Chapter 19
Retinitis Pigmentosa

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19.1 Definitions

Retinitis pigmentosa (RP) is a progressive retinal degenerative disorder with varying patterns of inheritance.

19.2 Symptoms

- *Early*: Nyctalopia and loss of peripheral vision
- *Late*: Decrease in central vision and photophobia

19.3 Signs

- *Early*: Vessel attenuation, vitreous cell, abnormal testing (ERG), and pigmentary deposits resembling bone spicules (perivascular) in the periphery (early-mid stage) (Fig. 19.1).
- *Late*: Waxy optic nerve pallor, RPE atrophy, posterior subcapsular cataract, cystoid macular edema, abnormal testing (ERG absent), and pigment deposition involving the macula.

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C.A. Medina et al. (eds.), *Manual of Retinal Diseases: A Guide to Diagnosis and Management*, DOI 10.1007/978-3-319-20460-4_19

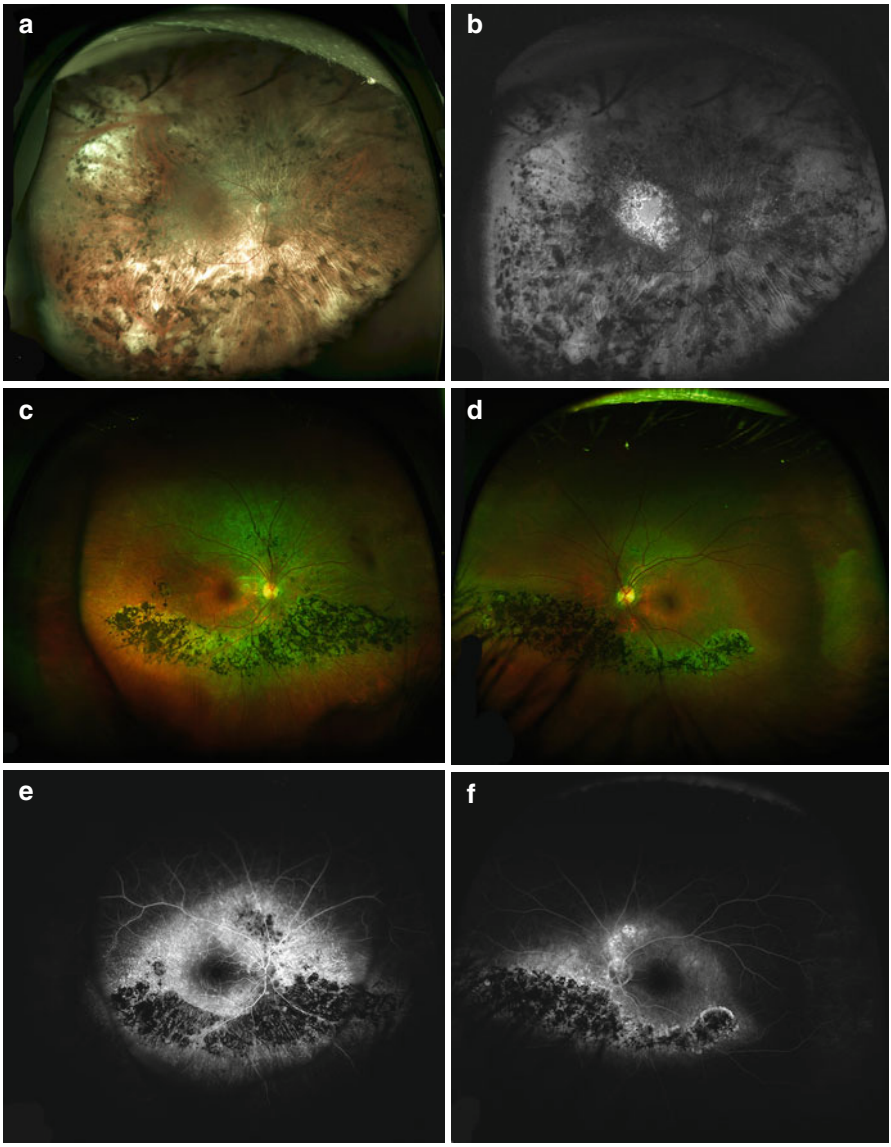

Fig. 19.1 Advance stages of retinitis pigmentosa; the right eye demonstrating RPE atrophy, pigmentary deposits, and waxy optic nerve (**a**). Fundus autofluorescence shows a parafoveal ring of hyperfluorescence with edge corresponding to loss of peripheral retina (**b**). Fundus photo and fluorescein angiogram demonstrate sectoral RP with focal RPE hypertrophy atrophic area extending towards the macular and vascular attenuation (**c**, **e** Right eye, **d**, **f** Left eye) (Courtesy of Hassan Rahman, MD, and Emmanuel Chang, MD, Houston, TX)

19.4 Epidemiology

Prevalence of 1 in 4000 to 1 in 5000 with over 1 million cases worldwide. Age of onset varies from early childhood to middle ages.

19.5 Inheritance

Non-syndromic: Over 50 genes and loci associated with non-syndromic RP (– 65 % of all RP).

- *Autosomal recessive*: 15–20 % of all RP with over 30 genes and loci associated with this form. RPE65 is involved in 2 % recessive RP and 16 % of Leber's congenital amaurosis (human gene replacement trials involving RPE65 underway).
- *Autosomal dominant*: Mildest form characterized by onset in adulthood (20 –25 % of all RP). Mutations in RHO associated with 30 % of AD. Mutant form of rhodopsin is toxic to rods by interfering with metabolism. Over 20 different genes associated with autosomal dominant form.
- *X-linked*: Rarest form of non-syndromic RP with early-onset and severe vision loss (8–15 % of all RP). Female carriers may have fundus pigmentary changes. Associated with myopia. Mutations in RPGR associated with 55–70 % of X-linked and 25 % of sporadic.
- *Digenic*: Heterozygous mutation in ROM1 in combination with a heterozygous mutation in RDS causes RP. Children of affected patients have a 1/4 risk of developing RP.
- *Sporadic.*

Syndromic: 25 % of all RP with over 30 different syndromes identified.

- *Usher syndrome*: Typically, autosomal recessive and mutations in USH2A in 30–50 % of cases (also in 16–20 % AR, non-syndromic RP). At least 11 other genes related to Usher syndrome.
- *Bardet-Biedl syndrome*: Autosomal recessive, 17 genes related to this systemic disease.

19.6 Associated Diseases

- *Usher syndrome*: The most frequent systemic disease with RP (10–20 % of all RP). Prevalence of 1 in 12,000 to 1 in 30,000. Characterized by sensorineural hearing loss. Three different forms: type 1 with profound deafness and ataxia, type 2 with moderate deafness and no ataxia, and type 3 with hearing loss that presents in childhood and progressively worsens.

- *Bardet-Biedl syndrome*: Prevalence is 1 in 150,000. Characterized by obesity, mental retardation, polydactyly, hypogenitalism, mild psychomotor delay, and renal abnormalities. 5 % of all RP.
- *Refsum's disease*: Deficiency of phytanoyl-CoA hydroxylase deficiency. Associated with elevated phytanic acid, deafness, ataxia, anosmia, liver disease, polyneuropathy, and cardiac abnormalities. Treat by restricted intake of milk products, green leafy vegetables, and animal fats (low phytanic acid diet).
- *Abetalipoproteinemia (Bassen-Kornzweig syndrome)*: Deficiency in apolipoprotein B leads to inability to absorb lipids and a deficiency in fat-soluble vitamins (A, D, E, and K). Findings include progressive ataxia, steatorrhea, and growth retardation. Diagnosis is based on lack of apolipoprotein B. Treat with vitamin A, E, and K supplements.
- *Cockayne syndrome*: Associated with dwarfism, mental retardation, deafness, and premature aging.
- *Neuronal ceroid lipofuscinosis (Batten disease)*: Findings include seizures, ataxia, and dementia.
- *Zellweger*: Associated with hepatosplenomegaly, hypotonia, and renal abnormalities.
- *Alstom*: Hearing loss, obesity, renal abnormalities, and hypogenitalism.

19.7 Differential Diagnosis

- *Leber's congenital amaurosis*: Severe visual impairment in infancy or early childhood. Frequently defined as an early form of RP.
- *Congenital stationary night blindness*: Relatively normal visual field and vision, nonprogressive.
- *Vitamin A deficiency*: Associated with keratitis or history of poor nutrition and malabsorption.
- *Congenital infections TORCH*: Pigmentary retinopathy from rubella or syphilis.
- *Kearns-Sayre syndrome*: Mitochondrial disorder associated with salt-and-pepper fundus, chronic progressive external ophthalmoplegia, ptosis, and cardiac conduction defects.
- *Cone-rod dystrophy*: Presenting symptom is decreased central acuity. ERG with a diminished waver form. Late stages of RP and CRD can appear very similar with flat ERGs. Differentiate by history of initial symptoms.
- *Secondary RP*: trauma, previous vascular occlusion, prior retinal detachment, uveitis, infection, metallic intraocular foreign body, or drug toxicity (chloroquine, phenothiazines).
- *Choroideremia*: X-linked disease caused by mutation in the CMH gene. Scalloped RPE atrophy early. Presence of RPE and choriocapillaris only in the macula in late stage.
- *Gyrate atrophy*: Autosomal recessive due to a deficiency in ornithine aminotransferase. Scalloped areas of absent RPE and choriocapillaris.

- *Workup/testing*: Obtain a detailed family history. Dilated fundus exam with above findings. Reduction of a- and b-wave amplitudes on ERG. Both rod and cone-isolated signals are reduced, but scotopic loss predominates. ERG is unrecordable in late stage. Visual field with ring scotoma that progresses to a central island. OCT may aid in diagnosing cystoid macular edema and reveal structural abnormalities in the photoreceptor layer. Unilateral RP is very almost nonexistent (single case confirmed genetically in publication), and acquired etiology should be ruled out. Non-syndromic RP can present in localized forms, which include sectoral RP (only 1–2 quadrants involved bilaterally), central RP (macula involvement early with visual field loss centrally that progresses peripherally), and pericentral RP (ring scotoma around central vision).

19.8 Prognosis and Management

Most patients are legally blind by 40s–50s due to severely constricted visual fields. Tinted glasses may aid with photophobia. Vitamin A therapy (15,000 IU daily) may reduce the rate in loss of ERG amplitude, but liver function should be monitored. Do not prescribe in women planning for pregnancy. Remove cataracts and treat cystoid macular edema with oral or topical carbonic anhydrase inhibitors. Experimental treatments currently being investigated include gene therapy, use of neuroprotective growth factors, tissue transplantation, and retinal prosthesis, promising genetic research involving the replacement of RPE65 gene (associated with autosomal recessive RP and Leber's congenital amaurosis).

- Family counseling and genetic testing. Low vision aids as need.
- Diet low in phytanic acid if Refsum disease. Supplementation with vitamin A, E, and K for abetalipoproteinemia.
- Refer to cardiology if suspicion for Kearns-Sayre syndrome.

19.9 Follow-Up

Annually.

References and Suggested Reading

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