

# Pearls and Oysters: Central fourth nerve palsies

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**CLINICAL PEARLS** Lesions of the fourth (trochlear) cranial nerve cause vertical or oblique diplopia by impairing the ability of the superior oblique muscle to intort and depress the eye. This binocular diplopia worsens in downgaze and lateral gaze away from the affected eye. Because intorsion is necessary to maintain fusion in ocular counter-roll, this diplopia also worsens with head tilt toward the affected eye.<sup>1,2</sup>

Diagnosis of a superior oblique palsy can be made using the Parks-Bielschowsky 3-step test: 1) determine which eye is hypertropic, 2) determine if the hypertropia worsens in left or right gaze, and 3) determine if the hypertropia worsens in right or left head tilt. In a superior oblique palsy, the hypertropia of the affected eye worsens with contralateral gaze and ipsilateral head tilt. Alternate cover, cover-uncover, and Maddox rod testing can be helpful examination techniques.<sup>3</sup>

Although the fourth nerve is most commonly injured peripherally along its intracranial course (the longest of all cranial nerves), the fourth nerve nucleus or fascicle may be implicated, resulting in a central fourth nerve palsy.

The fourth nerve nucleus is located within the midbrain adjacent to periaqueductal gray matter and dorsal to the medial longitudinal fasciculus (MLF) at the level of the inferior colliculus. After leaving the nucleus, the fascicles of the fourth nerve decussate in the anterior medullary velum at the roof of the aqueduct of Sylvius then exit the brainstem dorsally (figure 1). The fourth nerve is unique among the cranial nerves in that all of its fibers are crossed at the peripheral nerve level. Consequently, a lesion of the fourth nerve nucleus results in a superior oblique palsy of the contralateral eye.

While isolated central fourth nerve palsies have been reported, lesions of the fourth nerve nuclei or fascicles typically also affect adjacent brainstem structures.<sup>2,4-6</sup> A central fourth nerve palsy, therefore, should be suspected whenever a fourth nerve palsy is accompanied by brainstem signs, and the location of the lesion should be presumed to lie within the dorsal midbrain contralateral to the affected eye.

Central lesions within the dorsal midbrain may also result in bilateral fourth nerve palsies.<sup>7</sup>

Clinical features suggestive of bilateral fourth nerve palsies include right hypertropia in left gaze, left hypertropia in right gaze, and alternating hypertropia with head tilt to either side (i.e., right hypertropia with right tilt and left hypertropia with left head tilt).<sup>8</sup>

**CASE REPORTS** **Case 1.** A 20-year-old man presented to the emergency department complaining of 6 days of binocular vertical diplopia and a left eyelid droop. He had noted fatigue, bilateral eye pain, and flu-like symptoms 2 to 4 weeks prior to presentation.

Left-sided ptosis and miosis were present on examination, along with a left adduction deficit. He had a right hypertropia that worsened with left gaze, downgaze, and right head tilt. These findings were interpreted as a left Horner syndrome, left internuclear ophthalmoplegia (INO), and right fourth nerve palsy.

Brain MRI (figure 2) revealed a T2-weighted/fluid-attenuated inversion recovery (FLAIR) hyperintensity within the left dorsal midbrain which enhanced on T1, suggestive of demyelination. CSF contents were normal with no oligoclonal bands. Repeat brain MRI at 1 week (following a 3-day course of IV methylprednisolone) showed a reduction in size of the lesion.

Both the Horner syndrome and INO resolved within 2 months, but the fourth nerve palsy persisted. Years later, he experienced new neurologic signs and symptoms with corresponding MRI white matter lesions suggestive of multiple sclerosis.

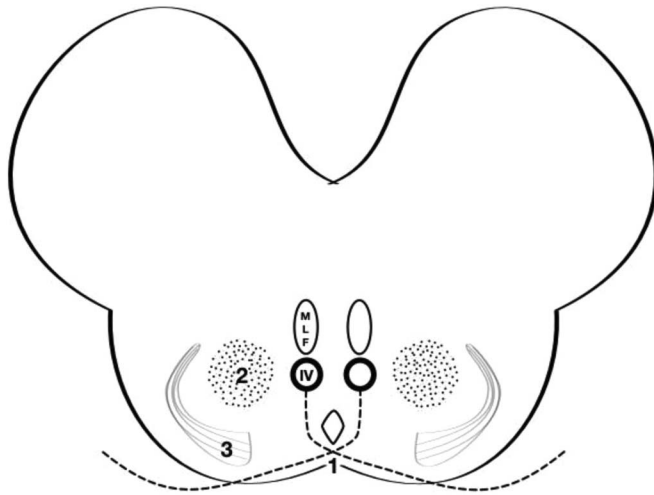
**Case 2.** An 18-year-old man presented to the neuro-ophthalmology clinic complaining of 8 months of intermittent binocular vertical diplopia following a traumatic brain injury.

On examination, he had right-sided ptosis and miosis, and right-sided dysmetria on finger-to-nose and heel-to-shin testing. He was orthophoric in primary gaze, but had a prominent left hypertropia in right gaze and left head tilt and a mild right hypertropia in left gaze and right head tilt. These findings suggested bilateral fourth nerve palsies, worse on the left, accompanied by right Horner syndrome and right cerebellar ataxia.

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**Figure 1** Cross-section of caudal midbrain at the level of the inferior colliculus

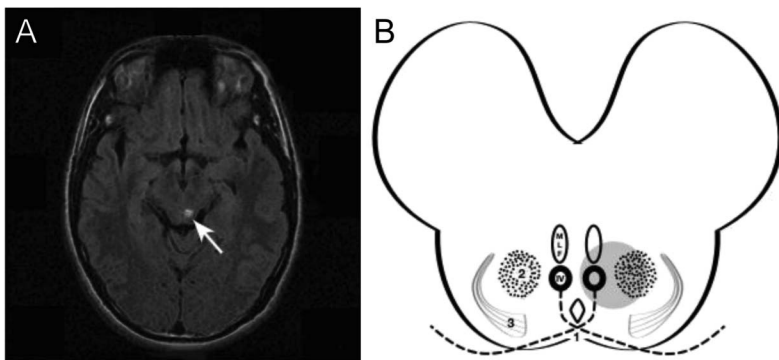


1) Decussation of the fourth nerve fascicles in the anterior medullary velum dorsal to the cerebral aqueduct; 2) oculosympathetic tract/reticular formation; 3) superior cerebellar peduncle prior to its decussation. IV = fourth nerve nucleus; MLF = medial longitudinal fasciculus.

Brain MRI 2 months after his accident showed evidence of diffuse axonal injury characterized by scattered T2/FLAIR hyperintensities and gradient echo T2\* (heme) sequence hypointensities. The right superior cerebellar peduncle and bilateral dorsal midbrain (worse on the right) were involved (figure 3).

**Case 3.** A 49-year-old woman presented to the emergency department after the abrupt onset of binocular vertical diplopia, left periorbital pain, numbness of the right arm, and tinnitus that progressed to hearing loss over minutes. She reported having experienced intermittent binocular horizontal diplopia over the past several months.

**Figure 2** MRI and midbrain cross-section demonstrate lesion (gray area) in case 1



(A) Axial fluid-attenuated inversion recovery hyperintensity in the left dorsal midbrain (arrow) causing contralesional fourth nerve palsy and ipsilesional Horner syndrome and internuclear ophthalmoplegia. (B) 1) Decussation of the fourth nerve fascicles; 2) oculosympathetic tract/reticular formation; 3) superior cerebellar peduncle. IV = fourth nerve nucleus; MLF = medial longitudinal fasciculus.

On examination, she had a right abduction deficit. In addition, she had a left hypertropia in right gaze and left head tilt and a right hypertropia in left gaze and right head tilt. Left-sided finger-to-nose dysmetria was noted. The alternating hypertropia with lateral gaze and head tilt strongly indicated the presence of bilateral fourth nerve palsies, which, accompanied by left cerebellar ataxia, argued for a focal brainstem localization.

Brain MRI revealed 2 discrete lesions: 1) a right cavernous carotid aneurysm, hyperintense on contrast-enhanced T1 and hypointense on T2\* heme sequence (figure 4, A and B, respectively), and 2) acute hemorrhage (with involvement of the left inferior colliculus) surrounding a left dorsal midbrain cavernous angioma, which was hypointense on T2\* (figure 5).

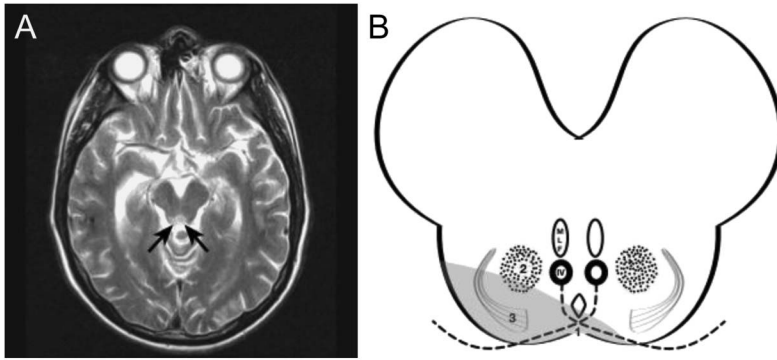
The bilateral fourth nerve palsies and ataxia resolved within 1 year. The right abduction deficit was attributed to the right cavernous carotid aneurysm. Three years later, she developed severe right-sided retrobulbar pain, internal and external ophthalmoplegia, and vision loss, and was treated for enlargement of the right cavernous carotid aneurysm with balloon occlusion. Five years later, she developed a left posterior cerebral aneurysm that required clipping.<sup>9</sup>

**DISCUSSION** In each of the 3 cases, fourth nerve palsies occurred contralateral to lesions within the dorsal midbrain and were accompanied by ipsilesional brainstem signs such as INO, Horner syndrome, or cerebellar ataxia. In case 1, the proximity of the left fourth nerve nucleus to the MLF and descending oculosympathetic pathways resulted in the combination of a contralesional (right) superior oblique palsy with an ipsilesional (left) INO and Horner syndrome (figure 2). As the MLF lies so close to the fourth nerve nucleus, the combination of INO and a fourth nerve palsy strongly suggests a nuclear lesion (figure 1). Injury to the left MLF results in an adduction lag or impaired adduction of the left eye in right gaze. Because the oculosympathetic pathway does not decussate, damage to the left oculosympathetic pathway anywhere along its course results in a left Horner syndrome.

In case 2, the central lesion was bilateral but more severe on the right, resulting in bilateral superior oblique palsies, more severe on the left. Horner syndrome was again present due to involvement of the ipsilesional (right) oculosympathetic pathway, but in this case it was accompanied by hemi-ataxia, the result of damage to the ipsilesional (right) superior cerebellar peduncle (figure 3). Because of uncrossed or doubly crossed fibers, lesions of the cerebellar hemispheres or cerebellar peduncles also result in ipsilesional symptoms.

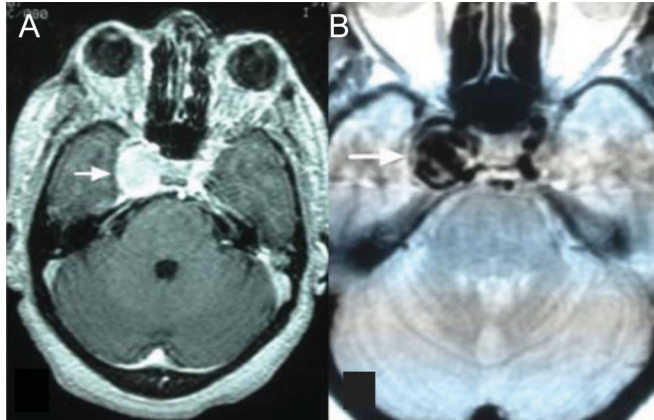
Case 3 was particularly complicated due to the presence of 2 lesions. Whereas subsequent events demonstrated that the right sixth nerve palsy was referable to

**Figure 3** MRI and midbrain cross-section demonstrate lesion (gray area) in case 2



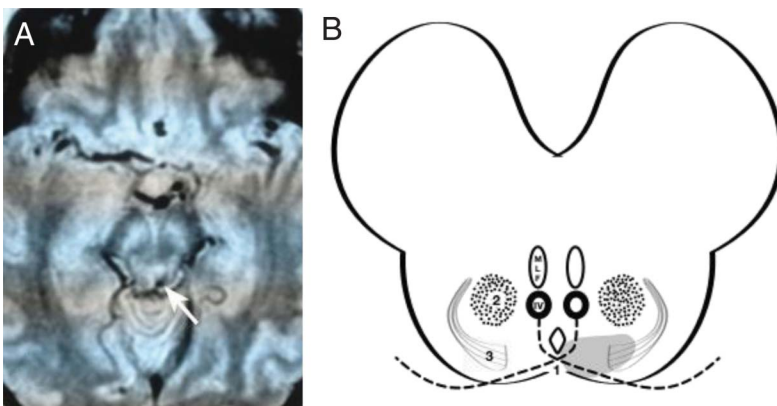
(A) Axial T2 hyperintensity along the right and left dorsal midbrain (arrows) causing bilateral fourth nerve palsies (both contralesional) and ipsilesional Horner syndrome and ataxia. (B) 1) Decussation of the fourth nerve fascicles; 2) oculomotor tract/reticular formation; 3) superior cerebellar peduncle. IV = fourth nerve nucleus; MLF = medial longitudinal fasciculus.

**Figure 4** MRI demonstrates aneurysm in case 3



Axial images demonstrate right cavernous sinus aneurysm (arrows) as (A) hyperintense on contrast-enhanced T1, and (B) hypointense on T2\* (heme) sequence causing ipsilesional sixth nerve palsy.

**Figure 5** MRI and midbrain cross-section demonstrate lesion (gray area) in case 3



(A) Axial T2\* hypointensity in the left dorsal midbrain (arrow) suggesting hemosiderin deposition causing bilateral fourth nerve palsies (both contralesional) and ipsilesional ataxia. (B) 1) Decussation of the fourth nerve fascicles; 2) oculomotor tract/reticular formation; 3) superior cerebellar peduncle. IV = fourth nerve nucleus; MLF = medial longitudinal fasciculus.

the right cavernous sinus aneurysm (figure 4), we attribute the remaining symptoms, including sudden vertical diplopia, left-sided ataxia, and right arm sensory symptoms, to the acute midbrain hemorrhage from the left-sided cavernous angioma (figure 5). The presence of bilateral superior oblique palsies and the ipsilesional cerebellar ataxia was similar to that observed in case 2. We presume that the auditory symptoms reflected involvement of the left inferior colliculus, which receives afferents from bilateral cochlea. An audiogram was not performed.

A skew deviation and a fourth nerve palsy present similarly, and distinguishing between the 2 may be a diagnostic challenge. A skew deviation is a pre-nuclear nonparalytic vertical ocular misalignment due to imbalance of utricular inputs to the ocular motor system, typically the result of a brainstem or cerebellar lesion.<sup>10</sup> It is often accompanied by features of the “ocular tilt reaction”—the triad of skew deviation, head tilt, and ocular counter-roll.<sup>10</sup>

Although it is rare for a skew deviation to precisely mimic an acute fourth nerve palsy, both entities may be associated with a positive head-tilt test. The hypertropia of a skew deviation may be comitant (ocular deviation is the same in all positions of gaze) in contrast to an acute fourth nerve palsy which shows an incomitant (ocular deviation varies with gaze position) deviation. When a skew deviation is associated with an incomitant deviation, the 2 entities may be best distinguished by the accompanying neurologic signs and the binocular ocular torsion associated with a skew deviation. In contrast to the compensatory head tilt seen in fourth nerve palsies (a contralateral head tilt that minimizes ocular misalignment), the head tilt and cyclotorsion (ocular counter-roll) associated with skew deviation occur in the same direction.<sup>10</sup> Postural testing may be of value since the vertical misalignment and torsion associated with a skew (but not with a fourth) typically abates after moving from an upright to a recumbent position (asymmetric utricular input is minimized).<sup>11</sup>

While peripheral fourth nerve palsies are commonly caused by trauma, central fourth nerve palsies are usually due to infarction or hemorrhage.<sup>2,4-8,12</sup> Although central fourth nerve palsies are rare, the combination of a superior oblique palsy and contralateral brainstem signs, particularly Horner syndrome, INO, or cerebellar ataxia, is highly localizing, signifying a dorsal midbrain lesion contralateral to the superior oblique palsy, and should raise suspicion for etiologies such as hemorrhage, demyelination, or trauma.

#### AUTHOR CONTRIBUTIONS

Daniel R. Gold, DO: conceptualization, drafting, and revising the manuscript. Robert K. Shin, MD: conceptualization, drafting, and revising the manuscript. Steven L. Galetta, MD: drafting and revising the manuscript.

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## DISCLOSURES

D. Gold reports no disclosures. R. Shin has received consulting honoraria from PRIME. S. Galetta has received consulting honoraria from Biogen Idec and Teva. **Go to [Neurology.org](http://Neurology.org) for full disclosures.**

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