CASE REPORT

Myelin Oligodendrocyte Glycoprotein-antibody-associated Disorder Presenting with Corticomeningeal Encephalitis prior to the Onset of Optic Neuritis

Takuya Ataka, Noriyuki Kimura and Etsuro Matsubara

Abstract:
We herein report a case of myelin oligodendrocyte glycoprotein-antibody-associated disorder (MOG-AD) presenting with corticomeningeal encephalitis. The patient exhibited oral ulceration, a mild impairment of consciousness, fever, nausea, nuchal rigidity, positivity for human leukocyte antigen type B51, and neutrophil-dominant pleocytosis and interleukin-6 level in cerebrospinal fluid (CSF). Magnetic resonance imaging (MRI) revealed a right temporal lesion with leptomeningeal gadolinium enhancement. The initial diagnosis was neuro-Behçet’s disease presenting with meningoencephalitis; however, a cell-based assay detected anti-MOG antibody in the serum and CSF and the patient also experienced bilateral optic neuritis. After administering steroid therapy, his neurologic symptoms and CSF abnormalities improved along with the disappearance of gadolinium enhancement and the lesion on MRI. This case suggests that MOG-AD may present with corticomeningeal encephalitis prior to the onset of optic neuritis.

Key words: MOG-AD, corticomeningeal encephalitis, neuro-Behçet’s disease, meningitis, Graves’ disease

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Introduction

Myelin oligodendrocyte glycoprotein (MOG)-antibody-associated disorders (MOG-AD) are classified as inflammatory demyelinating disorders of the central nervous system (CNS). Initially, anti-MOG antibody was detected in patients with neuromyelitis optica spectrum disorders, optic neuritis, and transverse myelitis (1, 2). In recent years, some cortical encephalitis cases related with MOG-AD have been reported (3). On the other hand, neuro-Behçet’s disease occurs in less than 10 percent of patients with Behçet’s disease. Neuro-Behçet’s disease can be categorized into parenchymal and non-parenchymal subtypes. The parenchymal type presents with brainstem lesions, cerebral lesions, spinal lesions, and rarely aseptic meningitis and meningoencephalitis (4, 5). Distinguishing MOG-AD from other inflammatory diseases of the CNS is a key imperative to guide treatment decision-making, because MOG-AD shows a good response to steroid therapy. We herein report a patient with MOG-AD who presented with corticomeningeal encephalitis prior to the onset of optic neuritis and who initially was suspected to mimic neuro-Behçet’s disease.

Case Report

A 37-year-old Japanese man presented with right orbital headache. His family history was unremarkable. The headache deteriorated despite taking over-the-counter analgesics. One week after the onset, the patient was admitted to a local hospital with a high fever (38.0°C), non-localized headache, nausea, and painless oral ulcers. Neurological examinations revealed nuchal rigidity, jolt accentuation, and Kernig’s sign. A cerebrospinal fluid (CSF) examination showed increased the cell count (164 cells/μL; 34% monocytes), total protein level (83.3 mg/dL), and a slightly decreased sugar level (45 mg/dL, blood sugar 102 mg/dL). The patient was treated with intravenous broad-spectrum antibiotics and antivirals for suspected acute infectious meningitis; however, he showed a gradual decrease in his consciousness level. Fig. 1

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Figure 1. The figure shows the clinical course of the patient. The treatments are described in the upper line, the changes in symptoms are described in the middle line, and laboratory data are described in lower line. IVMP: intravenous pulsed methylprednisolone, PSL: prednisolone, CSF: cerebrospinal fluid, MBP: myelin basic protein, N.A: not available

shows his clinical course. Ten days after onset, he was referred to our hospital for further evaluation. Neurological examinations showed a mild impairment of consciousness and nuchal rigidity, jolt accentuation, and Kernig’s sign. His visual acuity was normal (right/left: 1.6/1.25). Routine blood investigations showed leukocytosis (10,670 cells/μL) and a slightly elevated C-reactive protein level (0.36 mg/dL). He was suspected to have aseptic meningitis including autonomic diseases, and thus additional examinations were performed. He tested positive for human leukocyte antigen (HLA) type B51. The serum levels of thyroid-stimulating hormone, free triiodothyronine (T3), and free thyroxine (T4) were <0.005 μIU/mL (normal: 0.50-5.00 μIU/mL), 7.44 pg/mL (normal: 2.3-4.0 pg/mL), and 3.81 ng/dL (normal: 0.90-1.70 ng/dL), respectively. He exhibited positivity for thyrotropin receptor antibody (25.9 IU/L). In addition, serum anti-aquaporin 4-IgG detected by cell-based assay was negative. A CSF examination showed an increased opening pressure (240 mmH2O), increased cell count (682 cells/μL; 37% monocytes, 63% polymorphonuclear cells), total protein (113.9 mg/dL), and interleukin (IL)-6 level (5,500 pg/mL; normal <4.3 pg/mL). The sugar level in CSF had slightly decreased (47 mg/dL, blood sugar 110 mg/dL), while the IgG index had slightly increased (0.69). Oligoclonal bands were not detected in the CSF. Bacterial and fungal cultures were negative and the antibody indices to Herpes Simplex Virus, Varicella-Zoster Virus, Cytomegalovirus, Epstein-Barr Virus were not elevated. Fluid attenuated inversion recovery image (FLAIR) sequence of brain magnetic resonance imaging (MRI) revealed hyperintense cortical lesions with mild edema in the right temporal lobe (Fig. 2A). Gadolinium-enhanced T1-weighted image showed leptomeningeal enhancement in the right temporal lesions (Fig. 2B). Electroencephalography showed intermittent slow waves in the left frontal region and no epileptiform discharge. The initial laboratory findings were suggestive of neuro-Behçet’s disease. However, a cell-based assay detected anti-MOG antibody in the serum (titer 1:2,048; normal <1:128) and CSF (titer 1:64; normal <1:4). Finally, a diagnosis of MOG-AD presenting with corticomeningeal encephalitis and Graves’ disease was established. He was administered two courses of intravenous pulsed steroid therapy (methylprednisolone 1,000 mg/day for 3 days) followed by continuation therapy with oral steroids (prednisolone 30 mg/day); his symptoms showed a gradual improvement. Follow-up MRI at 26 days after onset showed disappearance of hyperintense lesions with leptomeningeal gadolinium enhancement on a FLAIR image (Fig. 2C, D). However, he experienced a recurrence of symptoms including bilateral visual impairment (visual acuity 0.09/0.7) at 36 days after onset; repeat MRI showed...
Figure 2. Magnetic resonance images of the patient on admission (A, B) and on 26th day after onset (C, D). (A) Axial fluid attenuated inversion recovery image (FLAIR) showing hyperintensity and swelling in right-dominant superficial cortex. (B) Gadolinium-enhanced T1-weighted image showing leptomeningeal enhancement in the areas corresponding to hyperintensity in FLAIR. (C) Images on the 26th day after onset showing an improvement of the hyperintensity and swelling (C), and the disappearance of leptomeningeal gadolinium enhancement (D).

Discussion

We herein described a patient with MOG-AD who developed corticomeningeal encephalitis followed by bilateral optic neuritis. We diagnosed him to have meningitis because he had fever, nuchal rigidity, nausea, jolt accentuation, Kernig’s sign. Considering the radiological findings which indicated the presence of cortical encephalitis, we finally diagnosed the patient to have corticomeningeal encephalitis, with hyperintensity in both optic nerves with mild edema on T2-weighted sequence (Fig. 3A, C) and gadolinium enhancement on gadolinium-enhanced T1-weighted images (Fig. 3B, D). He was administered an additional two courses of intravenous pulsed steroid therapy and his visual acuity thereafter fully recovered (visual acuity 1.6/1.25). He was discharged while continuing oral steroids (prednisolone 30 mg/day); the clinical course was uneventful after the tapering of steroid therapy.

The HLA type B51 was positive and both the cell counts (predominantly neutrophils) and IL-6 level were elevated in CSF. Therefore, our patient was initially suspected to have neuro-Behçet’s disease according to the International Criteria for Behçet’s disease (6) and probable neuro-Behçet’s disease, as per the International consensus recommendation criteria (7). Two cases of MOG-AD mimicking neuro-Behçet’s disease have been reported previously (8). Previous cases showed cerebral and brainstem lesions, whereas the present case showed cortical encephalitis. Although encephalitis in the brainstem or deep subcortical lesions are commonly associated with neuro-Behçet’s disease, both of aseptic meningitis and cortical encephalitis are rare manifestation of neuro-Behçet’s disease (5). On the other hand, cortical encephalitis has been recognized as a characteristic feature of MOG-AD (3, 9). Our patient was finally diagnosed to have MOG-AD presenting with corticomeningeal encephalitis based on the presence of anti-MOG antibody in serum and Graves’s disease as a co-existing disease.

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CSF, characteristic lesion: cortical encephalitis, and a favorable response to steroid therapy. Our findings suggest that MOG-AD may present with clinical and laboratory findings mimicking neuro-Behçet’s disease. Therefore, it is important to consider MOG-AD in the differential diagnosis of neuro-Behçet’s disease presenting with meningoencephalitis.

To the best of our knowledge, 7 cases of MOG-AD-associated meningitis, which were described to have fever, nausea, and nuchal rigidity, have been reported including our case (Table) (10-16). The mean age of these patients was 24.4 years (range: 3-55); four of these patients were male. Six of these patients had radiological cortical encephalitis, while six of these patients had subcortical lesions. Five of these patients had optic neuritis during their clinical course; however, six of these patients, including our case, either only had meningitis or had meningitis prior to the onset of optic neuritis. Only one patient experienced seizures. All patients had an increase in the cell counts and the total protein level in CSF. Four patients showed a mild decrease in the sugar level (40-60 mg/dL) in CSF. All patients were treated with intravenous steroid therapy and one patient received additional plasma exchange therapy during their clinical course. As maintenance therapy, seven patients were treated with oral steroids and two patients were treated with azathioprine. Three patients (including the present case) experienced a relapse. The clinical characteristics of our patient (increased cell count and total protein in the CSF; steroid-responsive meningitis) were consistent with these cases. Three of these patients (including our case) showed polymorphonuclear cell-dominant pleocytosis in the CSF, and a previous study showed neutrophils which frequently appear in the CSF of patients with MOG-AD during attack (17). These results possibly mean that polymorphonuclear-dominant pleocytosis can be seen during such attacks.

Previously, some types of cerebral cortical encephalitis have been reported (3, 9, 18). One is unilateral cerebral cortical encephalitis (UCCE) (3). UCCE is characterized by seizures and an unilateral radiological abnormality. Interestingly, only one of the cases with MOG-AD presenting with clinical meningitis with radiological cortical encephalitis experienced seizures.

The underlying mechanism for the development of meningitis in MOG-AD is not well characterized. Meningeal involvement may possibly occur as sequelae associated encephalitis because MOG-AD frequently presents with encephalitis. However, one case (16) had only subcortical encephalitis, it possibly means that inflammation spread to the

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**Figure 3.** Magnetic resonance images of the patient. A coronal T2-weighted image showing swelling in the bilateral optic nerves (A) with gadolinium enhancement (B). A horizontal T2-weighted image showing deflection in the bilateral optic nerves (C) with diffuse gadolinium enhancement (D) in the orbital region.
MOG-AD cases and describe such cases in detail.

Our patient had Graves’ disease based on the findings of hyperthyroidism, an increased blood flow in thyroid, and the serum positivity for thyrotropin receptor antibody. MOG-AD is less frequently associated with concomitant systemic autoimmune diseases than aquaporin-4 antibody-positive neuro- myelitis optica spectrum disorder (19). A few cases of MOG-AD had concomitant Hashimoto encephalopathy (20) and anti-N-methyl-D-aspartate receptor encephalitis (21). Our findings suggest that MOG-AD may also be associated with systemic autoimmune diseases. Further studies are required to elucidate the relationship between MOG-AD and systemic autoimmune diseases.

This case report highlights two important clinical issues. First, MOG-AD can present with menigitis as an initial symptom; therefore, MOG-AD should be considered in the differential diagnosis of menigitis. Second, patients with MOG-AD could also have concomitant systemic autoimmune diseases, such as Graves’ disease.

**Conclusion**

Although MOG-AD has a wide spectrum, the type is gradually being classified. We described a case of MOG-AD presenting with corticomeningeal encephalitis that had concomitant Graves’ disease. We should accumulate more MOG-AD cases and describe such cases in detail.

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

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| Authors Year Reference | Age | Sex | Lesion in cerebrum | CSF Cell (μL) + | MOG-ab Serum CF | Treatment Acute Chronic | Clinical course |
|-------------------------|-----|-----|---------------------|---------------|----------------|------------------------|----------------|
| Nagabushana et al. 2019 (10) | 22 | F | 1. bilateral cortical 2. bilateral subcortical | 57 | + | IVMP | 1.meningitis seizure (-) |
| Narayan et al. 2019 (11) | 28 | M | 1. bilateral cortical 2. brainstem 3. cerebellum | 143 | + | IVMP/PE | 1. ON |
| Suzuki et al. 2019 (12) | 55 | F | 1. left cortical 2. bilateral subcortical | 190 | + | IVMP | 1. meningitis |
| Zhong et al. 2019 (13) | 7 | F | 1. bilateral cortical 2. bilateral subcortical | 22 | 1:320 | IVMP | 1. ON |
| Leinert et al. 2020 (14) | 6 | M | 1. bilateral cortical 2. bilateral subcortical 3. brainstem | 56 | 1:5120 | IVMP | 1.meningitis seizure (-) |
| Vibha et al. 2020 (15) | 13 | F | 1. bilateral cortical 2. bilateral subcortical | 150 | + | IVMP | 1. meningitis |
| Shen et al. 2021 (16) | 3 | M | 1. bilateral subcortical | 7 | 1:100 | IVMP | 1. meningitis seizure (-) |
| Our case | 37 | M | 1. bilateral cortical | 682 | 1:2048 | IVMP | 1. meningitis |

N.A: not available. ON: optic nerve. IVMP: intravenous pulsed methylprednisolone. PE: plasma exchange. PSL: prednisolone. RTX: rituximab. AZA: azathioprine
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