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Case Report

Case of MOG-IgG-associated disease with ankylosing spondylitis: A rare coexistence

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ABSTRACT

Myelin oligodendrocyte glycoprotein-associated disease (MOGAD) is an inflammatory neurological disease. It progresses with attacks by affecting the optic nerves and spinal cord. Bilateral or recurrent optic neuritis are the most common findings in adult patients. Its association with systemic autoimmune disorders such as Sjögren syndrome, antiphospholipid syndrome, autoimmune thyroiditis, and celiac disease is rare. The first and only case of MOGAD in a patient with ankylosing spondylitis with a history of anti-tumor necrosis factor-alpha (anti-TNF-α) use was reported. Herein, we present the coexistence of MOGAD in a patient with AS who did not have a history of anti-TNF-α therapy.

Keywords: Ankylosing spondylitis, myelin oligodendrocyte glycoprotein antibody disease, optic neuritis.

Myelin oligodendrocyte glycoprotein-associated disease (MOGAD) is an inflammatory neurological disease. It progresses with attacks by affecting the optic nerves and spinal cord. Autoimmune demyelination and axonal damage are severe in the disease.[1] There are autoantibodies against myelin oligodendrocyte glycoprotein (MOG) found on the outer lamella of the myelin sheath in the central nervous system (CNS) in MOGAD. Anti-MOG antibodies reach the CNS by crossing the cerebrospinal fluid–brain barrier, which is usually damaged by infections.[2] The exact function of MOG is unclear, yet. However, it is thought to have an effect on the regulation of oligodendrocyte microtubule stability and modulation of the interaction between the immune system and myelin proteins.[3]

Bilateral or recurrent optic neuritis (ON) is common in adult patients with MOGAD. In neuromyelitis optica (NMO), severe attacks of ON and a contiguous inflammatory lesion in three or more vertebral spinal cords are seen. The NMO spectrum disorders (NMOSDs) are the limited form of the disease. Anti-aquaporin-4 (AQP4) antibodies are detected in most patients with NMOSD.[4] Approximately 42% of NMOSD patients who are negative for AQP4 antibodies are MOG antibody-positive.[5] The MOG antibody levels correlate with disease activity and treatment. The level of MOG antibody during an acute attack is higher than in remission.[6] Neuromyelitis optica is often associated with systemic autoimmune disorders. Anti-MOG positivity can be detected in

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systemic lupus erythematosus and Sjögren disease.[7] The coexistence of antinuclear antibodies (ANAs), anti-Sjögren syndrome A (SS-A), anti-Sjögren syndrome B (SS-B), and rheumatoid factor (RF) have been described in these patients.[8] Although autoantibodies are frequently seen in NMO, systemic symptoms or findings of autoimmune diseases may not be found.

Ankylosing spondylitis (AS) is an inflammatory disease in which sacroiliac (SI) joint and axial skeleton involvement is seen and, occasionally, peripheral joints can be affected. The association between AS and NMOSD is rarely defined in the literature. The first and only case of MOGAD development in a patient with AS with a history of anti-tumor necrosis factor-alpha (anti-TNF-α) use was reported by Luo et al.[9] In this article, we discuss the association of MOGAD in a patient with AS who did not have a history of anti-TNF-α therapy.

CASE REPORT

A 47-year-old male patient presented with blurred vision in his right eye that started three days ago. The blurred vision progressed to near-total vision loss of the right eye in the last three days. He also had post-traumatic visual loss sequelae in the left eye. On neurological examination, optic disc margins were obscure in the right eye, and the vision was almost completely lost in the right eye. There was no pathological finding on magnetic resonance imaging (MRI) with orbital, cranial, and spinal contrast. Cell cytology and biochemistry tests were normal in lumbar puncture samples, and oligoclonal immunoglobulin G (IgG) bands were negative. The AQP4 and MOG antibodies were sent for analysis. Considering isolated ON, intravenous methylprednisolone (1 g/day for seven days) was started. After steroid treatment, the patient could select hand movements. Since there was only one ON attack and there was no clear evidence for immunological disease, the steroid therapy was tapered gradually, while no additional immunosuppressive agent was used.

His medical history revealed that he was diagnosed with AS four years ago after a sacroiliac X-ray showed bilateral sacroiliitis (Figure 1). The MRI of the pelvis revealed medullary bone marrow edema in the mid-inferior part of both SI joints (Figure 2). The patient described inflammatory back pain 10 years. He was healthy otherwise. He had no prior surgeries, or trauma and did not smoke tobacco or drink alcohol. He denied sexually-transmitted infections, chronic diarrhea, and psoriasis in the past. His family history was negative. The patient met the Modified New York and Assessment of Spondyloarthritis International Society (ASAS) criteria.[10] Over the past four years, he was treated with only sulfasalazine and non-steroidal anti-inflammatory drugs for AS and had never used an anti-TNF agent or a biologic agent. His modified Schober was measured as 5 cm. Erythrocyte sedimentation rate was 13 mm/h, and C-reactive protein (CRP) was 5 mg/L. The ASDAS-CRP was calculated as 2.1 and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score was 2.5.

The patient, who remained without follow-up for four months, was referred again when his vision loss progressed. There were no lateralized motor or sensory deficits on neurological examination. Complete vision

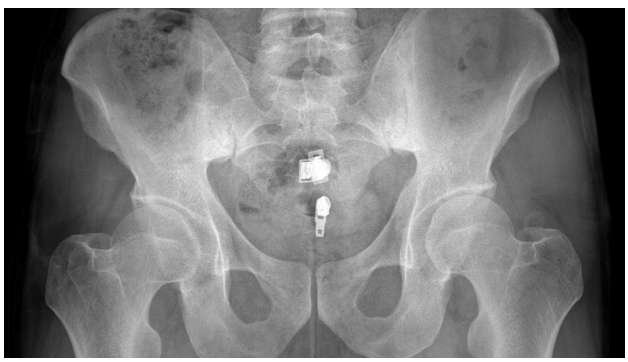

Figure 1. Bilateral sacroileitis on X-ray.

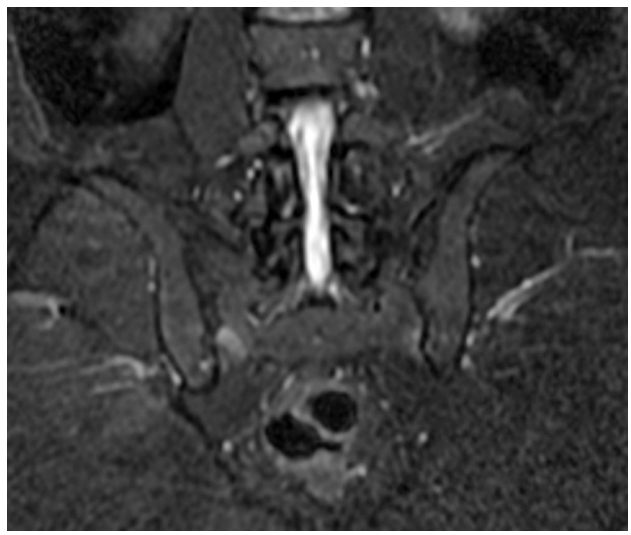

Figure 2. Bilateral sacroiliac bone marrow edema on magnetic resonance imaging.

loss and optic nerve head atrophy were observed in the right eye. No signal was received in the bilateral optic nerve visual-evoked potential (VEP) study. Contrast-enhanced cranial, orbital, and spinal MRI findings were normal. A lumbar puncture showed normal glucose, white blood cell, and protein. The oligoclonal band, which is an indicator of chronic or acute inflammation of the CNS or spinal nerve roots, was compatible with the type 4 pattern in which the same bands were seen in cerebrospinal fluid and serum. While pattern 2 or 3 is detected in multiple sclerosis patients, systemic IgG production is mentioned in pattern 4.[11] Anti-MOG positivity was detected, which was sent in the first attack but could not be checked, as the patient did not attend to follow-up. The patient, known to have AS, was also evaluated in terms of other rheumatological diseases. The rheumatological examination was AS compatible. Human leukocyte antigen-B27 (HLA-B27) and HLA-B5 were all negative. The ANA, RF, anti-cyclic citrulline peptide (CCP), anti-neutrophil cytoplasmic antibody (ANCA), SS-A, and SS-B were also negative.

Intravenous methylprednisolone (1 g/day for seven days) was administered rapidly to the patient for recurrent ON. Our case was diagnosed with MOG-associated ON, with serum NMO IgG (NMO IgG) negative, AQP4 negative, and anti-MOG-IgG positive for the first attack. Plasmapheresis was initiated for the steroid-resistant patient. He experienced marked improvement in vision and could count a finger at 2 meters. Rituximab infusion of 1,000 mg was started every six months at 15-day intervals. He took two cycles of rituximab. He did not have a new neurological attack. The final BASDAI of the patient who was still receiving non-steroidal anti-inflammatory drug for AS was calculated as 2.

DISCUSSION

Considering recurrent ON attack, serum AQP4 antibody negativity, and serum anti-MOG positivity, our patient with AS was also diagnosed with MOGAD. In a report, a female patient with AQP4-negative NMOSD and HLA-B27-negative AS was presented.[12] A female patient who was recently diagnosed with AQP4-positive NMOSD and HLA-B27-positive AS was also presented.[13] Coexistence of demyelinating CNS diseases in patients with AS was reported previously.[14]

Although the coexistence of AS and demyelinating disease is rare, in a study, asymptomatic demyelinating disease was detected on MRI in an AS patient who did not use anti-TNF.[15] The development of MOGAD in a patient with AS with a history of anti-TNF agent was reported.[9] Anti-MOG disease is less likely to occur in women than in those with NMOSD and is less associated with other autoimmune disorders.[16]

The pathogenesis of AS and NMOSD is unclear. The role of T cells in the pathogenesis of NMOSD is known. This suggests that there may be common pathogenesis in T cell dominance.[12] T cells and macrophages were detected in biopsies from active SI joints of spondyloarthritis patients.[17] T cell dominance is remarkable in both diseases. Interleukin (IL)-17-secreting Th17 cells, which are effective in the pathogenesis of autoimmune and chronic inflammatory diseases, are higher in NMOSD and AS patients compared to the healthy population.[18,19] However, more detailed studies are still needed for the role of IL-17 in the pathogenesis.

Amirzargar et al.[20] demonstrated that HLA-B27 was increased in ON patients. The HLA-B27 is a major histocompatibility complex (MHC) Class I protein that may present antigenic peptides to cytotoxic T cells. Misfold HLA-B27 proteins accumulate in the endoplasmic reticulum (ER), creating an ER stress and again causing activation of T lymphocytes via IL-17.[21] The IL-17 axis activation also stimulates inflammation in spondyloarthropathies. Previous studies have shown that HLA-B7, which is also increased in multiple sclerosis, a demyelinating disease, cross-reacts with HLA-B27. Cross-reactivity may affect the co-occurrence of diseases.[22] However, the role of HLA-B27 in the association of AS and NMOSD is still unclear.

Anti-TNF agents are contraindicated drugs for demyelinating diseases. Paradoxical autoimmune disorders and demyelinating CNS lesions may develop in the long-term use of these agents. The NMSOD cases with positive MOG antibodies have also been reported following anti-TNF therapy.[23] Our patient, also, did not receive anti-TNF treatment during the two-year period, when he was diagnosed with AS and was treated with sulfasalazine.

Our patient did not respond adequately to steroid treatment, and plasmapheresis improved vision. Although not used in the treatment of AS, rituximab was well tolerated in this patient with recurrent ON and was used for maintenance therapy.

In conclusion, knowledge of MOG-related diseases has been increasing in recent years. The widespread use of diagnostic tests, their availability, and more

consideration as a cause of recurrent ON play an essential role. The case of recurrent ON associated with seropositive MOG presented herein is important in that it is the first case, to the best of our knowledge, with AS who did not use anti-TNF, and that it shows the necessity of good questioning of the rheumatological entities that may accompany such cases.

Patient Consent for Publication: A written informed consent was obtained from the patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Concept: DK., SMT.; Supervision: SMT.; Materials: EG., DK.; Data collection and/or processing: DK., SMT.; Analysis and/or interpretation: DK., ZÖ., EG.; Writing: ZÖ., SMT.

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