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Primary Sjögren's Syndrome with Sensory Ganglionopathy and Painful Legs and Moving Toes Syndrome

Primer Sjögren Sendromunda Duyusal Ganglionopati ile Ağrılı Bacaklar ve Oynayan Parmaklar Sendromu

Mehmet Uğur Çevik[1], Sefer Varol[1], Eşref Akıl[1], Adalet Arıkanoğlu[1], İbrahim Batmaz[2], Ulaş Alabalık[3]

[1]Dicle University Faculty of Medicine, Department of Neurology, Diyarbakır, Turkey
[2]Dicle University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Diyarbakır, Turkey
[3]Dicle University Faculty of Medicine, Department of Pathology, Diyarbakır, Turkey

Summary

Sjögren's syndrome is characterized by the sicca syndrome, with dryness of the mouth (xerostomia) and the eyes (xerophthalmia). Sjögren's syndrome is the only connective tissue disease that is associated with sensory neuronopathy. The syndrome of painful legs and moving toes presents with pain in the lower limbs with spontaneous movements of the toes or feet. The co-occurence of Sjögren's syndrome and painful legs and moving toes syndrome is a rare condition. (Turkish Journal of Neurology 2014; 20:52-4)

Key Words: Sjögren's syndrome, painful legs and moving toes

Özet

Sjögren sendromu sikka semptomları olan kuru göz ve kuru ağız ile karekterizedir. Sjögren sendromu duyusal nöronopati ile ilişkili tek bağ doku hastalığıdır. Ağrılı bacak ve oynayan parmaklar sendromunda alt ekstremitelerde ağrı ve ayaklarda spontan hareketler görülmektedir. Sjögren sendromu ile ağrılı bacak ve oynayan parmaklar sendromu arasındaki ilişki nadir görülen bir durumdur. (Türk Nöroloji Dergisi 2014; 20:52-4)

Anahtar Kelimeler: Sjögren sendromu, ağrılı bacak ve oynayan parmaklar sendromu

Introduction

Sjögren syndrome (SS) is a chronic inflammatory autoimmune disease presenting with dry eyes (xerophthalmia), dry mouth (xerostomia) as a result of the mononuclear infiltration and destruction of lacrimal and salivary glands. Sjögren syndrome is also known as keratoconjunctivitis. Sjögren syndrome can be present either by itself (primary) or as accompanied by another autoimmune rheumatic diseases (secondary). It is commonly seen in middle-aged women. Women are 9 times more likely to be affected by the disease than men. A sensory ganglionopathy (neuropathy) can take place as a result of the infiltration of lymphocytic cells into dorsal root ganglia. Ten to fifteen percent of the primary SS patients show polyneuropathy. This polyneuropathy can involve motor and sensory tracts or remain as a purely sensory involvement (1,2).

The painful legs and moving toes syndrome is first described in 1971 by Spillane. This syndrome is a hyperkinetic movement disorder characterized by burning, stabbing pain during wakeful resting, and the involuntary toe flexion, extension and rotation to alleviate this pain (3).

We present a case which has sensory ataxia and hypoesthesia along with sensory neuropathy (ganglionopathy). To our knowledge, primary SS and painful legs and moving toes syndromes are rarely seen as together in the literature.

Case

50-year-old female patient had been followed in various centers for numbness in legs, loss of sensation and imbalance for the past 1-2 months. The case had been experiencing dryness in mouth and eyes and

Address for Correspondence/Yazışma Adresi: Mehmet Uğur Çevik MD, Dicle University Faculty of Medicine, Department of Neurology, Diyarbakır, Turkey
Phone: +90 412 248 80 16-4510 E-mail: mehmetugur.cevik@gmail.com
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had a history of chronic hepatitis B as a carrier. No other significant details were present in her history. Her cranial nerves found to be intact in the neurological examination. Deep tendon reflexes were not present in the upper and lower extremities; there were no pathological reflexes. There was a loss of precision in the upper extremity; she could walk only with help and in an ataxic way; Romberg sign was positive. She had losses in every sensory modality, proprioception and vibration senses being the most prominent ones. Both feet showed choreiform motion. In addition, there were transitory tonic jerks in the feet. She described pain and burning sensation at a significant severity on the lower leg and soles of the feet. In the nerve conduction studies, there were electrophysiological findings indicating pure sensory polyneuropathy. Her motor nerve conduction for median, ulnar, peroneal and posterior tibial nerves were normal. In her sensory nerve conduction studies, compound sensory action potential (CSAP) were not obtained for bilateral median and sural nerves and left ulnar nerve. Right ulnar nerve had a lower CSAP amplitude and the conduction speed was sluggish (Table 1).

The patient's cranial magnetic resonance imaging (MRI), cervical and thoracic spinal MRI studies were normal. Her lung graphy was normal. B12, folic acid, tumor markers, thyroid function tests, and vitamin E levels were normal. ANA, anti-ds DNA, anti-cardiolipin antibodies were also within normal limits. Anti-SSA antibody was positive. Due to the dryness of mouth and the presence of Anti-SSA antibody, Schirmer test and lip biopsy were planned after a pre-diagnosis for primary SS. In the Schirmer test, both eyes gave measurements that were less than 5 mm. Histopathological findings in line with SS were observed in the lip biopsy (Figure 1). Based on these findings, the patient was diagnosed with primary SS according to the American-European diagnostic criteria for SS published in 2002 (4). Symptomatic treatment was recommended for the dryness of mouth and eyes. The foot pain was relieved after 1800 mg/day gabapentin. For the neurological findings, 1 g/day intravenous methylprednisolone was given for 7 days. After the treatment, neurogenic findings did not seem to improve. Consequently, the patient who is a hepatitis B carrier was started on 700 mg/m^2/month cyclophosphamide following lamivudine treatment. The patient is still on lamivudine treatment.

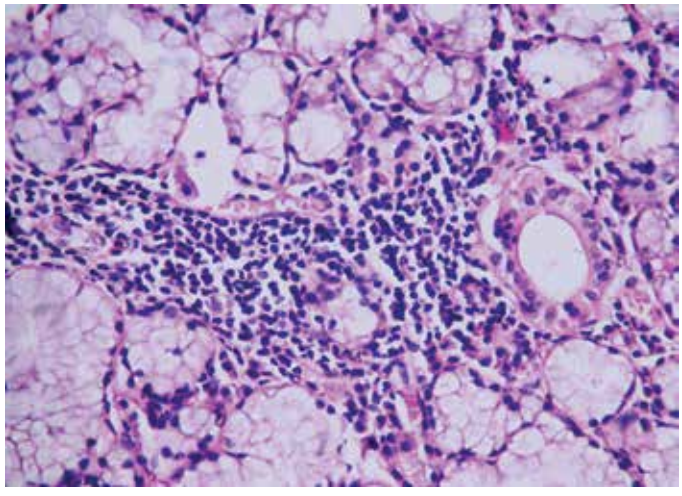

Figure 1. Salivary gland biopsy: Mild lymphocyte infiltration between salivary gland acini and gland (H&E,400X).

Discussion

In the etiology of pure sensory neuronopathy, primary SS, paraneoplastic, infectious causes, drugs and Friedreich syndrome should come to mind (5). Sjögren syndrome is the only connective tissue disease that presents with pure sensory neuronopathy (1). In the primary SS, pure sensory neuropathy has a subacute onset. Our patients started having neurological complaints in the past 1-2 months. It was shown that sensory neuronopathy patients show lymphocytic (primarily CD8 T-cells) infiltration and cell body degeneration in their dorsal root ganglia biopsies (6). Treatment is not effective in sensory ganglionopathies due to the cell body degeneration (7). She was also unresponsive to the high-dose steroid treatment. Sicca symptoms and neurological involvement is seen in 53% of the SS cases (8). It was reported that the SS diagnosis comes 6 years after the onset of sicca symptoms. Even though her sicca symptoms started 1 year ago, she did not go to the doctor and reported the dryness of her mouth and eyes only after it was asked specifically. The reasons why this question was asked were the ataxia and the pure sensory neuropathy in the nerve conduction studies. Nine of the 51 SS patients with peripheral nervous system involvement showed pure sensory neuropathy (8). Anti-SSA antibodies were found in 46% of the patients with peripheral nervous system involvement. In the same study, Anti-SSB antibodies were positive in 19%. Anti-SSA antibody was also positive in our patient.

The most common triggers for painful legs and moving toes syndrome is shown to be neuropathy and radiculopathy. Even though painful legs and moving toes syndromes appears to be originated centrally, it was suggested that peripheral mechanisms are the real triggers. The most common drugs for painful legs and moving toes syndrome are the GABAergic ones. These drugs relieve the pain and provide easier mobility (3). The conditions implicated in the etiology of painful legs and moving toes syndrome are neuropathy, radiculopathy, lumbar stenosis, SS, diabetes mellitus, IgG monoclonal gammopathy, Vitamin B12 deficiency and systemic lupus erythematosus (3). Alvarez et al. showed the co-occurrence of painful legs and moving toes syndrome with SS in 3 patients out of 14 patients recruited for painful legs and moving toes syndrome (3).

Restless leg syndrome should definitely be included in the differential diagnosis for painful legs and moving toes syndrome. These two conditions can easily mimic each other. Restless legs syndrome is characterized by the sudden desire to move legs and spasms, both disappearing when the person walks. It is more visible

Table 1. Sensory nerve conduction studies

Nerves	CSAP amplitude (μV)	NCV (m/s)
Right median	**NP**	**NP**
Left median	**NP**	**NP**
Right ulnar	**9.60** (>17)	**47.9** (>50)
Left ulnar	**NP**	**NP**
Right sural	**NP**	**NP**
Left sural	**NP**	**NP**

NP: no potential; NCS: Nerve conduction velocity; CSAP sensory action potantial, Normal values are in the parentheses; abnormal results are written in bold face.

during night than daytime. The arms can also be affected in some severe cases. Other findings supporting the diagnosis could be familial history, periodic leg movements in the polysomnography and positive response to dopaminergic treatment. Legs are more visibly affected in painful legs and moving toes syndrome. Sudden leg motions are often involuntary. It does not have a circadian property (9). In our case as well, there was no circadian character and the pain in the lower leg and sole of the feet did not disappear during walking.

Some rare cases with painful dystonic and tonic spasms on the feet due to medulla spinalis involvement in SS were also reported (10). The cause of the sensory ataxia in SS is the damage on the large radius proprioceptive nerve bundles (ganglionopathy). On the other hand, the reason for the dysesthesias is the degeneration of the axons in the small radius sensory cutaneous bundles (11). We think that the co-occurrence of SS and painful legs and moving toes syndrome can be explained by the axonal degeneration in the small radius sensory cutaneous bundles. We presented this case because the co-occurrence o f primary SS and painful legs and moving toes syndrome is extremely rare and primary SS should always be included in the diagnostic workup in cases of pure sensory neuropathies.

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