

## Anti-MOG Antibody Seropositive Neuromyelitis Optica: A Rare Pediatric Case

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### ABSTRACT

Neuromyelitis Optica spectrum disorder (NMO-SD) is a rare demyelinating disease detected in pediatric patients affecting the primary optic nerve and spinal cord. Clinical findings might overlap with other demyelinating diseases and compare to particularly multiple sclerosis the treatment regimens significantly differ. Therefore, to establish an immediate and definite diagnosis of NMO-SD is crucial. In the majority of patients, the aquaporin-4 antibody is detected in the serum as one of the supporting diagnostic criteria. The antibody against

myelin oligodendrocyte glycoprotein (MOG) is recently reported to be associated with serum aquaporin-4 antibody seronegative NMO-SD. Although not included in the diagnostic criteria, we believe that anti-MOG antibody may facilitate the diagnosis of NMO-SD. We herein report a pediatric case of NMO-SD with the anti-MOG antibody seropositivity.

**Keywords:** Neuromyelitis optica spectrum disorder, Devic syndrome, anti myelin oligodendrocyte glycoprotein antibody, aquaporin-4 antibody

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### INTRODUCTION

Neuromyelitis Optica spectrum disorder (NMO-SD), is a recently proposed unifying term for Neuromyelitis Optica (NMO) – also known as Devic's disease – and related syndromes. NMO-SD is an idiopathic inflammatory disease characterized by demyelination and axonal injury of the particularly optic nerve and spinal cord. It's relatively rare in pediatric patients and accounts for 4% of the acquired demyelinating diseases (1). Serum aquaporin-4 antibody is highly sensitive and specific for the diagnosis of NMO-SD (2). Differentiation of other demyelinating diseases of childhood in the absence of aquaporin-4 antibody due to overlapping clinical and radiological findings may be challenging. A recently discovered antibody against myelin oligodendrocyte glycoprotein (MOG) has been reported to be associated with aquaporin-4 antibody seronegative pediatric onset NMO-SD cases (3). Herein we report a pediatric case of NMO-SD in whom the diagnosis was established in the proper setting of clinical, radiological findings, and seropositivity for anti-MOG antibody in the absence of aquaporin-4 antibody.

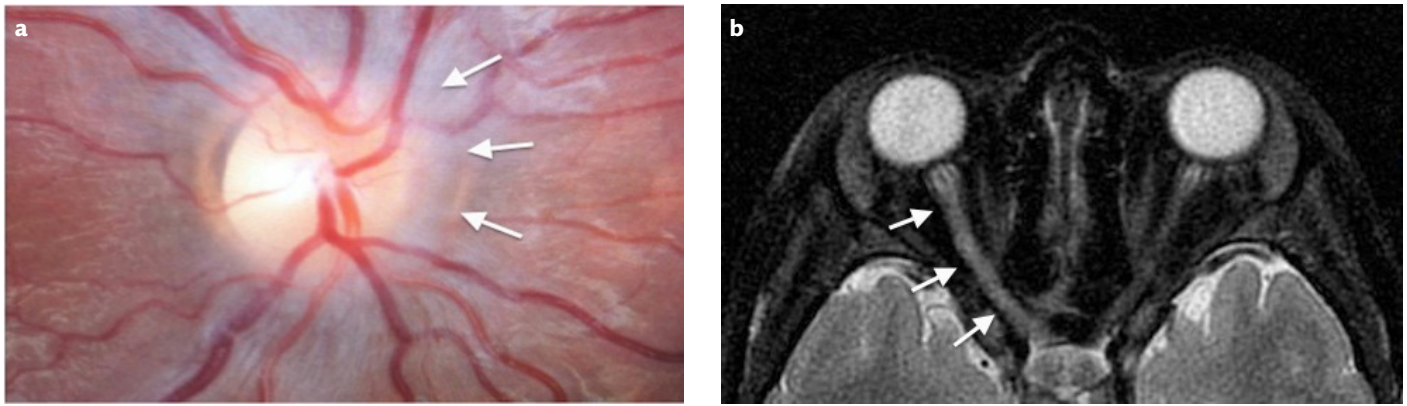
### CASE REPORT

A 12-year-old girl was admitted due to complaints of lower extremity weakness, blurred vision and urinary and stool incontinence began two days ago. Her medical history was unremarkable except upper respiratory tract infection that she experienced 3 weeks before. Her vital signs were within normal limits. Neurological examination revealed decreased

power of 0–1/5 and hyperactive deep tendon reflexes in bilateral lower extremities. Sensory system examination was normal. Abdominal skin reflex and Babinski's sign bilaterally were both negative. Her anal reflex was absent. Due to the dysfunction of the urinary bladder, catheterization was implemented.

In ophthalmic examination, pupillary and anterior segment examinations were normal in both eyes. Best-corrected visual acuity, assessed by Snellen 20-foot wall chart, was 0.05 in the right, 0.8 in the left eye. Retinal examination revealed hyperemia of the optic disc with slightly indistinct borders in the right eye (Figure 1a). Color vision, evaluated by Ishihara chart, was grossly reduced in both eyes. Peri-pupillary retinal nerve fiber layer thickness (PRNFLT), assessed by spectral-domain optical coherence tomography (Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany), was significantly increased. Visual fields testing, using the Humphrey Field Analyzer (Carl Zeiss Meditec AG, Jena, Germany), demonstrated bilateral generalized depression of sensitivity and constriction, more severe on the right eye compared to left. In the left eye, retinal examination and PRNFLT were normal.

Magnetic resonance imaging (MRI) of the brain was normal. Spinal MRI revealed the increased signal intensity of gray matter on T2-weighted sequence involving whole spinal cord beginning from 2<sup>nd</sup> cervical



**Figure 1.** Optic neuritis. Retinal examination revealed hyperemia of the optic disc with slightly indistinct borders in the right eye (arrows) (a). The right optic nerve along the intraorbital, intracanalicular, and chiasmatic segments is with increased calibration and signal intensity on T2-weighted fat saturated axial orbital MR image (b).

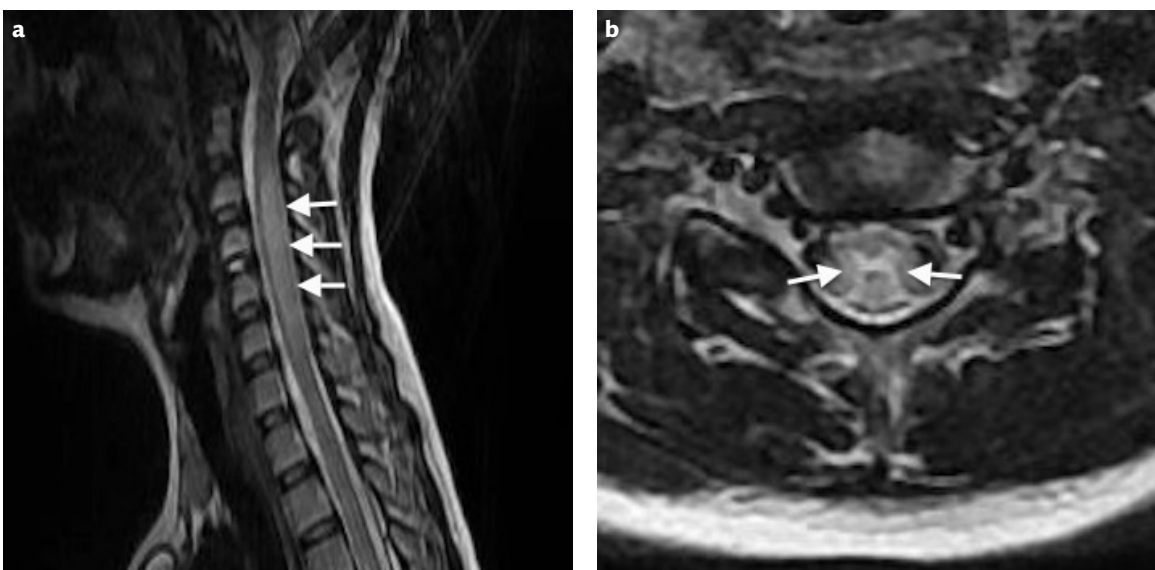
vertebrae (C2) and expansion of cervical spinal cord between the levels of C2-C5 (Figure 2). No pathologic enhancement was detected following intravenous gadolinium based contrast material administration. On orbita MRI, right-sided optic neuritis involving optic chiasm was detected (Figure 1b). Biochemical analysis of the blood and full blood count were within normal limits. She had increased erythrocyte sedimentation rate of 24 mm/h and normal C-reactive protein of 3.11 mg/l. Lumbar puncture showed neither white blood cells nor oligoclonal bands with normal levels of glucose and protein. Increased level of serum anti-MOG antibody was detected while serum and cerebrospinal fluid (CSF) were negative for the aquaporin-4 antibody. The diagnosis was made as NMO-SD based on the diagnostic criteria with the presence of myelitis, optic neuritis, and longitudinally extensive transverse myelitis on MRI (4). The patient was initiated on intravenous pulse methylprednisolone therapy of 30 mg/kg/day (maximum 1000 mg daily) for five days then oral prednisone tapered over a four weeks' period. She responded very well to corticosteroid therapy and was discharged with full recovery. Neuromuscular examination, cranial, spinal and orbital MRI findings were normal at 4 weeks after discharge. At the fifth month following the first episode, the patient was presented with blurred vision. The ophthalmic examination was compatible with optic neuritis in the left eye. The right

eye and neurological examination were normal. Therefore, a second time intravenous pulse methylprednisolone therapy was given. Subsequent azathioprine therapy was initiated as a preventive treatment.

## DISCUSSION

NMO-SD is an inflammatory disease of the central nervous system that rarely occurs in children and several reports of small case series or case reports exist (5, 6). Females are predominantly affected and in recent reports the mean age for the children is 10–14 years (7). Following a flu-like infection, patients are presented with either optic neuritis/transverse myelitis or both (6). In up to 90%, the disease is characterized by the number of attacks and results in more severe debility compared to multiple sclerosis (MS) (7).

In the recent multicenter study of Neuromyelitis Optica Study Group, 16% of the patients diagnosed with anti-MOG antibody seropositive NMO-SD were under 18 years of age (8). Either isolated optic neuritis or isolated myelitis was reported to typically present during the first acute episode while the association of simultaneous optic neuritis and myelitis was less frequent (9–10%) in the first visit (8, 9). In the current case, simultaneous



**Figure 2.** Transverse myelitis. T2-weighted sagittal MR image reveals expansion and increased signal intensity of the cervical spinal cord between the levels of C2-C5 (a, arrows). The gray matter involvement is shown on T2-weighted axial image (b, arrows).

optic neuritis and myelitis were detected at first episode. In the second attack, the patient was presented with optic neuritis in her left eye in the following fifth month. Correlatively, the mean duration between the first and second episodes of the NMO-SD patients with anti-MOG antibody seropositivity has been reported to be 5 months (8). In the study of Neuromyelitis Optica Study Group, paraparesis was the most common symptom associated with myelitis (48.3%) and 20.7% of the patients with paraparesis were graded as severe (8). About 50% of the patients presented with the purely sensory deficit and 67.9% had either pain or dysesthesia (8). The urinary bladder or bowel dysfunction was detected in 69% of the patients (8). Our patient also had severe paraparesis, bladder and stool dysfunction. Although she complained of pain there wasn't any clearly defined leveling sensory defect.

MRI is the imaging modality of choice to define the involvement of the optic nerve, spinal cord, and brain. Optic neuritis is characterized with increased signal intensity and calibration of optic nerve on T2-weighted and enhancement on post-contrast T1-weighted MR images. In contrast to MS, the optic neuritis in NMO-SD is typically more extensive including optic chiasm and optic tract (10). Transverse myelitis is longitudinally extensive involving more than 3 contiguous vertebral segments. Preferentially the gray matter of cervical and upper thoracic spinal cord is affected and exhibits increased signal intensity on T2-weighted MR image and patchy contrast enhancement (11). Brain involvement constitutes of lesions of periventricular ependymal lining in the cerebrum and brain stem, corticospinal tract, and cerebral white matter (10).

Examination of CSF may reveal mildly elevated levels of protein and white blood cell (>50 WBC/mm<sup>3</sup>) (7). In up to 27% of the patients, seropositivity of the oligoclonal band may be detected (12). Among pediatric patients, aquaporin-4 antibody seropositivity occurs up to 80% (13). Testing of CSF for the aquaporin-4 antibody might be reserved for the patients in whom serum is negative. Anti-MOG antibody has been reported to be seropositive in pediatric patients with NMO-SD whose serum aquaporin-4 antibody is negative and correlate with the better course (13). Anti-MOG antibody has also been described in various acute demyelinating diseases including acute demyelinating encephalomyelitis (ADEM) and recurrent optic neuritis (14).

The diagnosis of NMO-SD is based on the revised criteria of simultaneous/ sequential transverse myelitis and optic neuritis accompanied with either aquaporin-4 antibody seropositivity or MRI confirmation of transverse myelitis extending three vertebral segments (4). The differential diagnosis list constitutes MS and ADEM. Since the first line therapies for MS including interferon- $\beta$ ; natalizumab; humanized monoclonal antibody against the cell adhesion molecule  $\alpha$ 4-integrin; fingolimod; sphingosine-1-phosphate receptor modulator; are ineffective in NMO-SD and may exacerbate the disease, the discrimination of these two is crucial. Longitudinally extensive transverse myelitis and optic neuritis may also be the components of MS and ADEM (15, 16). So that, in the absence of aquaporin-4 antibody the differentiation of MS and ADEM from NMO-SD may be challenging. Although not accepted as diagnostic criteria, we believe that seropositivity of anti-MOG antibody might help establish the diagnosis of NMO-SD and rule out MS.

The treatment constitutes of the acute attack and preventive therapy: 1-The acute attack therapy is comprised of high dose intravenous methylprednisolone with the dose of 20–30 mg/kg/day for 3–5 days, plasma exchange and intravenous immunoglobulin in incomplete

response to high dose methylprednisolone. In attack prevention, immunosuppressive drugs including azathioprine, methotrexate, and mycophenolate mofetil are implemented (17).

In conclusion, when the aquaporin-4 antibody is seronegative in pediatric patients with NMO-SD, detection of anti-MOG antibody may help establish the definite diagnosis and differentiate from MS.

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**Conflict of Interest:** The authors declare no conflict of interest.

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