Complete Ophthalmoplegia
An Unusual Sign of Bilateral Paramedian Midbrain-Thalamic Infarction
Matthew J. Thurtell, MBBS, FRACP; G. Michael Halmagyi, MD, FRACP

Background and Purpose—Complete ophthalmoplegia, the combination of bilateral ptosis with loss of all extraocular movements, is rarely a consequence of ischemic stroke. We describe 3 patients who had complete ophthalmoplegia as a manifestation of bilateral paramedian midbrain-thalamic infarction, and we discuss possible pathophysiologic mechanisms.

Summary of Cases—Three patients presented with coma. All had complete ophthalmoplegia that initially persisted despite improvement or fluctuation in their other deficits. MRI revealed bilateral paramedian midbrain-thalamic infarction. Two patients died, with the ophthalmoplegia remaining unchanged before death. The surviving patient had a progressive improvement in ocular abduction but persisting third nerve and vertical gaze palsies.

Conclusions—Complete ophthalmoplegia is an unusual sign of bilateral paramedian midbrain-thalamic infarction. The ophthalmoplegia could result from combined third nerve, pseudoabducens, and vertical gaze palsies.

Key Words: ophthalmoplegia • mesencephalon • thalamus • infarction

Complete ophthalmoplegia, the combination of bilateral ptosis with loss of all extraocular movements, is rarely encountered in clinical practice. It can be produced acutely by conditions involving the neuromuscular junction (such as myasthenia gravis or botulism), ocular motor nerves (such as Miller-Fisher or Guillain-Barré syndromes), or brain stem (such as anticonvulsant drug intoxications or Wernicke syndrome).1 Although ischemic stroke has been identified as a cause in a minority of patients,1 the arterial territory of infarction has not been defined and a mechanism for the ophthalmoplegia has not been postulated. We describe 3 patients who had complete ophthalmoplegia attributable to bilateral paramedian midbrain-thalamic infarction. We suggest that the ophthalmoplegia results from bilateral pseudoabducens palsies combined with third nerve and vertical gaze palsies.

Case 1
A 30-year-old woman, with a history of rheumatic fever and left middle cerebral artery (MCA) territory infarction, presented after the sudden onset of coma. She was intubated and then transferred to our institution.

On examination, she was alert and following commands, so she was extubated. Her pupils were 7 mm in diameter and unreactive to light. She had bilateral ptosis and primary position exotropia. There were neither voluntary eye movements nor eye movements in response to vestibular stimulation. She had bilateral upper motor neuron facial weakness, dysarthria, and a spastic quadriplegia, yet she could move all limbs on command. Her reflexes were brisk and there were bilateral extensor plantar responses.

Brain MRI showed acute bilateral paramedian midbrain-thalamic infarction (Figure, A). The old left MCA territory infarct was noted.

Over the following days, she had fluctuating hypersomnia, but her ophthalmoplegia and pupils remained unchanged. She died 1 week after presentation, after a hemorrhagic transformation of the stroke.

Case 2
A 61-year-old woman, with a history of hypertension, presented after the sudden onset of coma. Brain CT showed no infarct or hemorrhage, so she was intubated and then transferred to our institution.

On examination, she was unresponsive but breathing spontaneously. Her pupils were 6 mm in diameter and unreactive to light. She had bilateral ptosis and primary position exotropia. There were neither spontaneous eye movements nor eye movements in response to vestibular stimulation. She coughed with suctioning. Her limbs were flaccid. There was finger flexion on the left in response to deep noxious stimuli. Her reflexes were symmetrically brisk. There was no response to plantar stimulation.

Brain MRI showed acute bilateral paramedian midbrain-thalamic infarction (Figure, B). MRA showed a filling defect in the P1 segment of the left posterior cerebral artery (PCA).
Within 24 hours, she was localizing to deep noxious stimuli with her left upper limb. Her pupils became asymmetrical, but remained unreactive, and her ophthalmoplegia persisted. As there was no further improvement over the following days, her family requested that active management be withdrawn. She died shortly after extubation.

**Case 3**

A 71-year-old man, with a history of hypertension, ischemic heart disease, and right PCA territory infarction, presented after the sudden onset of coma. Brain CT showed the old stroke but no recent infarct or hemorrhage. He was intubated and then transferred to our institution.

On examination, he was unresponsive but breathing spontaneously. His pupils were 6 mm in diameter and unreactive to light. He had bilateral ptosis. There were neither spontaneous eye movements nor eye movements in response to vestibular stimulation. He localized with both upper limbs in response to deep noxious stimuli. His reflexes were symmetrically brisk. There were bilateral extensor plantar responses. Over the following days, he had fluctuating hypersomnia, but his ophthalmoplegia and pupils remained unchanged. He was extubated when he was consistently alert. Brain MRI showed acute bilateral paramedian midbrain-thalamic infarction (Figure, C).

Ocular abduction progressively improved to normal from 5 days after presentation. His pupils remained fixed but became asymmetrical. Ultimately, he had residual bilateral third nerve palsies and a vertical gaze palsy.

**Discussion**

Paramedian midbrain-thalamic infarction results from occlusion of the midbrain-thalamic perforating arteries, which arise from the proximal PCAs or from a single artery (the artery of Percheron) that, in turn, arises from the proximal segment of one PCA. Bilateral infarction usually produces alterations in level of consciousness (decreased at onset, often fluctuating thereafter), cognitive abnormalities (confusion, amnesia), behavioral abnormalities (apathy, akinetic mutism), and ocular motor abnormalities (third nerve palsy, vertical gaze palsy, internuclear ophthalmoplegia). The pupils are often abnormal and can be unreactive, as in our patients. Pupil size varies depending on involvement of the Edinger-Westphal nucleus or oculomotor fascicles (large pupils), descending sympathetic fibers (small pupils), or some combination of these structures (midrange pupils).

Our patients were unusual in that their infarcts produced complete ophthalmoplegia; in addition to bilateral ptosis, all voluntary and reflex eye movements were lost. A similar deficit has been reported in 3 other patients with infarction and in 3 patients with hematomas at the midbrain-thalamic junction. Although complete ophthalmoplegia could potentially result from bilateral pontine and midbrain lesions, to the best of our knowledge, it has not been reported with infarction confined to any other single perforating artery territory.

The complete ophthalmoplegia can be partly accounted for by bilateral third nerve palsies (attributable to involvement of the oculomotor nuclei/fascicles) with a supranuclear vertical gaze palsy (attributable to involvement of the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF)). The loss of all abducting eye movements, including those in response to vestibular stimulation, suggests a lesion of the abducens motoneurons. However, no pontine abnormality was evident on imaging in any of our patients. Although we cannot be sure that there was no pontine lesion without histopathologic confirmation, we believe that our patients most likely had bilateral pseudo-abducens palsies. Initially described by Fisher, pseudoabducens palsy was defined by Caplan as an abducens palsy occurring in the absence of an abducens lesion. As most cases result from midbrain-thalamic junction lesions, it has been suggested that the deficit arises because of interruption of inhibitory vergence.
pathways traversing the paramedian thalamus. However, the observation that there is often an associated vertical gaze palsy suggests that a pathway or structure adjacent to the riMLF is responsible; thus, a lesion involving the adjacent fronto-pontine horizontal gaze pathway could give rise to pseudoabducens palsy. Alternatively, involvement of the medial rectus subdivisions of the oculomotor nuclei could explain the pseudoabducens palsies observed in our patients; reversible pharmacological lesions in the medial rectus subdivisions of the primate oculomotor nucleus produce a transient contralateral pseudoabducens palsy by inactivating excitatory interneurons passing from the oculomotor nucleus to the contralateral abducens nucleus.

The prognosis for recovery of the ophthalmoplegia is poor, with each of the previously reported cases with infarction showing modest, if any, recovery. Our sole surviving patient showed a gradual improvement in ocular abduction, with persisting bilateral third nerve and vertical gaze palsies, indicating that the pseudoabducens palsies can be transient rather than permanent.

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Disclosures
None.

References
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