Chapter 20
Cone-Rod Dystrophies

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20.1 Definitions

Cone-rod dystrophy (CRD) is a progressive degenerative disorder predominantly of retinal cones with varying patterns of inheritance.

20.2 Symptoms

Early: Decreased vision, dyschromatopsia, photophobia, and central scotoma
Late: Nyctalopia and progressive loss of peripheral vision

20.3 Signs

- *Early:* Normal-appearing fundus or fine, pigmentary changes (possibly resembling a bull's-eye maculopathy), and abnormal testing (OCT, FAF, ERG) (Fig. 20.1).
- *Late:* Vessel attenuation, waxy pallor of the optic nerve head, pigmentary changes resembling bone spicules in periphery and macula, RPE atrophy, and abnormal testing (ERG) (Fig. 20.2). Rod photoreceptor involvement will frequently occur late in cone dystrophy.

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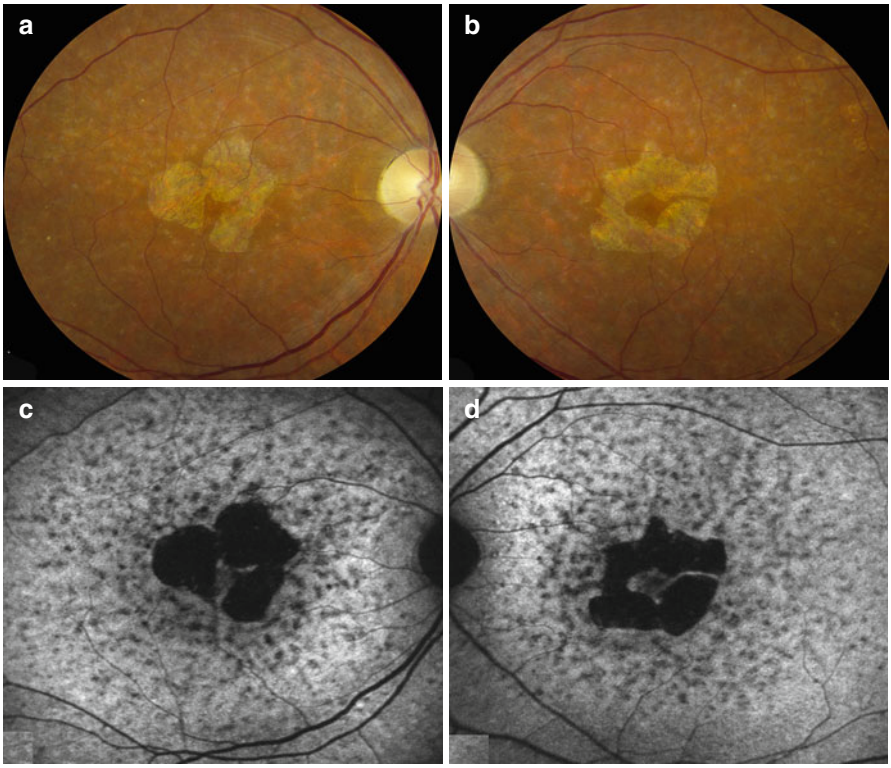

Fig. 20.1 Fundus photos of advanced "bull's-eye" maculopathy with discrete parafoveal RPE atrophy (**a**, right eye; **b**, left eye). Fundus autofluorescence shows a parafoveal ring of increased autofluorescence and central foveolar atrophy (**c**, right eye; **d**, left eye) (Courtesy of Hassan Rahman, MD, Houston, TX)

20.4 Epidemiology

Prevalence 1 in 40,000. One study found the mean age of onset as 12 years and mean age of legal blindness at 35 years. Cone dystrophy has been described in the literature and possibly represents a disease in the spectrum of cone rod dystrophy rather than an isolated disease process.

20.5 Inheritance

- Autosomal dominant, autosomal recessive, or X-linked depending on mutation.
  - Autosomal dominant: GUCY2D (also associated with Leber's congenital amaurosis) and CRX.

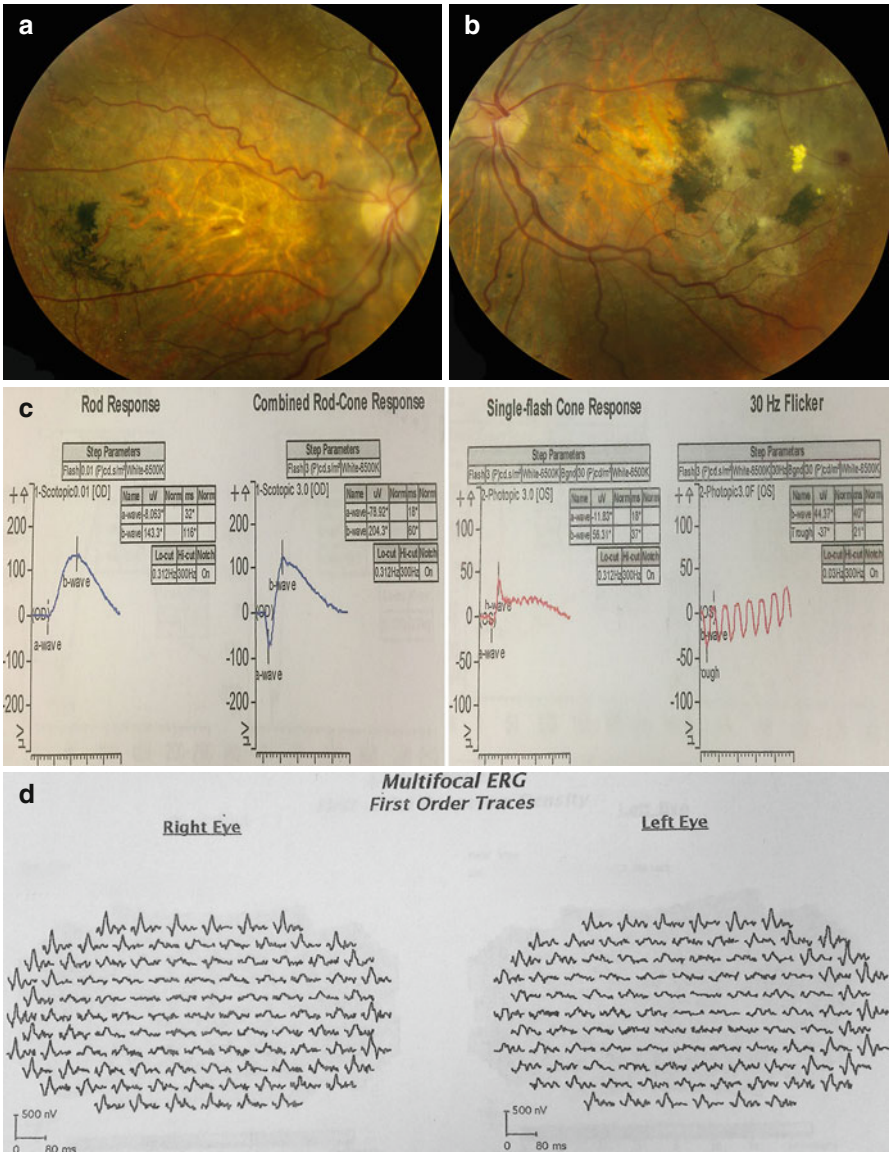

Fig. 20.2 Fundus photos of cone dystrophy (**a**, right eye; **b**, left eye), with a representative ERG demonstrating marked reduced and delay cone response with relatively normal rod response (**c**). Multifocal ERG demonstrated reduced waveform centrally (**d**) (Courtesy of Emmanuel Chang, MD, and Byron Lam, MD, Houston, TX)

  - Autosomal recessive: ABCA4 (associated with Stargardt disease) causes 30–60 % of autosomal recessive disease.
  - X-linked: RPGR (associated with X-linked RP). Also associated with both Bardet-Biedl syndrome and spinocerebellar atrophy type 7.
- Additional information available at the RetNet website.

20.6 Differential Diagnosis

- *Retinitis pigmentosa:* Initial symptom is nyctalopia with normal central vision. ERG with a diminished or abnormal response. Late stages of RP and CRD can appear very similar with flat ERGs. Differentiate by history of initial symptoms.
- *Leber's congenital amaurosis:* Can have reduced function of cones and rods. Poor visual acuity identified at or within a few months of birth, nystagmus, severely reduced ERG, and a pigmentary retinopathy. Delay in progression may be consistent with CRD.
- *Stargardt disease:* Early CRD may share a similar appearance. Peripheral retina typically not involved with Stargardt. Also, whitish-yellow flecks and dark choroid on FA, which are characteristic for Stargardt, are not typical of CRD.
- *Cone dystrophies:* Rods are spared during early and middle stages of the disease process. Present with decreased visual acuity, photophobia, and dyschromatopsia. ERG with decreased cone signal and preserved rod wave. May have rod involvement in later stages.
- *Congenital color blindness:* Normal visual acuity with onset at birth. Normal appearance of the fundus, normal rod function, and no progression.
- *Bull's-eye maculopathy:* If present on exam, then refer to the differential diagnosis of bull's-eye maculopathy in the chloroquine toxicity section.

20.7 Workup/Testing

Obtain a detailed family history. Due to the genetic heterogeneity, genetic testing not routinely done, but commercial tests are being developed to evaluate for some of the more frequently involved genes. Perform a complete ophthalmic exam including evaluation of color vision and dilated fundus examination. Consider obtaining fundus autofluorescence, (FAF) electroretinogram (ERG), and optical coherence tomography (OCT). These may show the following characteristic findings:

- FAF – may help identify RPE disturbances
- ERG – predominantly decreased photopic responses (flicker response, single-flash photopic response) early with development of abnormal rod signals. Severely reduced or flat ERG in late stage
- OCT – abnormalities of outer retinal layers

20.8 Prognosis and Management

Visual prognosis is poor with mean age of legal blindness at 35 years old. Tinted spectacles and miotic drops may help minimize photophobia. Genetic counseling and low vision aids should be prescribed as needed. Consider repeating ERG 1–2 years after initial diagnosis is made.

20.9 Follow-Up

Annually.

References and Suggested Reading

1. Hamel CP. Cone rod dystrophies. Orphanet J Rare Dis. 2007;2:7.
2. Michaelides M, Hardcastle AJ, Hunt DM, Moore AT. Progressive cone and cone-rod dystrophies: phenotypes and underlying molecular genetic basis. Surv Ophthalmol. 2006;51(3):232–58.
3. Thiadens AAHJ, Phan TML, Zekveld-Vroon RC, Leroy BP, Van den Born LI, et al. Clinical course, genetic etiology, and visual outcome in cone and cone-rod dystrophy. Ophthalmology. 2012;119(4):819–26.