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*Grand Rounds*

# A 20-year-old woman with abnormal eye movements

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## History

A 20-year-old woman was referred to the neuro-ophthalmology clinic at Beth Israel Deaconess Medical Center for evaluation of diplopia. Three months prior to presentation, she awoke with oblique binocular diplopia, which resolved spontaneously over a period of several weeks but recurred 1 month prior to presentation, accompanied by an inability to make facial expressions on her left side and difficulty with eye movements. She denied diplopia in primary gaze but complained of horizontal diplopia in right- and leftward gaze, worse in left gaze. She denied eye pain and any change in visual acuity. Associated symptoms included dry eye on the left, for which she was applying artificial tears four times daily and lubricating ointment at bedtime. She was previously healthy and took no medications. Family history was unremarkable. She had no history of head or eye trauma.

## Examination

On examination, her best-corrected visual acuity was 20/40 in each eye, and she identified 8/8 Ishihara color plates. There was no relative afferent pupillary defect or anisocoria. Confrontation visual fields were also full. External evaluation revealed inability to lift her brow or smile on the left, consistent with left facial nerve palsy. There was minimal lagophthalmos and an intact Bell's phenomenon. On ocular motility examination (Figure 1), her eyes were aligned in primary position at distance, with absent abduction in the left eye and slow adducting saccades in both eyes. Abduction was intact in the right eye, although there was abducting nystagmus. Gaze-evoked nystagmus was noted in upgaze, but there was no nystagmus in primary position (Video 1). On slit-lamp examination, there was superficial punctate keratopathy on the left cornea inferiorly, consistent with exposure keratopathy. Both optic discs were normal appearing, without swelling, hemorrhage or pallor. Retinal vessels and maculae also appeared unremarkable.

## Ancillary Testing

Magnetic resonance imaging (MRI) of the brain revealed a brainstem cavernous malformation. T1- and T2-weighted MRI demonstrated a "popcorn" hyperintensity in the left posterior pons, with adjacent hypointensities anterior and anteromedial to the lesion, consistent with remote hemorrhage (Figure 2). Given our patient's historical complaint, the oblique diplopia was thought to reflect a skew deviation rather than trochlear nerve involvement. In such a scenario, however, cessation of bleeding and clearance of blood products would have generally allowed neural tissue far from the center of the lesion to regain function.

## Treatment

Cavernous malformations are typically managed with surgical resection or observation with serial MRIs. Indications for surgical resection include progressive neurological deficits, recurrent hemorrhage, proximity to the pial surface, recurrent symptomatic episodes, and compression of surrounding brain tissue.[1] Our patient elected to proceed with neurosurgical resection 2 days aft her initial presentation to our department.

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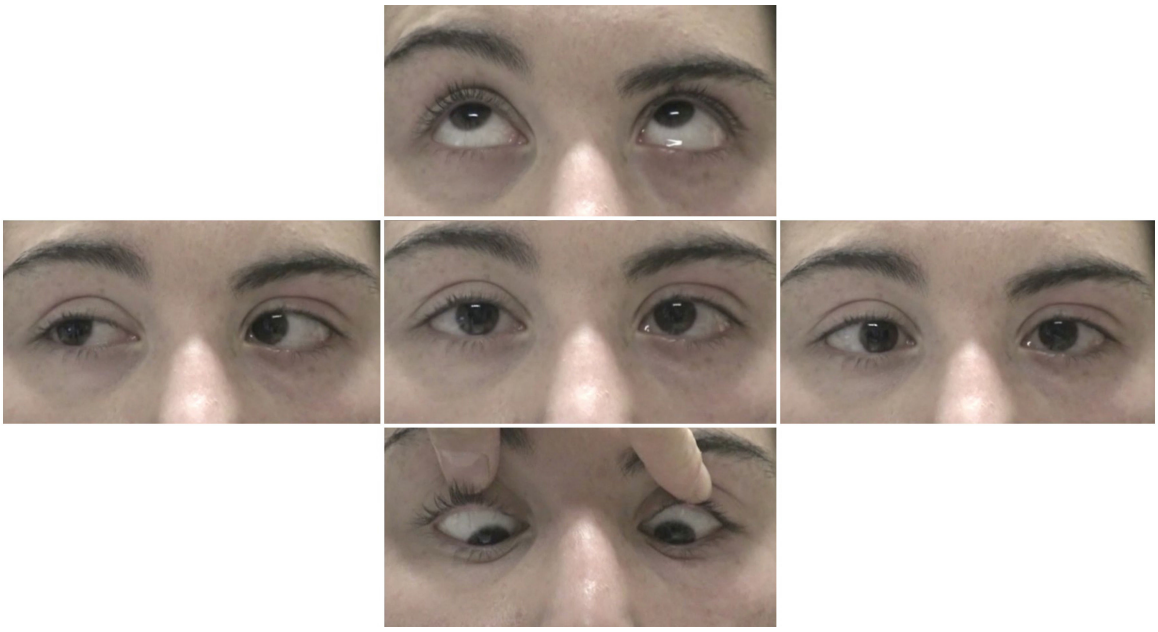
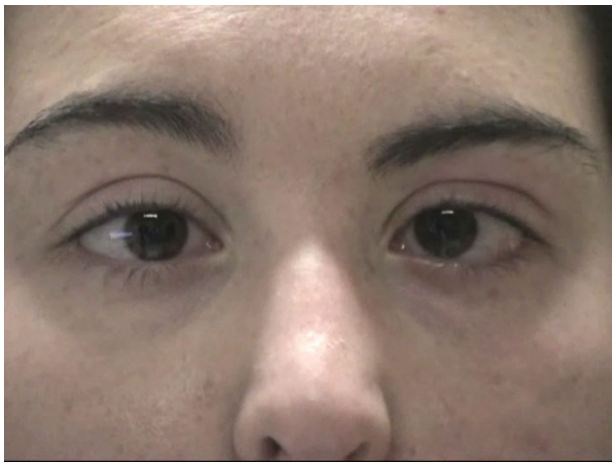


**Figure 1.** Clinical photographs of extraocular motility examination in a 20-year-old woman who presented with oblique binocular diplopia showing impaired leftward gaze in both eyes (middle row, right). Although right gaze appears intact (middle row, left), she had disconjugate eye movements, with slow adducting saccades in the left eye.



**Video 1.** Video of patient showing convergence at 1–2 seconds, right gaze at 5 seconds, attempted left gaze with leftward gaze palsy at 10–11 seconds, upgaze at 14 seconds, downgaze at 17 seconds, and a slowly adducting saccade in the left eye, indicating left internuclear ophthalmoplegia, at 21 seconds. Additionally, at 12 and 19 seconds the patient blinks, clearly showing lagophthalmos in the left eye due to left facial nerve palsy.

In addition, lubricating drops, four times a day, lubricating ointment at bedtime, and humidifiers were recommended because of underlying exposure keratopathy. Two weeks after surgery, however, she had an esotropia of 6 prism diopters in primary position at distance, without tropia at near. Fresnel stick-on prism lenses were prescribed. Overall, no improvement on either the motility or facial nerve function was noted postoperatively.

## Differential Diagnosis

One-and-a-half syndrome is most often localized to a unilateral lesion of the medial longitudinal fasciculus (MLF) and ipsilateral paramedian pontine reticular formation (PPRF) or the abducens nerve. The MLF forms a connection between the contralateral abducens nerve nucleus and the ipsilateral oculomotor nerve nucleus. Lesions of this tract result in internuclear ophthalmoplegia, with an ipsilateral adduction palsy and abducting nystagmus in the contralateral eye. The additional involvement of the PPRF or abducens nerve nucleus results in a conjugate gaze palsy to the ipsilateral side. Together, a lesion of the PPRF–abducens nerve nucleus (one) and MLF (half) combine to form the clinical entity known as one-and-a-half syndrome, as demonstrated in this patient.

The syndrome can be expanded based on involvement of additional brainstem structures. Additional facial nerve deficit may be present as fibers course around the abducens nerve nucleus before exiting the brainstem. When this occurs, the condition is termed eight-and-a-half syn-

Digital Journal of Ophthalmology, Vol. 27

Digital Journal of Ophthalmology, Vol. 27

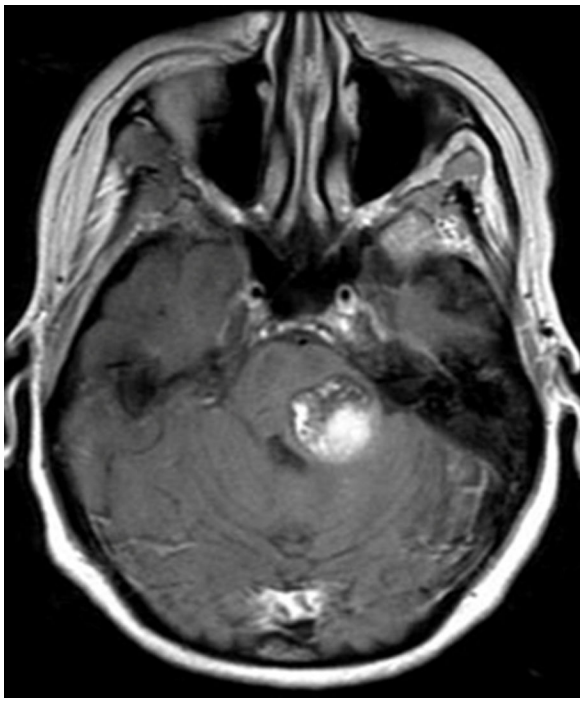


**Figure 2.** T1-weighted axial magnetic resonance imaging demonstrating a "popcorn" hyperintensity in the left posterior pons, with adjacent hypointensities anterior and anteromedial to the lesion consistent with remote hemorrhage, all in keeping with left pontine cavernous malformation.

drome, as was present in our patient.[2] Another example is the addition of ipsilateral trigeminal nerve involvement that produces a thirteen-and-a-half syndrome variant.[3]

These syndromes, as in our patient, result from a unilateral lesion in the dorsal pontine tegmentum. The differential diagnosis includes ischemia (eg, pontine lacunar infarction), compressive lesion (eg tumor), demyelinating disease, and infection.[3] Thorough medical history and physical examination along with neuroimaging are key to early diagnosis and treatment of these syndromes, because the prognosis is variable and the severity of the disorder is determined largely by the specifics of the underlying pathology.

On imaging, these lesions can resemble gliomas, hemorrhagic telangiectasias, such as those seen in Osler-Weber-Rendu disease, and even brain metastasis.[4]

## Diagnosis and Discussion

Eight-and-a-half syndrome was first described in 1998 by Eggenberger.[2] It is a rare pontine neuro-ophthalmologic syndrome characterized by a combination of one-and-a-half syndrome and ipsilateral facial nerve palsy and is most often caused by infarction. This syndrome has also been described in demyelinating disorders involving the pons level as well as space-occupying lesions such as tuberculomas or cavernomas.[5]

Cavernous malformations (CMs) are well-defined, tightly packed masses of thin-walled, dilated, sinusoidal capillaries with endothelial lining and fibrous adventitia. Although CMs may occur anywhere in the central nervous system, most are found in the cerebrum, accounting for up to 25% of all vascular malformations. In a meta-analysis of 11 natural history studies, brainstem CMs comprised 18 % of lesions.[6]

Because of the high density of cranial nerve nuclei and associated nerve tracts, patients with brainstem CMs commonly present with multiple cranial neuropathies and variable ophthalmic manifestations. Progressive neurological deficits are not uncommon and were observed in 39 % of patients in one case series.[1]

Characteristic T1- and T2-weighted MRI findings include a "popcorn" pattern of variable intensity due to evolving blood products. Remote bleeds may appear as a hemosiderin ring in the periphery of the lesion.

In conclusion, brainstem CMs can have variable ophthalmic manifestations owing to the close proximity of cranial nerve nuclei in the brainstem. Common ophthalmic manifestations include extraocular motility deficits that result in diplopia and long-term ocular surface sequelae due to lagophthalmos, with decreased or absent blink. Early recognition is of key importance for determining proper treatment of brainstem CMs, which should include the input of neurologists, neuro-ophthalmologists, and neurosurgeons for optimal results.

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Digital Journal of Ophthalmology, Vol. 27