Myelitis

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History

A 42-year-old man presented to the emergency department with altered sensation in the lower limbs and difficulty ambulating. He first noted paresthesia in his feet 1 week prior. The altered sensation gradually ascended to involve the length of both legs and his trunk to around the umbilicus. Over the preceding 2 days, he had noticed some difficulty walking longer distances and climbing stairs and had developed a sensation of incomplete bladder emptying. He had been systemically well and there was no prior history of neurological symptoms. He had a background history of mild hypertension but took no medication. There was no relevant family history.

Examination

Lower limb examination revealed non-sustained ankle clonus bilaterally, with brisk knee jerks and extensor plantar reflexes. There was mild weakness of left hip flexion and ankle dorsiflexion bilaterally. Pinprick sensation was decreased throughout the lower limbs, with a sensory level at approximately T9. There was reduction of distal proprioception and vibration sense. Examination of gait revealed difficulty walking on heels and performing a squat-to-stand manoeuvre. The upper limb and cranial nerve examinations were normal and there were no cerebellar signs. The systemic examination was unremarkable.

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Investigations

An MRI of the spine (Figure 2.1) revealed a T2 hyperintense cord lesion, extending from T2 to T5, with associated gadolinium enhancement. A brain MRI (Figure 2.2) revealed multiple T2 hyperintense white matter lesions, including callosal lesions, periventricular lesions extending perpendicular to the ventricles consistent with 'Dawson's fingers', and a left cerebellar lesion. Faint gadolinium enhancement of one periventricular lesion was noted.

A cerebrospinal fluid (CSF) examination revealed 47 mononuclear cells/μL and a normal protein level. CSF culture and viral polymerase chain reaction (PCR) analyses were negative, while CSF oligoclonal bands were positive. A blood screen for multiple sclerosis (MS) mimics was performed, including inflammatory markers, vitamin B_{12}, methylmalonic

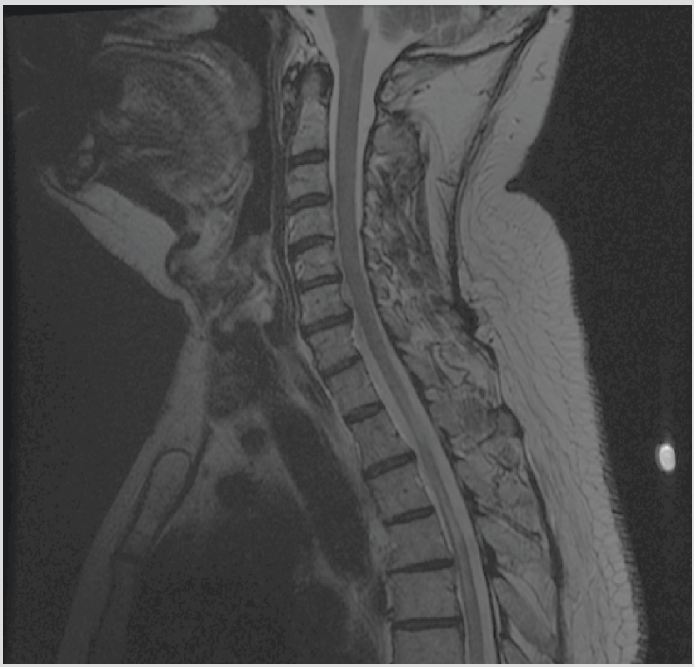

Figure 2.1 An axial T2-weighted MRI of the cervical spinal cord showing a hyperintense lesion extending from T2 to T5.

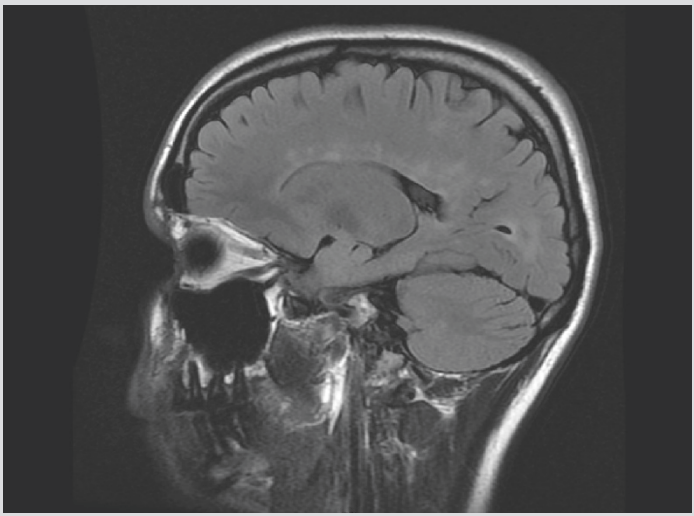

Figure 2.2 A sagittal FLAIR image of the brain showing multiple hyperintense white matter lesions, including 'Dawson's fingers.'

acid, folate, copper studies, aquaporin-4 antibodies, syphilis serology, angiotensin-converting enzyme, antinuclear antibodies, extractable nuclear antibodies, antineutrophil cytoplasmic antibodies, rheumatoid factor, double-stranded DNA antibodies, and antiphospholipid antibodies, all of which were normal or negative.

Outcome

This patient presented with myelitis and, given the absence of previous episodes of neurological symptoms, can be diagnosed with a clinically isolated syndrome (CIS). Following management of this acute episode and discussion of the diagnosis, the patient can be considered for commencement of a disease-modifying therapy (DMT), as there is established evidence for decreased relapse rates, slower accumulation of lesions, and reduced long-term disability with early treatment of MS. Given the presence of some unusual features in this case, reassessment of the diagnosis and repeat evaluation for a potential MS mimic should be considered in the future if his disease course or treatment response is atypical.

Discussion

The presence of brain lesions typical for MS strengthens the likelihood of underlying MS, although other diseases can mimic MS, both clinically and radiologically. In cases of CIS with features typical for MS, minimal testing may be required to help exclude alternative diagnoses, such as blood tests for inflammatory markers, antinuclear antibodies, and a nutritional deficiency screen (eg, Vitamin B_{12}, folate). While more extensive screening for MS mimics is not warranted in all cases of CIS, when atypical features are present, as in this case, a thorough search for differential diagnoses is warranted. Distinguishing a first presentation of MS from other mimics is important, as the use of MS therapies in other disorders can be both ineffective and even potentially harmful.

Typical myelitis related to MS is partial, usually affecting a peripheral portion of the cord and spanning less than two vertebral segments on imaging, and resulting in incomplete and often asymmetrical symptoms and signs below the level of the lesion. As with symptomatic lesions in other areas, symptoms and signs of MS myelitis tend to progress over days to several weeks, typically with ascending sensory changes, sphincter dysfunction, and mild-to-moderate lower limb weakness. Severe weakness, complete myelitis, and cauda equina syndrome are unusual in MS. Patients with acute partial myelitis are at an increased risk of recurrence and transition to MS [1]. On the other hand, complete myelitis, affecting all ascending and descending spinal tracts and usually resulting from a full-thickness lesion of the spinal cord, is uncommon in MS.

The differential diagnosis for myelitis is broad and includes infections, parainfectious myelitis, paraneoplastic syndromes, drug/toxin-induced myelitis, neurosarcoidosis, myelitis associated with systemic autoimmune diseases, and other inflammatory central nervous system diseases, including neuromyelitis optica (NMO) and acute disseminated encephalomyelitis. In 15–30% of cases of myelitis, no underlying cause can be determined [2].

In this case, the patient does not fit the stereotypical demographics for a new diagnosis of MS, being male and older than the usual age of onset of MS (20–40 years) [1]. The CSF pleocytosis is unusual; the cell

count is often normal and very rarely greater than 50 cells/μL in MS. While oligoclonal bands are present in up to 95% of cases of MS [3], they are not wholly specific for MS and may be seen in other inflammatory and infectious diseases.

The presence of a longitudinally extensive cord lesion (LETM), or a cord lesion spanning more than three vertebral segments on imaging, is also unusual in MS. On axial sections, LETM usually involves the central cord, unlike the typical eccentric lesions seen in MS, and may produce greater cord swelling than MS cord lesions. A number of diagnoses should be considered in the setting of LETM, although the most important of these are the NMO spectrum disorders. The aquaporin-4 antibody test, negative in this case, is positive in up to 89% of NMO cases [4]. Other clues to NMO are also absent in this patient, such as evidence of optic neuritis or distinctive brain MRI features, such as periependymal or area postrema lesions. Other causes of LETM, such as neurosarcoidosis, parainfectious and connective tissue diseases also appear unlikely given the lack of supportive features on history, examination, or blood tests.

Importantly, the MRI in this case fulfills the McDonald criteria (see Table 1.1) for both dissemination in time (DIT) and dissemination in space (DIS). Acute lesions in MS may show gadolinium enhancement for several weeks, thus the presence of both asymptomatic enhancing and nonenhancing lesions on a single MRI demonstrates lesions of differing chronicity and establishes DIT. MRI criteria for DIS require the presence of lesions in at least two of four regions typically affected in MS; in this case, three of the regions are involved radiologically (periventricular, infratentorial, and spinal cord). The McDonald criteria for MS also require that there is no better explanation for a patient's presentation, as the MRI criteria alone can be fulfilled by other disorders [5]. As the search for alternative diagnoses has been negative and the brain MRI lesions and CSF findings are suggestive, the most likely cause of this patient's CIS is MS.

Whilst initially difficult, receiving an earlier diagnosis of MS reduces patient anxiety related to diagnostic uncertainty and is preferred by patients, according to survey results [6,7].

Clinical pearls

- Spinal cord involvement in MS usually manifests as a partial myelitis, with incomplete and often asymmetrical involvement of ascending and descending tracts.
- Typical MS brain lesions are small ovoid T2 hyperintense lesions of the deep white matter, corpus callosum, and periventricular (including 'Dawson's fingers'), juxtacortical, and infratentorial regions. Spinal cord lesions in MS are typically short-segment lesions of the peripheral part of the cord.
- A thorough search for MS mimics is warranted in cases of CIS when there are atypical clinical or radiological features. The investigative approach must be tailored to the clinical presentation, but may include tests targeting vascular, inflammatory, connective tissue, infective, paraneoplastic, metabolic, and granulomatous diseases.
- Cases of CIS are by definition isolated in time. However, the presence of both asymptomatic nonenhancing and enhancing lesions on a single MRI is sufficient to fulfil DIT criteria for MS. DIS can be demonstrated by MRI lesions in more than one of four regions commonly affected in MS.
- An early diagnosis of MS allows consideration of early commencement of a DMT, which has been associated with a reduction in relapses and decreased long-term disability.

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