy that could be undertaken. This case dates from the era prior to the introduction of CT scan imaging. A CT scan would certainly have confirmed the area of infarction within the inferior cerebellum and likely would have confirmed the infarction within the brain stem. An MRI would have clearly indicated the area of brain stem and cerebellum involved. Any progression of symptoms: drowsiness, evolution of the extraocular findings would have prompted a repeat imaging study with the possibility of surgical therapy: shunting to relieve the hydrocephalus which often accompanies the compression of the 4th ventricle in these cases or removal of the infarcted cerebellar tissue.

We may indicate at the onset that the basic disease process was atherosclerosis with ischemia and infarction. The aneurysmal dilatation at the apex of the basilar artery was secondary to the atherosclerosis. This

aneurysm in any case was essentially above the level of the infarction and could not be implicated in the disease process from the standpoint of subarachnoid bleeding or brain stem compression. Surgical treatment of this aneurysm, even if feasible from a technical standpoint, would have little effect on the basic disease process.

In cases where recurrent episodes of transient basilar vertebral ischemia occur, anticoagulation therapy may be instituted with a reduction in frequency of the attacks. Occasionally patients with an occlusion or infarction in evolution may benefit from this therapy. Such therapy has little or no value in a completed infarction. Although the patient had “dizzy spells” 2 years previously, this probably related in a nonspecific manner to hypertension and does not necessarily indicate an earlier ischemic episode. Hypertension (present in this case) and a past history of gastrointestinal bleeding are contraindications for anticoagulation therapy. The combination of hypertension and anticoagulation may result in a secondary hemorrhagic infarction. Therapy in the present case was non specific: gait training, reasonable reduction of blood pressure, weight reduction, and dietary control.

When unilateral infarction of the corticospinal and corticobulbar tracts of the basilar pons occurs, the clinical effect is a contralateral, upper motor neuron paralysis of the face, arm, and leg. This produces a relatively pure motor syndrome as demonstrated in the following case of a patient with an upper pontine paramedian infarct.

Case13-5: This 70 year old right handed white male retired salesman, on the day prior to admission while working in his garden, had the acute onset of weakness of the right arm and leg. His daughter noted that he also had a right-sided facial weakness and slurring of speech. A similar episode had occurred 2 months previously but had resolved over 2 weeks. A duplex scan of the carotid and vertebral arteries at that time was negative. With neither episode did the patient have any aphasia, visual symptoms or diplopia. Past history: notable for non-insulin dependant diabetes mellitus for which the patient had been receiving an oral hypoglycemic agent. He had been taking 3 aspirin tablets per day (325mgx3). There was no history of hypertension or of cardiac disease.

Neurological examination:

1. *Mental status:* intact with no evidence of aphasia.
2. *Cranial nerves:* intact except for a flattening of the right nasolabial fold and slurring of speech.
3. *Motor system:* There was a pronator drift in the outstretched right arm with 4+/5 weakness in the right iliopsoas. The patient however could walk slowly without support.
4. *Reflexes:* deep tendon stretch reflexes were increased in the right arm. A Babinski sign was present on the right.
5. *Sensory system:* intact.

Clinical diagnosis: Lacunar infarct: pure motor syndrome probable location left internal capsule with paramedian pons less likely.

Laboratory data: *CT scan of head* had demonstrated a probable hypodensity left upper pons and possible minor old lacunar type lesions right posterior frontal and left medial temporal. The *MRI* was more definitive demonstrating a well-defined paramedian upper pontine infarct (Fig.13-18B). The *MRA* study was within normal limits.

Hospital course: The following morning the right arm was now plegic, and the patient needed assistance with walking. By the 4th hospital day, dysarthria, and strength in right leg were improving. He was discharged to a rehabilitation facility on the 5th hospital day.

Comment: This patient presented a relatively pure motor syndrome, one of several types of lacunar infarction. If all cases of a pure motor vascular syndrome involving the face, arm, and leg are considered, (Fisher and Curry, 1965), it is found that the most frequent site of infarction is the posterior limb of the internal capsule. The paramedian upper pons is the second most common site. The most common predisposing conditions for these small vessel occlusions are hypertension and diabetes. Often there is a considerable improvement from the effects of the lacunar infarction. In this case the most definitive study was the MRI. Note that the MRA essentially ruled out any large vessel disease. It is, moreover, important to realize, as demonstrated in Figures 13-16 and 13-17 that disease of the basilar artery often produces a bilateral paramedian syndrome with a bilateral infarction of the basilar pons. Basilar artery thrombosis thus occludes the paramedian branches in a bilateral manner.

The following case history presents an example of the more limited midbrain syndrome with paramedian posterior cerebral artery involvement.

Case 13-6: This 66 year-old white male awoke two days prior to admission with weakness of both his legs. He attempted to stand but fell to the floor. He had experienced no nausea or vomiting and no blurring of vision. There was no loss of consciousness.

Neurological examination: Blood Pressure - 148/82; pulse 82.

1. Mental status: Intact
2. Cranial nerves:
 - a. Right pupil was slightly larger than left; both were reactive to light.
 - b. Ptosis of the right lid was present.
3. Motor System:
 - a. Weakness of the left upper extremity was present.
 - b. Minor weakness of both lower extremities was present, more marked on the left.
 - c. The patient was unable to walk without support. When supported the patient walked with a left hemiplegic gait.
4. *Reflexes:* A left Babinski sign was present.
5. Sensory System: Intact.

Clinical diagnosis: Paramedian midbrain infarct: Weber's syndrome

Laboratory data: A *lumbar puncture* demonstrated normal cerebrospinal fluid.

Hospital course: Two days following admission, the patient demonstrated neurological progression with a significant dilation of the right pupil and weakness of the right superior rectus, right medial rectus, right inferior oblique and levator palpebrae muscles. During the subsequent hospitalization, improvement occurred. By the following one month, the patient had equal pupils, no ptosis and no extraocular palsies. He had minimal weakness of the left leg and a left Babinski sign.

Comment: The initial symptoms in this case of bilateral weakness of the lower extremities, taken in isolation did not allow for localization, in terms of spinal cord, medulla, pons midbrain or even bilateral parasagittal motor cortex. However the findings of a ptosis and a slightly larger pupil on the right in association with a left hemiplegia (altho minor weakness was also present in the right lower extremity) all suggested a possible Weber's syndrome of the paramedian penetrating branch territory of the posterior cerebral artery. The subsequent progression two days later to a more complete cranial nerve 3 syndrome confirmed the diagnosis. In retrospect, the initial bilateral lower extremity weakness suggested that the initial ischemic process involved the penetrating branches in a bilateral manner. The lumbar puncture was performed to rule out a possible subarachnoid hemorrhage secondary to an aneurysm of the posterior communicating artery and was negative.

The following case history 13-7 provides an example of a patient in whom symptoms and signs involved the larger territory of the posterior cerebral artery :both paramedian branches to midbrain and cortical branches were involved.

Case 13-7 : This 73 year old, white housewife, without a previous history of neurological disease, awoke on the morning of admission complaining of diplopia. She was noted by her husband to be drowsy and mumbling. She was brought to the emergency room at 9:20 AM where she was found to have a dilated and fixed right pupil with associated paralysis of right levator palpebrae, superior rectus, medial rectus and inferior rectus. The left pupil was pinpoint. A left facial weakness and a minor weakness of left hand were also present. The patient although drowsy was able to respond to commands.

Past history: Rheumatoid arthritis for many years. Iron deficiency anemia noted one year previously.

Neurological examination: (Approximately 11:50 AM).

1) *Mental Status:*

- a) The patient was drowsy—responding poorly to commands.
- b) She was disoriented to time and place.
- c) She reported the president as Johnson (Nixon was the President).

d) There was no evidence of an aphasia.

2) *Cranial Nerves:*

a) II- A questionable left homonymous hemianopsia was present.

b) III, IV, VI-The right globe was in a lateral position; no medial, upward or downward movement of the right eye was possible. The right pupil measured 6 mm. The left pupil was pinpoint. Horizontal movements of the left eye were intact. Vertical movements of the left eye were difficult to test.

c) Pain sensation was decreased on the left side of the face.

d) A left central facial weakness was present.

3) *Motor System:*

a) A complete paralysis of left upper extremity, except for slight movement at left shoulder was now apparent.

b) Tone was slightly decreased in left upper extremity.

c) Cerebellar tests were negative.

4) *Reflexes:*

a) Deep tendon reflexes were hyperactive bilaterally at biceps(4+) and triceps(4+). Patellar reflexes were 2+ bilaterally.

b) The left plantar response was markedly extensor; the right was also extensor but less markedly so.

c) No release of grasp or such was apparent.

5) *Sensory System:*

a) Position and vibratory sense were decreased in the left hand.

Clinical diagnosis: Posterior cerebral artery syndrome most likely embolic(? top of the basilar syndrome) with predominant involvement of the right paramedian midbrain and right occipital and mesial temporal areas.

Laboratory data

1) Hematocrit was 35-40.

2) *Cerebrospinal fluid* exam demonstrated pressure of 90 mm; no significant cells were present. Protein was normal at 31 mg%.

3) *Right common carotid arteriogram* demonstrated that reflux occurred into the right basilar and right vertebral artery. No aneurysm was present.

Hospital course: Examination approximately 10 days after admission indicated essentially a persistence of the following findings:

1) There was an inability to detect stimuli in the left visual field.

2) The right pupil was now 3-4 mm in diameter and responsive to light. However, a marked ptosis of the right lid was present with a partial paralysis of medial, upward and downward movements of the right eye.

3) A left central facial weakness was present.

4) A left hemiparesis was present with arm more involved than leg.

5) The plantar responses were extensor bilaterally, the left more markedly than the right.

Comment: The sudden onset of the total third cranial nerve paralysis associated with drowsiness, and confusion, and with a left homonymous hemianopsia, left central facial, left arm and left leg weakness could raise the possibility of several diagnosis.

1) A right hemisphere tumor or hemorrhage which was producing via temporal lobe herniation pressure effects on the right third cranial nerve and brain stem.

2) An aneurysm of the junction of the posterior communicating and internal carotid artery with secondary subarachnoid hemorrhage.

3) A hemorrhage within the substance of the midbrain involving the right cerebral peduncle and the adjacent third nerve. This was actually the pathology responsible for the initial patient described by Weber (see Wolf 1971).

4) Basilar-vertebral ischemic occlusive disease with predominant involvement of the penetrating paramedian vessels of the proximal posterior cerebral artery on the right, and of the distal posterior cerebral artery supplying the calcarine (Visual cortex).

The right common carotid arteriogram served to essentially rule out the right hemisphere mass lesion, temporal lobe herniation and an aneurysm of the posterior communicating-internal carotid artery junction. The normal cerebrospinal fluid examination also served to rule out a subarachnoid hemorrhage (today the diagnostic procedure to confirm the localization and diagnosis would be MRI and MR angiography - both noninvasive).

The persistent findings in this case consisted of a right third nerve paresis which was partial plus a paralysis of left face, arm and leg. These findings alone would be consistent with a Weber's syndrome of the right midbrain, peduncle and third nerve due to proximal posterior cerebral paramedian artery involvement. The persistent left field defect reflected involvement of the cortical territory of the right posterior cerebral artery due to ischemia or an embolus.

What then is the explanation for the other transient findings?

1) The drowsiness and confusion may have reflected involvement of any of the following structures:

a) paramedian tegmentum of the midbrain. The integrity of the reticular formation at this level is essential for maintaining an alert state.

b) the upward extension of these same structures into the diencephalon: hypothalamus, the medial thalamus and intralaminar nuclei. These also are supplied by the paramedian branches of the proximal posterior cerebral artery.

c) the hippocampal structures: The blood supply is derived from the longer medial temporal branches of the posterior cerebral arteries. When damage occurs the patient is often confused.

2) The left pin point pupil undoubtedly reflected involvement of the descending sympathetic fibers from the hypothalamus at some point on the left side of the brain stem-eg. midbrain or pons.

3) The sensory findings: decreased pinprick on the left side of the face and decreased position and vibration probably, reflected ischemia of the medial lemniscus at midbrain level or possibly of thalamic nuclei, Weber's original description included mention of but not emphasis on such sensory findings.

The right Babinski sign less evident than the left Babinski sign probably indicated involvement of the opposite cerebral peduncle. Thus the basic process may have been at the level of the upper basilar artery with multiple branches at the "top of the basilar" involved (See Caplan 1980 and Mehler 1989 for additional discussion of rostral brain stem syndromes).

The following case 13-8 illustrates a patient with thrombosis of the basilar artery in which several midbrain and pontine syndromes were present.

Case 13-8: This 64-year-old, white, right-handed, male house painter beginning 6 months prior to admission, had experienced a series of 15 to 20 attacks of unsteadiness of gait, attributed to transient weakness of the right or left side of the body (predominantly the left side) and associated with vertigo and occasional tinnitus ("motor sounds") of the left ear. Initially, head turning precipitated the vertigo. Six months prior to admission, because of a sensation of dizziness when climbing his ladder, the patient had been forced to stop his work. Seven days prior to admission, the patient was admitted, to his local community hospital with acute onset of paralysis and numbness of the left arm and leg of several hours duration. The patient was noted to be slightly confused and unable to speak clearly (dysarthric). These symptoms apparently improved; but approximately 7 days later, the patient had an onset of weakness of the right arm and leg accompanied by increased difficulty in speech, necessitating his transfer to a neurological center.

Past history: Hypertension had been present for at least 6 months. Weakness and cramps in the legs on walking, relieved by rest, had been present for 1 year (suggesting the intermittent claudication of peripheral vascular disease).

General physical examination:

1. Blood pressure was elevated to 200/90.
2. Pulses in the lower extremities were decreased or absent.

Neurological examination:

1. *Mental Status:* Although speech was severely dysarthric (speech was hardly intelligible to observers), the patient was alert and cooperative. He was able to follow commands, and to identify objects. There was no evidence of left-right confusion.

2. *Cranial Nerves:*

- a. The left pupil was slightly larger than the right.
- b. A right lateral rectus weakness was present.
- c. Nystagmus was present on gaze to the left or right.
- d. Pain sensation was decreased about the right corner of the mouth. The right corneal response was decreased.
- e. Jaw jerk was hyperactive.
- f. There was a paralysis of the lower half of the right side of the face.
- g. Gag reflex was decreased; the patient was unable to swallow on command. The uvula did elevate on phonation.
- h. The tongue was midline, but lateral tongue movements were weak.

3. *Motor system:*

- a. Strength was uniformly decreased in the right arm and leg, but intact on the left.
- b. Truncal ataxia was apparent in the sitting position.
- c. Ataxia was evident on the right in finger-to-nose and heel-to-shin tests. Interpretation of these findings was clouded by the presence of right-sided weakness.

4. *Reflexes:*

- a. Deep tendon reflexes were hyperactive throughout with clonus apparent at the patellar. As noted above, the jaw jerk was 3-4+.
- b. Plantar responses were extensor bilaterally (bilateral Babinski signs).

5. *Sensory system:*

- a. Pain sensation was decreased in the left leg.
- b. Vibratory sensation was decreased in both lower extremities.
- c. Position sense was defective in the toes of the left foot.

Clinical diagnosis: Transient ischemic attacks followed by infarction basilar –vertebral system. Possible thrombosis of basilar artery.

Laboratory data:

1. *Blood and spinal fluid serology* were normal.
2. *Cerebrospinal fluid* pressure was normal, with no cells. The protein content, however, was increased to 120-mg./100 ml. (explanation never certain).
3. *Skull x-rays* were negative except for calcifications in the internal carotids adjacent to the sella.

Hospital course: The patient's inability to swallow progressed so that by the third day in the hospital, it was necessary to make use of a nasogastric feeding tube. On the fifth day, a temperature elevation occurred, related to aspiration pneumonitis. Death occurred 14 days after admission.

Postmortem examination of the brain: The major supply of the basilar artery was derived from the left vertebral artery. The right vertebral artery was rudimentary. In the lower portion of the basilar artery, significant atherosclerosis and calcification was present with narrowing of the lumen. The lower- middle segment of the vessel was occluded by thrombus. The proximal (caudal) portion of the thrombus was older, fibrous, and well organized; the distal portion was more recent. This suggested distal propagation from the more proximal thrombus.

The pons was soft to palpation. Serial sections revealed a recent area of infarction (with swelling and some hemorrhagic component) involving the entire left cerebral peduncle at the level of the midbrain, extending in a

massive manner into the basilar pontis on the left. The areas of softening extended into the left and right paramedian areas of the pontine tegmentum (Fig. 13-17). A similar but possibly older lesion was present involving the right cerebral peduncle and right basilar pons. On the right the infarct extended up to the capsule of the red nucleus, to the subthalamus nucleus, and into the posterior and lateral portions of the thalamus.

Old small infarcts probably lacunae were also noted in the right lenticular nucleus and the head of the left caudate nucleus. In addition, the right occipital cortex demonstrated old infarction.

Comment: The symptoms and signs in this case would appear to be well correlated with the findings at postmortem examination. Thus, the appearance of the basilar artery and of the brain stem suggests several events from a chronological standpoint.

The recent massive lesion in the left cerebral peduncle and basilar pons corresponded to the right hemiparesis and right central facial weakness. The previous episodes of primarily left-sided involvement of the arm and leg would correlate with the older infarcts on the right side of the brain stem. The bilateral involvement of the basilar pons and cerebral peduncles must have resulted in a pseudobulbar syndrome, as regards the hyperactive jaw jerk and the movements of the tongue and the pharynx (reflecting bilateral corticobulbar involvement). The bilateral hyperactivity of deep tendon reflexes and the bilateral extensor plantar responses reflected bilateral corticospinal tract damage. The infarction of the right paramedian area of the pontine tegmentum must presumably correlate with the right lateral rectus muscle weakness and with deficit in position sense in the left toes. At some point, the infarction must have extended sufficiently lateral in the right pontine tegmentum to have involved the descending portion of the spinal tract and nucleus of the right fifth cranial nerve in addition to the lateral spinothalamic tract (decreased pain sensation in the left foot). In addition, the vertigo and tinnitus would suggest that the territory of the anterior inferior cerebellar artery had been involved to produce these symptoms in the lower pontine tegmentum.

The examination of the basilar artery indicated an old well-organized thrombus in the caudal portion of the artery that may have correlated with the transient ischemic attack beginning in May 1964. Presumably sufficient collateral circulation was present to prevent infarction until additional more recent thrombus extended to the middle portion of the artery. The specific syndromes associated with stenosis of the middle and distal segments of the basilar artery are discussed by Pessin et al 1987. Patients with basilar artery thrombosis may infarct the pons but leave the midbrain intact producing - "unlocked in syndrome". The patient remains awake but is able to communicate only with eye lid and vertical eye movements (refer to Fig.13-21). This condition must be differentiated from coma and is discussed in Chapter 29.

The Major Vascular Syndromes of the Brain Stem are Reviewed in the following Table 13-2 modified from Adams, Victor & Ropper

The following case demonstrates the features of a brain stem glioma.

Case 13-9: This 20 year old single female noted occasional horizontal diplopia and headache. Five months later, clumsiness and weakness of the left arm and leg were present and examination now also demonstrated evidence of increased intracranial pressure. CT scan and subsequently MRI (Fig.13-24) demonstrated a mass within the pons with compression of the 4th ventricle and cerebellum. Treatment with dexamethasone produced significant improvement of the diplopia and headache. Following a ventriculoperitoneal shunt procedure at the Massachusetts General Hospital to reduce hydrocephalus and radiotherapy (5400 rads) at the St Vincent Hospital, all neurological signs resolved and the tumor shrank on imaging studies. Two and a half years later over a three-year period, diplopia, progressive ataxia, left hemiparesis occipital headache and projectile vomiting recurred.

Neurological examination: the following abnormal features were now present:

1. *Mental status:* intact except for marked emotional lability.
2. Cranial nerves:
 - a. bilateral lateral rectus palsy.
 - b. horizontal nystagmus on gaze to left or right ,vertical nystagmus on upward gaze.
3. Motor system:
 - a. left hemiparesis
 - b. ataxic on attempting to sit or stand.
4. *Reflexes:* bilateral Babinski signs.

Clinical diagnosis: Progression of pontine glioma

Laboratory data: MRI (Fig 13-24) demonstrated additional enlargement of the pons with compression of the 4th ventricle and with extension of tumor and edema on the right side into the cerebellar peduncle, medulla, midbrain and thalamus.

Subsequent course: treatment with dexamethasone and chemotherapy produced temporary clinical and MRI improvement.

Comment: The occurrence of headache and diplopia in a 20-year-old certainly raises the question of an intracranial tumor. The localization is not certain based only on these symptoms. Thus 6th nerve palsy may occur with an increase in intracranial pressure without clearcut localization to the brain stem or even the posterior fossa. The subsequent development of clumsiness of the left arm and leg could have raised the question of cerebellar mass except that these symptoms occurred in the context of a left-sided weakness. Thus the clumsiness could have been nonspecific tumor in relationship to the 4th ventricle such as a medulloblastoma, or ependymoma, or cerebellar hemisphere lesion such as a cystic astrocytoma would not produce a left hemiparesis. The combination of a left hemiparesis and cranial 6th nerve palsy if progressive in nature could suggest a pontine glioma. The findings at the time of her recurrence left little doubt as to the diagnosis but did not entirely indicate the much more extensive nature of the tumor now present.

The following case history 13-10 indicates the total course to be seen with a brain stem glioma.

Case 13-10: This 24-year-old white housewife and secretary was referred for evaluation of progressive headache, diplopia, and left-sided weakness.:

In March 1960 approximately 2 weeks after the delivery of her second child, the patient had an onset of diplopia with an apparent horizontal separation of images. Her family noted that the right eye was "turned in". The symptom was intermittent for a week, then persistent and static for approximately one year. In June 1961 one year prior to admission, the double vision worsened. Moreover, a weakness of the left leg, an unsteadiness of gait, and clumsiness of the left hand were now noted. These symptoms steadily progressed so that the patient fell in November 1961, sustaining a fracture of the left ankle. Skull x-rays and lumbar puncture at that time were normal and the diagnosis of multiple sclerosis was entertained. As the previous symptoms worsened, the patient in the 3 months prior to admission noted a progressive numbness of both sides of her face and of the oral cavity. She had lost all of her ability to taste food or even to tell where food was located in the mouth. She had experienced increasing difficulty in attempting to swallow food. Liquids such as coffee were frequently regurgitated into the nasopharynx on swallowing. Her speech had developed a nasal quality and hoarseness had been noted. A bilateral occipital headache had developed, at times precipitated by flexion of the neck. In recent days, the headache had been accompanied by vomiting.

General physical examination:

No remarkable features were present.

Neurological examination:

1. *Mental status:*

- a. The patient was alert with intact memory and orientation.
- b. Although speech was slurred and the voice was low and hoarse, language function per se was intact with no evidence of aphasia.

2. *Cranial nerves:*

- a. Bilateral papilledema was evident on examination of the fundus with marked blurring of disc margins, elevation of the discs, and retinal hemorrhages. Visual acuity was intact.
- b. Bilateral lateral rectus weakness was present, more marked on the right than on the left. Vertical nystagmus was present on upward gaze.
- c. Pain and touch sensation were decreased over all three divisions of the trigeminal nerve, more marked on the right than the left. Corneal reflexes were absent bilaterally.
- d. A mild right central (supranuclear) facial weakness was present.

- e. The uvula deviated to the left on attempted elevation. The gag reflex was decreased bilaterally. Speech was of low tone and slurred.
- f. A bilateral weakness of the sternocleidomastoid muscles was present. The upper half of the left trapezius was weak.
- g. The tongue deviated to the right on protrusion.

3. *Motor system:*

- a. Marked weakness accompanied by spasticity was noted in the left arm and leg.
- b. Gait was unsteady with a spastic quality evident in the movements of the left leg.
- c. Coordination was poor on the left side. Whether this reflected cerebellar deficits in addition to weakness was not certain.

4. *Reflexes:*

- a. Deep tendon reflexes were symmetrical and physiologic.
- b. Plantar responses were extensor on the left, flexor on the right.

5. *Sensory system:* Except for the findings over the face, no deficits were present.

Clinical diagnosis: Pontine glioma

Laboratory data:

- 1. *Skull and chest x-rays* were negative.
- 2. *Electroencephalogram* was normal.
- 3. *Left brachial arteriogram* indicated a probably low position of the posterior inferior cerebellar artery, suggesting the possibility of cerebellar tonsillar herniation. Basilar and vertebral arteries were in a normal position.
- 4. A *pantopaque ventriculogram* revealed an intrinsic pontine and medullary tumor. The fourth ventricle and aqueduct were midline but were displaced posteriorly. This study was performed by instilling a radioopaque dye (pantopaque) into the ventricular system by means of a needle placed in the frontal horn.

Hospital and subsequent course:

A suboccipital craniotomy and removal of the lamina of C1 and C2 was performed by Dr. Samuel Brendler on July 3, 1962, with the aim of decompressing the cerebellum, brain stem, and cervical cord. The cerebellar hemispheres were found to be under marked tension. The medulla oblongata was markedly enlarged to twice the normal size, displacing the cerebellar hemispheres laterally. The upper cervical cord was also markedly enlarged. Although a firm yellow dicolored mass could be visualized within the medulla, no definite delineation from the surrounding normal tissue could be made. No cyst was present within the tumor mass. The upward extent of the tumor could not be visualized because the suboccipital approach does not allow inspection of the upper pons.

Surgical decompression was followed by x-ray therapy (total of 4846 roentgens). An improvement in neurological status was subsequently noted. At the time of hospital discharge, 10 weeks after surgery, papilledema had disappeared. Corneal reflexes had returned. Gag reflex was now present and swallowing was intact. Sternocleidomastoid muscles and tongue were intact. Bilateral lateral rectus weakness and bilateral facial weakness were still present. There was still a slight bilateral decrease in pain sensation over the face. The patient was able to ambulate using a walker. Strength in the left upper extremity had improved. Improvement continued to such an extent that the patient returned to her job as a secretary in April 1964 and walked to work each day. Her only residual symptoms were a minor degree of diplopia and a minor ataxia of gait.

Progression occurred in October 1965 with increased symptoms of diplopia and vertigo plus findings of nystagmus of a rotary type in all directions of gaze, moderate weakness of the sternocleidomastoid muscles and fasciculations bilaterally in the tongue.

In November 1965, the patient was readmitted to the hospital because of increasing ataxia, slurred speech, numbness of the right side of the face (pain and touch were now decreased over all three divisions of the trigeminal nerve), loss of taste, and decreased hearing in the right ear. In addition the gag reflex was decreased on the right. A greater degree of hoarseness was now evident and laryngoscopy demonstrated no movement of the right vocal cord. The sternocleidomastoid muscles were weak. Atrophy and fasciculation involving the right half of tongue was now evident. Intention tremor was now present. Pneumoencephalogram demonstrated an enlargement of the substance of the brain stem with posterior displacement of the fourth ventricle and narrowing of the pontine cistern. High voltage radiotherapy was started but had to be discontinued when symptoms progressed.

Follow-up evaluation in March 1966 demonstrated continued progression with additional neurological findings. Adduction and convergence of the right eye was now defective. A right peripheral facial weakness was now present. A marked intention tremor was present in the right upper extremity with a marked heel-to-shin ataxia in the right lower extremity.

Re-evaluation in May 1966 now indicated additional progression. A bilateral peripheral facial weakness was now present. Bilateral Babinski signs were present. In addition to the marked right-sided cerebellar findings previously noted, a significant involvement of the trunk and, to a lesser degree, of the left arm and leg was now apparent.

Despite treatment with steroid therapy (Decadron) and with an intraventricular infusion of an experimental chemotherapeutic drug, 8-azaguanine progression of the basic disease process continued at the time of hospital discharge in July 1966 with atrophy of the muscles of the left upper extremity. The patient was unable to stand and unable to arise from bed. The patient was transferred to a chronic disease hospital where death occurred on September 3, 1966.

Comment: The course of events in this case over a 6-year period clearly indicates the progressive involvement of cranial nerves and long fiber systems over a wide extent of the brain stem. In the later stages, the cervical spinal cord was involved as well. The initial diplopia was related to involvement of the right sixth nerve. The long duration of this finding, its unilateral nature, the fact that headache and other symptoms and signs of increased intracranial pressure were absent (despite examinations by ophthalmologists and neurologists all suggested that this was not the nonspecific effect of increased intracranial pressure. Such an increase in internal pressure may produce bilateral sixth nerve palsy).

With the subsequent development one year later of left-sided cerebellar findings, involvement of both sides of the brain stem was suggested, a somewhat unusual combination for a focal extrinsic compressive lesion. The subsequent development 3 months prior to admission of bilateral fifth nerve symptoms more clearly suggested a bilateral intrinsic lesion involving the pons. The difficulties in swallowing and the hoarseness in speech suggested involvement of the nucleus ambiguus or the vagus nerve at a medullary level. The loss of all sense of taste may have indicated bilateral involvement of the tractus solitarius or, less likely, of the various entering fibers passing via the facial and glossopharyngeal nerves. At later stages, the motor neurons or associated fibers at a medullary level supplying the tongue and sternocleidomastoid muscles were involved as indicated by the significant atrophy and fasciculations present in these muscles.

In very late stages, defects in adduction and convergence of the right eye suggested spread to a midbrain level with involvement of the third nerve nucleus supply to the right medial rectus muscle. The atrophy of muscles in the left upper extremity suggested spread to a spinal cord level.

Eventually increased intracranial pressure (with headache, vomiting, papilledema) was certainly present at the time of hospital admission in 1962. Thus diplopia was present for 2 years without evidence of an increase in pressure. This is the usual situation in intrinsic tumors of the brain stem—increased intracranial pressure is absent in early stages. In contrast, extrinsic tumors involving the brain stem usually manifest increased intracranial pressure early in their course.

Having concluded that an intrinsic lesion is present, the identification of the type of pathology as glioma should be evident when one considers the differential diagnoses. Vascular disease, multiple sclerosis, amyotrophic lateral sclerosis and syringobulbia represent other intrinsic diseases of the brain stem.

Vascular disease would be unlikely in view of the gradual but progressive nature of the problem and the age of the patient. Multiple sclerosis would be unlikely since both neurons and long tracts were involved. Moreover, the symptoms were limited to the brain stem (although certainly involving several rostral-caudal segments of the brain stem). The progressive nature of the problem without definite remissions is also to some extent against the diagnosis of multiple sclerosis. A bulbar form of amyotrophic lateral sclerosis would be unlikely in view of the early age of onset of symptoms, the presence of sensory signs and symptoms, the presence of cerebellar symptomatology. The relatively rare disorder syringobulbia is also unlikely. It is often associated with a relatively typical syndrome of syringomyelia. The brain stem involvement, which tends to be localized to several wedge or slit type areas extending in from the fourth ventricle at a medullary level, is often associated with a relatively typical syndrome of syringomyelia.

As regards treatment of brain stem gliomas, the general principles are similar to those considered for intrinsic tumors of the spinal cord. For most patients there is no surgical cure. Surgery often confirms the diagnosis and eliminates the possibility of extrinsic tumor. In occasional patients surgery may produce subtotal resection of exophytic extension of tumor into the fourth ventricle, or drainage of a focal cystic component. In addition, surgical decompression provides greater room for expansion of the brain stem. At times, when the tumor has produced obstruction of the fourth ventricle or aqueduct, the use of a bypass shunt will produce a considerable reduction in those symptoms related to an increase in intracranial pressure. The tumor often has a significant response to radiation with the production of a temporary remission as in the present case (see Strain et al, 1986).

The following example illustrates a case of multiple sclerosis with predominant involvement of brain stem and cerebellar pathways early in the course of the disease.

Case 13-11: This 38 year old divorced right handed white female employed as a tape library supervisor had been in excellent health until June, 1992, 1 year prior to admission when she developed vomiting, vertigo, numbness of her right leg and difficulty walking. She received medications for the vomiting and all symptoms cleared over 1 month. One year later in June she awoke to find that she had diplopia and both eyes were divergent. In addition if she attempted to use one eye, she found the vision in the left eye to be "out of focus". She had difficulty with walking, "she walked as though drunk". A physician saw her at that time and the examination indicated that the left eye was divergent. Neither eye could adduct in following objects or in attempted convergence. Upgaze was limited. She had mild ataxia in attempting to walk. A left Babinski sign was present. Following an MRI scan and progression of symptoms, she was admitted to the neurology service for acute treatment.

Neurological examination:

1. *Mental status:* intact except for a mild degree of indifference to her difficulties.
2. *Cranial nerves:* On primary gaze, the left eye was divergent (exotropia). Neither eye could adduct past the midline. Dissociated nystagmus was present in the abducting eye on attempted lateral gaze to right or left. Vertical gaze up and down was now intact.
3. *Motor system:* rapid alternating hand movements were somewhat slow. The gait was slightly broad based and mildly ataxic. She would fall to either side on attempted tandem gait.
4. *Reflexes:* Deep tendon reflexes were bilaterally hyperactive. The left plantar responses was extensor.
5. *Sensory system:* intact.

Clinical diagnosis: acute exacerbation of multiple sclerosis with predominant involvement of brain stem and cerebellar system.

Laboratory data:

1. *MRI* (Fig 13-27): there were well defined foci of increased signal particularly in the T2 weighted images in the periventricular white matter, the corpus callosum, the subcortical white matter of the right parietal lobe, the left midbrain and the cerebellar peduncles.
2. *CSF:* protein was high (60), 1 oligoclonal band was present, 3 lymphocytes were present (normal).
3. *ESR, ANA, VDRL, and Lyme titer* were all within normal range.

Subsequent course: The patient was treated with a 5-day course of high dosage intravenous methylprednisolone (1000 mg /day for 5 days) followed by a tapering course of oral prednisone. Within 10 days of the intravenous therapy, the patient had significant improvement: diplopia disappeared and walking improved. Her examination showed only rare dissociated jerks of the abducting eye. No divergence of the eyes was present in primary position. Convergence was intact. No diplopia was present on red glass testing. Significant nystagmus did develop with the hanging head maneuvers most marked with right ear

down. With rotation, sustained nystagmus occurred and this was clearly dissociated –more marked in the abducting eye on gaze to the right. Tandem gait was now very intact and she could stand or hop on one foot. Deep tendon reflexes were now physiologic and plantar responses were flexor. The patient had minor exacerbations. When beta interferon became available, she was begun on that medication in Sept 1994 and had no significant exacerbations until Aug. 1999 and Nov. 1999. When last evaluated in Mar.2000 she did have residual symptoms of 2x/month fecal incontinence more persistent cerebellar dysarthria and a hypophonia, increased reflexes on the left and a slightly broad-based gait. She had persistent symptoms over the years related to the common symptom in patients with multiple sclerosis of fatigue that improved when treated with methylphenidate (Ritalin) and amantadine (Symmetrel). She had a persistent but stable complaint that her memory and cognitive processes were not as good as before her illness. Urinary frequency responded to the use of oxybutynin (Ditropan) an anticholinergic.

Comment: This patient clearly met the criteria for a diagnosis of definite multiple sclerosis. Her symptoms and signs clearly indicated a disease process disseminated in time and space. Her major symptoms had clear-cut correlations on the MRI scan. The divergent position of the left eye and the inability to converge must have correlated with the left sided rostral midbrain lesion at the floor of the cerebral aqueduct involving the area of the left third nerve complex. This lesion extended across the midline and certainly was in a position to involve the convergence center and the medial longitudinal fasciculus. . The cerebellar symptoms correlated with involvement of the cerebellar peduncles. The complaints relevant to cognitive function most likely correlated with the changes in the lesions in cerebral white matter.

As regards treatment, acute exacerbations often respond to the intravenous administration of high dosage corticosteroids (1000mg /day of methylprednisolone is the usual therapy. This therapy reduces the inflammatory response and the edema of acute lesions. Oral therapy is not effective. The use of beta interferons has been demonstrated to significantly reduce exacerbations and to decrease progression of the disease. Serial MRI studies also confirm that beta interferon therapy also reduces the incidence of new lesions.

Case 13-12 concerns a patient with multiple sclerosis who began with symptoms and signs relevant to brain stem but then pursued a progressive 7 year course of increasing disability resulting in a bed ridden terminal state.

Case 13-12: This 43 year old right handed housewife was referred for evaluation of acute symptoms of ataxia, dizziness, diplopia, and tinnitus. In retrospect the patient had experienced urinary frequency and possible symptoms of a spastic bladder for several years.

Two months prior to admission, the patient experienced pain and a vague numbness-tingling on contact in both lower extremities followed by decreased strength in both legs. Examination by a neurosurgeon was reported to be negative.

Two-three weeks prior to admission, transient unsteadiness-ataxia was noted.

Three days prior to admission, the patient reported a poorly defined “dizziness”- not clearly vertigo-present all the time but clearly marked by accelerated by any attempt to roll over or to sit up. She could not walk without feeling “drunk”.

Two days prior to admission tinnitus was noted in the right ear and diplopia was first reported.

General physical examination: Normal

Neurological examination

1) *Mental Status.* Normal as regards orientation , memory function, and language function. However a considerable blunting of mood was present.

2) *Cranial Nerves.*

a) The patient had diplopia on gaze to either left or right with a horizontal separation of images. Red glass testing suggested bilateral involvement of medial rectus. In addition nystagmus was present on lateral gaze- particularly to the left. Although usually conjugate, at times, there was greater nystagmus in the abducting left or right eye. The total pattern suggested a possible bilateral internuclear ophthalmoplegia.

- b) The jaw jerk was hyperactive.
- 3) *Motor System*
 - a) Strength was intact.
 - b) Cerebellar function:
 - 1) The patient was ataxic when sitting; when standing or when attempting to walk-even on a broad or normal base.
 - 2) Finger to nose testing was intact but heel to shin test demonstrated a dysmetria with a problem in placement of heel to knee.
- 4. *Reflexes.*
 - a) Deep tendon reflexes were everywhere hyperactive including the finger jerks-(Hoffman signs)
 - b) Bilateral Babinski signs were present more marked on the left than on the right.
- 5) *Sensory system:.*
 - a) Vibration was decreased distally at toes and fingers.
 - b) Pain and position sensation were intact.

Laboratory data:

- 1) The *sedimentation rate, vitamin B12 level and serological tests for neurosyphilis and lupus erythematosus* were all negative.
- 2) *CT Scan of the brain* and pneumoencephalography were normal.
- 3) *Lumbar puncture* demonstrated normal pressure and no significant cells. Although the total protein was normal at 27mg%, gamma globulin at 15mg% constituted 55% of the total protein(Normal less than 14%). The serum gamma globulin was not significantly increased-thus the increased gamma globulin in the CSF must have been produced in relation to the central nervous system.

Subsequent course: Several days after admission the patient developed tingling paresthesias on the right side of the face involving the upper and lower lip in a pattern that suggested involvement of the descending spinal tract of the fifth cranial nerve. Despite treatment for several weeks with prednisone- a corticosteroid, some progression occurred with the development of numbness of left side of face, a left central facial weakness and slurring of speech. Eventually over 2-3 weeks a minor improvement in gait occurred. By July 1976 she was able to walk without assistance although she remained ataxic. On follow up in October 1976, in addition to an internuclear ophthalmoplegia, a gaze paralysis for conjugate lateral gaze to the right was present. as well as the prior cerebellar and pyramidal tract findings.

When seen in March 1977 one year after the acute episode of 1976, diplopia was no longer present, and gait although ataxic and slightly broad based was stable. However complaints of emotional lability and changes in memory began to appear followed by periods of depression. Evaluation in October 1979 indicated persistence of a spastic ataxic gait and a marked heel to shin ataxia. Over the years minor exacerbations occurred with incomplete remissions. With a severe exacerbation in Sept 1981, the patient was readmitted to the hospital with urinary incontinence and worsening gait. Mental status indicated marked emotional lability and poor recall of recent events. A homonymous left upper quadrant field defect was present. Nystagmus was present on gaze to the left and right. A left peripheral facial weakness was present. Speech was scanning and dysarthric. Weakness of left arm and leg were present with marked spasticity and clonus of left knee and ankle. The gait was broad based and unstable. The patient was confined to a wheelchair. Bilateral Babinski signs and frontal release signs were present.

CT scan with enhancement demonstrated multiple white matter lesions in both hemispheres as well as left pons. During the hospitalization a bilateral internuclear ophthalmoplegia, vertical nystagmus and worsening of gait occurred only to subsequently improve. The urinary incontinence related to an atonic bladder with overflow incontinence.

The patient returned home but subsequently had increasing motor disability affecting all four limbs, resulting in a bed ridden state. Progressive changes in mental status occurred with severe impairment of memory, hallucinations and agitation. She expired in a chronic care facility in December 1983.

Comment: The diagnosis of definite multiple sclerosis is based on evidence in the history and on the examination of lesions disseminated in time and space. Eventually there was then little question of the diagnosis in this case. However at the time of initial hospital admission, the patient had evidence of cerebellar, pyramidal tract and lower pontine findings. The dissociated nystagmus, greater in the abducting eye, on right or left lateral gaze, suggested a bilateral lesion of the medial longitudinal fasciculus. Multiple sclerosis is the most common cause of such a bilateral lesion. (Vascular disease with infarction may produce either a unilateral or bilateral type of internuclear ophthalmoplegia. A pontine glioma may also produce this syndrome). Initially there was little evidence of disease except at the possible pontine location. The pneumoencephalogram was performed to rule out a pontine glioma. This was prior to the clinical availability of the MRI scan. Today the MRI would be performed. Only a minority of cases(usually in far advanced cases) will the CT Scan reveal lesions.

At the time of the patient's second hospital admission, evidence of multiple sites of involvement was evident both from the clinical and CT standpoint.

Initially this patient presented with an evolving brain stem syndrome. The symptoms never completely resolved. Today (2002), she would have been treated with a 5 day course of high dosage (1000 mg per day) methyl prednisolone and then would have started on a beta interferon. This might have reduced subsequent exacerbations and reduced progression of the disease. See previous discussions in previous cases of this chapter and chapter 9. There is no specific therapy for primary progressive multiple sclerosis at this point in time although trials are in progress. Oral corticosteroids are no longer employed in therapy, such agents as demonstrated in earlier cases in chapter 9 have no benefit.

Case 13-13 Figure 13-28. Central pontine myelinolysis. MRI. This 49 year old male with a long history of alcoholism and poor nutrition was confused and lethargic with a low serum sodium of 99 mEq/liter which was corrected to 123 mEq/liter over 24 hours. He developed a mute; akinetic state with bilateral spasticity, bilateral Babinski signs, and difficulty in swallowing and respiration. MRI demonstrates an extensive area of demyelination involving the central areas of the pons and midbrain.

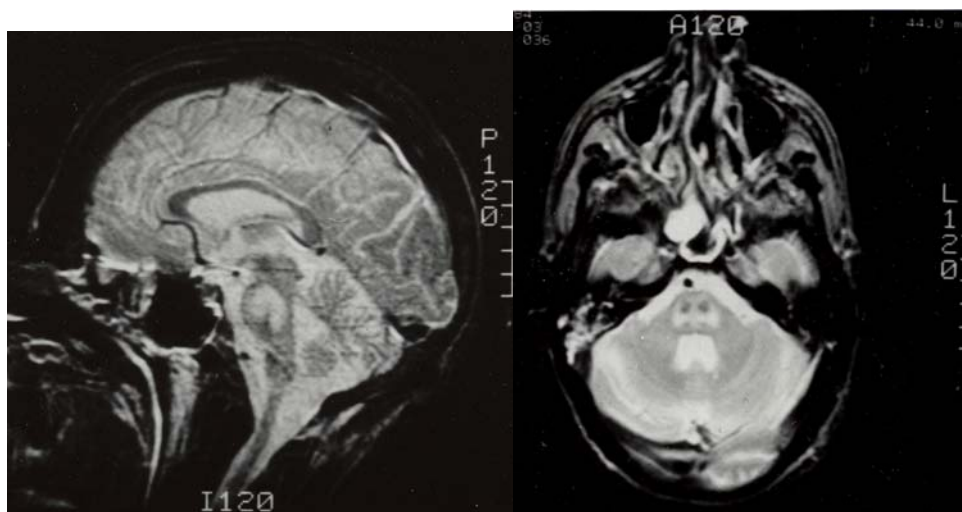


Figure 13-28. Case 13-13. Central pontine myelinolysis. A.) T-2 Sagittal. B T2 transverse Courtesy of Dr. Carl Rosenberg.