Extraglandular Manifestations of Primary Sjögren's Syndrome

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KEYWORDS

• Sjögren's syndrome • Extraglandular • Vasculitis • Arthropathy

KEY POINTS

- As many as 50% of patients with primary Sjögren's syndrome may experience extraglandular symptoms.
- Musculoskeletal symptoms include arthralgia and mild inflammatory arthritis, and myalgia.
- Neurologic involvement may occur in up to 20%. Peripheral neuropathy is fairly common; central nervous system involvement is rare.
- Respiratory symptoms reflect involvement of the upper airway with sicca manifestations, such as dry nose and dry cough; lower respiratory tract involvement usually involves interstitial lung disease.
- Vasculitis most often presents with palpable purpura and may be associated with risk for non-Hodgkin lymphoma.

Sjögren's syndrome is a chronic autoimmune disease that typically affects the salivary and lacrimal glands. It is also described as a lymphoinfiltrative disorder that affects exocrine glands producing dry eyes and dry mouth. Aside from the common glandular signs and symptoms, Sjögren's syndrome may also cause mononuclear infiltration and immune complex deposition involving extraglandular sites producing several extraglandular manifestations (EGMs) (**Box 1**). The prevalence of EGMs varies greatly depending on the particular manifestation. In some studies, EGMs are quite prevalent. For instance, in a report by Hernandez-Molina and colleagues[1] examining 109 patients with primary Sjögren's syndrome (pSS), 86% had at least one EGM. In this article we look at the ways that EGM may present in patients with pSS (see **Box 1**). The focus is specifically on the more prevalent and significant EGMs including involvement the nervous system, pulmonary manifestations, vasculitis associated with pSS, and arthropathy.

NERVOUS SYSTEM

Peripheral Nervous System

The prevalence of peripheral neuropathy in pSS has been reported to be anywhere from 2% to 60% in the literature (**Box 2**). The wide range reported is likely caused by the classification criteria used by the various studies and the criteria used to define neuropathy. Some reports used clinical symptoms with less objective inclusion criteria, whereas others relied on definitive criteria, such as nerve conduction studies.

The cause of peripheral neuropathy secondary to pSS is yet to be fully understood. Some have thought it because of vasculitis of the peripheral

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Box 1
Reported EGMs of primary Sjögren's syndrome

- Peripheral neuropathy[a]
- Central nervous system involvement[a]
- Trigeminal neuralgia[a]
- Autonomic neuropathy[a]
- Dementia/confusion[a]
- Pancreatitis
- Gastroparesis
- Autoimmune hepatitis
- Primary biliary cirrhosis
- Tubulointerstitial nephritis
- Cough[a]
- Dyspnea[a]
- Sinusitis[a]
- Septal perforation[a]
- Interstitial lung disease[a]
- Vasculitis[a]
- Arthralgias[a]
- Arthritis[a]
- Lymphoma
- Amyloidosis
- Fibromyalgia[a]
- Raynaud phenomenon

[a] Discussed in further in detail.

nerves.[2] Dorsal root ganglionitis with degeneration of dorsal root ganglion neurons and mononuclear cell infiltration without true vasculitis has been associated with the sensory ataxic form of Sjögren's syndrome–associated neuropathy.[3,4] Peripheral neuropathy is a term that seems to encompass a diverse subset of specific neuropathies associated with pSS as described next.

Box 2
Neurologic involvement

- Patients experiencing peripheral neuropathy associated with Sjögren's syndrome can present in multiple ways including abnormal vibratory sensation, impaired position sense, parethesias, and weakness.
- Central nervous system involvement in pSS can closely mimic multiple sclerosis. Clinical history, lumbar puncture, and magnetic resonance imaging findings may help differentiate the two.
- Patients with pSS have reported low mood, decreased quality of life, and impaired concentration, which can be significantly improved if addressed by supportive measures.

Sensory Ataxic Neuropathy

This form of neuropathy is caused by a lesion in the dorsal root ganglia and can involve all sensory modalities. Although this type of neuropathy can be seen with Sjögren's syndrome it is most commonly associated with paraneoplastic syndrome.[5] Other etiologies to consider when encountering this type of neuropathy are pyridoxine toxicity, human T-lymphotropic virus-1 infection, and HIV infection.[5] It is reported that patients with Sjögren's syndrome with this type of neuropathy do not have other prominent EGMs. The timing of the onset of the first symptom to its full-blown picture is typically months to years. It has been reported as mostly asymmetric in presentation.[2] On examination there are abnormal findings in vibratory sensation and impaired position sense, a positive Romberg sign, and absent deep tendon reflexes.[2,4,6] In one study examining 36 patients with this form of neuropathy, all were found to display pseudoathetosis.[2] Muscle strength is spared until late stages of the process when it begins to noticeably lessen.

Axonal Sensorimotor Polyneuropathy

This type of neuropathy usually presents with distal paresthesias and sensory deficits that are similar to other types of sensory neuropathy. The muscle weakness that accompanies the sensory deficits is also usually distal and also symmetric in distribution.[7] On physical examination, deep tendon reflexes are usually diminished or absent.[8]

Trigeminal Neuralgia

Patients with Sjögren's syndrome with trigeminal neuralgia may present either unilaterally or bilaterally and typically report numbness or paraesthesia.[2] Motor symptoms have not been reported in trigeminal neuralgia associated with Sjögren's syndrome. Fifteen patients studied were found to have a pure sensory neuropathy.[2]

Autonomic Neuropathy

Autonomic neuropathy is thought to be rare in Sjögren's syndrome but may be underreported. In a study examining 92 patients with pSS-associated neuropathy only three were found to have autonomic neuropathy. These patients were found to have Adie pupil (a dilated pupil that does not constrict to light); orthostatic