Grand Rounds

A 19-month-old girl with nystagmus, paradoxical pupillary response and low vision

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History

A 19-month-old girl presented to the ophthalmology clinic at Children's Hospital, Boston with bilateral horizontal nystagmus, first noticed at 3 months of age. Her parents stated that lately, the nystagmus was less noticeable; however, they became concerned because the patient did not seem to see things far away. Her parents also reported that she did not seem bothered by light. She had normal brain magnetic resonance imaging. Her past medical history was unremarkable and she had normal development. There was no difficulty with pregnancy, but the patient was delivered by C-section because of failure to progress. She had no known drug allergies and she was not taking any medication.

Examination

External examination demonstrated no abnormalities. Her visual acuity was assessed with the preferential looking test. With binocular viewing the result was 0.64 cpd (cycles per degree), corresponding to 20/960 Snellen acuity. For the right eye alone the visual acuity was 20/1,400 (Normal VA corrected for age is approximately 20/80). She was too restless for testing of the left eye. Her VEP (visual evoked potentials) acuities were 4.2 cpd on the right and 4.5 cpd on the left. These correspond to 20/143 and 20/133 Snellen acuity.

The pupils were round and equal and constricted in response to light. No afferent pupillary defect was seen. Additionally, using an infrared video system, paradoxical pupillary constriction to darkness was demonstrated. (see Video)

The cycloplegic retinoscopy was +5.50 sphere in both eyes. She was orthotropic on muscle balance testing. She had full ductions and versions. There was a small

Video. Infrared video system demonstrating the paradoxical pupillary constriction to darkness.

amplitude, high frequency, horizontal nystagmus. The direction of nystagmus did not change in different directions of gaze. There was no anomalous head posture and the patient did not appear to have a null point in which the nystagmus dampened.

The anterior segment examination was normal. There were no iris transillumination defects. The intraocular pressures were normal at 8 mmHg in both eyes. On visual field testing, she looked for the hand light in all quadrants with both eyes. On indirect ophthalmoscopy, the media were clear; the optic nerve heads were pink with sharp margins and were normal in diameter. In the maculae, foveal reflexes were identifiable. The retinal vasculature appeared to be of normal caliber and distribution and no abnormalities were seen in the extramacular fundi. (see Figures 1 & 2)

Ancillary Testing

Electroretinography

An electroretinogram (ERG) was performed and showed that the cone and cone-driven responses were absent or markedly attenuated. The rod responses were present but mildly attenuated. (See Figure 3)

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Figure 1. Ret Cam photograph of the right fundus.

Figure 2. Ret Cam photograph of the left fundus.

Figure 3. Electroretinogram (ERG) showing the absence of cone and cone-driven responses with decreased rod responses.

Treatment

Our patient was given +5.50 spherical refraction in both eyes and low vision aids.

Differential Diagnosis

The differential diagnosis includes several entities that can present with paradoxical pupillary response: achromatopsia, congenital stationary night blindness, cone-rod dystrophy. Uncommonly paradoxical pupillary constriction has been reported in retinitis pigmentosa, dominant optic atrophy, old bilateral optic neuritis, congenital nystagmus, Best disease, amblyopia, albinism and Leber's congenital amaurosis.

Diagnosis

This patient's ocular features of infantile nystagmus, paradoxical pupillary constriction to darkness, hyperopia and normal appearance of the retinas on ophthalmoscopy along with the ERG results make achromatopsia the most likely diagnosis.

Achromatopsia ("a-", lack of; "-chroma-", color; "-opsia", vision), also called rod monochromacy is a stationary autosomal recessive condition that affects 8,500 persons in the US (1 in 33,000). It is characterized by reduced visual acuity, nystagmus, deficits in color discrimination, normal fundus appearance and paradoxical pupillary constriction to dark.^{1,2} Hyperopia is common in individuals with achromatopsia, although a broad distribution of refractive errors has been reported.³ Patients with achromatopsia are usually photophobic (light sensitive). Our patient does not appear to be photophobic, but she is not yet ambulatory. Some children with achromatopsia do not have photophobia until walking on their own outdoors.

Achromatopsia is caused by a channelopathy of the photoreceptors.⁴ The most frequent molecular cause are mutations in the cGMP-gated cation channel genes *CNGA3* (Chrom 2) and *CNGB3* (Chrom 8)^{5,6} and less commonly, a mutation in the transducin protein *GNAT2*.⁷ As a result, cone and cone-driven ERG responses to full-field stimuli are markedly attenuated or non-detectable, but rod and rod-driven responses are normal or mildly decreased.^{8,9}

In our patient although achromatopsia is the most likely diagnosis, a progressive retinal disorder cannot be ruled out completely. For this reason regular ophthalmic follow-up is recommended.

Treatment and Recommendations

Patients should be prescribed glasses if there is a significant refractive error. Our patient was given +5.50 spherical refraction in both eyes. In our patient no additional treatment was offered at this point since she was not light sensitive and she is not ambulatory yet. She needs a follow up examination and the vision should be monitored with special tests that include measurement of the dark-adapted visual threshold and mapping of the visual fields. Other recommendations for patients with Achromatopsia include: Red/dark central contact lenses; sun filters to be worn outdoors to decrease light sensitivity and low vision aids including the use of large print materials, sitting in the classroom away from the windows and closing blinds to decrease glare on the board.

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