# CHAPTER 18

# Doyne Honeycomb Retinal Dystrophy (Malattia Leventinese, Autosomal Dominant Drusen)

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# General Features

In these conditions, drusen are present in childhood, but patients are asymptomatic, with good vision, until their 40s or 50s. Drusen are seen at the macula, around the edge of the optic nerve and/or nasal to the disc, in a radiating pattern (in particular, temporal to macula, as in Figs. 18.1, 18.2, 18.3, 18.4 and 18.5). The periphery is usually spared. Drusen increase in size and number with age. Peripapillary drusen are a characteristic finding. Visual loss later in life is due to pigment hyperplasia, geographic atrophy, and choroidal neovascular membrane (Figs. 18.6 and 18.7). Variability in the clinical picture is common within families.

Associated findings include hypertrophy of the retinal pigment epithelium (RPE) and irregular subretinal fibrosis. Drusen show areas of increased hyperautofluorescence, but reduced signal may be seen in areas of RPE atrophy. Optical coherence tomography (OCT) may show accumulation of the drusen material at the level of the RPE/choriocapillaris (CC) complex, under the RPE.

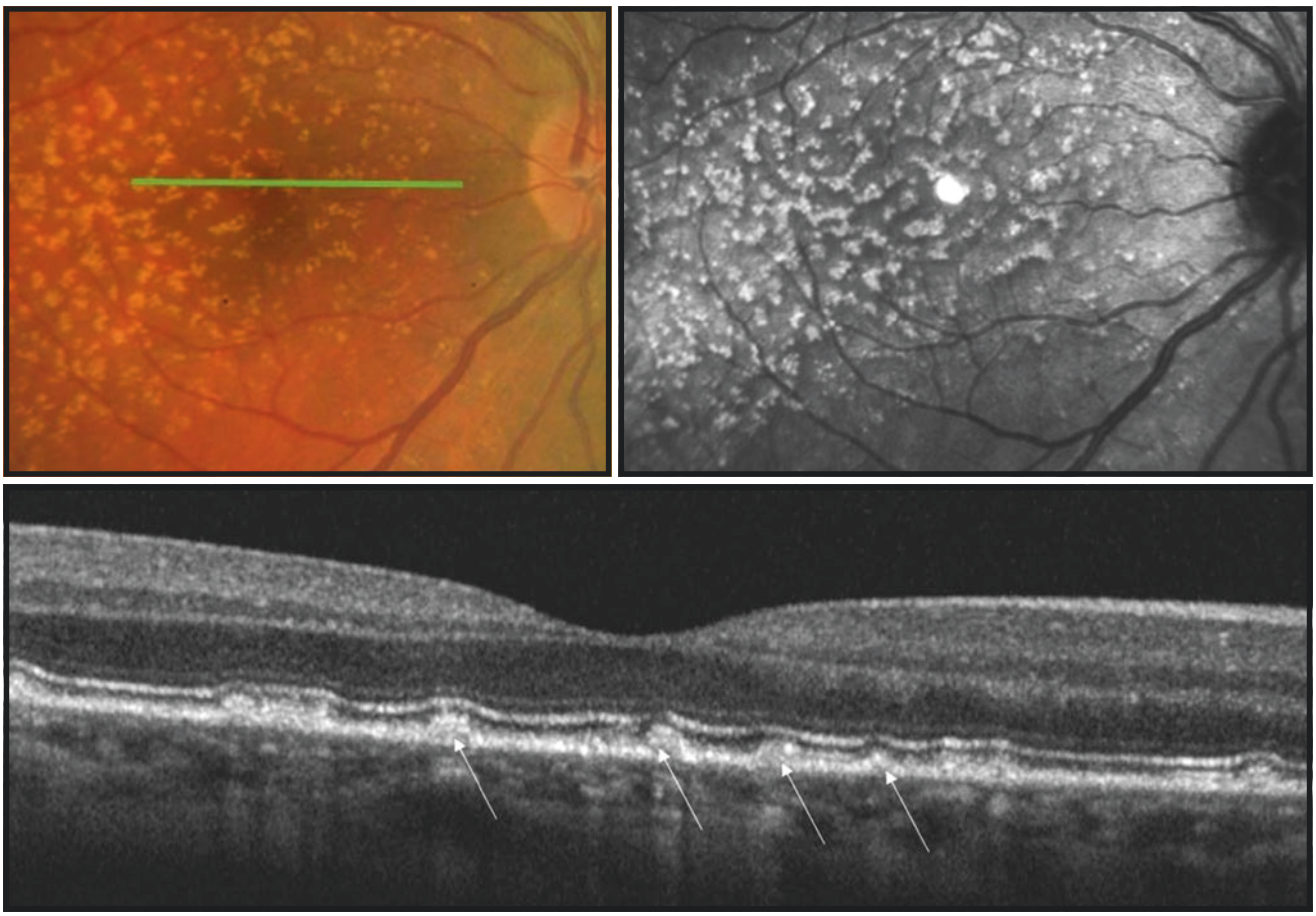

**Fig. 18.1** Radial pattern of autosomal dominant drusen (upper row). Optical coherence tomography (OCT) shows drusen located under the retinal pigment epithelium (RPE) (lower row, *arrows*)

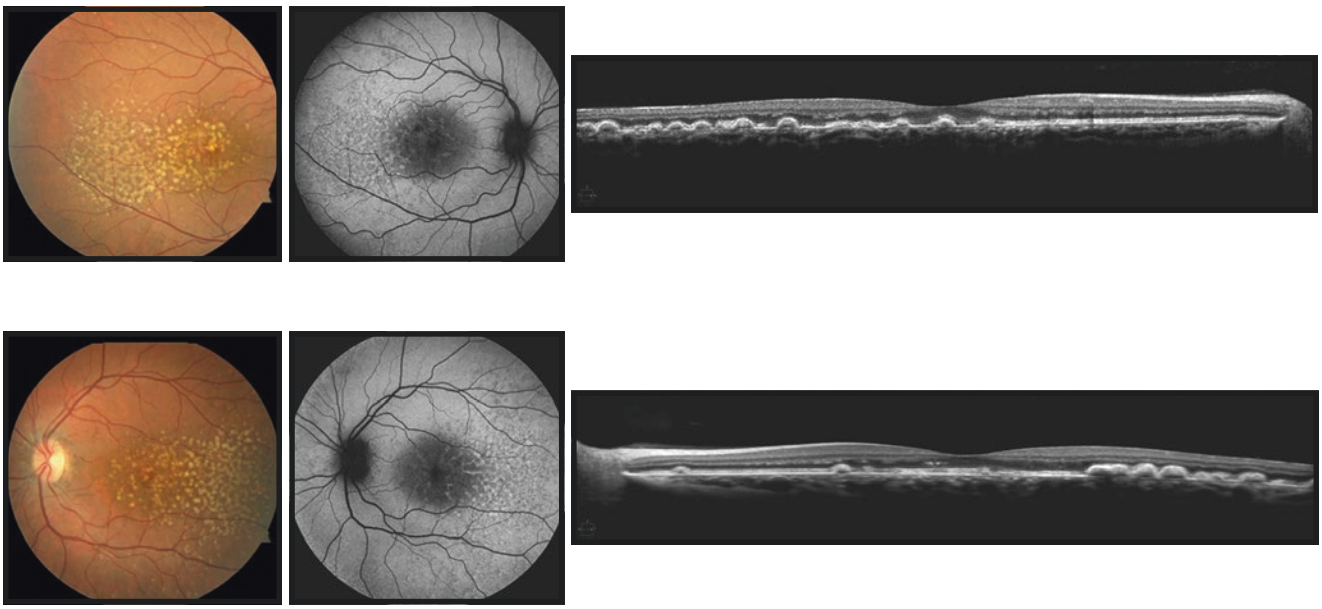

**Fig. 18.2** Multiple drusen (Doyne-like or Pseudo-Doyne) along the horizontal raphe; fundus autofluorescence (FAF) shows good RPE function. OCT shows multiple bumps beneath the RPE

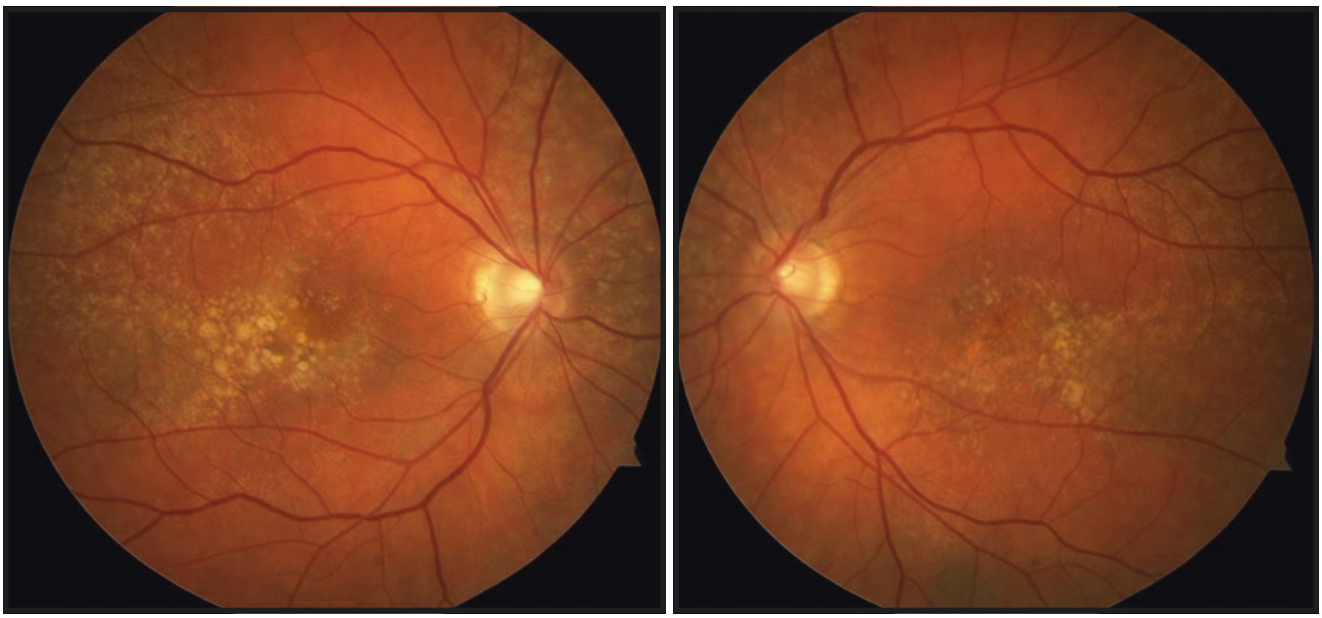

**Fig. 18.3** Drusen at the macula and nasal to the optic disc; some of the drusen show pigmentation and some RPE shows atrophic changes

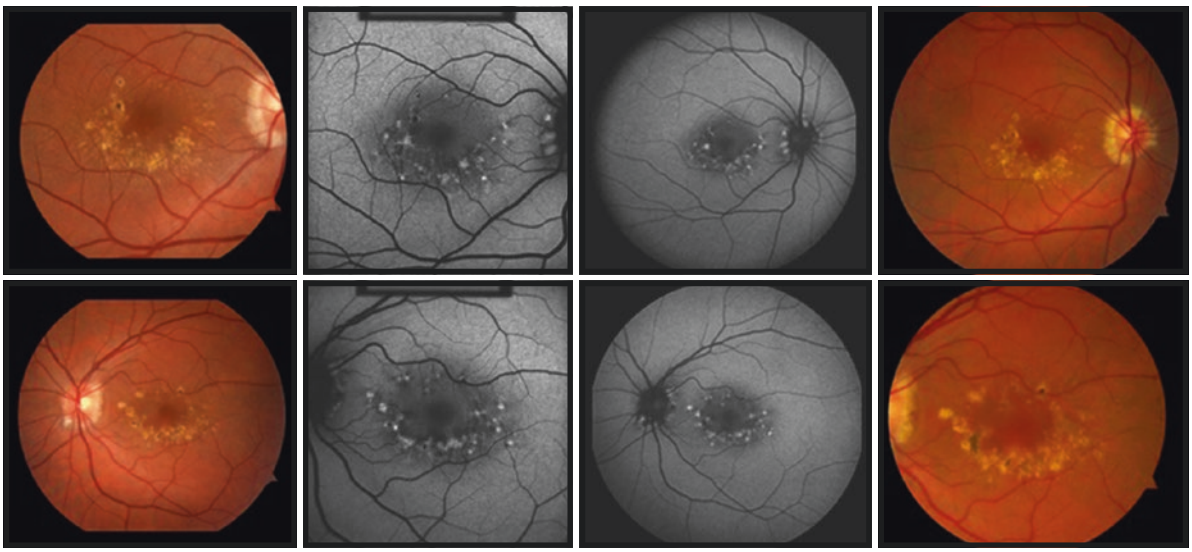

**Fig. 18.4** Drusen at the macula and in the peripapillary area; FAF shows stable RPE function at a 2-year follow-up (p.Arg345Trp)

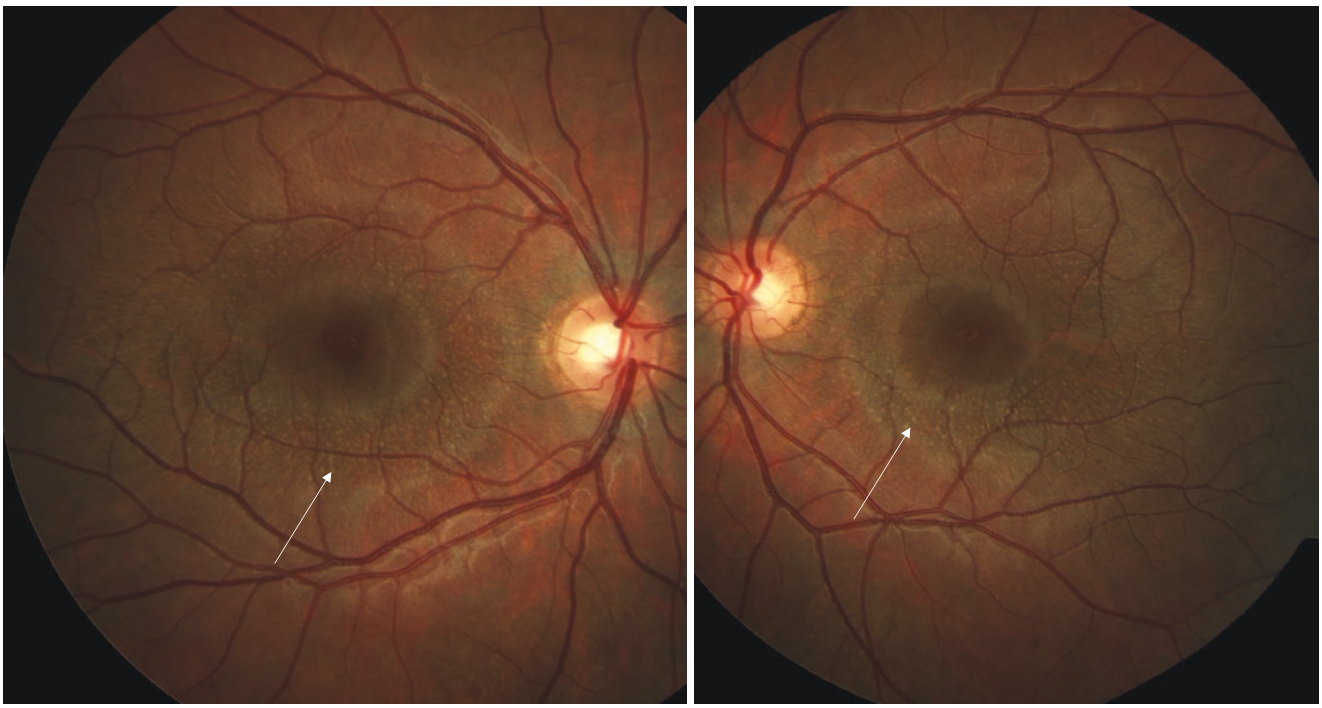

**Fig. 18.5** Bilateral Doyne (*arrows*) almost encircling the fovea, in a young boy (p.Arg345Trp)

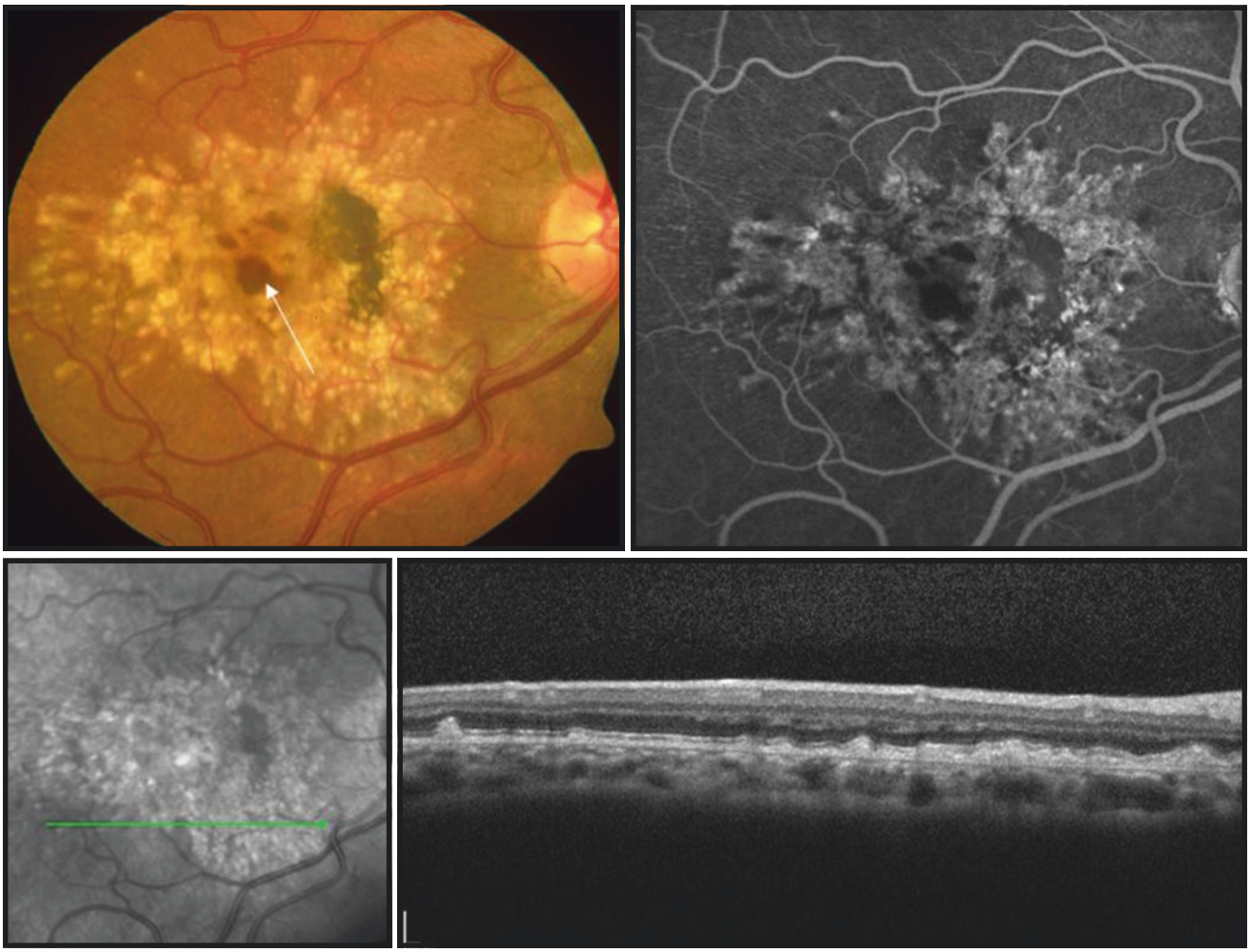

**Fig. 18.6** Confluent drusen and radial pattern are discernible; the presence of hemorrhage (*arrow*) is suggestive of choroidal neovascular membrane (p.Arg345Trp)

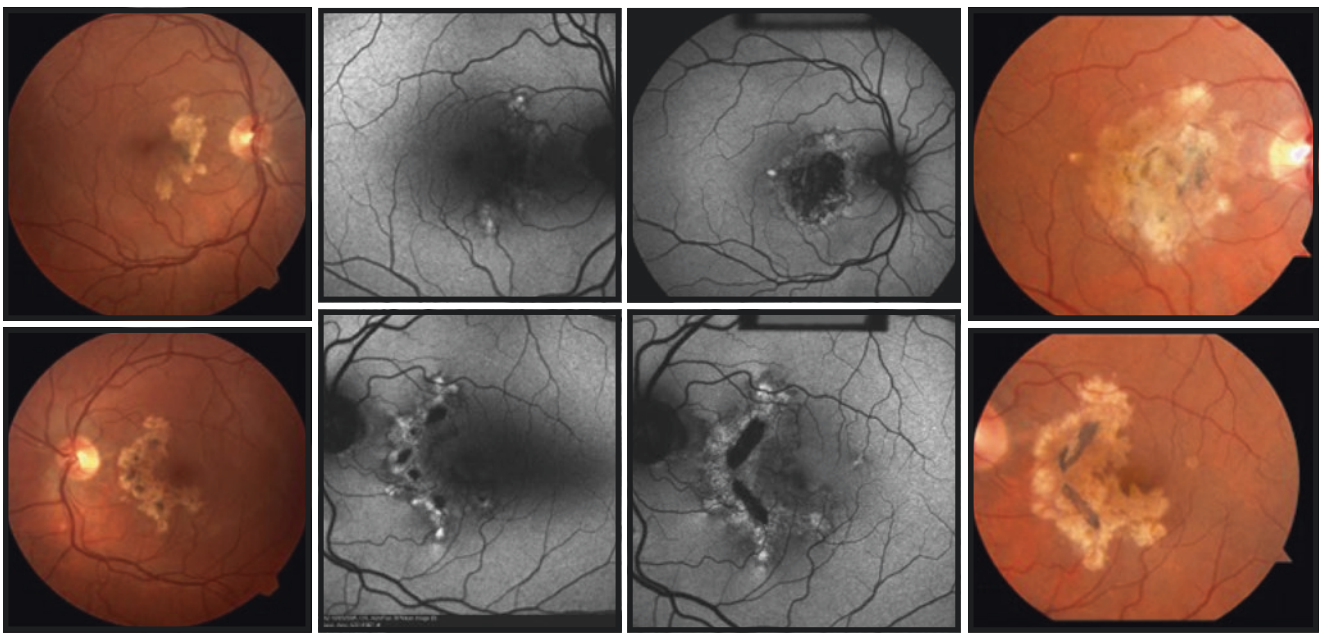

**Fig. 18.7** Ten-year follow-up shows progression of drusen, which are becoming confluent, and FAF shows progressive RPE dysfunction (p.Arg345Trp)

# Molecular Genetics

## *EFEMP1* Gene (*DHRD* or *DRAD* or *FBLN3* or *FIBL-3*)

- This gene is a member of the fibulin family of extracellular matrix glycoprotein.
- A single heterozygous missense mutation (p.Arg345Trp) in the *EFEMP1* (epidermal growth factor [EGF]–containing fibulin-like extracellular matrix protein 1) gene is responsible for this condition.
- Cytogenetic location: 2p16.1

# Suggested Reading

Stone EM, Lotery AJ, Munier FL, Héon E, Piguet B, Guymer RH, et al. A single *EFEMP1* mutation associated with both Malattia Leventinese and Doyne honeycomb retinal dystrophy. Nat Genet. 1999;22:199–202.

Takeuchi T, Hayashi T, Bedell M, Zhang K, Yamada H, Tsuneoka H. A novel haplotype with the R345W mutation in the *EFEMP1* gene associated with autosomal dominant drusen in a Japanese family. Invest Ophthalmol Vis Sci. 2010;51:1643–50.