

Impairment of Vertical Saccades From an Acute Pontine Lesion in Multiple Sclerosis

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Abstract: A 62-year-old woman with relapsing-remitting multiple sclerosis suddenly complained of diplopia associated with bilateral adduction impairment, nystagmus of the abducting eye bilaterally, and sparing of abduction, convergence, and vertical eye movements, consistent with bilateral internuclear ophthalmoplegia. Within 1 week, she had developed a complete horizontal gaze paralysis even with the oculocephalic maneuver. Vertical saccades were slow and convergence was preserved. There was a right lower motor neuron seventh cranial nerve palsy. Brain MRI showed a new enhancing lesion involving the pontine tegmentum. Clinical and MRI follow-up showed recovery after 6 months. The slowing of vertical saccades may have been due to spread of the demyelinating lesion to the adjacent paramedian pontine reticular formation, which contains omnipause neurons lying in the raphe interpositus nucleus thought to inhibit excitatory burst neurons for horizontal and vertical saccades. Our patient verifies the fact that vertical saccadic abnormalities may occur from a lesion apparently confined to the pons.

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Nearly 30% of patients with multiple sclerosis (MS) experience internuclear ophthalmoplegia (INO) at some time during the course of disease (1). This eye movement disorder is caused by a lesion of the medial longitudinal fasciculus (MLF). In some patients, adjacent

structures may be involved, causing a more complex clinical picture, including complete horizontal gaze paralysis (2). Recently, unusual ocular motor findings have been described in patients with MS, including bilateral third nerve palsy, opsoclonus, and isolated sixth cranial nerve palsy (3). Here, we report the case of a patient with MS who presented with acute bilateral INO followed 1 week later by complete transient horizontal gaze paralysis associated with slow vertical saccades. This patient verifies the fact that a lesion apparently confined, by imaging criteria, to the pons can cause a vertical saccadic impairment.

CASE REPORT

A 62-year-old woman with relapsing-remitting MS diagnosed at age 44 complained of diplopia for 4 days. She denied previous episodes of diplopia and previous examinations had revealed no ocular motor abnormalities. She was not undergoing immunomodulatory or immunosuppressive treatment.

Neurologic examination showed complete adduction loss and nystagmus of the abducting eye bilaterally. Abduction, convergence, and vertical eye movements were spared. A diagnosis of bilateral INO was made. Examination 48 hours later showed complete horizontal gaze paralysis even with the oculocephalic maneuver. The vertical vestibular-ocular reflex (VOR) was clinically normal, but vertical pursuit was interrupted by saccades. Vertical saccades appeared slow, but convergence was preserved. There was also a right lower motor neuron seventh cranial nerve palsy.

Treatment with intravenous methylprednisolone (1000 mg/day for 5 days) was started and, after a few days, adduction dramatically improved in both eyes, followed by gradual restoration of vertical eye movements.

Brain MRI, performed 21 days after the onset of complete horizontal gaze paralysis, showed a T2 lesion located at the right pontine tegmentum with extension to the left side. This lesion had not been present on an MRI performed 7 months earlier. Only the right side of the lesion enhanced on T1. No enhancing lesions were observed in the midbrain or elsewhere in the brain (Fig. 1).

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Two months later, vertical movements, bilateral adduction, and the right lower motor neuron seventh cranial nerve palsy had recovered completely, whereas abduction lag persisted and transient horizontal diplopia was reported. Six months later, there was complete recovery of ocular movement. MRI showed that the brainstem lesion had disappeared.

DISCUSSION

Complete unilateral or bilateral horizontal gaze paralysis implies lesions of the pontine tegmentum involving the sixth cranial nerve nucleus with or without involvement of the paramedian pontine reticular formation (PPRF) (4). Although seldom reported in MS, unilateral lesions of the sixth cranial nerve nucleus are usually associated with damage to the seventh cranial nerve fascicle and may involve other adjacent structures controlling horizontal and vertical eye movements, such as the MLF or PPRF (2,4). In our patient, bilateral INO occurred first, followed 1 week later by involvement of the right sixth cranial nerve nucleus and left sixth cranial nerve fascicle. This resulted in complete horizontal gaze paralysis.

We hypothesized a lesion involving the sixth cranial nerve nucleus and its fascicles on the right side, but restricted to the sixth cranial nerve fascicles on the left side, as function of the left seventh cranial nerve fascicles, which travel next to the sixth cranial nerve nucleus, was spared. There is a previous report (5) of two subjects with MS who had bilateral INO at onset, followed a few days later by bilateral loss of abduction resulting in complete horizontal gaze paralysis. The authors suggested that the demyelinating lesion first involved both MLFs and spread centrifugally to affect the sixth cranial nerve motor fibers

on both sides. In those 2 patients, however, vertical saccades were reported to be normal.

In our patient, we hypothesized lesion progression as shown in Fig. 2. Bilateral INO is often associated with impairment of vertical pursuit and VOR, as MLFs convey ascending signals for vertical vestibular reflexes, smooth pursuit, and gaze holding from the vestibular nuclei to the third and fourth cranial nerve nuclei and the interstitial nucleus of Cajal (6). Vertical saccades are not impaired by lesions of the MLFs. In our patient, the slowing of vertical saccades may have been due to spread of the demyelinating lesion to the adjacent PPRF. The PPRF consists of three subgroups of neurons from rostral to caudal: excitatory burst neurons (EBNs) lying in the medial part of the nucleus reticularis pontis caudalis (NRPC), omnipause neurons (OPNs) lying in the raphe interpositus nucleus (RIP), and inhibitory burst neurons (IBNs) lying in the nucleus paragigantocellularis dorsalis (PGD) (7). The slowing of vertical saccades could have been due to a lesion of RIP involving OPNs. In fact, OPNs have been shown to induce a prevalent glycinergic inhibition of EBNs in the pons and midbrain during fixation (8).

Indeed, EBNs in the PPRF discharge only weakly for vertical saccades (9), whereas damage confined to OPNs causes slowing of horizontal and vertical saccades (10). As previously observed by Milea et al (5), we also suggest that in our patient, the course of ocular abnormalities was due to medial-lateral progression of the brainstem lesion. However, in our patient, lesion extension was more evident on the right where the seventh cranial nerve fascicle was affected, causing a right seventh cranial nerve palsy. The MLFs, which were involved at onset, were the first to recover. Subsequent centrifugal spreading transiently involved OPNs in the RIP, and then the adjacent sixth cranial nerve fascicles,

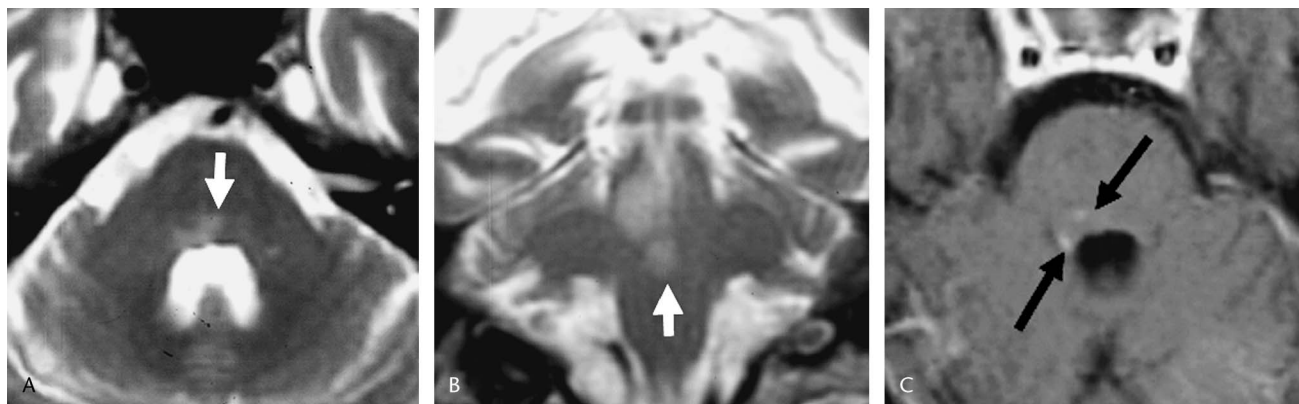


FIG. 1. Brain MRI performed at presentation. **A.** and **B.** T2 axial and coronal MRI show a right high signal lesion affecting the pontine tegmentum and extending across the midline in its lower portion (white arrow). **C.** Postcontrast T1 axial MRI shows that the lesion in the pontine tegmentum partially enhances (black arrows).

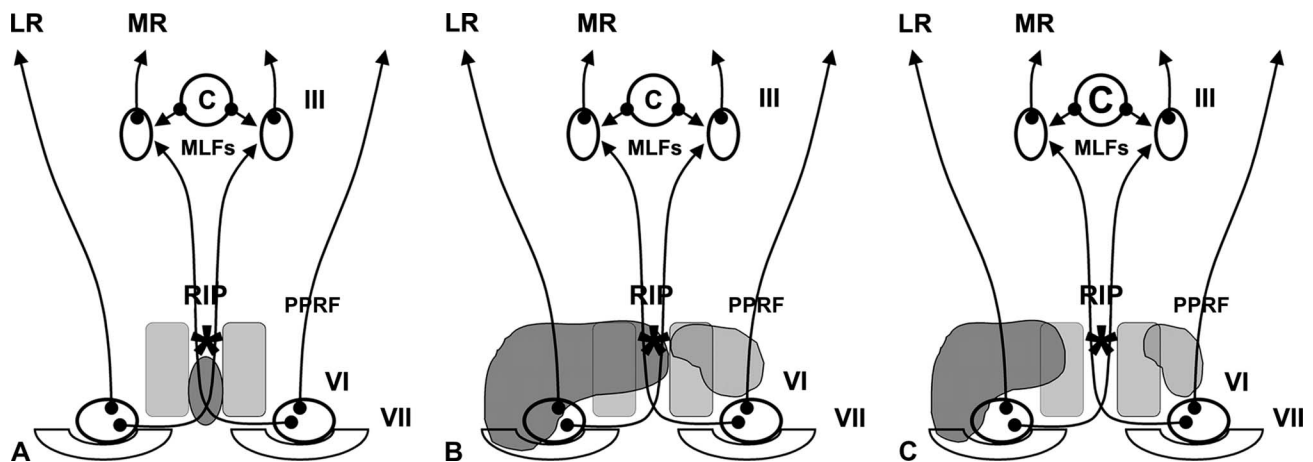


FIG. 2. Schematic illustration of hypothesized progression of the brainstem lesion in our patient. Gray areas show the extent of the brainstem lesion; dark gray indicates more severe tissue involvement than light gray. **A.** Phase 1. There is bilateral involvement of medial longitudinal fasciculi (MLFs) causing bilateral internuclear ophthalmoplegia. **B.** Phase 2. The lesion extends into the paramedian pontine reticular formation (PPRF, light gray rectangles) and involves the raphe interpositus nucleus (RIP, asterisk), right sixth cranial nerve nucleus and its fascicle, right seventh cranial nerve fascicle, and left sixth cranial nerve fascicle, causing complete horizontal gaze paralysis and right lower motor neuron facial palsy. **C.** Phase 3. The brainstem lesion has resolved in association with progressive recovery of the MLFs and PPRFs including the RIP, coincident with recovery of adduction and vertical gaze. Abduction and right peripheral facial palsy recover later. LR, lateral rectus; MR, medial rectus; C, convergence input; III, oculomotor nucleus; VI, sixth cranial nerve nucleus; VII, seventh cranial nerve fascicle; R, right.

which recovered more slowly, as suggested by persistence of the abduction lag 2 months later. Extension of the demyelinating lesion toward the rostral interstitial nucleus of the MLF (riMLF), which takes part in the generation of fast vertical eye movements, should also be considered as a possible explanation for the impaired vertical saccades. In humans, the riMLF nucleus lies just above the nucleus of Cajal and third cranial nerve nucleus and dorsomedially to the anterior pole of the red nucleus (11). However, the more recent lesion of this patient was in the pontine tegmentum and did not involve the midbrain. Furthermore, vertical eye movement limitations, convergence impairment, or diplopia had not been demonstrated earlier.

Our report suggests that demyelinating lesions confined to the pons may lead to impairment of vertical saccadic eye movements.

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