

Progressive Weakness, Cognitive Dysfunction and Seizures

A 45-year-old man developed recurrent partial seizures with secondary generalisation. Four years earlier, he had first presented with diplopia from left abducens palsy and right hemiparesthesia, followed by left hemiparesis 1 month later. His magnetic resonance imaging (MRI) brain scan done then is shown in Figure 1. His MRI cervical spine with contrast was unremarkable for any cord lesion. The erythrocyte sedimentation rate, anti-nuclear antibody, anti-double-stranded deoxyribonucleic acid, anti-extractable nuclear antigens, anti-neutrophil cytoplasmic antibodies, anti-cardiolipin antibodies, lupus anticoagulant test, and cerebrospinal fluid (CSF) analysis were unremarkable. He was treated with pulsed steroids and an immunomodulatory agent, but was lost to follow-up.

On re-evaluation during the current admission for seizures, his neurological function had been deteriorating progressively over the past 4 years. He had severe cognitive deficits (Mini-Mental State Examination 2/28), cerebellar dysarthria, and generalised pyramidal weakness with spasticity. Repeat MRI brain scan is shown in Figure 2. Serum

calcium, vitamin B12, lactate, pyruvate, caeruloplasmin, rheumatoid factor, anti-thyroid peroxidase antibodies, anti-glutamic acid decarboxylase antibodies, anti-gliadin IgA and IgG antibodies, human immunodeficiency virus and syphilis serologies, and very long chain fatty acid levels were unremarkable. Ophthalmological examination excluded retinal vasculitic lesions or inflammation; pathergy test was negative. Repeat CSF analysis was positive for oligoclonal bands. Computed tomography thorax showed no evidence of pulmonary sarcoidosis. He was treated with but did not respond to further courses of pulsed steroids.

What is the most likely diagnosis?

- A. Sjögren's syndrome
- B. Multiple sclerosis
- C. Cerebral lupus
- D. CADASIL
- E. Neurosarcoidosis

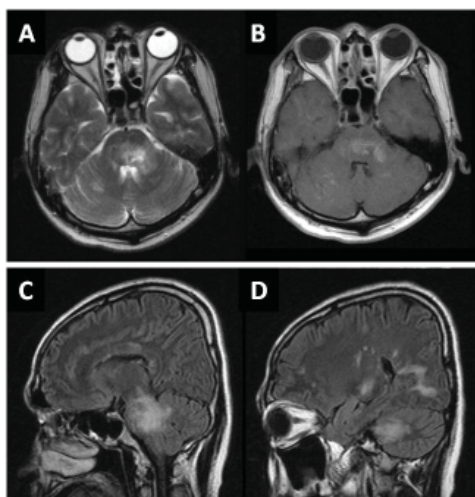


Fig. 1. Axial T2-weighted (A), T1-weighted post-contrast (B) and sagittal FLAIR (C, D) MRI images showing multifocal areas of T2 and FLAIR hyperintensities in both infra- and supra-tentorial regions, including the pons, bilateral subcortical, periventricular deep white matter and corpus callosum, with some of these areas demonstrating enhancement.

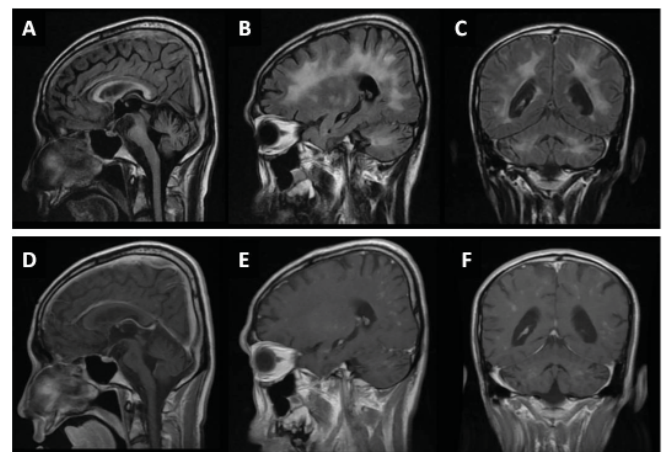


Fig. 2. Sagittal (A, B) and coronal (C) FLAIR, and sagittal (D, E) and coronal (F) T1-weighted post-contrast MRI images showing progression of T2 and FLAIR hyperintensities in the cerebral and cerebellar white matter and cortically, with multifocal patchy enhancement, as well as cerebral and cerebellar atrophy.

Answer: B

Discussion

The patient's progressive neurological dysfunction over 4 years without relapses, combined with the MRI brain lesions disseminated in time and space (in typical periventricular, juxtacortical and infratentorial regions), the presence of CSF oligoclonal bands, and an extensively unremarkable work-up for other autoimmune, infectious and metabolic diseases, is consistent with a diagnosis of primary-progressive multiple sclerosis (PPMS).¹ The lack of response to steroids and immunomodulatory therapy further supports the diagnosis of PPMS.^{2,3}

Although multiple sclerosis (MS) is a predominantly white matter disease, seizures have been reported to occur in about 2% of MS patients, approximately 2.5 to 5 times higher than in the general population.⁴ Seizures can occur throughout the disease course, and are sometimes the first symptomatic manifestation of MS. Seizures have been observed in relapsing-remitting and progressive MS. The aetiology of seizures is thought to be from cortical or juxtacortical lesions with or without inflammation.⁴⁻⁸

Studies suggest that partial seizures are more common in MS patients, accounting for more than 60% of seizures, and secondary generalisation frequently occurs.^{5,6} Data on the prognosis is conflicting, although most studies report good seizure control on standard anti-epileptic regimens.⁵ A few studies have noted an increased incidence of status epilepticus amongst MS patients, ranging from 17.6% to 38.4%, compared to 2% to 10% in the general population of epilepsy patients.⁴

Hence, MS should be considered as a differential diagnosis in patients presenting with seizures, with the relevant clinico-radiological features. The initiation of standard anti-epileptic drugs should be considered even after the first seizure in MS patients.

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