Sjögren’s Syndrome Related Sensory Motor Neuropathy and Autonomic Neuropathy: A Case Report

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Introduction

Neurologic involvement has been reported in primary Sjögren’s syndrome (SS) in approximately 10–25% of cases.1,2,3 Peripheral neuropathy is a major neurological manifestation of Sjögren’s syndrome1 and its etiology has been considered to be vasculitis in the peripheral nerves.2 While neuropathic symptoms of SS can be varied, it is unusual to have two different types of neuropathic presentations simultaneously in a patient. We describe a case of Sjögren’s syndrome presenting with autonomic symptoms who was noted to have large fiber neuropathy on EMG and inflammatory changes on nerve biopsy.

Case report

A 65 year old man presented with eight-month history of presyncopal and syncopal episodes lasting few seconds associated with change in position, mostly on standing up. He was hospitalized for multiple syncopal episodes. He denied any aura or prodromal symptoms, urinary incontinence, tongue biting, confusion, dysarthria, dysphagia, focal weakness, numbness. He had unintentional weight loss of about 40 lbs in one year. Patient had dry eyes and dry mouth and was diagnosed with Sjögren’s syndrome about five years ago based on serology (SS-A positive, SS-B negative). Plaquenil was tried for his SS but was not effective, hence stopped. He failed Fludrocortisone for his syncopal episodes. Other significant past medical history included anemia, hip replacement, and depression. Patient had history of smoking and he denied heavy alcohol use. His medications included albuterol, metoclopramide, midodrine 10 mg 3 times a day, pantoprazole 40 mg daily, pyridostigmine 60 mg 4 times a day, and Spiriva.

Examination showed positive orthostatic vitals (blood pressure lying down 103/68 with a pulse of 65, sitting 92/63 with a pulse of 70, standing 62/40 with a pulse of 75) and weight of 57 kg. Neurological examination patient showed normal speech, memory, attention, concentration. Cranial nerve examination was normal. Motor examination showed full strength throughout with no atrophy and normal tone. Reflexes were 2 throughout. Sensory examination showed decreased pinprick distal to mid-shin level bilaterally. Position and vibration sense were intact at the toes. Coordination was normal. The patient was able to get up from seated position, although slowly due to fear of passing out.

Work up showed normal cardiac enzymes, normal cortisol, lactate level, HBA1c was 5.6. Patient had a spinal tap that was normal for cerebrospinal fluid analysis except for high protein of 63, no oligoclonal bands, negative for malignant cells. Invitae cardiomyopathy panel, transthyretin amyloid panel, comprehensive neuropathy panel were negative. MRI brain showed chronic left posterior cerebellar stroke with ischemic white matter changes, which were minimal. Work up for malignancy was negative: CT chest, abdomen, and pelvis showed emphysematous changes and bilateral renal cysts. Testicular ultrasound noted no malignancy. Gastric endoscopy showed mild gastritis. Cardiac work up was included; electrocardiogram (EKG) showed normal sinus rhythm, left axis deviation, poor R-wave progression concerning for possible anterior septal infarct, and nonspecific ST-segment changes in the anterior precordium. Echocardiogram showed small to normal LV cavity size with normal systolic function, ejection fraction of 65%, mild mitral regurgitation, and mild tricuspid regurgitation.

An electrodiagnostic study from an outside facility showed mild generalized sensory motor peripheral polyneuropathy.

He had a left sural nerve biopsy done which showed moderate loss of large and small myelin axons and focal moderate perivascular chronic inflammation in the epineurium (Figure 1 and 2). Congo red-positive amyloid and onion-bulb formation were not seen.

Patient was started on Prednisone 50 mg daily for three months that was tapered slowly over several months. He was on lansoprazole for gastric prophylaxis. He had failed fludrocortisone at outside facility, so he was started on midodrine instead, which did not help either. A follow up visit few months later showed reduced frequency of dizzy spells when changing position and weight gain of about 5 pounds.
Sjögren’s syndrome is a systemic autoimmune disease characterized by xerophthalmia and xerostomia; it is associated with widespread systemic visceral involvement.\textsuperscript{5} The neurologic manifestations of primary Sjögren’s syndrome are varied and can be divided anatomically into two categories: peripheral neuropathies and central nervous system (CNS) conditions.\textsuperscript{6} Peripheral neuropathy is a major neurological manifestation.\textsuperscript{5} The reported neuropathies in primary Sjögren’s syndrome include distal sensory polyneuropathy, axonal sensorimotor polyneuropathy, chronic inflammatory demyelinating polyneuropathy (CIDP), multiple mononeuropathy, sensory neuronopathy and small fibre neuropathy.\textsuperscript{7} Sensory symptoms without substantial motor involvement are observed predominantly in sensory ataxic, painful sensory, trigeminal, and autonomic neuropathies.\textsuperscript{7} Motor impairment is apparent in multiple mononeuropathy, multiple cranial neuropathy, and radiculoneuropathy. Auto-

### Table 1. Nerve conduction studies in a patient with Sjögren’s syndrome-related neuropathy

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Sensory Distal Latency (ms)</th>
<th>Sensory Distal Amplitude (MicroV)</th>
<th>Motor Distal Latency (ms)</th>
<th>Motor Distal Amplitude (mV)</th>
<th>Motor Conduction Velocity (m/s)</th>
<th>F Wave Latency (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median*</td>
<td>NR (&lt;4.3)</td>
<td>NR (≥4.5)</td>
<td>7.7 (≥4.0)</td>
<td>49.7 (≥49.0)</td>
<td>39.6 (≤31)</td>
<td></td>
</tr>
<tr>
<td>Ulnar*</td>
<td>NR (&lt;4.1)</td>
<td>NR (≥8.0)</td>
<td>12.0 (≥5.0)</td>
<td>47.5 (≥49.0)</td>
<td>39.0 (≤32)</td>
<td></td>
</tr>
<tr>
<td>Radial**</td>
<td>3.3 (≤2.9)</td>
<td>23.2 (≥15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peroneal†</td>
<td>6.9 (≤6.1)</td>
<td>0.4 (≤1.5)</td>
<td>30.8 (≤35)</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibial**</td>
<td>7.2 (≤6.6)</td>
<td>0.2 (≤3.0)</td>
<td>38.4 (≤38)</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sural</td>
<td>NR (≤5.10)</td>
<td>NR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superficial Peroneal</td>
<td>NR</td>
<td>NR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NR = no response. Normal values in parentheses.

*Stimulating wrist, recording digits 2 or 5 (sensory) or recording abductor pollicis brevis or abductor digiti minimi muscle (motor).

**Stimulating forearm, recording anatomical snuff box.

†Stimulating ankle, recording extensor digitorum brevis muscle.

**Stimulating ankle, recording abductor hallucis muscle.

### Discussion

Sjögren’s syndrome is a systemic autoimmune disease characterized by xerophthalmia and xerostomia; it is associated with widespread systemic visceral involvement.\textsuperscript{5} The neurologic manifestations of primary Sjögren’s syndrome are varied and can be divided anatomically into two categories: peripheral neuropathies and central nervous system (CNS) conditions.\textsuperscript{6} Peripheral neuropathy is a major neurological manifestation.\textsuperscript{5} The reported neuropathies in primary Sjögren’s syndrome include distal sensory polyneuropathy, axonal sensorimotor polyneuropathy, chronic inflammatory demyelinating polyneuropathy (CIDP), multiple mononeuropathy, sensory neuronopathy and small fibre neuropathy.\textsuperscript{7} Sensory symptoms without substantial motor involvement are observed predominantly in sensory ataxic, painful sensory, trigeminal, and autonomic neuropathies.\textsuperscript{7} Motor impairment is apparent in multiple mononeuropathy, multiple cranial neuropathy, and radiculoneuropathy. Auto-

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**Figure 1.** H &E (Hematoxylin and Eosin) stained section (10 X objective) shows focal moderate chronic inflammation near a vessel in the epineurium.

**Figure 2.** Toluidine blue stained section (20 X) shows moderate loss of large and small myelinated axons with rare regenerative axonal clusters.
onomic symptoms such as abnormal pupils and orthostatic hypotension are particularly noted in patients with sensory ataxic, painful, trigeminal, and autonomic neuropathies.5

Our patient demonstrated autonomic symptoms along with sensory motor neuropathy findings on electrophysiological testing. The old stroke noted on MRI in the absence of vascular risk factors in our patient could be one of the central nervous system manifestations of Sjögren's syndrome.

The broad range of symptoms is in part derived from the varied pathophysiology of the disease. Central pathology can reveal direct infiltration of monocytes into the CNS versus indirect vascular compromise via autoimmune attack of the large and/or small vessels.8 Similarly, peripheral involvement can include either peripheral infiltration of autoimmune cells vs vascular disruption of the different structures eliciting varied effects, however direct antibodies against type 3 muscarinic receptors have also been described.9 Given the diverse pathology found in SS, electromyographic (EMG) findings would be equally assorted, fitting the associated structures damaged. Göransson discovered 55% of the SS patients studied revealed EMG abnormalities with 27% showing axonal polyneuropathy, but sensory only and motor only findings were also reported.10 The standard serological tests (anti-SS-A, SS-B) are less sensitive compared to minor salivary gland biopsy in the diagnosis of SS.11

For the therapy of neuropathy associated with Sjögren's syndrome, corticosteroids14 immunosuppressants,7 plasmapheresis,13 and immunoglobulin14,15,16 administration have been reported anecdotally and suggest a favorable therapeutic response. Several reports have documented success with rituximab for sensory ataxic neuropathy. Treatment of small-fiber neuropathy is aimed initially at symptomatic relief of the associated pain.15 In the long-term follow-up, these patients ultimately showed progression of symptoms.3

Our case highlights the need to recognize autonomic signs in patients with Sjögren's syndrome and consider a broad differential. The nerve findings of moderate perivascular inflammation of the epineurium helped solidify the diagnosis, as well as the quick response to steroids. The EMG findings show classic form of a sensorimotor axonal polyneuropathy that can occur in SS in addition to the focal neuropathies that happen secondary to the perivascular inflammation. Immune suppression is the mainstay treatment and can result in improvement of symptoms.

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References
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