Acute myeloneuropathy: An uncommon presentation of Sjögren's syndrome

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Abstract

Sjögren's syndrome is associated with central and peripheral nervous system involvement. The peripheral neuropathy is usually a sensory predominant neuropathy or a cranial neuropathy. Myelopathy is usually of focal, subacute, chronic or relapsing type. Acute myeloneuropathy as the predominant manifestation has not been described in the literature. We describe a middle aged woman who presented with an acute onset motor quadriparesis and bladder dysfunction. She had dryness of eyes and mouth for 8 months. Nerve conduction studies revealed motor axonal neuropathy and magnetic resonance imaging of spinal cord showed T2 hyperintensities involving entire cord. Mild perineural fibrosis, focal foamy changes in endoneurium and lymphocytic infiltration were seen in sural nerve biopsy specimen. Patient improved clinically after intravenous methylprednisolone therapy.

Key Words

Myeloneuropathy, sjögren's syndrome, vasculitis

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Introduction

Sjögren's syndrome (SS) is an autoimmune disorder characterized by decreased secretions of lacrimal and salivary glands (sicca symptoms). Central and peripheral nervous system involvement in SS is a result of vasculitis as well as direct immunological injury to neurons. Spectrum of SS-associated neuropathy include sensory ataxic neuropathy, trigeminal neuropathy, multiple mononeuropathy, radiculoneuropathy, painful sensory neuropathy without sensory ataxia, autonomic neuropathy with anhidrosis and multiple cranial neuropathy.[1] Acute motor axonal neuropathy resembling Gullaine Barre syndrome in SS is unusual and described in only a few case reports. SS-associated myelopathy manifests usually as acute transverse myelitis, which is found in about 1% patients.[2] However, extensive involvement affecting entire spinal cord is very unusual. We describe here, a woman with SS, which had unusual neurological features in the form of an acute motor axonal neuropathy and myelopathy affecting entire length of spinal cord.

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Case Report

A 40-year-old female presented to our hospital with complaints of diffuse low intensity pain in all four limb since 20 days. She also noticed tingling sensation in all four limbs, which started distally and progressed proximally within 24 h. Simultaneously she noticed weakness in all four limbs, which started proximally and progressed to distal muscles over 24-30 h in all 4 limbs. She also complained of dysuria, urinary retention and incomplete emptying of the bladder. She had a history of gritty sensation in both eyes and dryness of mouth for last 8 months, for which she had to repeatedly take sips of water while having her food. Clinical examination revealed normal higher mental functions and cranial nerves. Hypotonia was noted in all four limbs. Power was Medical Research Council (MRC) grade 3/5 proximally and MRC grade 2/5 distally in both upper and lower limbs. Both superficial reflexes and deep tendon jerks were absent. Sensory examination was normal. No neck rigidity, local spinal deformity or nerve thickening was noted.

Investigations showed normal complete hemogram blood sugars (fasting and post-prandial), serum Vitamin B12 levels, thyroid function tests, renal function tests, enzyme-linked immunosorbent assay for human immunodeficiency virus, hepatitis B surface antigen and anti- hepatitis C virus tests. Both erythrocyte sedimentation rate and C-reactive protein were raised 24 mm at the end of 1 h and 19 mg/L respectively. Liver function tests were normal except serum albumin was low (1.9 g/dl) with reversal of globulin

albumin ratio. Serum protein electrophoresis was normal. Magnetic resonance imaging (MRI) spine revealed diffuse T2 hyperintensity throughout the cord [Figure 1]. The nerve conduction studies revealed sensorimotor axonal polyneuropathy with absent F and H reflex [Figure 2]. Cerebrospinal fluid (CSF) analysis revealed mild pleocytosis with total cells of 20, predominantly lymphocytes (95%), CSF protein was raised (50 mg/dl) and CSF sugar was normal. CSF analysis for tuberculosis-polymerase chain reaction and virology (Epstein-barr virus, JE, cytomegalovirus and herpes simplex virus) was negative. Anti-nuclear antibodies were raised in the titre of 1:100. Anti-SS-A was positive, but anti –Sm was negative. Rheumatiod factor and anti-cyclic citrullinated peptide were negative. Histopathology of sural nerve biopsy showed mild perineural fibrosis, focal foamy changes in endoneurium with mild lymphocytic infiltration [Figure 3]. Wade Fite stain for *Mycobacterium leprae* was negative. Schirmer's test was positive in both eyes (2 mm/5 min in the right eye and 3 mm/5 min in the left eye). Patient didn't give consent for salivary gland biopsy. She was treated with IV methylprednisolone 1 g/d for 5 days followed by oral prednisolone 50 mg/day. She received anti-cholinergic medications for urinary incontinence. The clinical improvement was seen in the patient with power improvement to MRC grade 4+ in proximal as well as distal muscle groups in all 4 limbs. Follow-up MRI study demonstrated normalization of altered signals on the spinal cord [Figure 4]. However, urinary incontinence persisted and subsequent uroflowmetry showed hypocontractile bladder with low compliance, which partly improved with anticholinergic drugs.

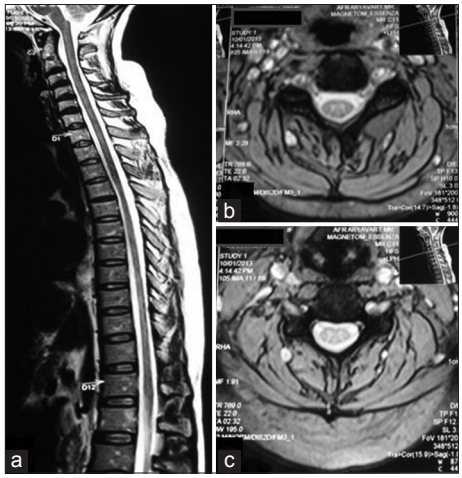

Figure 1: (a) Sagittal T2-weighted magnetic resonance imaging image shows diffuse hyperintensity throughout the spinal cord, (b and c) MRI T2-weighted (axial) cervical spine showing hyperintense signal

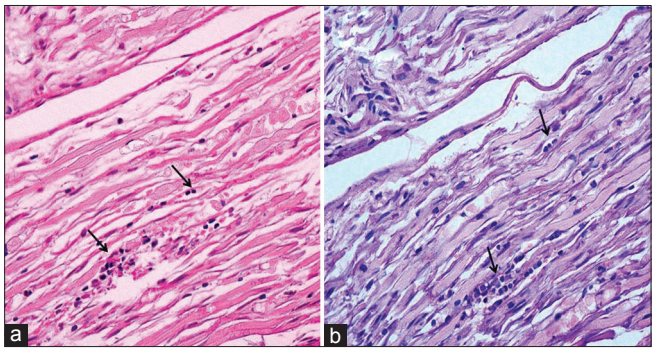

Figure 3: (a) Section of nerve showing several mononuclear inflammatory cells in the endoneurium (arrow) H and E, ×200, (b) Section of nerve showing collections of lymphocytes in endoneurial space (arrows) H and E, ×400

Discussion

SS is an autoimmune condition characterised by xerophthalamia, xerostomia due to the lymphocytic infiltration of exocrine glands. Diagnosis of primary SS requires the presence of 4 out of 6 following criteria: Ocular symptoms, oral symptoms, ocular signs, histpathology, salivary gland involvement and positive antibodies[3] our patient satisfied four out of these six criteria. Though SS is a common disorder in the western population, this disease is relatively uncommon in India, accounting for 0.5% of rheumatic diseases in a series from a tertiary care centre in India. Moreover, peripheral neuropathy occurred in only one out of 26 patients in that series.[4]

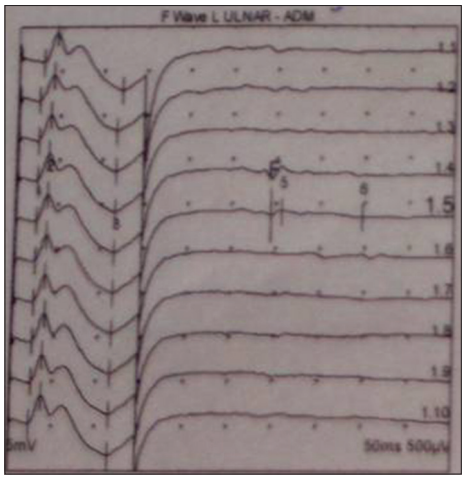

Figure 2: Absent F wave response on left ulnar nerve stimulation

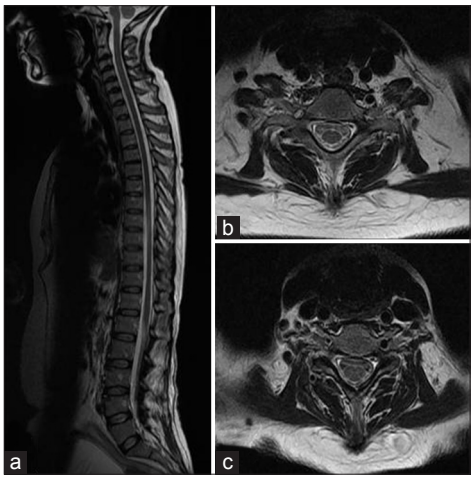

Figure 4: Follow-up magnetic resonance imagingT2W images (a) sagittal view of whole spine, (b and c) axial T2 images of cervical spine showing normalization of hyperintense signal

The neurological complications are relatively uncommon compared to other extraglandular symptoms in SS.[5] Various neurological manifestations have been reported in SS affecting both the peripheral as well as the central nervous system (CNS). Peripheral neuropathy is the commonest reported manifestations of SS, which usually has a predominant sensory component. In a large series of 92 patients, pure sensory ataxic neuropathy without any weakness was the most common presentation followed by painful sensory neuropathy.[1] Optic neuritis, oculomotor, trochlear, trigeminal, facial, ninth and tenth cranial neuropathies (isolated as well as multiple) have been reported.[1,5] However, a pure motor axonal type neuropathy has been reported in only a few case reports.[6,7] In SS associated axonal type neuropathy, the loss of axons usually occurs due to ischemic damage to axons as a consequence of vasculitis. However, in our patient, sural biopsy showed diffuse lymphocytic infiltration of the nerve. This observation shows that the axonal damage occurred due to an autoimmune process primarily directed against neuronal antigens, rather than ischemic damage due to vasculitis. Similarly, mononuclear infiltration of dorsal root ganglia has been observed previously. On this basis, anti-neuronal antibodies and anti-Ro antibodies have been implicated in the pathogenesis of neurological manifestations of SS.[1,5,8] Conventionally, corticosteroids constitute the mainstay of therapy in SS and in extra-glandular disease associated with SS. Hence, we treated our patients with methylprednisolone and patient showed satisfactory response. Mochizuki *et al*. treated a similar patient with acute motor predominant neuropathy and another patient having SS-associated chronic inflammatory demyelinating polyneuropathy with intravenous immunoglobulins and found a favourable response.[6]

In another study, CNS involvement was also found along with peripheral neuropathy. The disease course mimicked multiple sclerosis and 30% of patients with CNS lesions had oligoclonal bands. In this study, symmetrical sensorimotor axonal neuropathy with predominant sensory neuropathy was most commonly seen.[8] However, Arai *et al*. state that myelopathy is a very rare condition in SS and only 12 cases, including their case, had been reported. The clinical manifestations of myelopathy were acute or subacute transverse myelitis, chronic progressive myelopathies or relapsing and remitting cord syndromes. Most commonly, thoracic spinal cord was affected.[9] In SS associated myelopathy, predominant posterior column involvement has been reported.[1] However, as per current literature, an acute onset extensive myelopathy involving entire length of spinal cord as in our case, is very unusual. Acute or chronic myelopathy and myeloneuropathy due to SS have been reported to respond well to cyclophosphamide.[8,9] However, larger prospective cohort studies of such patients are needed to give better insight regarding management protocols such as the choice, dose and duration of immunomodulation.

Thus, our case demonstrates the importance of evaluation of appropriate patients with neuropathy or myeloneuropathy for rheumatological disorders, especially SS.

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