Case Report

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Sjögren's syndrome with rapidly progressive motor neuron disease: a case report

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Abstract

Sjögren's syndrome is an autoimmune disease that can affect multiple systems. Sjögren's syndrome with motor neuron disease is rarely reported. Herein, we describe a patient with rapidly progressive motor neuron disease secondary to Sjögren's syndrome. A 42-year-old woman was admitted to our hospital with a 2-month history of progressive limb weakness. Neurological assessment revealed fasciculation in the lower limbs and amyotrophy in the bilateral supraspinatus, interosseous, and thenar muscles. Serological examination and labial gland biopsy revealed Sjögren's syndrome. In addition, electromyography demonstrated neurogenic damage to the upper and lower limbs. The patient received a short course of high-dose corticosteroids, intravenous immunoglobulins, and immunosuppressant treatment, including a weekly dose of 0.4 g cyclophosphamide and a daily dose of 0.2 g hydroxychloroquine. However, the patient's limb weakness was further aggravated and her respiratory function was compromised. Electromyography re-examination demonstrated extensive neurogenic damage, and she was diagnosed with Sjögren's syndrome with motor neuron disease. The patient died of respiratory failure after 2 months. We suggest that more effective maintenance treatments should be sought. Further investigation is required to elucidate the association between autoimmune motor neuron disease and Sjögren's syndrome.

Keywords

Sjögren's syndrome, motor neuron disease, anti-Ro/SSA, anti-Ro/SSB, central nervous system, immunotherapy

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Introduction

Sjögren's syndrome is an autoimmune disease that can affect multiple systems. Fauchais et al.[1] reported that between 8.5% and 70% of patients with primary Sjögren's syndrome develop neurological symptoms, which occur 24 months earlier, on average, than the onset of dryness symptoms or a diagnosis of Sjögren's syndrome. In a study of 82 patients with neurological involvement in primary Sjögren's syndrome, 47% showed signs of nervous system involvement 6 years before the onset of dryness symptoms.[2] Sjögren's syndrome causes peripheral nervous system lesions, in which sensory nerves are the most often affected;[2–5] its pathogenesis may be related to lymphocyte infiltration in the dorsal root ganglia.[1] In contrast, central nervous system involvement is relatively rare in patients with Sjögren's syndrome (2%–25%). When the central nervous system is affected, symptoms can include cognitive dysfunction, aseptic meningitis, headache, seizures, transverse myelitis, neuromyelitis optica, disseminated encephalopathy, multiple sclerosis, and cranial nerve injury.[1,6–8]

Case report

A 42-year-old woman was admitted with a history of limb weakness for approximately 2 months. Two months before admission, she had complained of hand weakness, difficulty getting up after squatting, and weakness of the right upper limb that had developed gradually and spread to all limbs. The patient also reported dryness in her oral cavity and eyes, which had occurred for approximately 30 years. She had no other history of neurological or psychiatric illness and took no regular medication. She had lost approximately 5 kg in the preceding 3 months. Neurological examination revealed fasciculation in the lower limbs and amyotrophy in the bilateral supraspinatus, interosseous, and thenar muscles. Muscle strength, as measured using the Medical Research Council scale, was 4/5 in the proximal muscles and 3/5 in the distal muscles of her upper limbs. Her lower limbs had muscle strength of 4/5, and her tendon reflexes in the lower limbs were very brisk. Electromyography (EMG) revealed neurogenic damage in the upper and lower limbs. The patient's tear film breakup time and Schirmer I scores were decreased compared with normal values. Serological examination revealed positive anti-Ro/SSA and anti-Ro/SSB anti-nuclear antibodies at a titer of 1:320. Serum creatine kinase concentration was normal (76 IU/L). Based on the patient's personal history of dryness of the mouth and eyes, as well as the results from the serological examination and ophthalmology, we highly suspected a diagnosis of primary Sjögren's syndrome. Thus, after obtaining written informed consent, we took a biopsy from the minor labial salivary gland. This biopsy showed lymphatic infiltration of the labial gland tissue with >1 focus (Figure 1), consistent with a diagnosis of xerostomia. The EULAR Sjögren's syndrome disease activity index (ESSDAI) score was 5. The patient received a short course of high-dose corticosteroids (intravenous methylprednisolone [IVMP];

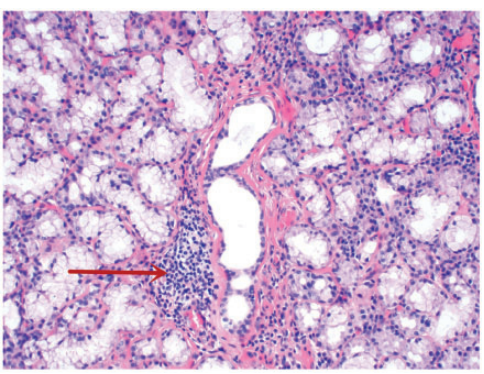

Figure 1. Lymphocyte infiltration (arrow) was observed in a labial gland biopsy.

Table 1. Nerve conduction velocity and needle electromyography findings.

Motor nerve conduction studies

Nerve	Incubation ms	Amplitude mV	Conduction velocity m/s	Distance mm
Ulnaris motor (R)				
Wrist–ADM	2.50	7.10		
Below elbow–wrist	4.52	5.80	64.4	130.0
Above elbow–below elbow	6.15	6.70	52.1	85.0
Medianus motor (R)				
Wrist–APB	3.37	5.60		
Elbow–wrist	6.38	4.30	59.8	180
Tibialis motor (R)				
Ankle–AH	3.7	7.0		
Peroneus motor (R)				
Ankle-EDB	3.15	5.7		
Fibular head–ankle	8.52	5.0	49.3	265

Sensory nerve conduction studies

Nerve	Incubation ms	Amplitude μV	Conduction velocity m/s	Distance mm
Medianus sensory (R)				
Digit I–wrist	1.64	45.5	55.5	91.0
Digit III–wrist	2.25	23.7	60.0	135
Ulnaris sensory (R)				
Digit V–wrist	1.50	16.0	68.0	102
Tibialis sensory (L)				
Digit I–ankle	3.95	5.8	42.5	168
Tibialis sensory (R)				
Digit I–ankle	3.65	6.0	47.1	172
Peroneus sensory (L)				
Calf–fibular head	4.31	4.0	60.3	260
Peroneus sensory (R)				
Calf–fibular head	4.72	3.2	56.1	265

	Spontaneous		Motor unit potential	
	Fibrillation potential	Positive shape wave	Time limit	Amplitude
Needle electromyography				
(R) Tibialis anterior	2+	2+	17.5	2065
(L) Tibialis anterior	2+	2+	16.5	1391
(R) Sternocleidomastoid	1+	1+	11.7	597
(R) Quadriceps femoris	2+	2+		
(R) ADM	3+	3+	13.7	1171
(L) ADM	2+	2+	12.5	973
(R) Musculus biceps brachii	2+	2+		
(L) Rectus abdominis	2+	2+		

ADM: abductor digiti minimi; AH: abductor hallucis; APB: abductor pollicis brevis; EDB: extensor digitorum brevis; L: left; R: right.

1000 mg/day for 3 days and 500 mg/day for 3 days) followed by oral prednisolone over 6 weeks. She also received intravenous immunoglobulin (IVIG; 0.4 g/kg per day for 5 consecutive days) therapy, a weekly dose of 0.4 g cyclophosphamide, and a daily dose of 0.2 g hydroxychloroquine. However, her limb weakness became further aggravated and her respiratory function was compromised. After 6 weeks of cyclophosphamide treatment, the patient decided to discontinue this medication because of insufficient relief of symptoms. EMG re-examination demonstrated extensive neurogenic damage (Table 1) and no signs of any demyelinating or axonal damage. The patient was diagnosed with Sjögren's syndrome with motor neuron disease. She died of respiratory failure after 2 months.

Discussion

We reported a case of Sjögren's syndrome with rapidly progressive motor neuron disease. The patient received a short course of high-dose corticosteroids, intravenous immunoglobulins, and immunosuppressant treatment. However, these treatments were ineffective and the patient's condition deteriorated further.

Seeliger et al.[9] systematically investigated 184 patients with polyneuropathy associated with limb weakness. Of these, 24% (44/184) were diagnosed Sjögren's syndrome, indicating that severe neuropathy with limb weakness is often associated with Sjögren's syndrome. Furthermore, in 1999, Katz et al.[10] reported two patients with multisystem neuronal involvement associated with Sjögren's syndrome. One had lower motor neuron syndrome, while the other had upper motor neuron symptoms and sensory neuronopathy. The symptoms of both patients were alleviated following treatment with high-dose corticosteroids. In addition, in 2008, Hagiwara et al.[11] presented two patients with primary lateral sclerosis-like upper motor neuron disease with accompanying subclinical Sjögren's syndrome. Both patients showed significant neurological improvement after an initial course of intravenous immunoglobulin therapy. In contrast to the patients from these previous reports, our patient was highly resistant to immunotherapies; muscle weakness rapidly developed, and she eventually died of respiratory failure after 2 months. Despite the use of immunosuppressive agents, the patient's condition progressed rapidly, leading us to hypothesize that Sjögren's syndrome may play an additive role in the progression of motor neuron dysfunction. Based on the patient's lack of a response to treatment with high-dose prednisone and immunoglobulin, we also speculate that Sjögren's syndrome and motor neuron disease may be independent conditions that were coincidentally found in the same patient; whether there is a causal relationship between the two requires further study.

Conclusions

We described a case of Sjögren's syndrome presenting with rapidly progressive motor neuron disease. Compared with previously published cases of Sjögren's syndrome with motor neuron disease, our patient was highly resistant to immunotherapy. As such, we suggest that more effective maintenance treatments should be sought, rather than simply repeating IVMP and IVIG. Further investigation is required to elucidate the association between autoimmune motor neuron disease and Sjögren's syndrome.

Ethics statement

Written informed consent was obtained from the patient for the publication of this case report, and for the use of all information and images.

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We are grateful to the patient, who was willing to share her medical data.

Author contributions

DM, XJ, JY, and HY contributed to the conception and design of the study. HY wrote the first draft of the manuscript, and XJ wrote some sections of the manuscript. JY provided a much guidance and many corrections. DM critically revised the manuscript and gave final approval for its publication. All authors have read and approved the manuscript.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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