CASE REPORT

Anti-myelin Oligodendrocyte Glycoprotein Antibodies in a Patient with Recurrent Optic Neuritis Involving the Cerebral White Matter and Brainstem

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Abstract

We herein report a case of recurrent optic neuritis involving the cerebral white matter and brainstem in a patient positive for anti-myelin oligodendrocyte glycoprotein (MOG) antibodies. The patient had an initial attack at 24 years of age. Optic neuritis recurred over 14 years, and she was admitted to our neurology unit at 38 years of age. She showed bilateral optic neuritis, high-intensity lesions in the cerebral white matter and brainstem on T2 MRI with contrast enhancement, and elevated serum anti-MOG antibodies. Immunotherapy improved the MRI lesions. Recurrent optic neuritis in patients with anti-MOG antibodies may thus involve the cerebral white matter and brainstem.

Key words: MOG, white matter, brainstem, MRI, NMO

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Introduction

Myelin oligodendrocyte glycoprotein (MOG) antibodies have been described in patients with pediatric acute disseminated encephalomyelitis (ADEM) (1, 2). Recent studies have documented patients with neuromyelitis optica spectrum disorder (NMOSD) who were negative for anti-aquaporin 4 (AQP4) antibodies and positive for anti-MOG antibodies (3, 4). Sato et al. also reported clinical and radiological findings of NMOSD in patients positive for anti-MOG antibodies (5). The pathomechanisms of these antibody-positive demyelinating disorders are unknown. Moreover, cerebral brain magnetic resonance imaging (MRI) abnormalities of patients with optic neuritis with anti-MOG antibodies occur less frequently than optic nerve lesions (6). We herein report the case of a patient who had optic neuritis with a long-term follow-up, anti-MOG antibodies, and abnormalities in the cerebral white matter and brainstem.

Case Report

In 1998, a 24-year-old Japanese woman developed right optic neuritis two months after delivering her first child and she was treated with methylprednisolone (mPSL) pulse therapy in an ophthalmology department. She had no notable personal or family medical history or history of drug abuse. After treatment, her visual acuity was fully restored. The next year, she developed left optic neuritis with optic pain and had three recurrences of right optic neuritis. In 2000, after her second pregnancy, she complained of right visual loss, however, she was not admitted to the hospital due to financial problems and thereafter showed right blindness. In 2007, after her third pregnancy, she had a recurrent attack of left optic neuritis and was again treated with mPSL. Brain MRI showed left optic neuritis and no other abnormality. In 2009, after her fourth pregnancy, she had another episode of left optic neuritis. A neurological examination revealed left visual loss. Brain MRI showed left optic neuritis and no other abnormality, and serum anti-AQP4 antibody was nega-
After two courses of mPSL, her left critical flicker frequency improved from 10 Hz to 13 Hz. She was administered oral PSL for one month. In November 2013, when she was 38 years of age, she had an attack of left optic neuritis and was treated with three courses of mPSL and oral PSL for six months. Brain and spinal cord MRI with contrast enhancement showed no abnormality, and serum anti-AQP4 antibody was again negative. In 2014, she had an attack of left optic neuritis without any known trigger, such as infection, and was admitted to the department of ophthalmology of our hospital and then transferred to our neurology department.

General medical examinations showed no abnormal findings. Neurological examinations showed right visual loss and left visual disturbance. Her visual acuity was 10 cm hand motion for the right eye and 0.6 for the left eye. Her visual field was not measurable on the right side and was limited on the left side. The light reflex was lost in the right eye and prompt in the left eye. Her critical flicker frequency was not measurable on the right side and 18 Hz on the left side. She showed no other neurological abnormalities. A blood biochemical analysis and urinalysis showed no abnormalities. Autoantibodies including antinuclear, anti-SS-A, anti-SS-B, anti-double-stranded DNA, anti-thyroid peroxidase, and anti-neutrophil cytoplasmic antibodies were negative. Tumor markers including carcinoembryonic antigen, CA19-9, alpha-fetoprotein, and soluble intereukin-2 receptor were also negative. Cerebrospinal fluid (CSF) examinations revealed normal pressure, a monocyte count of 6/μL, 29 mg/dL of total protein, and an IgG index of 0.114. CSF culture and cytology were negative. Myelin basic protein and oligoclonal bands were also negative. Brain T2-weighted MRI showed high-intensity areas in the left external capsule and extreme capsule (Figure A) and precentral white matter (Figure B) with partial contrast enhancement (Figure C), as well as the pontine base and tegmentum of the midbrain (Figure D), left cerebral peduncle (Figure E), and right medial thalamus with contrast enhancement (data not shown). Spinal cord MRI showed no abnormality. Whole-body computed tomography revealed no malignancy. Visual evoked potentials by flash stimulation showed no response in the right eye, and P100 was 129 ms in the left eye. Sensory evoked potentials and auditory brain responses were normal. Nerve conduction studies of the extremities were within the normal range, and electroencephalography showed no abnormalities. We retrospectively analyzed the serum anti-MOG antibodies in samples collected in 2009 and 2014 and found a high titer of MOG antibodies (1:2048 at each time) using a cell-based assay (7).

After the patient was treated with mPSL for two courses, she was administered oral PSL (1 mg/kg), which was tapered by 20 mg/day. Her left visual disturbances and right

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**Figure.** MRI scans of the cerebrum and brainstem on admission and after treatment. (A-E) On admission, there were T2 high-intensity areas in the external capsule and extreme capsule (A, arrow), left precentral white matter (B, arrow) with partial contrast enhancement (C), pons and midbrain tegmentum (D), and left cerebral peduncle (E). (F-J) After treatment, these lesions diminished (F, G, I, J) and no longer showed any contrast enhancement (H).
vision loss did not improve, however, the high-intensity areas of the brainstem and right thalamus disappeared, and the left white matter lesions were diminished (Figure F-J). She has not suffered from recurrent optic neuritis or white matter lesions for six months.

**Discussion**

We herein described the case of a patient with anti-MOG antibody-positive optic neuritis involving the cerebral white matter and brainstem. Our patient presented with the NMOSD characteristics proposed by Wingerchuk et al. (8). Sato et al. reported that patients with MOG antibodies have distinctive clinical features, as compared with patients seropositive for AQP4 antibodies: they are more frequently male; have more optic nerve lesions than spinal cord lesions, with the latter often located in the lower portion of the spinal cord; more frequently have optic neuritis in both eyes simultaneously; are more likely to have a single attack; and usually have more extensive functional recovery (5). Moreover, in the report by Sato et al., cerebral lesions were reported in six out of 16 cases, with two of the six being pediatric cases. Our present case does not fit this clinical pattern. The reason for the involvement of the cerebral white matter and brainstem in this case is unknown. Kitley et al. reported that patients with MOG antibodies were significantly more likely to have ADEM-like lesions, defined as lesions in the deep gray nuclei or fluffy white matter, than were patients with AQP4 antibodies (4). Our case supports this observation. Amano et al. reported a case of influenza-associated transverse myelitis in a patient positive for MOG antibodies and considered influenza infection as a possible trigger for myelitis (9). Considering that the anti-MOG antibody titers in our patient were the same before and after the brain MRI abnormalities developed, the combination of anti-MOG antibodies and an external trigger may have led to brain MRI abnormalities. Because our patient’s recurrent optic neuritis often occurred shortly after a pregnancy, pregnancy may have been a trigger for her recurrences. Although the possibility of reversible cerebral vasoconstriction syndrome was considered, she showed no thunderclap headache, magnetic resonance angiography abnormalities or posterior white matter involvement. The fact that immunosuppressive treatment improved the white matter lesions suggests that inflammatory changes of the cerebral white matter were the main manifestations of this disorder in our patient.

MOG is expressed in the central nervous system on the outermost surface of the myelin sheath and the plasma membrane of oligodendrocytes (10). MOG might act as a cell adhesion molecule, a regulator of microtubule instability, or a mediator of interactions between myelin and the immune system (11). Anti-MOG antibodies are frequently observed among pediatric patients with recurrent optic neuritis (1, 12). In a Japanese case series of NMOSD, 64.7% were AQP4 positive and 7.4% were MOG positive, while double-positive cases were very rare (13). Among anti-AQP4 antibody-seronegative NMO patients, 21.1% were reported to have anti-MOG antibodies (4). In a recent report of patients with idiopathic optic neuritis, 27.6% were positive for MOG antibodies and 3.4% were positive for AQP4; these patients often showed optic pain and high CSF levels of myelin basic protein (6). Although our patient showed cerebral involvement with contrast enhancement lesions, myelin basic protein was not elevated in her CSF, and no oligoclonal bands were present. It is therefore difficult to identify whether anti-MOG antibodies alone mediated the cerebral demyelination. Because our patient was positive for anti-MOG antibodies and had MRI lesions atypical for multiple sclerosis, no oligoclonal bands, no IgG index elevation, and recurrent optic neuritis, we diagnosed her NMOSD even though she did not fit new international consensus diagnostic criteria for NMOSD (14). In accordance with the diagnosis of NMOSD, we treated the patient with immunotherapy. In patients with recurrent optic neuritis with anti-MOG antibodies, both careful clinical examinations and serial MRI scans are necessary for the treatment of these patients without any neurological manifestations except for optic neuritis.

The authors state that they have no Conflict of Interest (COI).

**References**