Isolated Relative Afferent Pupillary Defect Secondary to Contralateral Midbrain Compression

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Background: Relative afferent pupillary defects are typically related to ipsilateral lesions within the anterior visual pathways.

Objective: To describe a patient who had a workup for headache and was found to have an isolated left relative afferent pupillary defect without any other neurological findings.

Design: We review the neuroanatomy of the pupillary light reflex pathway and emphasize the nasotemporal bias of decussating fiber projections, which accounts for the relative afferent pupillary defect contralateral to the described lesion.

Result: Magnetic resonance imaging of the brain revealed a pineal tumor compressing the right rostral midbrain.

Conclusion: While rare, a relative afferent pupillary defect can occasionally occur secondary to lesions in the postchiasmal pathways. In these circumstances, the pupillary defect will be observed to be contralateral to the side of the lesion.

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A relative afferent pupillary defect (RAPD) is characterized by pupillary dilation upon illuminating the eye during the swinging flashlight test. The presence of this sign signifies an abnormality in the transmission of light information within the pupillary light constrictor pathway from the retina to the rostral midbrain circuitry involved in this reflex. Relative afferent pupillary defects are most frequently associated with lesions in the optic nerve. For example, patients with unilateral optic neuritis have a slowing in conduction velocity in the affected nerve. During illumination of the unaffected eye, both direct and consensual pupillary responses can be appreciated. The rapid transmission of this information results in simultaneous innervation of the Edinger-Westphal nucleus, which ultimately provides parasympathetic innervation to the sphincter fibers of the iris via the oculomotor cranial nerve. However, during the rapid movement of the light source to the affected side, the abnormality in optic nerve conduction velocity (or the loss of optic nerve axons) delays the arrival of pupillary light information entering the brainstem, and the examiner can identify an escape or dilation of the pupils. Although retinal fibers concerned with this reflex transmit information to both the ipsilateral and contralateral midbrain, there is a slight crossing bias, with about 53% of the fibers crossing in the optic chiasm (chiefly derived from the nasal retina) and 47% remaining ipsilateral. This anatomical organization of the pupillary constrictor pathway results in the possibility of producing an RAPD during illumination of the eye opposite to an optic chiasm, tract, or midbrain lesion (Figure). Here, we describe a patient who had an isolated sign of a left RAPD secondary to a pineal tumor compressing the right dorsal midbrain at the level of the brachium of the superior colliculus.

REPORT OF A CASE

A 27-year-old man with no medical history was referred to the neurology clinic for evaluation of a headache. Results of his physical examination were normal with the exception of the presence of a left RAPD. Visual acuity was 20/20 bilaterally with full visual fields by bedside testing. The pupils were equal in size and reactivity to direct light illumination. However, during the swinging flashlight test, we noted the
unmistakable presence of a left RAPD. Funduscopic examination revealed normal optic discs without evidence of papilledema, pallor, or atrophy. There was no evidence of head tilt, ptosis, internuclear ophthalmoparesis, fourth nerve palsy, or skew deviation. Extraocular movements were full. There were normal ocular alignment and normal ductions and versions. There was no evidence of vertical or oblique strabismus on alternate cover testing. Pursuit and vestibular eye movements were normal. There was no evidence of primary position, gaze evoked, rebound, or convergent retraction nystagmus.

Magnetic resonance imaging of the brain with gadolinium infusion revealed a large pineal tumor. The mass was found to compress the right dorsal midbrain at the level of the brachium of the superior colliculus (Figure). Despite the apparent involvement of the cerebral aqueduct, there was no evidence of hydrocephalus. No abnormalities of the optic nerves were identified. The patient’s headache subsequently resolved spontaneously, and he was referred to the departments of neurosurgery and neuro-oncology for further evaluation.

**COMMENT**

The size of the resting pupil is controlled by the amount of light falling on the retina and depends on the integrity and relative activity of these discrete autonomic pathways. The axons of the ganglion cells of the nasal retina decussate in the optic chiasm to join the fibers derived from the temporal retina from the other eye. Collectively, these fibers constitute the optic tract. Photoreceptors have been identified to be more densely distributed in the nasal vs the temporal portion of the retina. Given this anatomical arrangement, there is a corresponding asymmetric parcelling of nerve fibers within the optic tracts arising from the nasal and temporal retina. In particular, it has been estimated that the ratio of crossed to uncrossed afferent pupillary fibers is 53:47 (Figure).

The majority of retinal axons provide afferent information to the lateral geniculate nucleus en route to the primary visual areas on the calcarine cortex. However, approximately 10% of the fibers bypass the lateral geniculate nucleus and are relayed to the pretectal area of the rostral midbrain. These fibers travel through the brachium to synapse at the level of the superior colliculus. Second-order neurons subsequently relay pupillary light information to Edinger-Westphal nuclei bilaterally. This dual and near-simultaneous innervation provides the anatomical basis for both the direct and the consensual light reflexes. From the Edinger-Westphal nuclei, tertiary parasympathetic neurons travel in the superficial dorsomedial aspect of the ipsilateral oculomotor nerve to reach the ciliary ganglion. The ganglion then gives rise to 8 to 10 short ciliary nerves, which subdivide into 16 to 20 branches. The majority of these branches supply the ciliary muscle to control the shape of the lens. Approximately 3% of these fibers ultimately converge upon and innervate the pupillary sphincter muscles (promoting constriction), thereby contributing to the regulation of pupil size.

Relative afferent pupillary defects have been classically associated with lesions in the ipsilateral retina or op-
tic nerve. Because of the asymmetric distribution of photoreceptors in the nasal and temporal retina and the ratio of crossed to uncrossed fibers in the chiasm, an RAPD can also result from contralateral optic tract and midbrain lesions. The pretectal afferent pupillary pathway is a continuation of the fibers within the optic tract. As such, a lesion affecting those fibers that have branched off from the optic tract during their trajectory to the dorsal midbrain can also result in a contralateral RAPD. Unlike retinal, optic nerve, and optic tract lesions, no visual field defect should be produced when the lesions affect this terminal portion of the afferent pupillary pathway. Furthermore, an RAPD without visual dysfunction may occur with lesions that selectively interrupt the pupillary afferents to the pretectal nucleus or as a result of damage to the pretectal nucleus itself. Most patients characterized in the literature with an RAPD contralateral to an anterior pathway lesion also manifested additional neurological signs and symptoms. Ultimately, an RAPD may occur with ipsilateral lesions in the retina, optic nerve, and optic chiasm, or with contralateral lesions in the optic tract, brachium of the superior colliculus, and pretectal area.

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REFERENCES