The Pattern Dystrophies

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Abstract

The pattern dystrophies form a clinically and genetically heterogeneous group of retinal phenotypes including adult-onset foveomacular vitelliform dystrophy (AFVD), butterfly-shaped pigment dystrophy (BPD), reticular dystrophy of the retinal pigment epithelium, pseudo-Stargardt pattern dystrophy (multifocal pattern dystrophy simulating Stargardt disease/fundus flavimaculatus), and fundus pulverulentus. The pattern dystrophies constitute a group of retinal disorders characterized by a variety of deposits of yellow, orange, or gray pigment, predominantly in the macular area. The age at onset in pattern dystrophies is highly variable, but patients tend to remain asymptomatic until the 5th decade or may even remain asymptomatic throughout life. The course of pattern dystrophies is often benign, although severe vision loss occurs in up to 50 % of the affected individuals after the age of 70, as a result of chorioretinal atrophy and/or the development of choroidal neovascularization.

Keywords

Pattern dystrophy • Adult-onset foveomacular vitelliform dystrophy • Butterfly-shaped pigment dystrophy • Reticular dystrophy of the retinal pigment epithelium • Pseudo-Stargardt pattern dystrophy • Fundus pulverulentus

2.1 The Pattern Dystrophies: Introduction

The clinically and genetically heterogeneous group of pattern dystrophies (PD) is characterized broadly by a variety of deposits of yellow, orange, or dark pigment, predominantly in the macular area. The term was originally suggested by Hsieh and colleagues [1] and Marmor and

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colleagues [2]. A wide variety of clinical presentations and patterns has been included in the group of PD, and Gass has classified PD into five major subgroups [3]: adult-onset foveomacular vitelliform dystrophy (AFVD), butterfly-shaped pigment dystrophy (BPD), reticular dystrophy of the retinal pigment epithelium, multifocal pattern dystrophy simulating Stargardt disease/fundus flavimaculatus, and fundus pulverulentus. Yet, Gass and others also noted that additional forms of PD are observed and that even the eyes of the same patient may manifest different forms of PD.

Since Gass description of the classification more than three decades ago, important insights into PD were obtained. Among these insights, which will be discussed in this chapter, were the identification of various genetic defects associated with some of these phenotypes and a more detailed understanding of the lesion composition and their pathogenesis based on multimodal imaging, histological, and laboratory studies.

2.2 Adult-Onset Foveomacular Vitelliform Dystrophy

2.2.1 Background

Adult-onset foveomacular vitelliform dystrophy (AFVD) is the most common form of PD. AFVD was first described by Gass in 1974 and was initially termed "peculiar foveomacular dystrophy" [4], and later adult-onset foveomacular vitelliform dystrophy (AFVD). Following Gass' description, multiple authors have described this phenotype, and multiple terms were utilized to describe the phenotype [5–19]. Among the terms used were adult macular vitelliform degeneration [10], adult vitelliform macular degeneration [8, 11, 17], pseudovitelliform macular degeneration [16], adult-onset foveomacular pigment epithelial dystrophy [18], adult foveomacular vitelliform dystrophy [5, 7], and adult vitelliform macular dystrophy [6, 15]. This conflicting terminology generated confusion in the field and hampered accurate diagnosis and study of the phenotype [15].

While AFVD was initially described as an autosomal-dominant trait, it was later reported that most cases are sporadic. Mutations in *PRPH2*, *BEST1*, and *IMPG1* and *IMPG2* genes were associated with this phenotype [20–23]. Mutations in these genes can cause a spectrum of clinical pictures, including other maculopathies or panretinal dystrophies. Furthermore, most AFVD patients do not carry mutations in the *PRPH2*, *BEST1*, and *IMPG1* and *IMPG2* gene. Sporadic AFVD was associated with an *HTRA1* single nucleotide polymorphism (SNP) which is also associated with age-related macular degeneration [24].

Interestingly, *PRPH2* is expressed in rods and cones, whereas *IMPG1* and *IMPG2* are components of the interphotoreceptor matrix, and *BEST1* is expressed exclusively in the RPE. Since mutations in each of these genes can result in the AFVD phenotype, it is conceivable that altered photoreceptor outer segments, intercellular matrix, or RPE function can each lead to formation of vitelliform lesions which characterize AFVD. Thus, AFVD may be the result of altered RPE-photoreceptor complex function, probably due to defective photoreceptor intake by the RPE leading to the buildup of the subretinal vitelliform material. Currently, there is no treatment for AFVD.

2.2.2 Clinical Findings

Gass, in his original description of nine cases, has suggested that AFVD usually manifests between 30 and 50 years of age and shows bilateral subfoveal vitelliform yellowish deposit at an average size of one-third disc area with a central pigmented spot (Fig. 2.1) [4]. In fact, AFVD often manifest in elderly individuals and the vitelliform lesion is often considerably larger. Vitelliform lesions in AFVD can also demonstrate characteristics and stages such as a pseudohypopyon or a vitelliruptive lesion which can also be seen in Best vitelliform macular dystrophy. In some cases, multifocal vitelliform lesions are present [25]. With time, lesions can show more pigment changes, progressive atrophy and/or choroidal neovascularization with corresponding vision loss. Some older patients may show drusen in

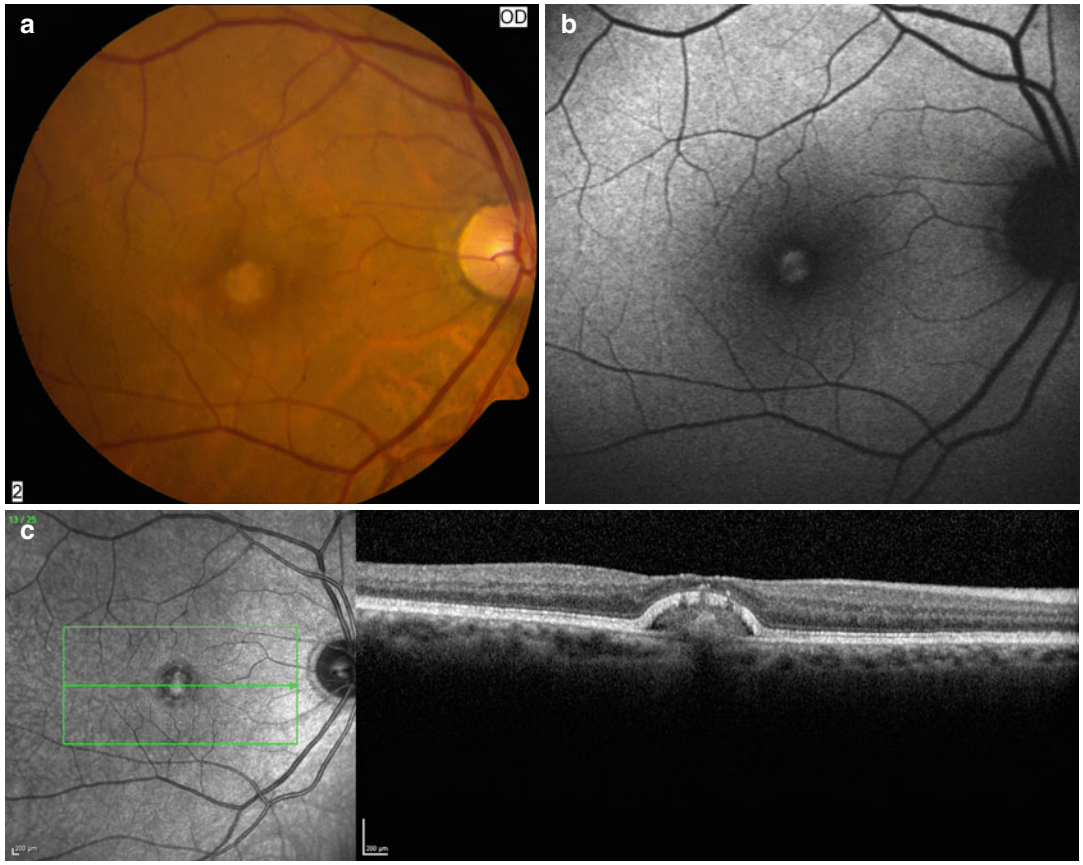

Fig. 2.1 Adult-onset foveomacular vitelliform dystrophy (AFVD). (**a**) Color fundus photograph of a 69-year-old male diagnosed with AFVD. The visual acuity was 0.8 in each eye. Patient was negative for *PRPH2*, *BEST1*, and *IMPG1/2* gene mutations. A vitelliform lesion of approximately one-third disc diameter in size is evident. Few drusen are also seen. (**b**) Fundus autofluorescence shows a hyperautofluorescent signal from the vitelliform lesion. (**c**) Spectral-domain optical coherence tomography (SD-OCT) demonstrates a dome-shape subretinal vitelliform lesion

combination with vitelliform lesions, a phenotype that apparently overlaps with age-related macular degeneration, and may therefore be different from "classical" AVFD with isolated vitelliform lesions without drusen. Data from multiple cohorts suggested that the majority of AFVD cases actually manifest in elderly individuals and that vitelliform lesions are often up to one disc diameter in size. In addition, AFVD is commonly accompanied by RPE atrophy or hyperpigmentation [5–7, 10, 11, 15–18] and by pigment epithelium detachment (PED) [14, 19, 26].

On fluorescein angiography (FA), vitelliform lesions in AFVD show blockage of fluorescence in the early phase of the angiogram, with late staining that can be difficult to distinguish from occult choroidal neovascularization (CNV). Optical coherence tomography (OCT) shows a hyperreflective dome-shape subretinal lesion in the vitelliform stage (see Fig. 2.1). This may be replaced by heterogeneous lesion reflectance in the pseudohypopyon and vitelliruptive stages of the lesion, with photoreceptor and RPE cell loss in the atrophic stage. On fundus autofluorescence (FAF; see Fig. 2.1), the vitelliform material demonstrates hyperautofluorescence, with progressive hypo-autofluorescence with advancing atrophy of the lesion [4, 5, 12, 14, 27]. Electrophysiology and color vision studies are generally normal except for a slightly subnormal electro-oculogram (EOG) in some of the cases of AFVD. Multifocal ERG may show suppressed

central amplitudes, and microperimetry demonstrates reduced sensitivity over the vitelliform lesion which may extend to surrounding seemingly unaffected retina [4, 12, 15, 19, 28].

Histological studies have demonstrated the subretinal location of the vitelliform lesion. The lesion is composed of photoreceptor outer segment remnants, lipofuscin components (corresponding to increased fundus autofluorescence), pigment-containing macrophages, and RPE cells. Outer photoreceptor segment disruption and outer nuclear layer loss are observed over the vitelliform lesion. RPE cells at the base of the lesion are initially hypertrophic and are later hypopigmented at the lesion center and hyperpigmented at its circumference. RPE cell loss occurs at later stage of the disease [4, 29–31].

2.2.3 Disease Course

AFVD may be diagnosed while the patient is asymptomatic or when it is associated with variable visual symptoms including reduced visual acuity or metamorphopsia. Often, the visual acuity is well preserved at diagnosis. Disease progression in AFVD is usually associated with slow visual deterioration which occurs over years [10, 11, 16]. For example, Renner and colleagues evaluated 120 eyes of 61 patients with a mean age of 55 years having a central, yellow, subretinal lesion smaller than one disc diameter in at least one eye. Approximately half of the eyes showed disease progression with vision loss in many cases and other visual symptoms such as metamorphopsia, central scotoma, and visual disturbance [15]. Ten cases had follow-up of longer than 5 years and preserved 20/50 in at least one eye.

Querques et al. described the natural course of AFVD using SD-OCT in 46 eyes of 31 patients with a mean age of 75 years and a mean follow-up of 16 months (range 12–30 months) [14]. The authors classified the lesions based on OCT characteristics into vitelliform, pseudohypopyon, vitelliruptive, and atrophic stages. During follow-up, the mean visual acuity reduced from 0.32 logMAR to 0.39 logMAR. Visual decline was associated with progression of the vitelliform lesion stage and disruption of the ellipsoid zone. Overall, 61 % of the lesions remained vitelliform during the course of the study while 11 % became atrophic during follow-up. Vision loss was also associated with thinning of the outer nuclear layer over the vitelliform lesion, probably reflecting photoreceptor cell loss [9].

AFVD eyes can also develop CNV which by itself can lead to visual loss [10, 18, 26, 32–35]. If CNV develops, anti-vascular endothelial growth factor therapy may be helpful in reducing exudation and limiting the angiogenic process [33, 35]. Yet, the visual outcome is usually limited by the presence of the vitelliform foveal lesion and its progression.

2.2.4 Differential Diagnosis

Vitelliform foveal lesions similar to those observed in AFVD can be seen in several ophthalmic and systemic conditions. Often, AFVD is confused with AMD. Both diseases may develop sporadically in aged individuals. Drusen were described in some AFVD cases and are also the hallmark of AMD, and CNV may develop in both. Both AFVD and AMD also share an *HTRA1* risk SNP. In fact, there is no consensus where the line of distinction between AMD complicated with a vitelliform lesion and AFVD with drusen should be drawn. Some have suggested that AFVD may be a specific phenotype of AMD [10]. Others consider typical AFVD as a phenotype without drusen and would classify cases with adult vitelliform lesions associated with drusen as a form of AMD. Further insights into the pathogenesis of this phenotype are required to resolve this issue.

Vitelliform lesions in Best vitelliform macular dystrophy, an autosomal-dominant condition which is associated with *BEST1* mutations, develop at childhood, and a diagnosis of genetically confirmed Best disease over the age of 40 years is uncommon. Vitelliform foveal lesions can also develop secondary to vitreomacular traction and epiretinal membrane, both of which are readily recognized on OCT. Chronic presence of subfoveal fluid in conditions such as central

serous choroidopathy (CSC) or following retinal detachment repair can also result in lesions with a vitelliform aspect. Systemic conditions associated with vitelliform lesions include pseudoxanthoma elasticum maculopathy [9], mitochondrial retinal dystrophy associated with the m.3243A>G mutation [36], Kearns-Sayre syndrome [37], desferrioxamine-related retinopathy [38, 39], and binimetinib treatment [40]. Vitelliform lesions can also appear as multifocal and acute in acute exudative polymorphous vitelliform maculopathy [41]; this may be a paraneoplastic manifestation of variety of cancers with potential association with anti-RPE antibodies [42–47].

2.2.5 Conclusion

AFVD, the most common form of PD, is associated with mutations in several genes, but most cases are sporadic. AFVD is characterized by vitelliform lesions in the fovea, in association with a usually normal EOG. The disease is diagnosed in adults and generally follows a course of slow visual decline, which may eventually be accelerated because of the development of foveal atrophy or CNV.

2.3 Butterfly-Shaped Pigment Dystrophy

2.3.1 Background

Butterfly-shaped pigment dystrophy (BPD) was first described by Deutman and colleagues [48]. In this autosomal-dominantly inherited macular dystrophy, a spoke-like pigment pattern that may resemble the shape of a butterfly is observed in the macula [49]. Other phenotypes of the pattern dystrophy group that can be caused by *PRPH2* mutations include AFVD and pseudo-Stargardt pattern dystrophy (multifocal pattern dystrophy simulating Stargardt disease/fundus flavimaculatus) [49]. BPD is genetically heterogeneous: besides mutations in the *PRPH2* gene and the *CTNNA1* gene, a locus on 5q21.2–q33.2 is also associated with autosomal-dominant BPD [49–54].

2.3.2 Clinical Findings

Patients can present with mild loss of visual acuity and/or metamorphopsia after the age of 40, but BPD patients are often asymptomatic. Patient with BPD caused by mutations in the *PRPH2* gene has yellowish lesions in the macula at the level of the outer retina and retinal pigment epithelium (RPE) [49]. The lesions have three or more branches that can resemble wings of a butterfly (Fig. 2.2a). The butterfly-shaped lesions can evolve from lesions similar to adult-onset foveomacular vitelliform dystrophy. Some patients with *PRPH2* mutations show a BPD lesion in the macula together with multiple flavimaculatus-like yellow flecks in the posterior pole (Fig. 2.2) [55]. These cases can be regarded as pseudo-Stargardt pattern dystrophy. On fluorescein angiography, the pigmented regions of the lesion are hypofluorescent, whereas surrounding depigmented zones and areas of chorioretinal atrophy are hyperfluorescent (see Fig. 2.2) [49, 56]. On FAF, lesions show variably increased and decreased autofluorescence (see Fig. 2.2) [57]. On optical coherence tomography, the lesions correspond to hyperreflective granular changes at the photoreceptor-RPE interface. The central visual field is normal or shows slightly decreased central sensitivity in cases without profound chorioretinal atrophy. The peripheral visual field is normal. Full-field electroretinography (ERG) is normal, except in cases that advance to extensive pseudo-Stargardt pattern dystrophy [49, 56, 58, 59]. The electrooculogram (EOG) in BPD is normal to slightly subnormal.

2.3.3 Disease Course

Most patients with BPD have a good visual acuity in at least one eye for many decades. The development of choroidal neovascularization is very rare [60]. However, a marked decline in visual acuity can develop after the seventh decade by progressive photoreceptor and RPE atrophy in the macula [32, 61].

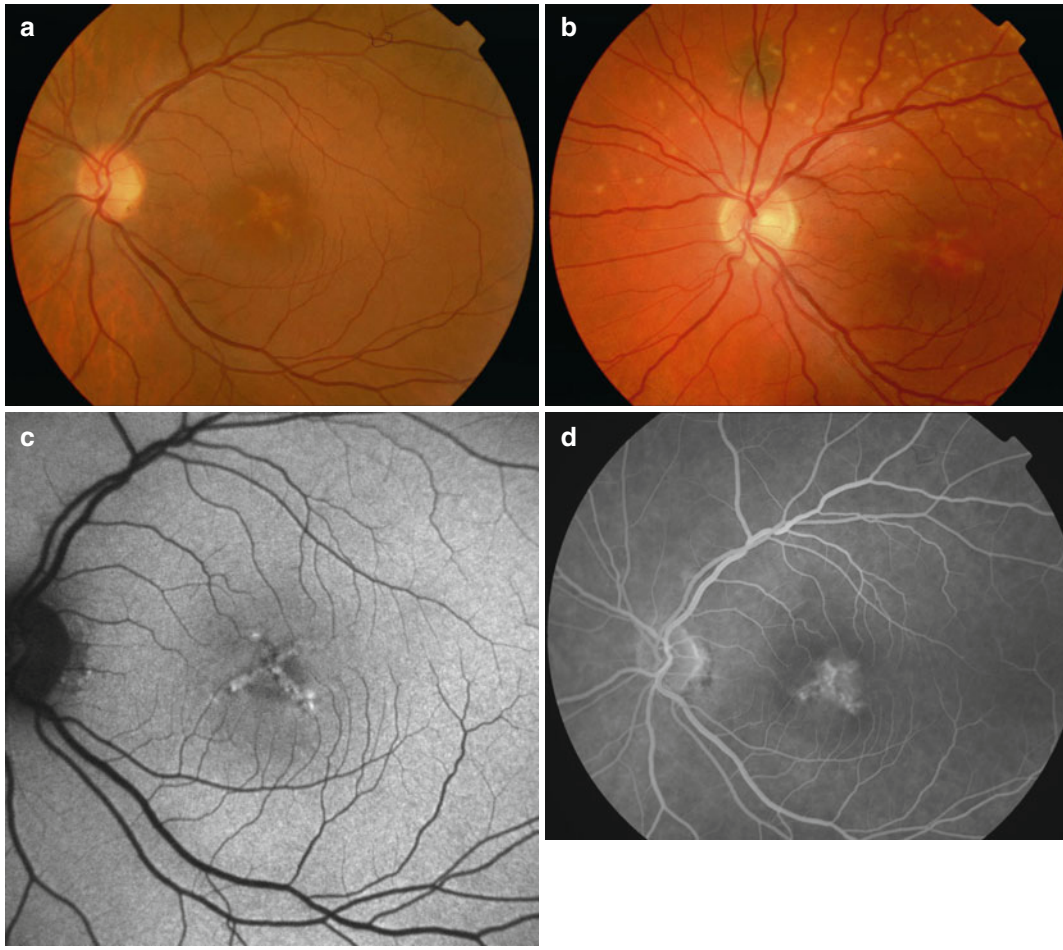

Fig. 2.2 Butterfly-shaped pigment dystrophy (BPD). (**a**) Color fundus photograph of a butterfly-shaped hypopigmented lesion in a 62-year-old patient carrying an autosomal-dominant mutation in the *PRPH2* gene. In some patients with BPD, more darkly pigmented, branching lesions can be seen in the macula, but such cases are usually not associated with *PRPH2* gene mutations. (**b**) Butterfly-shaped lesions can be associated with irregular yellowish flavimaculatus flecks, in association with *PRPH2* mutations, thus showing overlap with pseudo-Stargardt pattern dystrophy. (**c**) Fundus autofluorescence shows relatively marked autofluorescence changes typical of hereditary macular conditions. (**d**) Fluorescein angiography in this case shows hyperfluorescence due to a retinal pigment epithelium (RPE) window defect but can also show blockage in cases of hyperpigmentation at the level of the RPE

2.3.4 Differential Diagnosis

BPD should be differentiated from the other *PRPH2*-associated macular dystrophies, long-standing atrophic RPE detachments, atrophic age-related macular degeneration, and atrophic central serous chorioretinopathy. Pattern dystrophies can also be observed in association with maternally inherited diabetes and deafness (mitochondrial retinal dystrophy; see Chap. 8), myotonic dystrophy, pseudoxanthoma elasticum, and Crohn's disease.

2.3.5 Conclusion

BPD is an autosomal-dominantly inherited macular dystrophy at the mild end of the clinical

spectrum of dystrophies. However, central vision loss can still become more pronounced in the elderly population due to progressive atrophy and/or neovascularization.

2.4 Pseudo-Stargardt Pattern Dystrophy (Multifocal Pattern Dystrophy Simulating Stargardt Disease/Fundus Flavimaculatus)

2.4.1 Background

The human *PRPH2* gene causes a broad spectrum of retinal dystrophies, ranging from purely macular phenotypes to retinitis pigmentosa [49]. The PRPH2 protein localizes to the rim region of rod and cone outer segment discs and lamellae and plays an important role in photoreceptor outer segment morphogenesis [49]. *PRPH2*-associated phenotypes are inherited autosomal dominantly with the exception of digenic retinitis pigmentosa, which also requires a mutation in the *ROM1* gene.

Identical *PRPH2* mutations are associated with decreased penetrance and variable expression, which can result in a markedly variable spectrum of clinical pictures even in families carrying the same mutation [55]. A *PRPH2*-associated dystrophy that appears purely macular at first may eventually evolve into a clinical picture with widespread retinal involvement. The pseudo-Stargardt pattern dystrophy phenotype, as the name coined by Boon et al. [62] indicates, can closely mimic autosomal recessive Stargardt disease (*STGD1*). Up to 20 % of patients with presumed autosomal recessive Stargardt disease of the fundus flavimaculatus subtype, in whom no *ABCA4* gene mutation is found, actually carry an autosomal-dominant *PRPH2* mutation. This finding underscores the importance of genetic testing, as such findings greatly influence the visual prognosis, genetic counseling, and possible future therapeutic perspectives.

2.4.2 Clinical Findings

Most pseudo-Stargardt pattern dystrophy patients start to notice vision loss in their fifth decade, but some patients can remain asymptomatic [55]. Initial symptoms can include metamorphopsia, central vision loss, and/or scotoma. There are varying degrees of night blindness in up to half of the patients, generally with more advanced disease. On funduscopy, patients show irregular yellowish flecks in the posterior pole (Fig. 2.3), and these flecks closely resemble flavimaculatus flecks that can be seen in Stargardt disease. The flecks can gradually become confluent to form a mildly atrophic oval zone that encircles the macula and optic disc (see Fig. 2.3). The aspect of macular lesions in pseudo-Stargardt pattern dystrophy is variable: some lesions consist of a few clustered yellowish or slightly pigmented spots or have the aspect of butterfly-shaped pigment dystrophy [55]. In other cases, macular lesions can show large confluent and irregular flecks or spots.

On fluorescein angiography, the Stargardt-like flecks and the macular lesions are hyperfluorescent, sometimes with a central hypofluorescent spot (see Fig. 2.3). In contrast to most cases of Stargardt disease, there is no blockage of choroidal background fluorescence ("dark choroid"). On FAF, the Stargardt-like flecks are initially highly increased autofluorescent (see Fig. 2.3). The flecks are often bordered by small zones of decreased autofluorescence. When these flecks merge, the resulting oval zone is visible as a band of generally increased autofluorescence with granular zones of decreased autofluorescence (see Fig. 2.3) [55]. The macular lesions correspond to various patterns of increased and decreased autofluorescence. OCT shows that the Stargardt-like flecks and macular lesions correspond to abnormalities on the photoreceptor outer segment-RPE level (Fig. 2.3).

The full-field ERG is normal in early pseudo-Stargardt pattern dystrophy, when the Stargardt-like flecks are still well defined and principally located in the posterior pole. With disease progression, full-field ERG can reveal generalized cone and/or rod dysfunction [55]. In

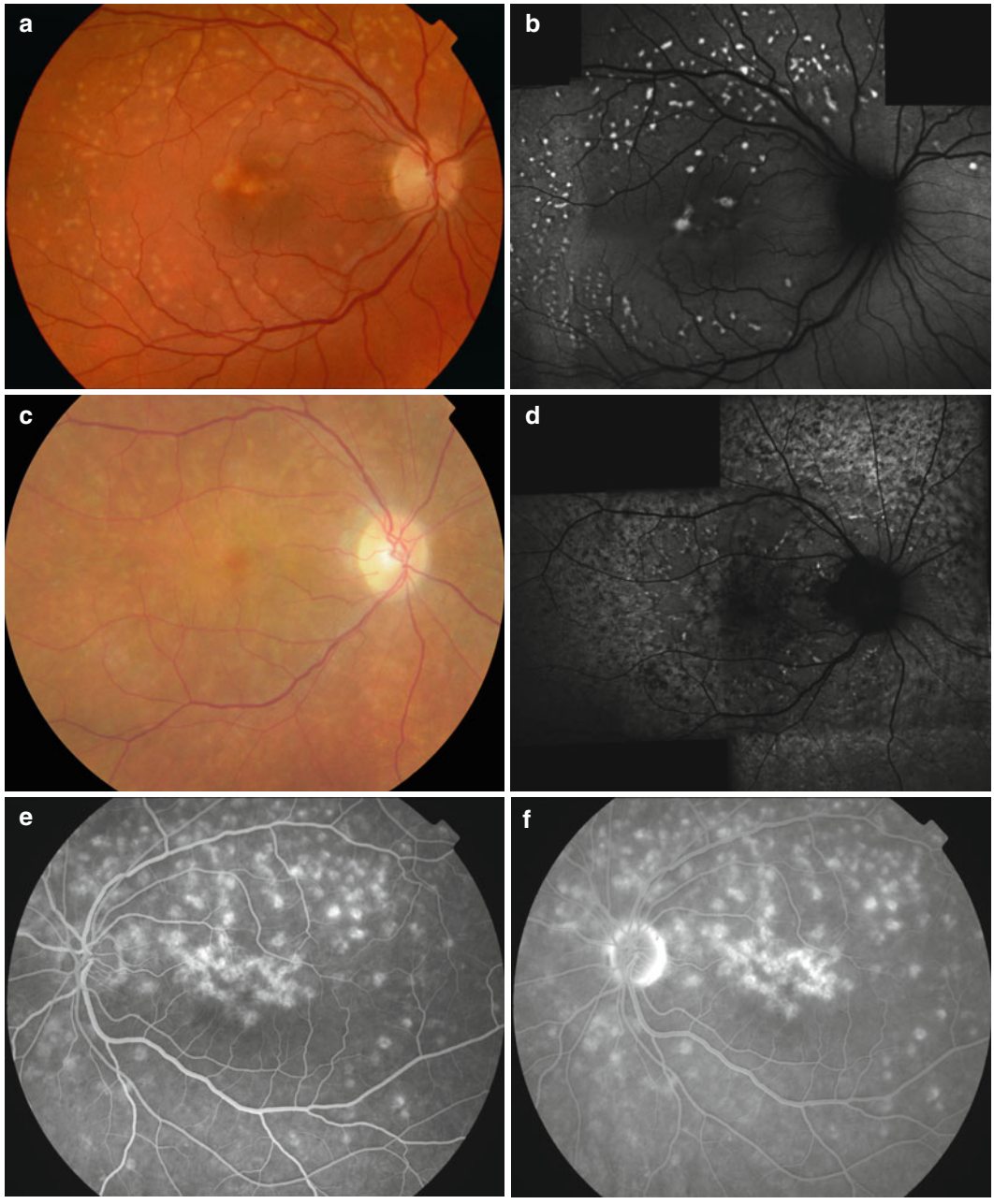

Fig. 2.3 Pseudo-Stargardt pattern dystrophy. (**a**) Color fundus photography of typical pseudo-Stargardt pattern dystrophy (caused by autosomal-dominantly inherited mutations in the *PRPH2* gene) with Stargardt-like flavimaculatus flecks in combination with multifocal pigmentary changes in the macula. (**b**) These lesions are typically markedly hyperautofluorescent in the earlier stages of the disease. (**c**) With advancing disease, lesions in the macula and flecks around the arcade become confluent and mildly atrophic, which is also reflected on fundus autofluorescence (FA) (**d**). Still, visual acuity at this stage, which is reached beyond the age of 45–50, can be fairly good (>20/30). On fluorescein angiography, lesions are hyperfluorescent in the early (**e**) and late (**f**) phase, compatible with mild retinal pigment epithelium (RPE) atrophy and possibly some late staining. Unlike in many Stargardt disease cases, the angiogram in pseudo-Stargardt pattern dystrophy does not show marked masking of choroidal background fluorescence ("dark choroid"). (**g**) Spectral-domain optical coherence tomography in pseudo-Stargardt pattern dystrophy shows irregularities at the outer photoreceptor-RPE level. (**h**) In some elderly patients, the disease can eventually progress to profound chorioretinal atrophy of the posterior pole, which is clearly reflected on FAF as black areas corresponding to RPE atrophy (**i**)

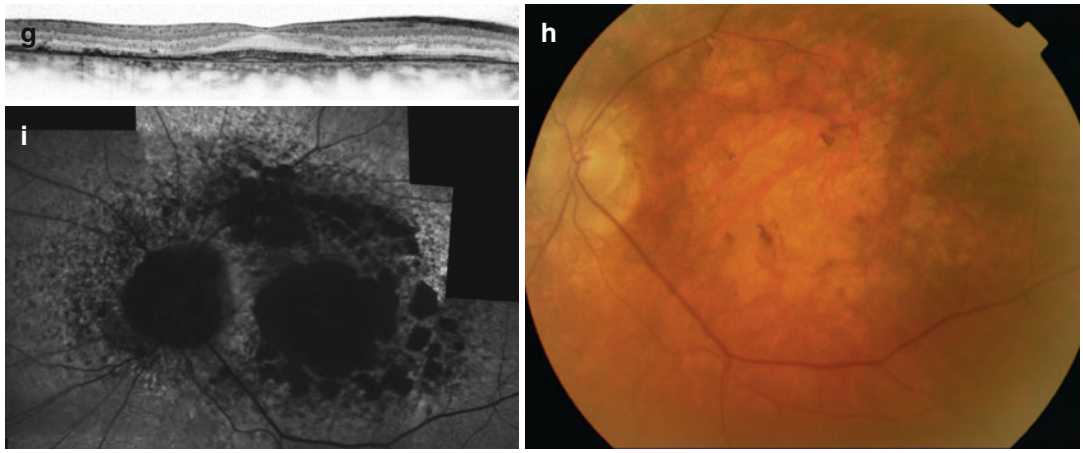

Fig. 2.3 (continued)

advanced cases, the photopic and scotopic full-field ERG responses become severely abnormal to non-recordable. These ERG findings indicate that pseudo-Stargardt pattern dystrophy can evolve from a dystrophy that initially appears localized to the macula—both functionally and anatomically—to widespread panretinal photoreceptor dystrophy. The EOG results vary widely but may show a subnormal to absent light rise in more than half of advanced cases [55].

2.4.3 Disease Course

In advancing disease, the retinal abnormalities extend beyond the posterior pole and do not tend to spare the peripapillary retina in contrast to Stargardt disease (see Fig. 2.3). Profound macular atrophy and marked vision loss (to as low as finger counting) generally do not develop before the age of 55. In advanced disease, patients may also show slight retinal arteriolar attenuation, perivascular and retinal hyperpigmented clumping, and temporal pallor of the optic disc [55].

2.4.4 Differential Diagnosis

In contrast to typical Stargardt disease, see Chap. 3, pseudo-Stargardt pattern dystrophy has an autosomal-dominant pattern of inheritance, a relatively late age at onset, a comparatively good visual acuity, and no dark choroid on fluorescein angiography. Other differential diagnostic entities that should be considered include autosomal-dominant Stargardt-like dystrophies such as STGD3 (caused by mutations in the *ELOVL4* gene), STGD4, and pattern dystrophy associated with maternally inherited diabetes and deafness (m.3243A>G mitochondrial retinal dystrophy, see Chap. 8).

2.4.5 Conclusion

Pseudo-Stargardt pattern dystrophy is a progressive autosomal-dominant retinal dystrophy caused by mutations in the *PRPH2* gene. This phenotype is characterized by multifocal irregular yellowish flecks in the posterior pole and should be differentiated mainly from autosomal recessive Stargardt disease.

2.5 Reticular Pattern Dystrophy

2.5.1 Background

In 1950, Sjögren described a new form of retinal degenerations which he termed "dystrophia reticularis laminae pigmentosae retinae" [63]. The phenotype was later termed reticular dystrophy and was classified as one of the pattern dystrophies

[2, 3]. Autosomal-dominant and autosomal recessive inheritance patterns have been described in association with this phenotype.

2.5.2 Clinical Findings

In reticular pattern dystrophy, a network of (hyper) pigmentary abnormalities extends to the periphery of the macula in forms resembling a chicken wire or fishnet with knots. The patterns are more readily detected on fluorescein angiography, on which a network of hypofluorescent patterns surrounded by hyperfluorescent lines is evident.

OCT may demonstrate small RPE elevations in over half of patients. An altered ellipsoid zone and outer limiting membrane (OLM) are also observed in approximately half of the eyes. The subretinal material appears densely hyperreflective in most eyes, while some may show hypo-reflective areas [64, 65]. Electrophysiology including ERG and EOG testing and psychophysical tests such as color vision and dark adaptation may be unaffected or impaired [66]. A mild, relatively common, asymptomatic, and relatively stable form of reticular hyperpigmentation in the (mid)peripheral retina can also be seen in elderly patients. Thus far, this variant of reticular retinal changes has not been associated with any genetic abnormalities.

Ocular features which may be associated with reticular dystrophy include spherophakia with myopia and luxated lenses, partial atrophy of the iris, scleral staphyloma, convergent strabismus, and choroidal neovascularization [63, 67]. Deafmutism and choreatiform behavior was also described in association with reticular dystrophy in the original description of Sjögren [63].

2.5.3 Disease Course

The pigmentary changes often first appear in proximity to the fovea center; they later extend to the macula periphery manifesting an oval pattern which may encompass the entire posterior pole. The hyperpigmented areas gradually fade, leaving corresponding areas of RPE atrophy.

2.5.4 Differential Diagnosis

The differential diagnosis of reticular pattern dystrophy mainly includes maculopathies with RPE pigmentation and atrophy involving deposition of subretinal material. The combination of ophthalmoscopy, fluorescein angiography, OCT, and genetic tests can readily distinct reticular dystrophy from Stargardt disease, Best vitelliform macular dystrophy, other pattern dystrophies, and dominant drusen.

2.5.5 Conclusions

Reticular dystrophy is an uncommon form of pattern dystrophy. Lesion location between the RPE and photoreceptors is similar to other pattern dystrophies. Yet, material deposition images in OCT are more similar to the ones observed in fundus flavimaculatus than the ones seen in adult-onset foveomacular vitelliform dystrophy [64]. Eventually, vision loss may occur secondary to the development of choroidal neovascularization and macular atrophy.

2.6 Fundus Pulverulentus (Coarse Pigment Mottling of the Macula)

2.6.1 Background

Fundus pulverulentus is an uncommon macular phenotype that was first described by Slezak and Hommer in 1969 [68]. It was later suggested to group with other RPE dystrophies [69]. An autosomal-dominant inheritance pattern may be present [68, 69], but affected family members may also manifest other forms of PD [70, 71]. Association with *PRPH2* gene mutation has also been described [71].

2.6.2 Clinical Findings

Gass has described the phenotype rather aspecifically as a coarse mottling of the RPE in the macula

area [3]. The visual field, color vision, full-field ERG, and dark adaptation are normal, but the EOG can in some cases be subnormal [70].

2.6.3 Disease Course

Little is known on the disease progression of this subtype of PD, but mild visual loss has been described. Fundus pulverulentus can also be associated with the development of CNV [72].

2.6.4 Differential Diagnosis

This phenotype shows similarities to the other forms of PDs. It was also associated with pseudoxanthoma elasticum where progression from fundus pulverulentus to BPD was reported [73]. Mitochondrial retinal dystrophy (maternally inherited diabetes and deafness and MELAS syndrome) [36] and toxic maculopathies such as desferrioxamine retinopathy can have a similar phenotype [74].

2.6.5 Conclusions

Fundus pulverulentus is an uncommon and nonspecific form of PD that can be seen in association with pseudoxanthoma elasticum. The disease is more a description of an atypical macular pigmentation pattern rather than an isolated clinical entity.

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