CASE REPORT

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Acute bilateral hypotropia and esotropia complex as first manifestation of multiple sclerosis: a case report

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ABSTRACT

A 21-year-old Japanese woman presented with sudden eye movement disorders. An ophthalmic examination revealed bilateral hypotropia and esotropia complex. Brain magnetic resonance imaging revealed abnormal signals in the posterior and medial part of the lower pontine tegmentum (including periventricular and subcortical white matter) that were suggestive of demyelination. A cerebrospinal fluid test was positive for oligoclonal bands. She was subsequently diagnosed with multiple sclerosis and was administered intravenous methylprednisolone and oral dimethyl fumarate, with complete recovery from hypotropia and esotropia after two months. Bilateral hypotropia and esotropia are important clinical signs for the accurate diagnosis of multiple sclerosis.

Keywords: multiple screlosis, internuclear opthalmoplegia, hypotropia and esotropia, magnetic resonance imaging

Abbreviations:
MS: multiple sclerosis
MRI: magnetic resonance imaging
MLF: medial longitudinal fasciculus

INTRODUCTION

Ocular motor disorders such as internuclear ophthalmoplegia and skew deviation are common symptoms of multiple sclerosis (MS), and their physiopathological mechanisms have been extensively studied.[1] However, rare manifestations linked to internuclear ophthalmoplegia such as complex ocular motor disturbances[2-4] are still being described, and their relationship with specific magnetic resonance imaging (MRI) findings has not yet been completely elucidated. The study of rare oculomotor symptoms in MS patients may help understanding the anatomical mechanisms underlying this disease. Herein, we report a patient with the unusual oculomotor disorders of

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bilateral hypotropia and esotropia complex as the first manifestation of MS.

CASE REPORT

A 21-year-old Japanese woman presented to the outpatient clinic of our hospital with sudden-onset diplopia. She had no history of diabetes, glucose intolerance, arterial hypertension, hypercholesterolemia, systemic vasculitis, smoking, obesity, or other risk factors for ischemic oculomotor nerve palsy. In addition, the patient had no personal or family history of neurological disorders. A general physical examination revealed no abnormalities. Her blood pressure was 110/56 mmHg. A neurological examination revealed bilateral oculomotor palsy manifested as abduction deficits of hypotropia and esotropia complex with downbeat nystagmus. In other words, mixed lateral and horizontal-vertical gaze palsy and gaze nystagmus consistent with internuclear ophthalmoplegia were noted in both the eyes (Fig. 1). The pupils of both the eyes were normal and responded promptly to light stimulus. Cranial nerves appeared to be intact on examination. No symptoms of limb weakness, ataxia, or sensory disturbance were observed. Her deep tendon reflexes were all normal, and her plantar responses were flexor. Her visual disturbances prompted a consultation with the ophthalmology department. On examination, her visual fields were full on confrontation, intraocular pressures were within normal limits, and the results of her pseudoisochromatic plates test were normal. Her pupils were of equal size and reactive to light, without any afferent pupillary defect. No sign of optic neuritis associated with inflammation of the optic nerve was found. General laboratory screening tests yielded normal values. An examination of the cerebrospinal fluid (CSF) revealed a mononuclear cell count of 1 cell/mm^3, a CSF protein level of 19 mg/dL, and a CSF glucose level of 62 mg/dL with a plasma glucose level of 79 mg/dL. These values were all within the normal range, but the IgG index (0.8) was above the normal value (<0.66). Endocrine examinations revealed no abnormalities in the thyroid function (thyroid-stimulating hormone level, 1.778 μIU/mL; free T3 level, 2.26 pg/mL; free T4 level, 0.94 ng/dL). PCR tests from blood and CSF cultures were negative for varicella-zoster virus, herpes simplex virus, and cytomegalovirus. No indicators of autoimmune disease, including serum anti-acetylcholine receptor, IgG4, anti-Aquaporin 4 antibodies, anti-myelin oligodendrocyte glycoprotein antibody, or myelin basic protein were present, but oligoclonal IgG bands were detected in the CSF samples.

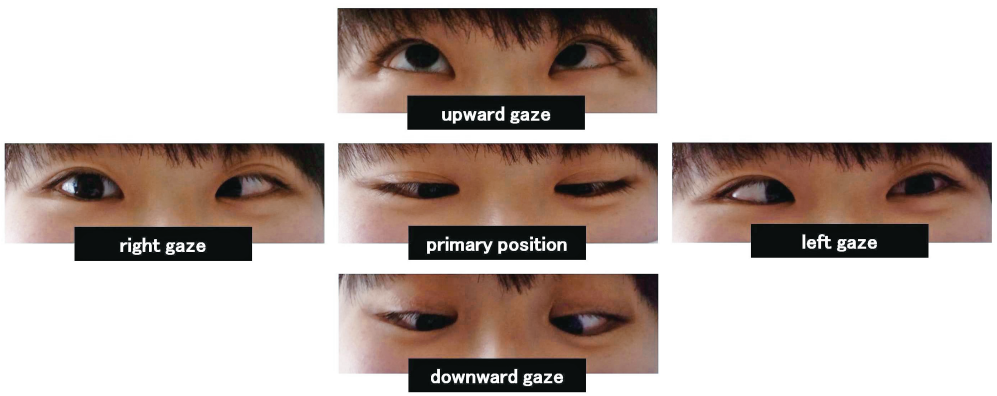

Fig. 1 Photographs of ocular movements exhibited by the patient on the first day after hospital admission Bilateral internuclear ophthalmoplegia manifested as hypotropia and esotropia complex could be observed.

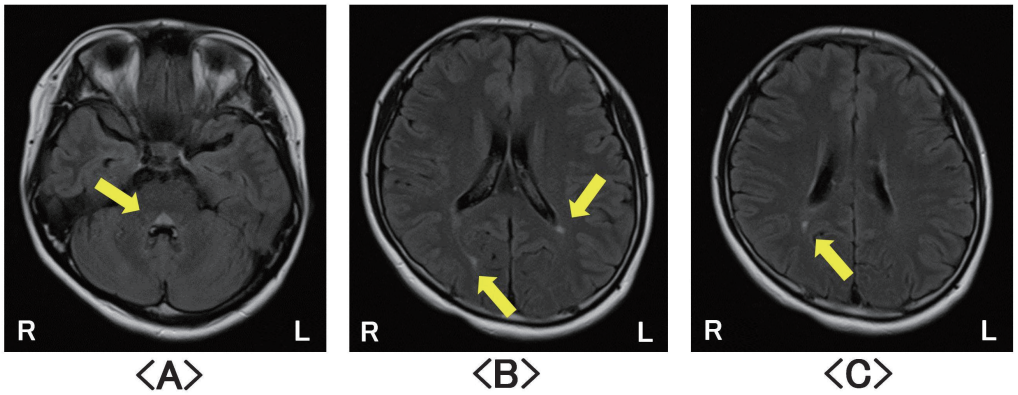

Fig. 2 Magnetic resonance images obtained on the first day after hospital admission
Fig. 2A: Fluid-attenuated inversion recovery (FLAIR) revealed areas with abnormally high signal in the posterior and medial part of the lower pontine tegmentum (arrow).
Fig. 2B, 2C: Other FLAIR-derived images also revealed abnormal signals in the periventricular, juxtacortical, and deep white matter (arrows).
R, right; L, left.

MRI signals observed via fluid-attenuated inversion recovery (FLAIR) imaging (1.5T Siemens MAGNETOM Aera, Munich, Germany) were abnormally high in the posterior and medial part of the lower pontine tegmentum (Fig. 2A). Lesions associated with an abnormally high MRI signal were scattered in the periventricular, juxtacortical and deep white matter (Fig. 2B, 2C). No abnormalities were revealed by the intraorbital and spinal cord MRI scans or by magnetic resonance angiography in the brain. Moreover, no significant enhancement was observed in any other region via gadolinium-enhanced MRI.

The case was diagnosed as definite MS based on the revised McDonald criteria from 2017.[5] The patient's symptoms gradually improved after the administration of intravenous methylprednisolone (1,000 mg/day for 3 days and then reduced to 500 mg/day for the next 2 days) later replaced by oral methylprednisolone (40 mg/day during the first week, followed by gradually decreasing by 10 mg each week). After this initial round of treatment, the patient started

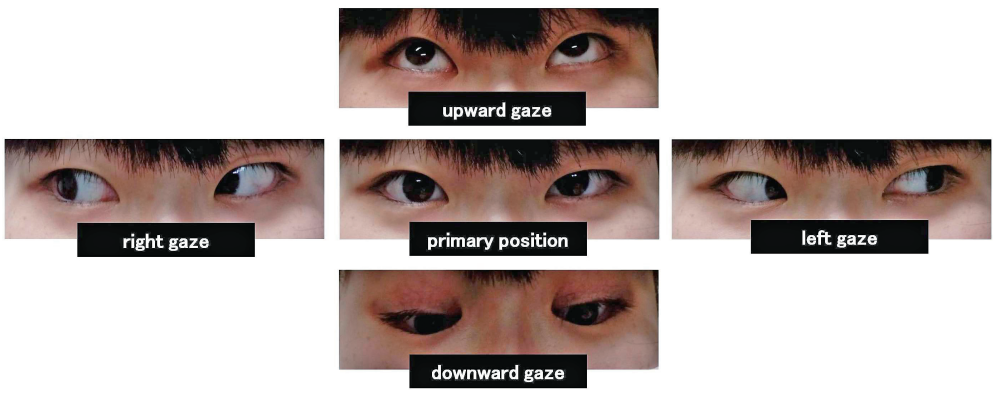

Fig. 3 Photographs of ocular movements obtained two months after the start of treatment
The patient fully recovered from the internuclear ophthalmoplegia.

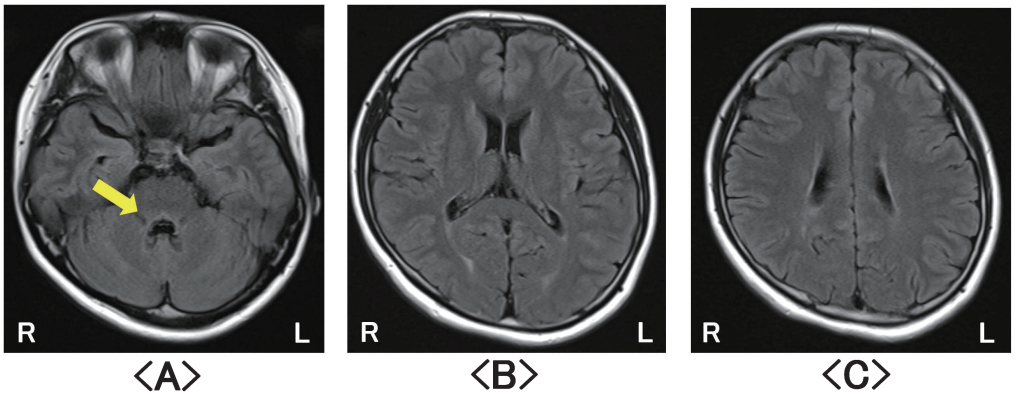

Fig. 4 Magnetic resonance images obtained six months later
Fluid-attenuated inversion recovery (FLAIR) showed the improvements in the abnormal signals on FLAIR images, especially in the posterior and medial part of the lower pontine tegmentum (arrow).
R, right; L, left.

disease-modifying therapy consisting of oral dimethyl fumarate (240 mg/day as initial dose for the first week, followed by a maintenance dose of 480 mg/day). No additional antibiotic, antiviral, or antifungal medications were administered during this period. Complete recovery from ophthalmoparesis on both sides was recorded after two months (Fig. 3). Six months later, follow-up MRI showed the improvements in the abnormal signals on FLAIR images, especially in the posterior and medial part of the lower pontine tegmentum (Fig. 4).

DISCUSSION

We herein describe the case of a patient with MS initially presenting with bilateral oculomotor abnormalities consisting of sudden-onset bilateral hypotropia and esotropia complex detected using MRI. MS is frequently accompanied by both visual and oculomotor complications. Unilateral or bilateral internuclear ophthalmoplegia is also common in MS. The oculomotor abnormalities associated with MS include abducens nerve palsy, nystagmus, oblique deviation, and gaze palsy. Some cases of one-and-a-half syndrome, medial longitudinal fasciculus (MLF) syndrome, and unilateral third or sixth nerve palsy have been described in association with MS.[2-4,6,7] In the acute or severe phase of MLF disorders, bilateral horizontal gaze limitation has been reported,[3] and the eye on the affected side may be abducted.[7] In addition, bilateral horizontal gaze limitation has been reported.[3] Thus, we speculate that the bilateral oculomotor abnormalities observed in this case were the result of a combination of bilateral MLF syndrome and oculomotor nucleus involvement. This conclusion is based on the fact that the case included bilateral horizontal gaze nerve palsy without ptosis or pupil abnormalities, which is indicative of a disorder on the third cranial nerve.

Limited eye adduction and abduction to either side leads to an isolated partial bilateral horizontal gaze palsy. The culprit lesion for this syndrome is located in the brainstem, and it commonly affects the abducens nuclei[4,8] or the abducens fibers and the MLF[4,9] in the medial part of the lower pontine tegmentum. The abducens nuclei contain motor neurons that innervate the lateral rectus muscle and internuclear neurons connecting to the medial rectus subdivision of the contralateral oculomotor nucleus through the MLF.[8] Lesions of the abducens nucleus

cause ipsilateral conjugate gaze palsy, whereas MLF lesions are associated with internuclear ophthalmoplegia.[9] Overall, these facts provide the explanation for the bilateral hypotropia and esotropia complex resulting from the demyelinating lesions in the posterior and medial part of the lower pontine tegmentum in this case.

Internuclear ophthalmoplegia is usually associated with MS, and it should be considered as an important sign for demyelinating disease when found in young undiagnosed patients.[10-12] In previous studies, the etiologies of internuclear ophthalmoplegia revealed that approximately one-third of the cases were derived from stroke, another third from MS, and the rest from infectious disease. All of the cases derived from stroke were unilateral, making bilateral disease more suggestive of MS.[11,12]

Disease-modifying therapies are commonly used in adult patients with MS, with the highest effectiveness achieved when they are initiated early in the disease course.[13] Several studies revealed a decreasing risk of MS progression after initiation of immunomodulatory drug therapy.[14,15] Moreover, to our knowledge, this is a first report that a full recovery from bilateral oculomotor abnormalities was achieved with corticosteroids and disease-modifying therapy using dimethyl fumarate.[16] Therefore, further investigations will be required to determine the most appropriate treatment strategy for cases such as the one described in this report.

Demyelinating lesions in MS cause characteristic visual syndromes. Detection of these oculomotor abnormalities during an ophthalmologic evaluation should lead to quick diagnosis and treatment and, consequently, better outcomes for MS. Careful attention to both neurological and ophthalmological findings in MS, as in the case presented here, not only reveals information about current disease burden but also about the underlying structural and functional abnormalities in the nervous system and provides evidence on the effectiveness of standard and novel therapies for demyelinating disease.

AUTHOR CONTRIBUTION

Joe Senda and Ryota Hirao contributed equally as first authors to this work.

CONFLICT OF INTEREST

The authors declare no conflicts of interest in association with the present study.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of this case report and any accompanying images/photographs.

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