Isolated third nerve palsies as the initial manifestation of multiple sclerosis

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A 24-year-old man presented 10 days after the onset of binocular horizontal diplopia, left upper eyelid ptosis, and mild left eye pain. He denied any previous episodes of numbness, weakness, or transient vision loss. On examination, his visual acuity was 20/20 in both eyes. He demonstrated 1 mm of anisocoria, with the left pupil larger than the right. Color perception was normal in both eyes as assessed by Ishihara color plates. There was 1 mm of left upper eyelid ptosis. There were supraduction, infraduction, and adduction deficits on the left. There was no adduction slowing or contralateral abducting nystagmus to suggest an internuclear ophthalmoplegia. The slit-lamp and dilated fundus examination were both unremarkable. The remainder of the complete neurologic examination was normal. MRI revealed enhancement of the left medial cerebral peduncle along the course of the third cranial nerve (CN), as well as the proximal cisternal portion of the nerve, on T1 postcontrast images (figure 1A). Multiple other nonenhancing hyperintense lesions on T2 fluid-attenuated inversion recovery (FLAIR) were observed throughout the brainstem and periventricular regions, consistent with a diagnosis of multiple sclerosis (MS) (figure 1B). Lumbar puncture revealed >5 oligoclonal bands not present in the serum. The patient was treated with 5 days of IV methylprednisolone and discharged on an oral prednisone taper. Two weeks after completion of steroids, extraocular motility was full and the ptosis and anisocoria had resolved.

PRACTICAL IMPLICATIONS

Consider demyelinating disease in the differential diagnosis of cranial nerve III palsy, particularly in a younger patient without typical microvascular risk factors.

Another patient, a 40-year-old woman, presented 4 days after the onset of binocular diplopia and ptosis of the right upper eyelid (figure e-1, links.lww.com/CPJ/A45). She denied any previous episodes of numbness, weakness, or transient vision loss. Visual acuity was 20/20 on the right and 20/30 on the left with a left afferent pupillary defect. Color perception was normal in both eyes. There was 4 mm of upper eyelid ptosis and a supraduction deficit on the right. The anterior segment examination was unremarkable. Dilated funduscopy demonstrated moderate optic nerve pallor on the left. The remainder of the neurologic examination was normal. MRI revealed enhancement of the right cerebral peduncle and proximal cisternal portion of CN III on T1 postcontrast images (figure 1, C). T2 FLAIR images showed bilateral periventricular and right temporal subcortical white matter hyperintensities (figure 1, D) as well as increased signal in the left optic nerve consistent with a diagnosis of MS with a previous subclinical episode of optic neuritis. Lumbar puncture demonstrated >5 oligoclonal bands not present in the serum. The patient was started on IV methylprednisolone and discharged on an oral prednisone taper. Six weeks after discharge, the patient's diplopia and ptosis had resolved completely and ocular ductions were full.

Discussion

MS may affect both the afferent and efferent visual systems. Internuclear ophthalmoplegia and nystagmus are the most common efferent manifestations, with isolated CN palsies occurring less often.^{1,2} The rarity of CN symptoms is thought to be a function of the relative lack of myelination surrounding the CN nuclei compared with the extensive myelination seen in other

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Figure 1 MRI sequences on presentation with cranial nerve III palsy

Case 1: (A) T1 postcontrast image shows enhancement of the left medial cerebral peduncle and proximal cisternal portion of the third nerve. (B) T2 fluid-attenuated inversion recovery (FLAIR) sequence shows additional white matter lesions. Case 2: (C) T1 postcontrast sequence shows enhancement of the right cerebral peduncle and proximal cisternal portion of the CN III. (D) T2 FLAIR sequence shows bilateral periventricular hyperintense lesions.

portions of the brainstem such as the medial longitudinal fasciculus. Lesions involving CN III are particularly rare.³ Here, we describe 2 patients with CN III palsy as the presenting symptom of MS. Both were found to have enhancement of the cerebral peduncle as well as the proximal cisternal

portion of the third nerve. The latter finding of “peripheral” cranial nerve enhancement in MS is interesting and relates to the transitional anatomy at the brainstem exit zone, where a short projection of central myelination envelops the cisternal portion of the nerve^{e1} (links.lww.com/CPJ/A45).

Table Case reports detailing cranial nerve III palsy as the initial manifestation of multiple sclerosis

Case/reference	Age, y	Sex	Unilateral or bilateral	Complete or partial palsy	Pupil involved	Ptosis	Pain
Our case 1	24	M	Unilateral	Partial	Yes	Yes	Yes
Our case 2	40	W	Unilateral	Partial	No	Yes	No
3	30	F	Unilateral	Complete	Yes	Yes	Yes
4	35	F	Unilateral	Partial	No	Yes	Yes
5	27	M	Unilateral	Partial	No	Yes	No
6	23	F	Unilateral	Partial	Yes	Yes	Yes
7	30	M	Bilateral	Partial	No	Yes	No
e1 (links.lww.com/CPJ/A45)	27	F	Unilateral	Partial	No	No	No

Thömke et al.¹ estimated that only 1.6% of patients with MS will develop an isolated CN palsy (CN III, IV, VI, VII, VIII) over the course of their disease. Zadro et al.² reported a higher rate of 10.4%, with CN VI palsies accounting for half of the cases. A review of the literature reveals only 6 prior case reports of isolated CN III palsy as the initial presentation of MS.^{3–7,e2} Five out of the 6 cases were unilateral and partial. Two of 6 patients presented with anisocoria. Three of 6 patients reported eye pain on presentation (table). On aggregate, these cases mirror our findings.

Despite the rarity of CN III palsy as a primary manifestation of MS, demyelinating disease should remain on one's differential diagnosis, particularly in a younger patient without typical microvascular risk factors.

Author contributions

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References

1. Thömke F, Lensch E, Ringel K, Hopf HC. Isolated cranial nerve palsies in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1997;63:682–685.
2. Zadro I, Barun B, Habek M, Brinar VV. Isolated cranial nerve palsies in multiple sclerosis. *Clin Neurol Neurosurg* 2008;110:886–888.
3. Bhatti MT, Schmalfuss IM, Williams LS, Quisling RG. Peripheral third cranial nerve enhancement in multiple sclerosis. *AJNR Am J Neuroradiol* 2003;24:1390–1395.
4. Belezá P, Machado A, Soares-Fernandes J, et al. Isolated oculomotor nerve paresis as the presenting sign of multiple sclerosis. *Arq Neuropsiquiatr* 2008;66:254–255.
5. Newman NJ, Lessell S. Isolated pupil-sparing third-nerve palsy as the presenting sign of multiple sclerosis. *Arch Neurol* 1990;47:817–818.
6. Uitti RJ, Rajput AH. Multiple sclerosis presenting as isolated oculomotor nerve palsy. *Can J Neurol Sci* 1986;13:270–272.
7. Seery LS, Hurliman E, Erie JC, Leavitt JA. Bilateral pupil-sparing third nerve palsies as the presenting sign of multiple sclerosis. *J Neuroophthalmol* 2011;31:241–243.