

A Case of Sjogren's Syndrome with Sensory Ganglionopathy

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Abstract: Sensory ganglionopathy may associate with Sjögren's syndrome (SS) and its clinical presentation is dominated by symptoms of damage to the type 1a large sensory fibers. Here we describe a case of SS with sensory ganglionopathy. A 27-year-old lady presented with imbalance and tingling-numbness of all limbs for 4 months. Imbalance aggravated during standing and walking, and was more marked in the dark. Tingling and numbness were asymmetrical, more marked in the upper limbs. She also complained of dry mouth and feeling of stickiness during swallowing for 9 months along with significant weight loss (about 25-kg over 6 months). Examination revealed hypotonia and areflexia, but muscle power was normal. There was an athetoid movement of the upper limbs, more marked after closing eyes. All modalities of sensation were impaired in all limbs. Romberg's sign was positive and she had an unstable gait. Investigation revealed positive ANA, positive RNP, and positive SS-A. Schirmer's test and saliva flow test was positive. Histopathological examination of labial mucosa revealed a Focus score of >1. Nerve conduction study (NCS) revealed absent sensory nerve action potentials (SNAP) both upper and lower limb nerves. Magnetic resonance imaging (MRI) of the spine revealed mild thickening of dorsal root ganglia and corresponding nerve roots. A diagnosis of primary Sjogren's syndrome with ganglionopathy was made and the patient was started on corticosteroids and azathioprine. Neurologists should be aware of possible autoimmune origins of neuropathies and neuronopathies, as these are potentially treatable condition.

Keywords: Sjögren's Syndrome, Ganglionopathy, Imbalance

1. Introduction

Sjögren syndrome (SS) is a systemic autoimmune disease. It predominantly affects middle-aged women (male/female ratio 1:9) and the prevalence is 0.1 to 3 per 1,000 population in different epidemiologic surveys [1]. Exocrine glands, particularly the salivary and lacrimal glands, are predisposed to SS. [2]. However, Widespread extraglandular neurological, rheumatological, pulmonary, or gastrointestinal symptoms are present in at least one-third of patients. In SS, neurological symptoms are not uncommon. The prevalence

of neurological manifestations in primary SS varies between 10 and 60% [3]. Five to fifteen percent of people with Sjögren's disease have polyneuropathies, of which forty percent have large-fiber sensory ganglionopathies and twenty percent have small-fiber sensory neuropathies or ganglionopathies [4]. SS may not be identified in such patients before the appearance of neurological symptom [5]. Here, we present a primary SS case who presented with predominant neurological symptoms.

2. Case Report

A 27-year-old lady, a known case of hypothyroid and hypertension, was admitted to hospital with the complaints of imbalance and tingling-numbness of all limbs for 4 months. Her complaints were insidious and progressive. Imbalance aggravated during standing and walking, and was more marked in the dark. These symptoms were also associated with clumsiness while holding objects, writing, and buttoning. Tingling and numbness were asymmetrical and were more marked in the upper limbs. She also complained of dry mouth and feeling of stickiness during swallowing for last nine months along with significant weight loss. She had lost about 25-kg weight over a period of six months. She experienced difficulty in swallowing solid and dry food and tried to manage by drinking excess water with food. These difficulties were not associated with nasal regurgitation or slurred speech. There was also an occasional sandy feeling within the eye. Her bowel-bladder habit was normal, having no history of fever, joint pain, skin rash, chronic loose motion, diabetes, or cough.

She was being treated with thyroxine for one year and multiple antidepressants and anxiolytic medications.

On examination, the lady was cautious and oriented, the speech was normal and all cranial nerves including the fundus were normal. Motor examination revealed hypotonia and areflexia, but muscle power was normal. There was an athetoid movement of the upper limbs, more marked after closing eyes. All modalities of sensation were impaired in all limbs. Romberg's sign was positive and she had an unstable gait.

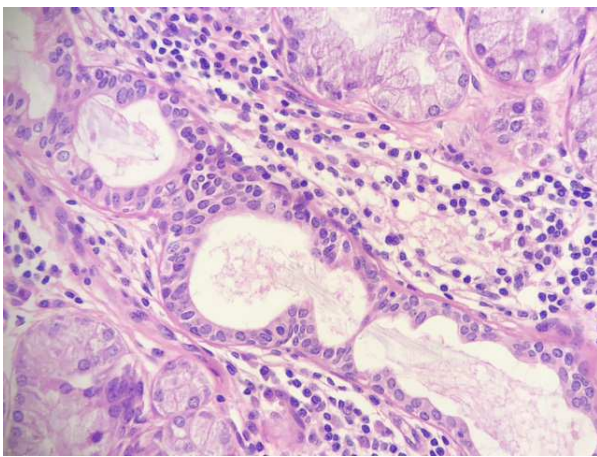


Figure 1. Histopathology of labial mucosa biopsy showing Focus score >1.

Investigation revealed a normal blood count with moderately elevated erythrocyte sedimentation rate (ESR). Blood glucose and other biochemical parameters were normal. Cerebrospinal fluid (CSF) study revealed an elevated protein level (77.7 mg/L); although other parameters including glucose level and cell count were normal. Nerve conduction study (NCS) was performed which revealed that sensory nerve action potentials (SNAP) were absent in both upper and lower limb nerves, which was consistent with sensory polyneuropathy.

Magnetic resonance imaging (MRI) of the spine was done which revealed mild thickening of dorsal root ganglia and corresponding nerve roots. Shirmer's test and saliva flow test were positive. Screening of autoimmune antibodies revealed positive anti-nuclear antibody (ANA), antibodies to ribonucleoprotein (RNP), and anti Sjögren's-syndrome-related antigen A (SS-A) antibody were positive. Histopathological examination of labial mucosa revealed a Focus score of more than one, which is typical of Sjögren syndrome (Figure 1). A diagnosis of primary Sjögren's syndrome with ganglionopathy was made and the patient was started on corticosteroids and azathioprine. She is currently under follow up.

3. Discussion

A wide spectrum of neurological manifestations may be present in patients with primary SS. The neurological manifestations may be the initial symptom or may appear later on in the progression of the illness. Sensory neuropathies, axonal sensorimotor polyneuropathy, mononeuropathy, multiple mononeuropathy, demyelinating polyradiculoneuropathy, cranial neuropathy, and autonomic neuropathy are the peripheral polyneuropathy subtypes seen in SS. The subtypes of peripheral neuropathy vary in how they present clinically. But all of them may lead to deterioration of quality of life. In a group of patients with primary SS, a recent investigation found a significant prevalence (46%) of peripheral nerve system involvement [6]. The symptoms of dry eye and dry mouth in primary SS may be underdiagnosed because of vagueness of the complaints. So comprehensive immunological testing to evaluate this condition is vital [7].

Due to the porous blood-nerve barrier created by the fenestrated endothelial cells, sensory ganglia may be vulnerable to autoimmune attack. Sensory ganglionopathy associated with Sjögren's syndrome is likely to be mediated by cytotoxic T cells [8]. In sensory ganglionopathy or neuronopathy all modalities of sensations may be impaired. However, ganglionopathy differs from conventional sensory neuropathies in that its symptoms first manifest on the face, trunk, and arms before moving to the distal legs as sensory ganglionopathies are not dependent on the length of axons. Sensory ganglionopathies do not cause weakness as they are confined to sensory neurons. Typically, signs of injury to the type 1a big sensory fibers, which transmit signals from muscle spindles, predominate the clinical manifestations [4]. As a result, the main sign is an unstable gait with a wide base of support which was also present in index patient. In some cases, involuntary, irregular athetosis-like movements (pseudoathetoid movements) of limbs may be observed [9]. Electrophysiological study in ganglionopathy reveals reduced amplitudes of sensory-nerve action potentials (SNAPs) with relative sparing of sensory latencies and conduction velocities, which was also evident in the index case. The findings support a pattern of involvement that is not nerve-length-dependent and is typical of a sensory ganglionopathy

when SNAPs in the arms (e.g., radial, median, or ulnar) or the blink reflex (assessing trigeminal sensory ganglion) are affected but those in the lower legs (sural and superficial peroneal) are normal. However, electrophysiological study may be normal early in the course of the disease. Electromyographic studies as well as motor-nerve conduction studies are typically normal. The reductions in SNAPs usually corresponds to the clinical pattern of sensory symptoms and can be asymmetric or generalized.

MRI may reveal swelling, increased signal on T2-weighted images, or enhancement in the dorsal root ganglia. Degeneration of the posterior columns in the spinal cord may also be observed [10]. Rarely is a dorsal root ganglia biopsy advised, despite the fact that it may reveal an autoimmune response by CD8+ T cells on sensory ganglia neurons. A factor that may assist distinguish neuropathy from axonal neuropathy is the selective loss of big myelinated fibers and the absence of clusters of small regenerating fibers, according to sensory-nerve biopsy results. These results are not specific, though, and nerve biopsy is not usually done. Immunostaining of skin sample may show reduced intraepidermal nerve-fiber density in a way independent of nerve length (e.g., a greater reduction in the density of fibers in the thigh or arm than in the distal leg) [11].

In 2016, ACR-EULAR proposed a new diagnostic criterion for SS [12]. The new classification criteria are based on five objective tests. These include focal lymphocytic sialadenitis in labial salivary gland with a focus score ≥ 1 , positive anti-SS A and positive Schirmer's test; all of which were present in the index case. Here The number of mononuclear cell infiltrates with at least 50 inflammatory cells in a 4 mm² glandular section is referred to as the focal score [13]. Other criteria include ocular staining score and unstimulated whole saliva flow rate.

A variety of immunotherapies (e.g., glucocorticoids, immunosuppressive agents, plasma exchange, intravenous immune globulin, and rituximab) have been tried in different forms of immune-mediated sensory ganglionopathies with variable success [9]. In SS associated ganglionopathy, data regarding management strategy derived mostly from case reports and case series. Corticosteroids and IVIG are the most commonly utilized first-line treatments for recent-onset sensory ataxic neuropathy, although response may be variable. Mycophenolate mofetil (MMF) is the most frequently but not invariably reported effective treatment of sensory ataxic neuropathy after IVIG [4]. Response to Rituximab was also variable [14, 15]. Other documented treatments include d-penicillamine, infliximab, tacrolimus, azathioprine, hydroxychloroquine, cyclophosphamide, and interferon alpha [4].

4. Conclusion

Neurologists should be aware of possible autoimmune causes of neuropathies and neuronopathies, as these are potentially treatable condition. Moreover, patient may present with predominant neurological features. One must be

very cautious to illicit symptoms and signs of autoimmune disease like SS in such patients.

Conflict of Interest

The authors declare that they have no competing interests.

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