Optic Neuritis Leading to Vision Loss: A Case of MOG-Associated Disease with Successful Immunotherapy

A 42-year-old woman presenting with loss of vision due to optic neuritis was admitted to the Naval Medical Center in October 2022. She had optic disc edema, blurred visual margins, optic disc pallor, and deficient visual field in both eyes. Cranial magnetic resonance imaging (MRI) showed bilateral optic nerve thickening, tortuosity, and swelling, especially on the right side. Orbital MRI T2 sequence showed the typical “double track sign” change. The titers of MOG-IgG in CSF and serum were 1: 1 (+) and 1: 32 (+) separately, so MOGAD was diagnosed. The primary treatment was intravenous methylprednisolone for 2 weeks, after which the blurred vision improved and MRI showed the optic nerve lesions disappeared. She was discharged and oral corticosteroids were tapered gradually, and 1 month later, the symptom had vanished without recurrence, cranial MRI was normal, and MOG-IgG in CSF and serum were negative. Low-dose oral corticosteroids were continued for 6 months, with no relapse and normal cranial MRI, so we stopped corticosteroid therapy. At 1-year follow-up, the symptoms had not recurred.

Conclusions: A 42-year-old woman presented with loss of vision due to optic neuritis and positive antibody testing for MOG. MOGAD was diagnosed, and timely immunotherapy was effective.

Keywords: MOG Peptide 97-108 • Neuromyelitis Optica • Case Reports

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Introduction

Myelin oligodendrocyte glycoprotein (MOG)-associated disease (MOGAD) is a recently described inflammatory demyelinating disease of the central nervous system (CNS), and has clinical and MRI phenotypes that can distinguish it from the main differential diagnoses of: a) aquaporin-4 (AQP4)-IgG-positive neuromyelitis optica spectrum disorder (AQP4-IgG+NMOSD), and b) multiple sclerosis (MS). [1]. The mean incidence of MOGAD is 0.16/100,000 per year, with higher positive rate at 0.31/100,000 in children, and the prevalence is estimated at 2/100,000 [2]. MOGAD has a younger age of onset and is more common in children than adults, and it has a more balanced male-to-female ratio (approximately 1: 1.1 male-to-female), and no significant racial predilection [3]. The proportion of patients with a history of antecedent infection is higher [4]. The clinical manifestations are closely related to the patient’s age, with acute disseminated encephalomyelitis (ADEM)-like manifestations in children and optic neuritis (ON) in adults, as well as myelitis, brainstem encephalitis, and meningitis [1-3]. ON is the most common clinical subtype of MOGAD, which is often combined with spontaneous ocular pain, ocular rotational pain, and orbital pain, and unilateral or bilateral visual acuity, visual field defects, color vision changes, and visual acuity decline may occur in the acute phase. Magnetic resonance imaging (MRI) shows the injured segment usually includes anterior optic pathway and the retrobulbar nerve and rarely involves the optic chiasm and the optic tract [4]. In contrast to MS, in which ON is mostly unilateral and with injury of the shorter segment optic nerve, ON in MOGAD is bilateral and longitudinally extensive [5]. Unlike MS of cranial MRI, in which periventricular lesions are generally larger and not perpendicular to the ventricular canal, MOGAD usually has fewer lesions and the area involved is wide, including the thalamus, basal ganglia, brainstem, cerebellum and cerebral cortex [6]. The proportion of patients with combined autoantibodies is low, indicating that about 20% of MOG-positive patients have combined autoimmune antibodies, mainly thyroid-related antibodies and antinuclear antibodies [7]. Most AQP-4-positive patients have combined antinuclear antibodies, anti-SSA antibodies, anti-RO52 antibodies, or anti-SSB antibodies [1,7].

MOGAD is a rare disease with few reported cases and no large-scale clinical trials related to treatment. A number of small clinical studies have indicated that the treatment of MOG antibody-related diseases usually involves high-dose intravenous methylprednisolone, intravenous immunoglobulin (IVIG), and plasma exchange, followed by sequential standard immunomodulating and immunosuppressive therapies, such as oral corticosteroids [8]. It is emphasized that the oral corticosteroids dose should be reduced slowly or even maintained at small doses for a long time because the risk of recurrence of MOG antibody-related disease is closely related to the rate of prednisone reduction. If the prednisone is completely reduced in less than 3 months, the probability of recurrence of the disease doubles [8]. Therefore, low-dose oral prednisone maintenance therapy should last for at least 3 months or even several years, followed by sequential immunosuppressive therapy including methotrexate, azathioprine, and mycophenolate mofetil, which has become the current recommendation for the treatment of MOG antibody-related disease [9]. Overall, the prognosis of MOG antibody-associated diseases is better than that of AQP4-IgG+NMOSD and MS [10].

Our patient was a 42-year-old woman presenting with loss of vision due to optic neuritis, without any symptom of cranial and spinal cord injury, and positive antibody testing for MOG. We completed the relevant examinations in time to carry out accurate and effective treatments, and the patient had a good recovery.

Case Report

A 42-year-old woman was admitted to the Naval Medical Center Ophthalmology Department on Oct 10th, 2022 with “blurred vision in both eyes for 4 days, aggravated for 3 days”.

On Sep 14th, 2022, she started to have fever with a maximum temperature of 38.9°C, no headache or dizziness, no nausea and vomiting, no cough and sputum, and no abdominal pain and diarrhea. After repeatedly failing to improve, she was hospitalized in a local hospital on Sep 27th, with routine blood tests indicating leukocytes of 16.24×10^9/L and neutrophils of 13.49×10^9/L (83.0% of the total). Except for positive EBV-IgG antibody, other etiological tests were negative. After symptomatic treatment, the body temperature returned to normal and she was discharged on Oct 4th, denying any history of chronic diseases, infectious diseases, surgical trauma, or family history.

On Oct 6th, the patient had blurred vision in both eyes without any obvious cause, and the symptoms persisted and gradually worsened. On Oct 7th, she suddenly became unable to see in both eyes, without obvious eye distension, ophthalmalgia, eye rotation pain, visual distortion, headache, nausea, vomiting, or other discomforts. On Oct 9th, in the local hospital, her examination showed findings including bilateral optic papillary edema, total visual field loss in both eyes, corrected visual acuity index/20 cm in the right eye and 0.05 in the left. She was diagnosed as having “optic neuritis (optic neuromyelitis?)” and was treated with methylprednisolone iv 1 g/day. On Oct 10th, she was admitted to the ophthalmology ward. The visual acuity of the right eye was manual/1 foot, and the visual acuity of the left eye was 0.02. The lens of both eyes was cloudy and the fundus optic disc boundary was unclear, edematous, and slightly pale. The retina was flat, the macula was dark, and the central concave reflection was not seen; the
conjunctiva of both eyes were not congested, the cornea was old ring, the anterior chamber was clear, and there was pupil-to-light reflex; the intraocular pressure of the right eye was 18.7 mmHg and that of the left eye was 14.0 mmHg. Methylprednisolone was continued at 1 g/day iv, and the treatment was changed to oral prednisone tablets 60 mg/day 2 days later. On Oct 14th, she was rechecked for visual acuity, showing right eye 0.08, -4.25DS→0.6, left eye 0.12, -4.25DS→0.8. The fundus edema improved, and visual field and fundus abnormalities became significantly better than before in both eyes. Cranial MRI showed no significant intracerebral abnormalities, but presented bilateral optic nerve thickening and swelling, especially on the right side. After neurologist consultation, the patient was referred to the Neurology Department for further therapy on Oct 14th.

Figure 1. Initial cranial magnetic resonance imaging (MRI) of a 42-year-old woman with positive antibody testing for myelin oligodendrocyte glycoprotein (MOG). (A, B) the T2 sequence shows bilateral optic nerve thickening, tortuosity, and swelling, and the involvement ranges from the intraorbital segment nerve without involving the optic cross, especially on the right side. (C, D) T2 pressure lipid sequence shows bilateral optic nerve thickening, tortuosity, and swelling. The involved area extends from the intraorbital segment nerve without the optic cross, especially on the right side. MOG – myelin oligodendrocyte glycoprotein; MRI – magnetic resonance imaging.
Figure 2. (A, B) Initial orbital magnetic resonance imaging (MRI) T2 sequence of a 42-year-old woman with positive antibody testing for myelin oligodendrocyte glycoprotein (MOG). There is a high signal of the optic nerve sheath around the right optic nerve, showing the typical “double track sign” change. MOG – myelin oligodendrocyte glycoprotein; MRI – magnetic resonance imaging.

Figure 3. Initial spinal magnetic resonance imaging (MRI) of a 42-year-old woman with positive antibody testing for myelin oligodendrocyte glycoprotein (MOG). There were no significant abnormalities in the cervical medulla (A) and thoracic medulla (B). MOG – myelin oligodendrocyte glycoprotein; MRI – magnetic resonance imaging.
After she was admitted to our department, we performed routine blood, liver, and kidney function tests, coagulation, electrolytes, blood lipids, blood glucose, thyroid function, C-reactive protein, procalcitonin, autoantibody spectrum, tumor markers, and other blood tests, as well as urine and stool routine tests. The next day, we performed a lumber puncture for cerebrospinal fluid (CSF) analysis. MOG, AQP-4, Myelin basic protein (MBP), glial fibrillary acid protein (GFAP), autoimmune encephalitis antibodies, and pathogenic organisms (including HIV, other viruses, bacteria) in serum and CFS were tested. She had a lgG synthesis rate of 24 h and oligoclonal band in CFS. All antibodies were detected by cell-based assay (CBA). Cranial, orbital, and whole spinal cord MRI scans were performed. The neurological examination showed no significant abnormalities except a slight decrease in visual acuity in the right eye. On Oct 17th, routine blood test results indicated serum antinuclear antibodies (+), and the routine blood, biochemistry, coagulation, thyroid, and other test results were normal. Routine biochemical examination of cerebrospinal fluid showed total cell count 40×10⁶/L, chloride 119.0 mmol/L, glucose 3.71 mmol/L, and protein 387.21 mg/L. On Oct 19th, there were no significant abnormalities according to the cervical and thoracic spine MRI examinations. On Oct 20th, results showed that the titer of MOG-IgG in CSF was 1: 1 (+), and the titer in serum was 1: 32 (+), normal lgG synthesis rate of 24 h and oligoclonal band in CSF, MBP, GFAP, autoimmune encephalitis antibodies, and pathogenic organisms in both serum and CSF were negative. Cranial MRI T2 sequence and T2 pressure lipid sequence showed bilateral optic nerve thickening, tortuosity, and swelling. The involved area extended from the intraorbital segment nerve without the optic cross, especially on the right side (Figure 1). Orbital MRI T2 sequence showed the typical “double track sign” change (Figure 2). There were no significant abnormalities in the cervical medulla and thoracic medulla (Figure 3). Based on the patient’s symptoms, signs, and ancillary tests, the diagnosis of “MOG antibody-associated optic neuritis” was clear. The patient was treated with intravenous methylprednisolone 500 mg/d×3 days, 240 mg/d×3 days, 120 mg/d×3 days, and then changing to oral Prednisolone tablets 60 mg/d. After she was discharged, the dose was reduced by 10 mg per week to 30 mg and then maintained. A follow-up 1 month later showed no recurrence of symptoms, with normal fundus examinations, cranial MRI showed no obvious abnormalities (Figure 4A), and the MOG antibody in serum and cerebrospinal fluid had become negative. Therefore, the treatment plan was adjusted – prednisone was slowly reduced to 10 mg oral administration per day, as maintenance therapy for 6 months and the drug was to be stopped if all results were normal. Corticosteroid therapy was stopped based on lack of relapse and a normal cranial MRI scan (Figure 4B). At 1-year, the symptoms had did not recurred.

Discussion

MOG, a member of the human immunoglobulin superfamily, is a myelin glycoprotein specifically expressed by oligodendrocytes in the central nervous system and is a highly conserved protein consisting of 218 amino acids. It constitutes the outermost layer of myelin and accounts for a very low percentage (<0.05%) of all myelin components. The biological functions of MOG are not yet clear, but it has been suggested that it can play a role in stabilizing myelin structure, regulating the cell membrane architecture, and activating complement [11]. As for the
production of MOG antibody, it has been found in animal studies that intestinal flora can assist in the generation and activation of MOG-specific CD4+ T cells and B cells, promoting the production of MOG antibodies [12]. When the blood-brain barrier is damaged again, peripherally generated MOG antibodies will enter the CNS and lead to neurological damage through cytotoxicity mediated by complement and antibody [12].

According to the criteria proposed in Lancet Neurol, 2023, MOGAD is typically associated with optic neuritis, acute disseminated encephalomyelitis, or transverse myelitis, and is less commonly associated with brainstem presentations, cerebral cortical encephalitis, or cerebellar presentations. Diagnoses such as MS and NMOSD need to be excluded. The presence of MOG-IgG in serum and/or CSF is a core criterion for the diagnosis of MOGAD [1]. The main symptom of our patient was loss of bilateral vision due to optic neuritis—the titer of MOG-IgG in CSF was 1: 1 (+) and the titer in serum was 1: 32 (+), with a normal IgG synthesis rate of 24 h in CSF, and the oligoclonal band in CSF was normal, and all these tests were used to diagnose typical MOGAD.

Optic neuritis is the most common clinical symptom of MOGAD, mainly manifesting as visual acuity loss, which may be accompanied by visual field defects, opthalmalgia, and increased intraocular pressure [1]. Compared with AQP4-positive optic neuritis, MOG-positive optic neuritis mostly involves the bilateral optic nerves, accounting for more than 70% of cases. The visual acuity loss is severe and develops rapidly, with visual acuity dropping to finger movement or even disappearing completely after the disease reaches its peak. MOGAD shows better response to acute immunotherapy and less frequently results in severe disability, such as ambulatory and visual disturbances [13]. However, most patients recover well from those symptoms after timely immunotherapy, and only about 10% of patients have reduced visual acuity to less than 0.1, with a low rate of blindness. MRI shows that MOG-positive optic neuritis is dominated by lesions in the anterior part of the optic nerve (especially in the retrobulbar and intraorbital segments), showing T2 sequence high signal, thickening and swelling of the optic nerve, enhancement of the optic nerve sheath (specific image changes), and the lesion length often exceeds 1/2 of the intraorbital segment, which may extend to the intraorbital soft tissue and combine with inflammation of the intraorbital soft tissue, but rarely involves the optic cross [1,14]. In terms of the development of myelitis, 56% of MOG-positive patients have long-segment transverse myelitis, with cervical and thoracic spinal cord involvement being the most common [15], and some cases involve the lumbar and sacral medulla, with sphincter dysfunction, paraplegia, and sensory impairment [1,16]. In addition, involvement of the conus medullaris is one of the characteristic manifestations of the disease [1]. In this case, MRI T2 sequence showed bilateral optic nerve thickening, tortuosity, and swelling, and the involvement ranged from the intraorbital segment nerve without involving the optic cross, especially on the right side.

MOG-positive disease is often found to present with “severe imaging lesions and mild clinical symptoms”. Regarding possible mechanisms, MRI in 70% of patients with this lesion shows significant swelling and enhancement of the spinal cord, without necrotic lesions [16]. For some MOG antibody-positive patients, there is no large inflammatory cell infiltration or complement aggregation in the neomyelinating lesions [17]. Injection of MOG antibodies into mice triggers a mild inflammatory response, but no large inflammatory cell infiltration or neuronal necrosis was found [18]. The lesions returned to normal within 2 weeks, suggesting that the MOG antibody-induced lesion may be reversible [19]. In our patient, the visual acuity of both eyes recovered rapidly after 3 days of corticotherapy and approached normal level. Long-term oral maintenance treatment with small doses of prednisone was used during the follow-up period, and there was no recurrence of the disease. This suggests that the degree of pathological damage to MOG antibody-involved tissues may be mild and reversible, and has a good prognosis. However, whether the pathological damage becomes more severe with recurrent disease, as in classical AQP4 antibody-positive disease, needs to be further explored.

MOGAD is a pathological manifestation, with fused white matter demyelination being the most common, and inflammatory cell infiltrates containing large numbers of CD4+ T cells that synergistically upregulate helper T cells and other cytokines, especially interleukin-6 [12,18]. Consistent with this, serologic testing in our patient revealed an increase in CD4+ T cells and a decrease in B cells in the acute phase, and the indexes returned to normal 1 month later. As for the suspected cause of the disease, the onset of the disease is after repeated fever due to no clear pathogenic infection, and whether it is related to the immune response triggered by EBV infection is yet to be explored. Our patient’s serology was positive for ANA antibody (1: 1000), serum EBV-IgG antibody (IgM-negative), and hepatitis E IgG antibody, but she had no arthralgia, dry mouth and eyes, rash, abdominal pain, diarrhea, or other related symptoms. However, the role and relevance of these antibodies in the disease process need to be further clarified.

Approximately 35% of patients with MOG antibody disease present with a relapsing course, with optic neuritis as the most common relapse symptom, generally independent of the first episode [20]. It has also been reported that the risk of recurrence of MOGAD increases as the titer of MOG-IgG increases at initial onset and as the duration of MOG-IgG-positivity increases in patients. In contrast, patients with low MOG-IgG titers at the onset of disease and who turn negative within a short period of time often show a monophasic disease.
course [15–17]. The prognosis for our patient was excellent, with rapid recovery of near normal vision in both eyes after 3 days of corticosteroid therapy. She was treated with oral maintenance therapy with small doses of prednisone (30 mg/day) orally. At 1-month follow-up, she showed no recurrence of symptoms, and the treatment was adjusted—prednisone was slowly reduced to 10 mg per day, which was maintained for 6 months, the symptoms did not recur, so the drug was stopped, and telephone follow-up 1 year later determined that her peripheral symptoms had not returned.

Conclusions

MOGAD is a recently described inflammatory demyelinating disease of the CNS, and has clinical and MRI phenotypes that can distinguish it from the main differential diagnoses of AQP4-IgG+NMOSD and MS. Our patient was a 42-year-old woman whose symptoms started with acute bilateral optic neuritis, with a sharp decrease in visual acuity in both eyes within a short period of time. The orbital MRI suggested the lesions involved the anterior segment of the optic nerve bilaterally, with a length of more than 1/2 of the intraorbital segment, without involving the optic chiasm. She had no numbness or weakness. The cervical and thoracic MRI results were normal. MOG antibody in CSF was 1: 1 (+) and serum MOG antibody was 1: 32 (+). MOGAD was diagnosed, and corticosteroid therapy was effective, with no recurrence at 1-year follow-up.

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