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What Started This? Debilitating Longitudinally-extensive Myelitis

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PRESENTATION

The patient's recurring symptoms suggested neurologic disease but the problem was, in fact, rheumatologic. A 50-year-old right-handed woman presented with focal motor and sensory deficits in both her upper and lower extremities. This was the fourth time in a year that she had developed various acute neurologic deficits. Each previous episode began with acute subscapular back pain followed by variable lower extremity weakness and muscle spasms. Magnetic resonance imaging (MRI) had consistently demonstrated an acute noncompressive spinal myelopathy, but diagnosis had otherwise remained elusive.

On each occasion, pulsed-dose intravenous methylprednisolone, 1000 mg daily for 3 days, provided interval improvement, but the patient would relapse in weeks to months. Her medical history included 5 years of xerophthalmia, confirmed by Schirmer's test, which was severe enough to require treatment with punctal occlusions. She also had dental disease that had necessitated implants and dentures. Her mother and brother had Sjögren's syndrome.

ASSESSMENT

On examination, the patient had Lhermitte's sign and left hand-grip weakness. She also had a Babinski reflex, increased tone, hyperreflexia, and decreased sensation to proprioception and temperature in the left lower extremity. Decreased sensation to vibration was evident in the right lower extremity. She had an L4 sensory level bilaterally. A wide-based antalgic gait was noted in conjunction with a right foot drop. Her musculoskeletal examination did not identify synovitis in any small or large joints and was generally unremarkable. A fluid-attenuated brain MRI showed scattered areas of hyperintensity consistent with small vessel ischemia, such as is often seen with atherosclerosis. A T2-weighted spinal MRI demonstrated acute longitudinally-extensive myelitis with central enhancement from C7- T1 and T3-T4 (**Figure**).

To eliminate important diagnoses such as multiple sclerosis, Devic's disease (neuromyelitis optica [NMO]), infection, or inflammatory processes, many tests and studies ensued. Test results for anti-double-stranded DNA, anti-ribonucleoprotein, anti-Smith, anti-human T-lymphotropic virus 1 were all negative, as was testing for Devic's disease; no NMO-IgG (specifically, aquaporin-4 antibodies) were present. Similarly, her serum was negative for *Treponema pallidum* and human immunodeficiency virus; serum protein electrophoresis was negative for abnormal bands.

Results from a visual evoked potentials test were normal. The patient's cerebrospinal fluid contained no oligoclonal bands and no indication of herpes simplex virus, enteroviruses, bacterial infection, or a paraneoplastic process that might cause her symptoms. A chest radiograph showed no evidence of hilar adenopathy. However, laboratory data demonstrated strongly positive levels of anti-Sjögren's syndrome A (anti-SS-A or anti-Ro) and anti-Sjögren's syndrome B (anti-SS-B or anti-La), as well as reduced complement levels (C4, 6 mg/dL; C3, 69 mg/dL) (**Table**).

DIAGNOSIS

The patient received a new diagnosis of Sjögren's syndrome. Acute noncompressive myelitis can occur as a manifestation of infarction, systemic inflammatory disorders (eg, systemic lupus erythematosus, sarcoidosis, etc.), demyelinating diseases, and infectious/post-infectious causes.

While patients with Sjögren's syndrome most often present with xerophthalmia and xerostomia, systemic manifestations including neurological deficits can occur (**Table**). Peripheral nerve involvement is well described and occurs with an estimated prevalence of up to 20%. In contrast,

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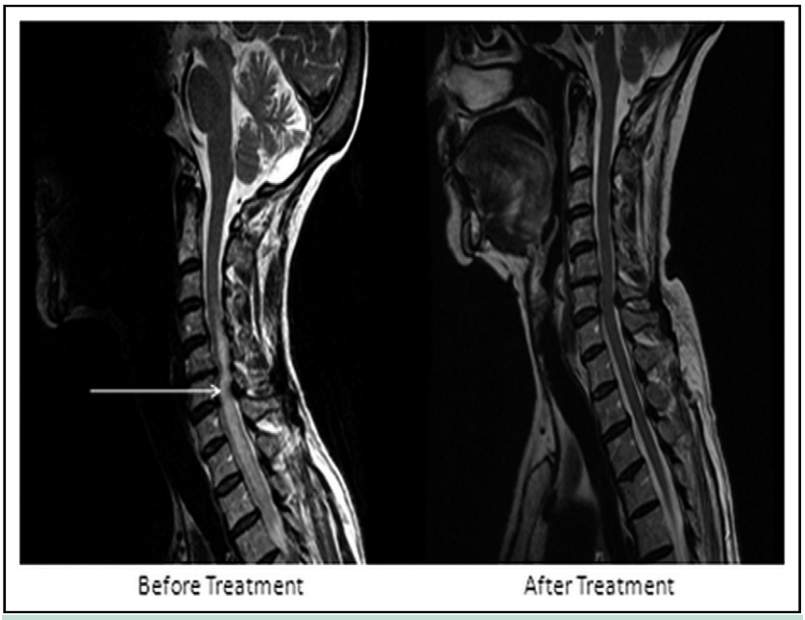

Figure (**A**) A T2-weighted spinal MRI demonstrated acute longitudinally-extensive myelitis with central enhancement from C7- T1 and T3-T4. (**B**) Another T2-weighted spinal MRI showed resolution after treatment.

central nervous system manifestations are uncommon, with a reported prevalence of only 4.8%.[1] When spinal cord involvement is present, it manifests most frequently as acute transverse myelitis, Brown-Séquard syndrome, or progressive myelopathy.

Table Revised American-European Consensus Group Criteria for the Diagnosis of Sjögren Syndrome

I Ocular Symptoms	Dry eyes for more than 3 months, foreign-body sensation, or the use of tear substitutes more than 3 times daily
II Oral Symptoms	Feeling of dry mouth for more than 3 months, recurrently swollen salivary glands, or frequent use of liquids to aid swallowing
III Ocular Signs	Schirmer test performed without anesthesia ($<$ 5 mm in 5 min) or positive vital dye staining results
IV Oral Signs	Abnormal salivary scintigraphy findings, abnormal parotid sialography findings, or abnormal sialometry findings (unstimulated salivary flow $<$ 1.5 mL in 15 min)
V Histopathology	Positive minor salivary gland biopsy findings showing focal lymphocytic sialoadenitis
VI Auto-antibodies	Positive anti-SSA or anti-SSB antibody results

For a Diagnosis of Sjögren Syndrome must have: 4 of the 6 criteria including either item V (Histopathology) or VI (Auto-antibodies) OR any 3 of the 4 objective criteria (items III, IV, V, VI).

MANAGEMENT

Regardless of the etiology, the symptoms and sequelae of longitudinally-extensive myelitis are often catastrophic and debilitating, making prompt diagnosis and treatment paramount. Evidence-based data are limited due to the dearth of patients with Sjögren's syndrome and central nervous system manifestations, and this has led to the anecdotal recommendation that treatment consist of a T-cell immunosuppressant and corticosteroid. Importantly, Devic's disease, in which NMO antibodies are present, results in a relapsing-remitting course of longitudinally-extensive myelitis with optic nerve involvement and also must be considered, as it is often responsive to B-cell, rather than T-cell, targeted therapy.[2]

In 4 case series, the majority of patients improved when given intravenous cyclophosphamide. Therefore, it has been suggested as a first-line immunosuppressant for the central nervous system manifestations of Sjögren's syndrome.[3-5] Additionally, there are 2 reports demonstrating that azathioprine plus corticosteroids has shown promising results with variable rates of relapse.[6]

In addition to prednisone, 60 mg daily, our patient received monthly intravenous cyclophosphamide, initially dosed at 750 mg/m^2. This was then adjusted based on a white cell count nadir. After her third infusion, the prednisone was tapered, and following the sixth infusion, maintenance therapy with azathioprine was initiated. She currently remains free of neurological symptoms, and an MRI following the completion of her treatment indicates resolution of the lesions seen at initial presentation (**Figure**).

Very few reports of acute longitudinally-extensive myelitis in patients with Sjögren's syndrome exist in the literature. Our case adds to the limited body of evidence for treatment regimens.

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