Devic’s disease associated with anti-Ro/SSA antibodies

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Date accepted for publication 14 November 2010

Abstract

Neuromyelitis optica (NMO) and systemic inflammatory diseases are not mutually exclusive. Even when other autoantibodies are present, myelitis extending over 3 vertebral segments with NMO-IgG positivity discloses the diagnosis of NMO. We report the case of an isolated myelitis extending over 6 vertebral segments due to neuromyelitis optica (NMO). Despite the absence of optic nerve involvement, the absence of NMO-IgG in the blood and the presence of symptoms and autoantibodies suggestive of Sjögren syndrome, the diagnosis was founded on spinal magnetic resonance imaging and the detection of NMO-IgG specific antibodies in cerebrospinal fluid.

Keywords

Devic; neuromyelitis optica; aquaporin-4; Sjögren syndrome; antinuclear antibodies; anti-Ro/SSA.

Introduction

Transverse myelitis has an incidence of 1–4 cases per million people per year. This disorder of the spinal cord results in motor, sensory and autonomic dysfunction depending on the level involved. Transverse myelitis can be an initial presentation of numerous diseases. The differential diagnosis is broad but must be done thoroughly as treatment and prognosis varies with etiology.

Case report

We report the case of a 43-year-old woman presenting with gradual paraparesia. Two weeks before admission, she noticed the presence of tingling in her right arm that progressively extended to the ipsilateral leg. The night before admission, she developed left hemi-anesthesia sparing the face and gait was impossible because of weakness in her lower limbs and sensory disturbances. She did not smoke or drink alcohol and has not left northern Europe recently. A thorough interrogation highlighted recurrent xerophthalmia and a previous episode of left hemi-paresthesia lasting no more than 24 h a year ago. Physical examination was unremarkable except for bladder distension. Neurological examination disclosed brisk tendon reflexes on both arms and legs with bilateral Babinski and Hoffmann signs. Vibration sense was abolished up to the right knee and to the left hip. Touch and pain sensation were diminished in both legs and in the left hemi-body up to the clavicle. For both lower limbs, movements against resistance were
possible but impaired. Gait was impossible mainly because of sensory ataxia. Laboratory investigations revealed increased erythrocyte sedimentation rate at 26 mm/h, the presence of antinuclear antibodies identified as anti-Ro/SSA antibodies at a 1/640 titer, immunoglobulin G1 (IgG1) at 16.8 g/L (normal <15 g/L). Double-stranded anti-DNA antibodies, anti-neutrophil cytoplasmic antibodies and anti-phospholipid antibodies were looked for and were negative. Complement testing was normal. Cerebrospinal fluid (CSF) analysis revealed 4 red blood cells per mm³, 40 white blood cells per mm³ (82% lymphocytes) and increased protein at 0.71 g/L (normal <0.45 g/L). Glucose was within normal range and there was no oligoclonal banding. Serological testing on both blood and CSF were negative for hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), cytomegalovirus, Epstein-Barr virus, human T-lymphotropic virus, Coxsackie viruses, adenovirus, enterovirus, herpes simplex virus (HSV)-1, HSV-2, human herpes virus-6, varicella zoster virus, syphilis, Brucella, Lyme disease, Q fever, and Mycoplasma. A Schirmer test was asymmetric with 5 mm on the left eye and 17 mm on the right eye after 5 min. Visual evoked potentials, fundus examination, cutaneous pathergy test and accessory salivary gland biopsy were normal. Spinal magnetic resonance imaging (MRI) showed an extensive C1 to Th1 T2-hyperintense signal enhancing after gadolinium injection (diameter of 11 mm at the C6 level, Fig. 1) and brain MRI was normal. Isolated extensive longitudinal myelitis led us to suspect a diagnosis of neuromyelitis optica (NMO) and the detection of antibodies directed against aquaporin-4 in the CSF confirmed the diagnosis.

**Discussion**

Paraparesis associated with bilateral pyramidal syndrome, sensory level and bladder dysfunction is suggestive of spinal cord involvement. In this case, MRI ruled out compression. Five categories of diseases were thus considered: vascular, infectious, demyelinating, inflammatory and neoplastic[1]. Gradual onset over several hours argues against an ischemic origin. Medical history including a previous episode of hemi-paresthesia makes the infectious origin unlikely. Relapsing acute transverse myelitis has been reported during HSV-1 and -2, HBV, HCV or *Brucella* infections[2]. All the serological/polymerase chain reaction screenings for infectious myelitis on blood and CSF were negative. Tumors of the spinal cord do not present with a relapsing/remitting course and the onset of symptoms is longer than several hours except for intratumoral hemorrhages. In our case, the former episode and the absence of bleeding argued against a neoplastic origin. The most difficult part of the differential diagnosis is to distinguish

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**Fig. 1.** MRI slice showing the extensive C1 to Th1 T2-hyperintense signal.
demyelinating from inflammatory lesions. Multiple sclerosis (MS) myelitis is typically short segmented and associated with brain white matter lesions and oligoclonal banding in the CSF. An isolated lesion extending over 6 vertebral segments makes it unlikely. Connective tissue and granulomatous diseases may present with acute or subacute myelitis. Systemic lupus erythematosus (SLE), Sjögren syndrome, mixed connective-tissue disease, systemic sclerosis, sarcoidosis, Behçet disease and anti-phospholipid syndrome have all been associated with myelitis. Detection of anti-Ro/SSA antinuclear antibodies, the result of the Schirmer test and a high IgG1 level suggested the diagnosis of primary Sjögren syndrome (PSS). In PSS, neurological manifestations may precede the diagnosis. Among 82 patients with PSS, acute transverse myelitis was the only symptom in 17 patients. Neuromyelitis optica classically associates optic neuritis with extensive spinal cord lesions and few if any brain white matter lesions. A definite diagnosis of NMO is made when there is acute myelitis or optic neuritis and at least 2 of 3 supportive criteria: continuous spinal cord lesion extending over 3 or more vertebral segments, brain MRI not meeting diagnostic criteria for MS and NMO-IgG positive status. Myelitis over 3 vertebral segments with NMO-IgG has a 73% sensitivity and a 100% specificity for NMO diagnosis. Antinuclear antibodies are found in 53% of patients with NMO and an anti-SSA characterization is found in 17% of patients with NMO and NMO-IgG. A recent study showed that for myelitis meeting criteria for NMO with positive NMO-IgG and antinuclear antibodies, the diagnosis should be NMO. However, as NMO may coexist with PSS or SLE, clinicians should be careful in the follow-up for systemic manifestations of any systemic disease.

Conclusions

Our case illustrates the difficult etiological assessment of myelitis. Despite thorough investigations, 17% of cases of relapsing myelitis remain idiopathic. Extensive myelitis should raise the possibility of NMO even in the absence of optic nerve involvement. NMO and systemic inflammatory diseases are not mutually exclusive. Extensive myelitis over 3 vertebral segments and NMO-IgG positivity is due to NMO even in the presence of other autoantibodies. The presence of NMO-IgG does not exclude PSS or SLE as these conditions can coexist. Therefore the clinician must always be vigilant for systemic manifestations in the follow-up care of these patients.

Teaching points

- NMO-IgG may be present in the CSF even if they are absent in the blood. This observation highlights the importance of the CSF analysis in the diagnostic workup of suspected Devic’s disease.
- Bilateral paraparesia, bladder dysfunction and the presence of a sensory level evolving over hours or sometimes over a week or two are suggestive of myelitis.
- Causes of myelitis are vascular (19%), infectious (17%), demyelinating (11%), associated with systemic disease (20%), NMO (17%) and idiopathic (16%).
- Extended myelitis should raise the possibility of NMO even without optic neuritis.
- Neuromyelitis optica and systemic inflammatory diseases are not mutually exclusive. Even when other autoantibodies are present, myelitis extending over 3 vertebral segments with NMO-IgG positivity discloses the diagnosis of NMO.

References