CASE REPORT

Spontaneous Improvement of Visual Acuity in a 13-Year-Old Boy with Neuromyelitis Optica Spectrum Disorder

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ABSTRACT

Ophthalmic and MRI evaluations of a 13-year-old boy who reported loss of visual acuity in his right eye demonstrated the presence of unilateral optic neuritis. After serological tests showed positivity for anti-aquaporin 4 antibody, he was diagnosed with neuromyelitis optica spectrum disorder. Encephalopathy and myelitis were not observed. Since his unilateral optic neuritis was considered to reflect mild disease activity, only follow-up observations were performed. Visual acuity and central scotoma improved 1 week after the first examination. In the absence of any specific treatments, good visual acuity has remained for 20 months, with no relapse of optic neuritis.

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Introduction

Neuromyelitis optica (NMO) is an inflammatory demyelinating disease that affects both the optic nerve and the central nervous system. Anti-aquaporin 4 (AQP4) antibody has been detected in patients with NMO.¹ AQP4 is a component of the dystroglycan protein complex that is located in the astrocytic foot processes at the blood-brain barrier.¹ NMO is predominantly diagnosed in middle-aged females. According to the 2015 international consensus diagnostic criteria, NMO spectrum disorder (NMOSD) with anti-AQP4 antibody diagnostic criteria are as follows: (1) presence of at least one core clinical characteristic such as optic nerve, spinal cord, dorsal medulla, brainstem, diencephalon, or cerebrum; (2) positive test for the anti-AQP4 antibody; and (3) the exclusion of an alternative diagnosis.² Although steroid pulse therapy or plasma exchange therapy is performed during the acute phase, these diseases are often refractory to any treatment. Furthermore, as NMOSD is characterized by frequent relapses and accrual of irreversible disability,³ spontaneous remissions are rare.⁴

Here, we report an unusual case of a 13-year-old boy who met the 2015 criteria for NMOSD with anti-AQP4 antibody who spontaneously achieved recovery from the visual disturbance without any treatment.

Case report

A 13-year-old male Japanese patient reported blurred vision and retrobulbar pain in his right eye (oculus dexter, OD) at one month before his first visit to our department at the Katsushika Medical Center, Jikei University Hospital. As Goldmann perimetry performed by his previous doctor revealed the patient had a central scotoma in his OD, he was referred to our department for further evaluation. His family history was negative for any type of visual disturbance. At the time of his first examination, he had headache and retrobulbar pain in the OD. Encephalopathy and myelitis were not observed. His logMAR best-corrected visual acuity (BCVA) was 0.4 in the OD and −0.3 in the left eye (oculus sinister, OS). Intraocular pressure was 13 mmHg (OD) and 11 mmHg (OS). Relative

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afferent pupillary defect was positive in his OD. The critical flicker frequency (CFF) values were 8 Hz (OD) and 38 Hz (OS). He had no other neurological findings such as paralysis of limbs, back pain, and hearing loss. Slit lamp examination, funduscopy, and fluorescein angiography showed no remarkable findings in either eye (data not shown). Although visual field testing using Goldmann perimetry revealed central scotoma of the I-4e isopter in OD and supratemporal desensitization of the I-1e isopter in OS, therefore suggesting junctional scotoma (Figure 1). Using spectral-domain optical coherence tomography (OCT) (Cirrus, Carl Zeiss Meditec AG, Dublin, CA, USA), we accessed the circumpapillary retinal nerve fibre layer (RNFL) thickness and conducted a macular ganglion cell analysis. Since normative data were not available for individuals younger than 20 years of age, the OCT findings were evaluated based on the supposition that the patient was 20 years of age. OCT findings demonstrated that while there was no thinning of the RNFL, there was

significant thinning of the macular ganglion cell layer (Figure 2). Gadolinium contrast-enhanced T1-weighted SPACE (sampling perfection with application optimized contrasts using different flip angle evolutions) magnetic resonance imaging (MRI) of the brain revealed that there were no remarkable findings such as multiple sclerosis lesions. However, there was thickening and enhancement from the right posterior optic nerve close to the optic chiasm (Figure 3), which suggested the presence of retrobulbar optic neuritis. To exclude Leber hereditary optic neuropathy (LHON), genetic testing for the mitochondrial DNA was performed. Results were negative for three primary mutations of G3460A, G11778A, and T14484C, which account for 95% of LHON. In addition, we tested for the anti-AQP4 antibody using both the enzyme-linked immunosorbent assay (ELISA) and the cell-based assay (CBA) since it is reported that the ELISA had a slightly lower sensitivity when compared to the CBA.⁵ Interestingly, ELISA results were negative for the

Figure 1. Visual fields using Goldmann perimetry. At the first examination, the visual field of the left eye shows a subtle upper temporal defect (A) in the right eye there is a central scotoma (arrow) of the I-4e isopter (B). One week later, improved central scotoma is seen in the right eye (C). Four months later, the visual fields in the right eye are normal (D).

Figure 2. Spectral-domain optical coherence tomography (OCT). While the OCT findings demonstrate that there is no thinning of the retinal nerve fiber layers in both eyes (A), there is significant thinning of the macular ganglion cell layer only in the right eye (B).

anti-AQP4 antibody while the CBA results were positive. In addition, the anti-myelin oligodendrocyte glycoprotein antibody was negative. Based on the above-mentioned clinical and MRI findings, the current laboratory data for this patient were considered to meet the requirements of the diagnostic criteria for NMOSD. Thus, this patient was diagnosed with unilateral retrobulbar optic neuritis associated with NMOSD.

Follow-up observations were subsequently performed in the patient without the use of any interventional treatment, such as steroid pulse therapy or plasma exchange because the patient reported subjective vision improvement several days after the onset. Spontaneous remission occurred 1 week after the initial examination, with the logMAR BCVA recovering to 0.0 in the OD, and the visual fields showing improvement of the central scotoma

(Figure 1). The central scotoma disappeared 4 months after the first examination (Figure 1). Although possible brain stem symptoms, such as hiccups, were noted from time to time, there was no myelitis lesion observed during the whole-spine MRI examination that was performed at 8 months after the first visit. Based on these findings, further observation of the patient was continued without any treatment (Figure 4). At 12 months following the first visit, CFF values were 43 Hz (OD) and 43 Hz (OS). At 20 months after the first visit, the logMAR BCVA remained stable at -0.1, without relapse of the optic neuritis or any other particular events.

Discussion

This case report provided details on a 13-year-old NMOSD boy with anti-AQP4 antibody in whom

Figure 3. Gadolinium contrast-enhanced T1-weighted SPACE (sampling perfection with application optimized contrasts using different flip angle evolutions) MRI of the head reveals thickening and enhancement (arrows) from the right posterior optic nerve close to the optic chiasm in the coronal (A) and sagittal (B) planes.

visual acuity loss recovered to normal without any treatment. The patient's good visual acuity has continued for 20 months after the first visit.

Development of NMO/NMOSD is rare in young boys during childhood. There have been several studies of childhood NMO, including a study of 58 patients aged up to 18 years reported in the United States,⁶ and a study of 18 patients aged up to 15 years in Japan,⁷ along with a retrospective, multicentre study that examined the long-term outcomes of these patients.⁸ In all of these studies, girls accounted

for a greater proportion of the patients, with male: female ratios of 1:9,⁶ 1:3.5,⁷ and 1:3,⁸ respectively.

In the study of the 58 childhood NMO patients in the United States, the initial symptom cited by 57 (98%) patients was either optic neuritis ($n = 48$; 83%) or transverse myelitis ($n = 45$; 78%), or both, and twenty-six (45%) had episodic cerebral symptoms (encephalopathy, ophthalmoparesis, ataxia, seizures, intractable vomiting, or hiccups).⁶ In the present case, the patient's initial symptom was unilateral optic neuritis, which appears to be typical.

Figure 4. Follow up of logMAR best-corrected visual acuity over one year.

In NMO, brain lesions are often observed on MRI images. Furthermore, while cerebral lesions are also found in up to 60% of the adult NMO patients, these are usually clinically silent.^{9,10} In contrast, a study that examined 58 children with NMO found that 66% of these patients had brain lesions while 68% had clinical symptoms that included hiccups, dizziness, hyponatremia, diabetes insipidus, and menstrual irregularities.^{6,9} Refractory hiccups and vomiting are common concomitant symptoms, and have been found to be associated with the area postrema.^{11,12} Typically, these symptoms last for several weeks, and precede other clinical signs. Hiccups were also repeatedly observed in the present case, and may be an early sign of the brain lesion. However, in this case, there were no abnormalities noted in the brain and whole-spine MRI.

Children with NMO exhibit a variety of symptoms. In addition, it has been reported that some NMO children do not have typical symptoms such as optic neuritis and myelitis, and thus these cases can be difficult to diagnose.⁹ Moreover, it is also difficult to make a differential diagnosis for other neurological diseases such as acute disseminated encephalomyelitis, which is an inflammatory demyelinating condition that predominately affects the white matter of the brain and spinal cord. Furthermore, it has been reported that the progression of childhood NMO takes longer than that of adult NMO.⁸

In the present case, however, there was early spontaneous recovery of the visual acuity and there was no relapse of the optic neuritis. These

changes might be associated with the negative ELISA and the positive CBA for anti-AQP4 antibody that were observed in this case. Valentino et al. report that the anti-AQP4 antibody titres were correlated with disease activity, with higher titres observed during and preceding relapses versus during remissions.¹³ Takahashi et al. demonstrated that anti-AQP4 antibody titres became lower after methylprednisolone treatments as compared to levels before the treatment.¹⁴ Taken together, the clinical findings for the present case suggest that there was a low disease activity, and that there was no disease progression.

In order to make a definitive early diagnosis and determine an initial treatment, it is important to measure the anti-AQP4 antibodies. Relapses are commonly seen with childhood NMO, with the relapse rate in the anti-AQP4 antibody-positive cases reported to be as high as 93%.¹⁵ Since it is also possible that a relapse could occur in the present case, careful follow-up examinations will need to be performed.

In summary, we reported a 13-year-old NMOSD boy with anti-AQP4 antibody in whom after losing his visual acuity and visual fields, recovered to nearly normal without any treatment. After this recovery, the patient has exhibited no relapses during the 20 months following his first visit.

Declaration of interest

None to disclose.

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