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Aquaporin-4 Antibody Negative Transverse Myelitis in Sjögren Syndrome

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Abstract

Sjögren's syndrome is an autoimmune disease that classically presents with sicca symptoms and arthralgias, yet a small subset of patients develops central nervous system involvement. We report a 64-year-old woman with Sjögren's syndrome (ANA positive, anti-SSA 8) who developed abrupt bilateral lower-extremity and abdominal numbness with back pain and urinary retention. Non-contrast thoracic MRI demonstrated a non-enhancing anterior cord lesion from T3 to T6 consistent with transverse myelitis. Cerebrospinal fluid revealed IgG of 10.1 with an IgG/albumin ratio of 0.31, and negative aquaporin-4 (AQP4) IgG. She received IV methylprednisolone 1 g daily for five days, followed by an oral prednisone taper and inpatient rehabilitation. Hydroxychloroquine was trialed intermittently for sicca symptoms but discontinued due to poor tolerance. Neurology initiated mycophenolate mofetil 500 mg twice daily, later titrated to 1g twice daily, as maintenance therapy; after two years, it was held because of recurrent household viral infections. Over nine months without immunosuppression, her neurologic status remained stable, and catheterization frequency decreased from multiple times daily to every few days, leading to sustained discontinuation of mycophenolate. This AQP4-negative presentation highlights diagnostic uncertainty at the Sjögren's syndrome-transverse myelitis interface, the importance of antibody testing beyond AQP4 and the need to balance relapse prevention against infection risk through close rheumatology-neurology coordination and symptom-guided re-imaging.

Keywords

Aquaporin-4 Antibody, Neurologic Manifestations of Rheumatic Disease, Sjögren's Syndrome, Lupus

1. Introduction

Sjögren syndrome is an autoimmune disorder, which classically presents with nonspecific joint pain and immune-mediated lacrimal and salivary gland dysfunction [1]. This dysfunction often results in sicca symptoms and inflammation of the parotid and submandibular glands [1] [2]. The condition frequently impacts adult females, with 60% - 80% of patients being female and the majority of patients being between 30 and 70 years old [3]. Symptoms can traverse many organ symptoms, resulting in skin, lung, kidney, or nervous system involvement [1]. Diagnostically, a large subset of patients with Sjögren's syndrome display ANA positivity as well as increased levels of Anti-SSA/Ro and Anti-SSB/La antibodies [1]. Central nervous system (CNS) manifestations are sparse, occurring in 3% - 6% of cases [4]. CNS involvement is customarily noted as optic neuritis, multiple sclerosis, and neuromyelitis optica spectrum disorders (NMOSD) [5]-[7]. Within the sparse neurologic symptoms that can present with Sjögren's syndrome, transverse myelitis is a rare subset that can be diagnosed with aquaporin-4-IgG antibodies [1] [3] [4].

2. Case Presentation

A 64-year-old woman with asthma, heart failure with preserved ejection fraction, and hypertension presented to establish care for Sjögren's syndrome. Her labs depicted ANA positivity with an anti-SSA level of 8. She developed abrupt bilateral lower-extremity and abdominal numbness with concurrent back pain and urinary retention. Non-contrast MRI of the thoracic spine revealed a non-enhancing anterior cord lesion from T3-T6 consistent with transverse myelitis. CSF opening pressure was 9 cm H_2O with 165 nucleated cells, elevated protein levels, IgG 10.1 with an IgG/albumin ratio of 0.31, and negative cultures. CSF was also negative for aquaporin-4 IgG antibodies (AQP4).

3. Clinical Course

IV methylprednisolone 1g was administered daily for five days, followed by an oral prednisone taper and inpatient rehabilitation. Hydroxychloroquine was also administered intermittently to address sicca symptoms, but it was discontinued due to poor tolerance. She also started oral gabapentin 300 mg to be taken up to three times daily for neuropathic leg pain. The following year, neurology initiated mycophenolate mofetil 500 mg twice daily, later titrated up to 1 g to be administered twice daily. After two years of treatment, her mycophenolate was held owing to recurrent viral infections in her household. Despite the halt of immunosuppressants, neurologic status remained stable for 9 months and catheterization frequency decreased from multiple times daily to every few days. As such, the mycophenolate mofetil has been discontinued. The patient will be evaluated by neurology to determine if re-imaging is necessary. Ongoing management balances relapse prevention with infection risk. Close rheumatology-neurology coordination and re-imaging are planned if new symptoms emerge.

4. Discussion

Sjögren syndrome is an autoimmune disorder, which causes arthralgias as well as lacrimal and salivary gland dysfunction [1]. CNS manifestations include optic neuritis and multiple sclerosis, whereas peripheral neurological manifestations, can mimic different variants of Guillain-Barre syndrome, such as miller-fisher syndrome [5]. Neurologic symptoms, such as episodes resembling multiple sclerosis, can be the presenting symptom of Sjögren's syndrome [5] [7]. As the disease is slowly progressive, maintaining vigilance for neurologic symptoms can have serious implications on prognosis, especially when neurologic symptoms precede hallmark sicca symptoms [5] [7].

Transverse myelitis is an uncommon neurologic manifestation of Sjögren's syndrome [1] [4]. It is an inflammatory myelopathy, which affects the spinal cord and presents with muscle weakness and sensory deficits, which can in turn lead to dysautonomia [8] [9]. Although transverse myelitis can be seen in accordance with autoimmune conditions, the etiology can also be independently inflammatory, trauma-induced or idiopathic [7]-[11]. Transverse myelitis can be precipitated by viral infections in those with and without autoimmune diseases, such as Sjögren's syndrome [12]. Of the patients with transverse myelitis who present with Sjögren's syndrome, there is a 20% sensitivity for diagnosis via CSF analysis and spinal MRI [2]. On T2 MRI, hyperintense lesions can predominantly be visualized in the cervical spine [2]. Aquaporin 4 antibodies are often positive in patients with NMOSD [12] [13]. Aquaporin-4-IgG antibodies can be helpful for diagnosis as they are implicated in patients with Sjögren's syndrome that present with transverse myelitis [9]-[11] [14] [15]. Fascinatingly, aquaporin-4 and aquaporin-5 share approximately half of their sequencing identity, which could potentially demonstrate a connection between astrocyte and salivary gland autoimmunity [14]. If AQP4-IgG is negative in patients with Sjögren's syndrome who present with symptoms of transverse myelitis, it becomes increasingly difficult to establish both diagnoses [3] [14] [15].

The AQP4-IgG is not only helpful in establishing diagnosis but it can also provide prognostic information regarding relapse and subsequent disability [10] [12] [16]. AQP4 positivity has been associated with worse prognosis; thus, those diagnosed with AQP4 positive transverse myelitis are to be treated more aggressively [12] [16]. Anti-SSA/Ro antibodies, which are present in this patient, have also been associated with recurrent transverse myelitis [17]. Initial treatment for transverse myelitis is high-dose IV corticosteroids with an option for plasma exchange in refractory cases [7]. Maintenance therapy typically consists of azathioprine, mycophenolate mofetil (MMF), or rituximab [10]. Inebilizumab, an anti-CD19 monoclonal antibody, has demonstrated profound efficacy in refractory AQP4-positive NMOSD [14] [15]. In those with seronegative transverse myelitis and other NMOSD, it is difficult to optimize treatment as diseased modifying therapy and immunosuppressants are targeted therapies [15]. Our patient received IV methylprednisolone followed by MMF, later discontinued due to infection risk.

Oral gabapentin was given up to three times daily to address her neuropathic pain and provide symptom relief. Her stable neurologic course and reduced catheterization over nine months suggests a monophasic or less aggressive disease progression. This points to a lesser need for indefinite immunosuppression as can be the case in patients with refractory AQP4-positive NMOSD [14] [15] [18].

For our patient, indefinite treatment will likely remain unnecessary, which is consistent with her AQP4 negativity and the associated disease progression. This case highlights the necessity of antibody testing beyond AQP4. The absence of MOG testing represents a limitation in this case. Autoimmune small-vessel injury and perivascular lymphocytic infiltration underlie Sjögren's syndrome's neurologic manifestations, but overlap with NMOSD biology may account for shared phenotypes [6]. AQP4-negative NMOSD can also demonstrate MOG-IgG positivity [6]. As our patient is AQP4-negative, it could be helpful to consider testing patients with transverse myelitis for MOG-IgG positivity [6]. This marker is associated with a more benign course that tends to be steroid-responsive [6]. Establishing MOG-IgG positivity can be a crucial step in treatment if patients with transverse myelitis demonstrate the pattern witnessed in patients with Sjögren's syndrome-related NMOSD [6]. In the future, it could be helpful to test both MOG and AQP4 to establish a dichotomy between the antibodies and respective treatment courses. Further biomarker establishment and exploration is needed to stratify relapse risk in AQP4-negative neuro-Sjögren and to refine long-term immunotherapy decisions.

5. Conclusion

In this Sjögren-associated AQP4-negative transverse myelitis case, early high-dose corticosteroids produced clinical stability, while long-term management required continued reassessment of maintenance immunosuppression as infection risk evolved. The patient's nine months of stability, barring immunosuppressing therapy and reduced catheterization, suggest a monophasic or less aggressive course aligned with AQP4 negativity. This case demonstrates the value of comprehensive antibody evaluation beyond AQP4, notably, MOD, and the importance of multidisciplinary follow-up with readiness to re-image if symptoms recur. An individualized approach can balance risk stratification for subsequent infections and vigilant relapse prevention.

Patient Consent

Written informed consent was obtained from the patient for publication of clinical details and images.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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