Principles and Practice of Clinical Electrophysiology of Vision

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Blue Cone Monochromatism

Michael K. Farley
John R. Heckenlively

X-linked blue cone monochromatism (XLBCM) is a congenital ocular cone disorder that was first described by Spivey and associates in 1964.[14] The disorder is due to unequal homologous recombination and point mutation or else a nonhomologous deletion of sequences adjacent to the red and green pigment gene cluster on the long arm of the X chromosome.[10, 11] These changes prevent formation of functional blue cones, which constitute a very small proportion of cones in the retina and which have properties different from medium- and long-wavelength cones.[1, 5, 9, 13] On standard electroretinography (ERG) blue cone monochromatism has the typical changes of a cone dystrophy.[2, 3] The photopic ERG and 30-Hz flicker is poor to nonrecordable (Fig 104–1), while the rod-isolated ERG is normal to subnormal. Spectral sensitivity testing demonstrates blue cone function.[4, 12]

A characteristic clinical picture of this disorder consists of young males presenting with reduced visual acuity, color blindness, photosensitivity, a fine nystagmus, and macular retinal granularity or depigmentation.[8] Myopia is often present.[7] Males are fully affected by this X-linked recessive disease.

Clinically, most carriers are normal but, on careful testing, will demonstrate abnormalities in color vision, delays in dark adaptation, and abnormal ERG flicker and dark-adapted red-flash responses; fluorescein angiography often demonstrates minor changes in the macula.[6, 8, 14]

REPRESENTATIVE CASES

Four males and four obligate females from two X-linked families will be presented. The pedigree of one large family is presented in Figure 104–2. The ages of affected males ranged from 2 to 20 years. The three older males had a history of subnormal visual acuity, poor color vision, mild photosensitivity, and better vision in dim illumination. The mothers of the affected individuals affirmed that nystagmus was noted within the first few months of life.

The visual acuity of the affected males varied between 20/80 to 20/400. The 2-year-old had central fixation. All four affected males showed nystagmus, pendular in three and jerk waveform in two. Horizontal nystagmus was present in two, and the nystagmus remained horizontal in vertical gaze. In one patient there was a second intermittent pendular nystagmus of high velocity and low amplitude.

The refractive errors ranged from mild hyperopia in two patients to mild and high myopia in the remaining two patients. Anterior segment examination and intraocular pressures were normal in all affected males. Ophthalmoscopy demonstrated irregular pigmented foveal areas in both eyes of patients A. and D., but the fluorescein angiograms were normal. All males had high abnormal error scores on the Farnsworth-Munsell 100-hue test.

The photopic ERG was nonrecordable in all XLBCM males, and the flicker response was nonrecord-

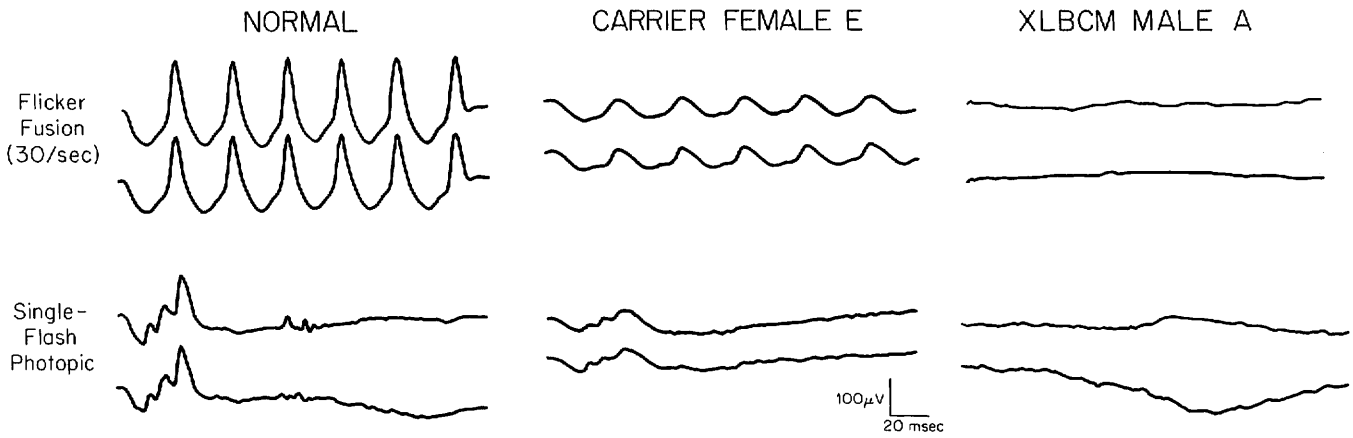

FIG 104–1.
Comparison of photopic and 30-Hz flicker fusion in a normal, a patient with blue cone monochromatism, and an obligate carrier from the pedigree in Figure 104–2. The photopic ERG is nonrecordable by single-flash techniques in the patient, while the carrier has a half-normal response.

able in three of four. In the 2-year-old the flicker fusion study was barely recordable at 10 Hz and nonrecordable at 20 Hz. The cone portion of the red-response dark-adapted ERG was absent in all four (Fig 104–3). The scotopic rod-mediated ERG demonstrated normal amplitudes in all cases, with an average implicit time of 86 ms (normal implicit time, 67 ± 12 ms).

The four carrier mothers had no visual complaints. The visual acuity of the carrier females ranged from 20/20 to 20/30. Three were mildly myopic and the fourth mildly hyperopic. Anterior segment and applanation tensions were normal. Two carriers had irregular foveal pigmentation in both eyes, but no window defect was seen on fluorescein angiography. Eye movement was normal in all four carriers.

On color vision testing with the Farnsworth-Munsell 100-hue test, one carrier had error scores of OD 140, OS 137 with a monopolar deutan axis; another carrier had error scores of OD 113, OS 140 that were scattered without a discernible axis.

The flicker ERG up to 60 Hz was recordable in all four carriers, but diminished amplitudes were evident in three carriers (see Fig 104–1). Diminished photopic b-wave amplitudes were found in the same three carriers. Upon a dim red flash after 30 minutes of dark adaptation, the cone portion of the red response was absent in two carriers and barely detectable in the other two (see Fig 104–3).

The diagnosis of blue cone monochromatism can be made more accurately on a molecular genetic level. Clinically, it is necessary to demonstrate residual blue cone function psychophysically in a patient

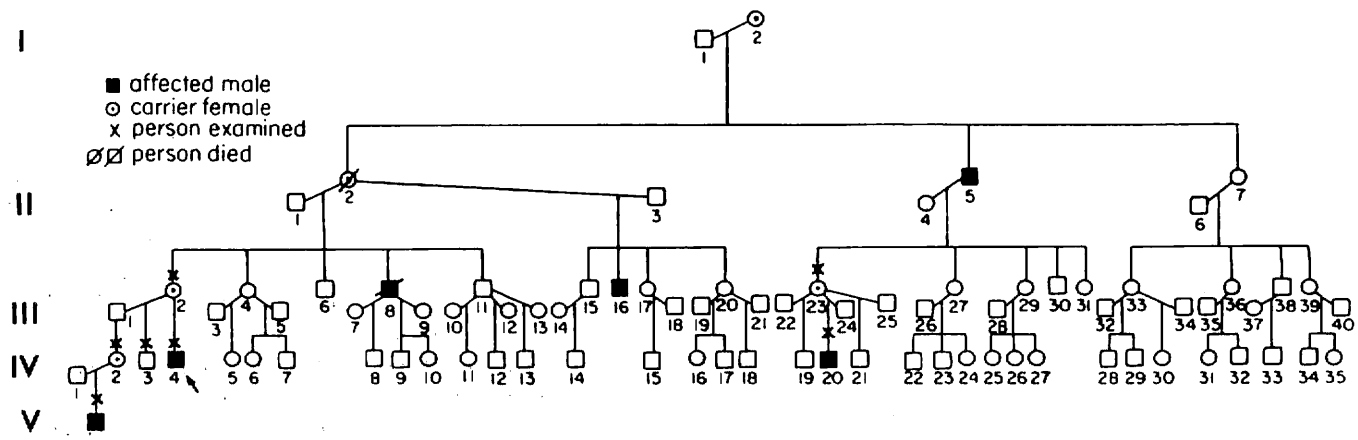

FIG 104–2.
Pedigree of a family with typical X-linked recessive blue cone monochromatism.

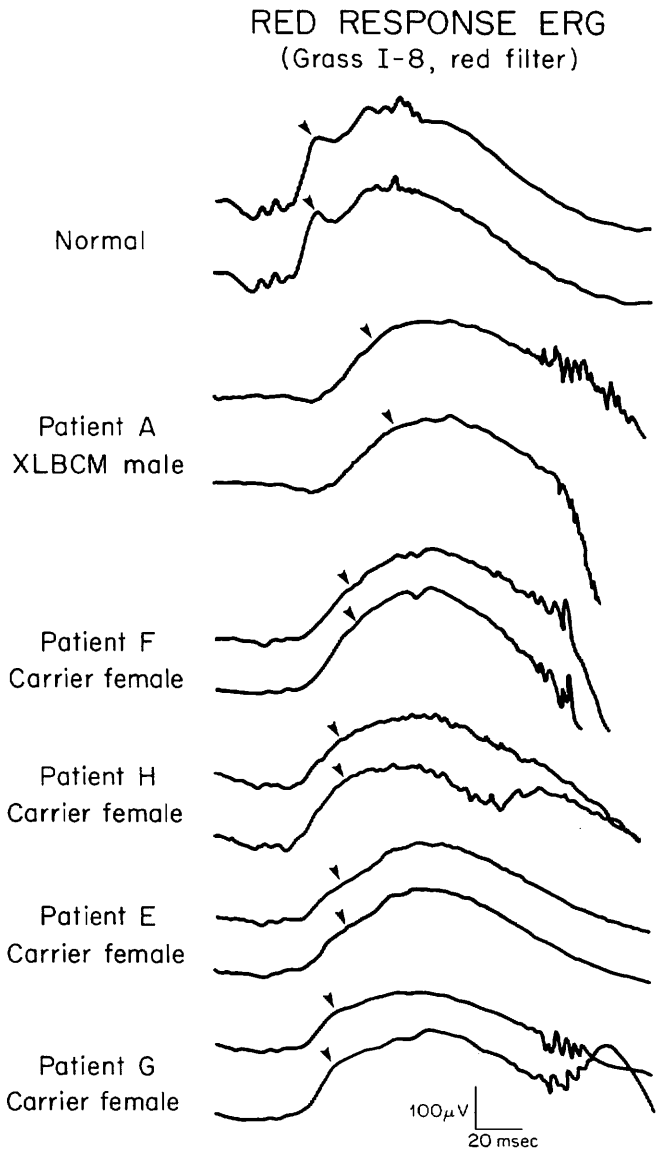

FIG 104–3.
Red response under dark-adapted conditions in a normal, a person with blue cone monochromatism, and obligate carriers. In the five patients after the control, the *arrows* represent the location where the cone portion would normally be present. Two carriers (F. and H.) had no cone portion, while carriers E. and G. exhibited barely recordable cone portions.

with X-linked cone congenital dystrophy. Since sophisticated psychophysical testing is available in few centers, the diagnosis is presumptive without the molecular genetic confirmation.

The management of affected males is dependent on recognizing the X-linked inheritance so that genetic counseling can be performed. Molecular biological testing should be more readily available in the future; this will provide greater accuracy in the diagnosis of X-linked cone dystrophies. It is important to emphasize the relative stationary nature of the disorder because many patients and parents worry about the possibility of blindness. Tinted lenses are advisable for better vision indoors and outdoors.

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