Sjogren's Syndrome Complicated with Optic Neuromyelitis and Dual Positivity of AQP4 and GFAP Antibodies: A Case Report

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ABSTRACT

A patient diagnosed with Sjogren's syndrome (SS) developed weakness and numbness in both lower limbs, accompanied by abdominal distension and sensory impairment in the left index and little fingers. Cervical magnetic resonance imaging (MRI) indicated the presence of longitudinal inflammatory lesions in the C3-C6 segments of the cervical spinal cord. The serum tests showed positive anti-aquaporin-4 (AQP4) and anti-glial fibrillary acidic protein (GFAP) antibodies. After treatment with steroid pulse and immunosuppressive agents, the symptoms of limb numbness, abdominal distension, and sensory impairment in the left finger were significantly improved. Cervical spinal cord MRI indicated significant improvement in inflammatory lesions. Anti-GFAP antibodies are quite uncommon in cases of SS complicated with neuromyelitis optica, and it is necessary to identify the true autoimmune GFAP-astrocytopathy (GFAP-A), if it is positive.

Key Words: *Sjogren's syndrome, Neuromyelitis optica, Anti-aquaporin 4 antibody, Anti-glial fibrillary acidic protein antibody*.

How to cite this article: Qiang F, He Q, Liu J, Sheng J. Sjogren's Syndrome Complicated with Optic Neuromyelitis and Dual Positivity of AQP4 and GFAP Antibodies: A Case Report. *JCPSP Case Rep* 2025; **3**:212-214.

INTRODUCTION

Sjogren's syndrome (SS) is a chronic autoimmune disorder that impacts the exocrine glands. Neuromyelitis optica (NMO) is characterised by inflammation of the optic nerve and spinal cord and can occur in SS patients.[1] Although dual positivity for anti-aquaporin-4 (AQP4) and anti-glial fibrillary acidic protein (GFAP) antibodies has been observed in NMO, it is rarely found in SS patients with NMO.[2] We present a case of SS complicated by NMO, showing dual positivity for AQP4 and GFAP antibodies.

CASE REPORT

A 43-year woman experienced dry mouth and left shoulder joint pain. Autoantibody tests were positive for anti-SSA-60KD, anti-SSA-52KD, and anti-SSB antibodies. The scores for the Schirmer and Saxon tests were 7 mm in 5 minutes and 1.5 g in 2 minutes, respectively. Pathological examination revealed multifocal lymphocytic infiltration in the salivary gland. She was diagnosed with SS, and her symptoms improved with low-dose prednisone and hydroxychloroquine treatment.

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Received: November 14, 2024; Revised: February 03, 2025; Accepted: February 16, 2025
DOI: https://doi.org/10.29271/jcpspcr.2025.212

Two years after her SS diagnosis, the patient developed weakness in both lower limbs, along with itching and numbness but no visible skin lesions. She also experienced decreased sensation in her left index and little fingers, as well as abdominal distension. Neurological examination confirmed significant loss of tactile and pain sensation in the affected fingers.

Laboratory tests showed an erythrocyte sedimentation rate (ESR) of 87 mm / 1st hour, IgG of 29 g/L, and IgG-RF of 91.2 IU/mL. A complete blood count, liver function tests, renal function tests, tumour marker assessments, urinalysis, cardiac enzyme tests, complement levels, C-reactive protein (CRP), thyroid function, hepatitis, syphilis, human immunodeficiency virus (HIV), anti-cyclic citrullinated protein (CCP) antibody, anti-cardiolipin antibody, anti-β2 glycoprotein antibody, bone marrow, immunoglobulin monoclonal light chain electrophoresis, and abdominal ultrasound examination were all negative. The biochemical, routine, and microbiological tests performed on the cerebrospinal fluid (CSF) yielded negative results. The immunoglobulin levels in CSF were within the normal range. Furthermore, the CSF analysis revealed no oligoclonal IgG bands. The MRI of the cervical spine revealed extensive longitudinal T1-weighted hypointensity and fat-suppressed T2-weighted hyperintensity in the cervical spinal cord (C3-C6) (Figure 1A-C). No abnormal findings were detected in the brain MRI and thoracic spinal cord (Figure 1D, G, and H). Both anti-AQP4 and anti-GFAP antibodies tested positive, while the anti-myelin oligodendrocyte glycoprotein (MOG) antibody was negative in both serum and CSF. The patient was diagnosed with SS complicated by NMO, and the Expanded Disability Status Scale (EDSS) score was 3.5. The patient received 1000 mg of intrave-

nous methylprednisolone for three days, followed by 500 mg for two days. The maintenance treatment consisted of a gradually tapering high dose of oral prednisolone (1 mg/kg/d). Additionally, an intravenous administration of cyclophosphamide at a dosage of 1 g was commenced monthly. The patient's abdominal distension and limb numbness were alleviated, and the tactile and pain sensations in the left finger were restored. Exudative lesions in the C3-6 segments of the cervical spinal cord showed significant improvement after six months of treatment (Figure 1E, F). During this period, the patient did not experience any adverse events.

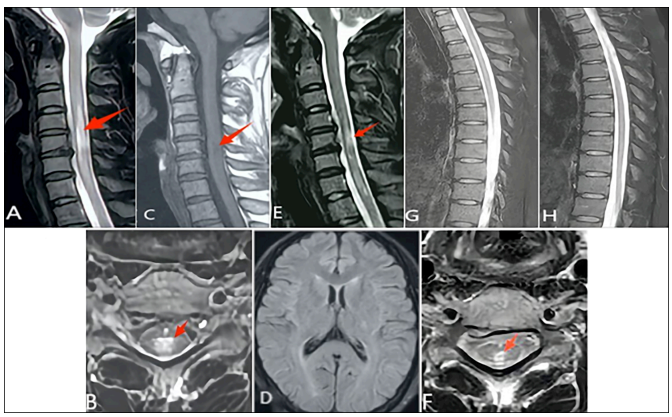

Figure 1: MRI of the cervical and thoracic spinal cords, as well as the brain, of the patient. (A-C) The MRI revealed T1-weighted hypointensity and T2-weighted hyperintensity longitudinally in the cervical spinal cord (C3-C6). (D, G, and H) No abnormal findings were observed in brain MRI and thoracic spinal cord. (E, F) The exudative lesion in the C3-6 segments of the cervical spinal cord showed significant improvement after four months of treatment.

DISCUSSION

NMO spectrum disorder (NMOSD) is an autoimmune demyelinating disease that affects the optic nerves, spinal cord, and brain. Among connective tissue diseases, SS is the most prevalent disorder associated with NMO.[3] However, compared to isolated NMOSD, those with combined SS do not show significant differences in EDSS scores or recurrence rates.[4] In this case, the patient's clinical features support the diagnosis of SS in conjunction with NMO, indicating a potential shared pathophysiological mechanism between these two conditions. The AQP4 antibody is crucial in the pathogenesis of NMOSD, and its high specificity makes it an essential tool for clinically differentiating NMOSD from multiple sclerosis. This case presents typical neurological symptoms, signs, spinal cord MRI findings, and elevated titers of AQP4 antibody, fully conforming to the 2015 diagnostic criteria for NMOSD.[5] However, GFAP antibodies are rarely detected in patients diagnosed with SS complicated by NMO. GFAP antibody is a specific biological marker for autoimmune GFAP-astrocytopathy (GFAP-A), which was first proposed by Fang in 2016.[6] GFAP-A typically presents acutely or subacutely with fever, headache, mental disturbances, and cerebellar ataxia. CSF analysis shows increased white blood cells, mainly lymphocytes and monocytes, along with elevated protein levels. Cranial MRI often displays vascular-like radiographic enhancement in the white matter of the ventricles.[7] In this case, although the patient tested positive for the GFAP antibody, the patient did not present the typical clinical symptoms, cranial MRI findings, or abnormal changes in CSF associated with GFAP-A. Therefore, the diagnosis of GFAP-A remains debatable. As GFAP is an intracellular antigen in astrocytes, its serum levels are normally very low and only become detectable when astrocytes are damaged, and studies have also found a positive correlation between serum GFAP concentration in NMOSD patients with AQP4 antibody and disease activity and severity.[8,9] Consequently, the hypothesisis that the GFAP antibody present in this patient is a consequence of GFAP being released into the bloodstream due to astrocyte damage associated with NMOSD. The patient exhibited bilateral lower limb weakness and numbness, along with abdominal distension. These symptoms are generally not associated with cervical spinal cord injuries. We hypothesise that these symptoms may be linked to concurrent lumbar spinal cord involvement. Unfortunately, the medical records indicated that the patient refused a lumbar MRI.

In summary, the concurrent presence of anti-AQP4 and anti-GFAP antibodies in patients with SS complicated by NMO is uncommon. The underlying pathophysiological mechanisms of this phenomenon warrant further investigations.

PATIENT'S CONSENT:

Written consent was obtained from the patient to publish the data concerning this case.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

FQ: Conceptualisation, data curation, investigation, software, and writing of the original draft.
QH: Data curation, methodology, supervision, writing review, and editing.
JL: Formal analysis and methodology.
JS: Conceptualisation, supervision, writing review, and editing.
All authors approved the final version of the manuscript to be published.

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