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Case report

MRI-negative myelitis associated with MOG-IgG antibody: A case report and literature reviews

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ABSTRACT

According to few case reports, myelin oligodendrocyte glycoprotein-associated disease (MOGAD) could present as myelitis subtype with normal spine MRI, though it is rare. Herein, we report a case of clinically myelitis but MRI was normal, with strongly positive anti-MOG-IgG antibody in the sera. The patient showed a rapid improvement following a high dose methylprednisolone treatment.

Myelitis is one of the core clinical features of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). Its characteristics including frequent involvement of conus medullaris and gray matter (e.g., H-sign), and longitudinally extensive lesions extending over more than three vertebral segments have been well described. However, a few myelitis/myelopathies associated with MOG-IgG could result in normal spinal magnetic resonance imaging (MRI) at the time of disease onset [1]. We hereby report a case of MRI-negative myelitis/myelopathy with strongly positive results for serum anti-MOG-IgG antibody and review relevant literatures.

A 62-year-old female presented with chest tightness and painful paresthesia originating from the left leg and spreading to the right leg, and further to the left arm four weeks ago. One week before the symptom onset, the patient was vaccinated against COVID-19 for the fifth time. Her past medical history included hypertension, type 2 diabetes mellitus, and dyslipidemia since past 15 years. She was an active smoker with a history of 10 packs per year. Initially, the patient was admitted to the internal medicine department of a different general hospital due to her symptoms of chest tightness. During that time, the severe limb pain and paresthesia worsened with a further progression in limb weakness. MRI scans (1.5 T) of the brain, cervical spine, and thoracic spine did not reveal any cord signal abnormality or compressive myelopathy (Fig. 1). She was then transferred to our hospital following which meticulous neurological examination was performed, which revealed no abnormalities of cognition, language, cranial nerves, or brainstem function. She experienced weakness in both legs, which was more pronounced on the left side and needed some support when walking. Sensory examination revealed subtly diminished pinprick sense up to bilateral L1; however, vibratory sense was normal. Chest tightness, in other words, tight band-like sensation still existed. Bilateral patellar and Achilles tendons exhibited enhanced myotatic reflexes. Hoffmann's sign was positive bilaterally. Babinski's sign and ankle clonus were absent. The patient did not complain of bowel or bladder dysfunction.

Spinal cord involvement was the most likely diagnosis, considering the patient's symptoms and neurological deficits. After a careful review of MRI conducted at the other hospital, a normal spinal cord signal was evident; and cervical, thoracic, and lumbar spine MRIs (3.0 T) were re-examined to detect any newly developed lesions in 26 days following the initial scan. Follow-up spine MRI was unremarkable (Fig. 1). Cerebrospinal fluid (CSF) analysis indicated normal white blood cell counts (WBC 5 cells/mm^3) and mildly elevated protein levels (66.7 mg/dL). CSF cytology and oligoclonal band were negative. CSF immunoglobulin G index was 0.47. In a neurophysiological analysis, the nerve conduction study revealed normal findings, except for mildly slowing conduction of both median nerves. The bilateral median and posterior tibial somatosensory evoked potentials (SEP) depicted normal central conductions, though amplitude was diminished at left median SEP. Blood tests including the levels of vitamins, folate, and thyroid hormones were within the normal reference ranges. Tests for the autoantibodies associated with connective tissue disorders, such as antinuclear antibodies and antineutrophil cytoplasmic antibodies, serum paraneoplastic panel, and infectious testing for syphilis, hepatitis, and HIV were all negative. Serum anti-aquaporin-4 IgG was also absent; however, the results for MOG-IgG were strongly positive (mean fluorescence intensity ratio =

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60.12; positive when >3.65), when tested using the fluorescence-activated cell sorting live cell-based assay (Eone Laboratories, Republic of Korea). The patient was treated with intravenous methylprednisolone (1 g per day for three consecutive days) at 38 days after symptoms onset, and neurological symptoms rapidly improved. She was discharged on low-dose prednisolone and at the time was able to walk independently.

MOGAD has emerged as a discernible disease entity, which is different from neuromyelitis optica spectrum disorders (NMOSD) and multiple sclerosis. In accordance with the diagnostic criteria that had been recently proposed by the international panel group [2], diagnosis of MOGAD requires core clinical demyelinating event, and a clear positive cell-based assay result of serum MOG-IgG antibody. Core clinical demyelinating events include optic neuritis, myelitis, and acute disseminated encephalomyelitis. Myelitis is defined by an acute disturbance in one or more functions among the motor, sensory, sphincter, or sexual functions that can be referred to the spinal cord, and can be identified by a T2 high signal intensity of the MRI spinal cord with or without gadolinium enhancement, and/or by CSF inflammation. MRI features of MOGAD-associated myelitis have been established recently, although up to 10% (7 of 73 patients) of the patients can have a normal spine MRI at onset [1]. According to a previously conducted study, myelitis lesion was still absent in three of the six patients who underwent follow-up MRI [1]. Reports of patients similar to our case, indicating an image-negative myelitis/myelopathy associated with MOG-IgG, have been assimilated and accumulated (Table 1) [1,3–6]. The common findings in these patients include: (1) a clear neurological deficit suggestive of spinal cord involvement, (2) unremarkable results despite thorough evaluation, except for positive serum MOG-IgG, and (3) good treatment response to corticosteroids. Presence of preceding viral infection and either isolated myelitis or concurrent/subsequent demyelinating symptoms varied across the cases. Various intensities of serum MOG-IgG positivity were revealed, and our case was strongly positive for serum MOG-IgG, that was less likely to be a potential false positive. This case series, including our patient, suggests that image-negative myelitis/myelopathy can occur within the spectrum of

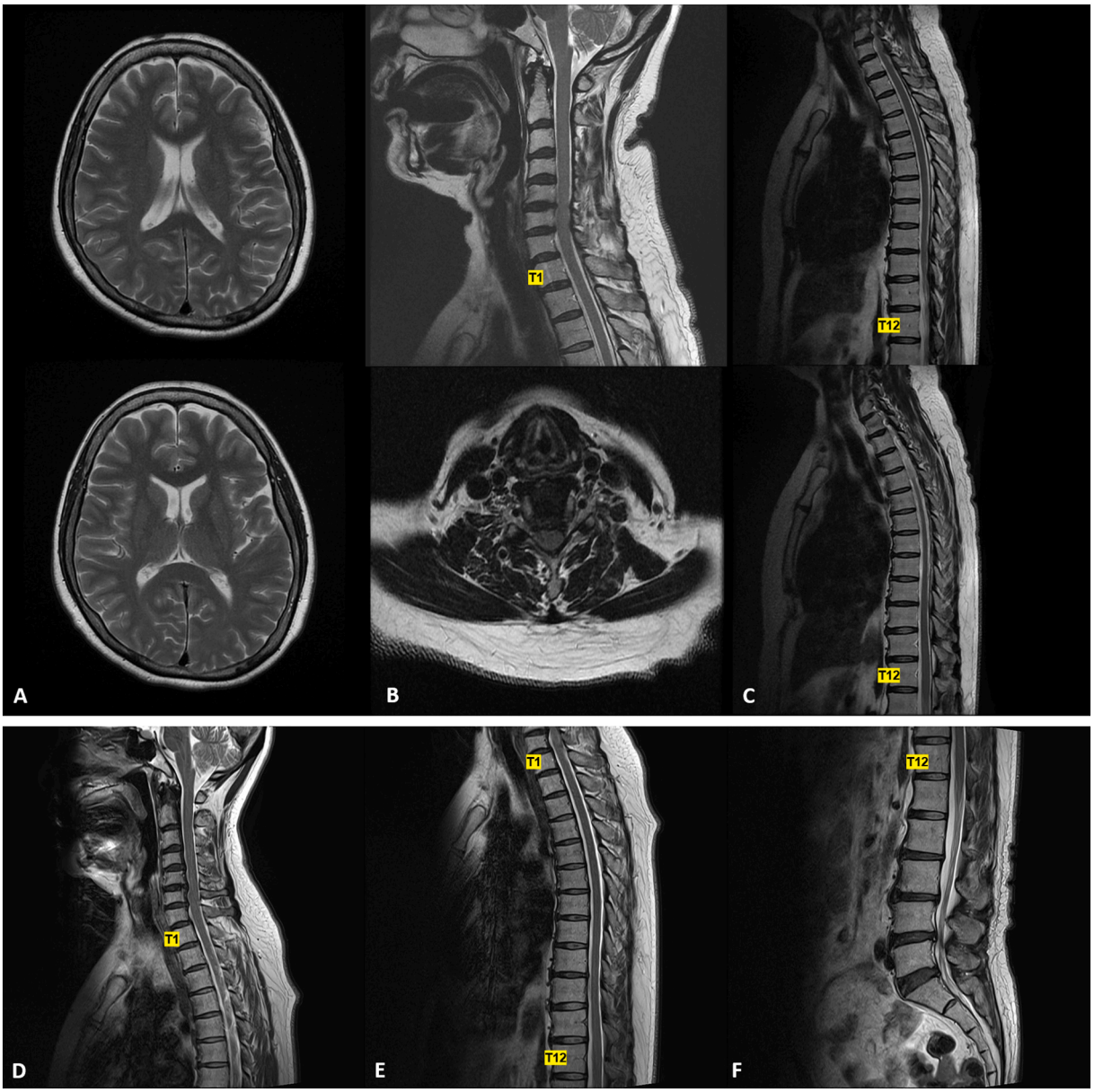

Fig. 1. MRI of brain (A), cervical spine (B), and thoracic spine (C) at day seven after symptom onset. Follow-up MRI of cervical spine (D), thoracic spine (E), and lumbar spine (F) at day 33 after symptom onset. Both MRI scans did not reveal any convincing evidence of signal abnormality in the brain or in the cord.

Table 1
Summaries of case reports for MRI-negative myelitis/myelopathy associated with myelin oligodendrocyte glycoprotein-IgG antibody.

	Macaron and Ontaneda, 2020	Perez et al., 2019	Hwangbo and Oh, 2023	Sechi et al., 2021			Kolcava et al., 2022	Our case, 2023
Age	57-year-old	8-year-old	37-year-old	35-year-old	46-year-old	80-year-old	29-year-old	62-year-old
Sex	Male	Male	Female	Female	Male	Male	Male	Female
Clinical manifestation	Isolated myelitis	Isolated myelitis	Cognitive change and myelitis	Visual disturbance and myelitis	Visual disturbance and myelitis	Isolated myelitis	Isolated myelitis	Isolated myelitis
Preceding illness	Upper respiratory tract infection	None	None	None	Upper respiratory tract infection	Fever, fatigue	None	COVID-19 Vaccination (mRNA)
Previous demyelinating event	None	1 episode of optic neuritis and 1 episode; 1 episode of unprovoked seizure (MRI and EEG unremarkable)	1 episode of encephalomyelitis	None	None	None	1 episode of presumptive myelopathy (not evaluated at that time)	None
Neurological deficits at nadir	Muscle weakness Right hand 4+/5 Both legs 2 to 3/5; Sensory and sphincter disturbance	Muscle weakness Left ankle 4/5; Sensory and sphincter disturbance	Sensory and sphincter dysfunction; Normal muscle strength	Sensory and sphincter dysfunction	Muscle weakness, sensory and sphincter dysfunction	Spastic paraparesis, sphincter dysfunction	Sensory and sphincter dysfunction, gait ataxia, normal muscle strength	Muscle weakness Both legs 3 to 4/5; Neuropathic pain and sensory disturbance
CSF	WBC 19cells/μL, Protein 75 mg/dL, Glucose 96 mg/dL, IgG index 0.46, OCB absent	WBC 7cells/μL, Protein 97 mg/dL, Glucose 24 mg/dL, IgG index N/A, OCB absent	WBC no pleocytosis, Protein 48.2 mg/dL, Other results not available	WBC 48cells/μL, Protein 100 mg/dL, OCB absent, Other results not available	WBC 161cells/μL, Protein 52 mg/dL, OCB absent, Other results not available	Not available	WBC no pleocytosis, Protein 224 mg/dL, OCB absent	WBC 5cells/μL, Protein 66.7 mg/dL, Glucose 66 mg/dL, IgG index 0.47, OCB absent
Brain MRI	Normal	Normal	Normal	Normal	Optic nerve swelling and enhancement	Not available	Normal	Normal
Spine MRI	Normal at 48 h, 5 and 121 days after symptom onset	Normal	Normal	Normal	Normal at 2and 4 weeks after symptom onset	Normal	Normal	Normal at 7 and 33 days after symptom onset
Neurophysiological study (SSEP or MEP)	Not done	Not done	Normal	Not done	Not done	Suspicious spinal cord lesion	Suspicious spinal cord lesion	Normal
MOG-IgG	Titer of 1:10,000 (positive when >1:20)	Titer of 1:100 (cut-off level not defined)	MFI ratio of 6.49 (positive when >3.65)	Titer not available (1:100 or more)	Titer not available (1:100 or more)	Titer not available (1:100 or more)	Titer of 1:80	MFI ratio of 60.12 (positive when >3.65)
Treatment	5-day course of IV methylprednisolone (1 g/day) followed by an oral prednisolone taper	5-day course of IV methylprednisolone (1 g/day) followed by an oral prednisolone taper	Steroid pulse treatment followed by oral prednisolone taper	5-day course of IV methylprednisolone (1 g/day)	5-day course of IV methylprednisolone	Oral corticosteroid for 1 month	3 g of methylprednisolone with oral prednisolone taper	3-day course of IV methylprednisolone with oral prednisolone taper
Neurological outcome	Prompt improvement	Recovery to normal	Rapid improvement	Improvement	Improvement	Improvement	Improvement	Rapid improvement

Abbreviations. MEP, motor evoked potentials; MFI, mean fluorescence intensity; MOG, myelin oligodendrocyte glycoprotein; OCB, oligoclonal band; SSEP, somatosensory evoked potentials.

MOGAD. The reason why MRI appears negative or normal in some MOG-IgG associated myelitis is uncertain; but possible explanations might be related to the limited MRI sensitivity, particularly lesions limited to the gray matter or short length, timing of scan (early or late imaging missing an evolving or a transient lesion), high MRI sensitivity to motion artifact and tissue interfaces, and insensitivity to detect functional disturbances of oligodendrocyte cytoskeleton mediated by MOG-IgG antibody [1,3,7]. Another causes of image-negative myelitis/myelopathy include paraneoplastic myelopathy, Sjögren syndrome, systemic lupus erythematous, stiff-person syndrome, and autoimmune disease with antibodies directed against glial-fibrillary acidic protein, glutamic acid decarboxylase-65 and glycine receptor antibodies. Myelitis/myelopathy with normal MRI in MOGAD and aforementioned diseases are similar to each other in that autoantibodies are involved and it might be relevant to functional disturbances of spinal cord without frank demyelination nor axon loss, though it has to be proven [8,9]. A small proportion of patients whose clinical manifestations and conventional MRI findings were dissociated, and were referred to as "normal-appearing imaging-associated, neuroimmunologically justified, autoimmune encephalomyelitis," demonstrated extensive white matter abnormalities in diffusion tensor MRI scans [10]. Whether this advanced MRI technique would be helpful in demonstrating image-negative myelitis with MOG-IgG needs to be further evaluated. International panel group for MOGAD diagnostic criteria have recommended avoiding MOG-IgG screening of all patients with CNS inflammatory demyelination, and a cautious interpretation of positive results in patients with atypical findings for MOGAD [2]. We agree that such a prudent stance is appropriate; however, since atypical manifestations including progressive myelopathy or combined peripheral neuropathy with MOG-IgG have been reported [11,12] and the significance of clear positivity of serum MOG-IgG in patients with atypical phenotype is yet to be elucidated, more substantial data are needed for defining the spectrum of MOGAD phenotype. MOG-IgG testing should be considered in these contexts in image-negative myelopathy patients, particularly if no better explanation is identified even though extensive work-up yields negative results.

CRediT authorship contribution statement

Jiwon Yang: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Yeong-Bae Lee:** Writing – review & editing. **Hyeon-Mi Park:** Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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