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Chapter

New OCT and OCTA Insights in Inherited Retinal Dystrophies

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Abstract

Optical coherence tomography (OCT) and OCT angiography (OCTA) radically changed the diagnostics of inherited retinal dystrophies (IRD), providing new information regarding the microstructural changes occurring in each disease. The introduction of quantitative metrics provided even more steps forward in the understanding of IRD pathogenesis and course, allowing to propose new ways to categorize different subgroups of patients, characterized by remarkably different characteristics and prognosis. All these informations provided insights regarding how heterogeneous the clinical spectrum of IRD is. In the present study, we provide an updated description of OCT and OCTA findings in the main IRD, including retinitis pigmentosa, Stargardt disease, and Best vitelliform macular dystrophy. Moreover, we discuss imaging findings in pigmented paravenous retinochoroidal atrophy, a rare condition that is undergoing even growing scientific and clinical interest. In addition, we provided a brief updated scenario on imaging findings in pattern dystrophies. We discuss in detail the current state-of-the-art and the new insights provided by quantitative OCT and OCTA approaches, offering a complete description that might be helpful both for expert and nonexpert researchers interested in IRD.

Keywords: OCT, OCTA, IRD, STGD, RP, BVMD, PPCRA, pattern dystrophy

1. Introduction

Inherited retinal dystrophies (IRD) represent a group of extremely heterogeneous retinal disorders. In recent years, several steps forward in the understanding of IRD pathogeneses and clinical courses have been provided by the use of quantitative multimodal retinal imaging, namely a set of noninvasive diagnostic techniques allowing to reach a very high, histology-like level of details. The main multimodal retinal imaging technologies are based on fundus autofluorescence (FAF), optical coherence tomography (OCT), and OCT angiography (OCTA), although many other ancillary techniques are even more employed both in research and clinical contexts [1]. The combined use of these imaging modalities allows to obtain highly detailed information regarding the morphological and biochemical properties of retinal diseases.

The even larger use of multimodal retinal imaging provided undoubted advantages in retinal diagnostics, and IRD highly benefitted from this, watching the increasing interest of research groups and companies in developing new treatment strategies [2]. From this point of view, the next years will provide meaningful changes regarding the management of IRD, providing new potential treatments and changing the clinical course of these genetically determined retinal diseases. These are the reason why ophthalmologists and retinal specialists should be more focused on reaching a good level of knowledge regarding IRD imaging findings, especially looking at OCT and OCTA ones. The main goal of this chapter is to provide an updated and complete scenario regarding OCT and OCTA characteristics of the most common IRD, namely retinitis pigmentosa (RP), Stargardt disease (STGD), and Best vitelliform macular dystrophy (BVMD). In addition, we dedicated a section to pigmented paravenous retinochoroidal atrophy (PPCRA), a rare retinal disorder characterized by still unknown pathogenesis, which is currently an object of very high research interest. A brief description regarding the current literature findings in pattern dystrophies is also provided.

2. Retinitis pigmentosa

RP is the most common IRD form, characterized by very high genotypical and phenotypical heterogeneity [3]. RP is a progressive, centripetal disease characterized by primary damage of rod photoreceptors followed by cone photoreceptors involvement in later stages [3]. The clinical presentation is mainly characterized by night blindness and peripheral visual field alterations; central vision impairment occurs in more advanced stages of the disease. The classic fundoscopic triad is made by optic disc pallor, attenuated retinal vessels, and "bone-spicule" peripheral retinal pigment deposits. A complete noninvasive multimodal retinal imaging RP case is shown in **Figure 1**.

FAF examination is characterized by peripheral diffuse hypoautofluorescence. The central retina is surrounded by the typical Robson-Holder hyperautofluorescence ring, interpreted as RPE reactive phenomenon correlating with the integrity of the outer retinal bands and the progression of the disease [4, 5]. The central retina may be characterized by different amount of FAF alterations, depending on the status of the outer retina and the occurrence of macular edema. FAF deterioration was found strictly related with the electrophysiology evidence of retinal functional decline [4].

OCT provided undoubtedly advantages in detecting the changes occurring at the level both of inner and outer retinal layers. It offers the most detailed representation of the status of outer retinal bands, correlating with visual acuity, retinal sensitivity, and RP progression [6]. In particular, the status of an external limiting membrane (ELM), ellipsoid zone (EZ), outer nuclear layer (ONL), and outer hyperreflective bands ruled the central vision and peripheral visual field [7, 8]. Electrophysiology investigations also highlighted a relationship between the integrity and thickness of inner retinal layers and the functionality of the central retina [9]. Many times, myopia-related alterations coexist with typical signs of retinal degeneration related to RP [10]. In advanced stages, outer retinal tubulations (ORT) can be identified on structural OCT [10]. ORT is defined as round outer retinal structures with hyperreflective borders surrounding a mixed reflectivity core, usually located at the borders of, or centrally within, regions of outer retinal atrophy [11]. ORT formation is made by the gradual remodeling and invagination of the ELM-photoreceptors complex and is commonly interpreted as a degenerative sign. Although RP is mainly considered an outer retinal disorder, even growing evidence are suggesting a major involvement
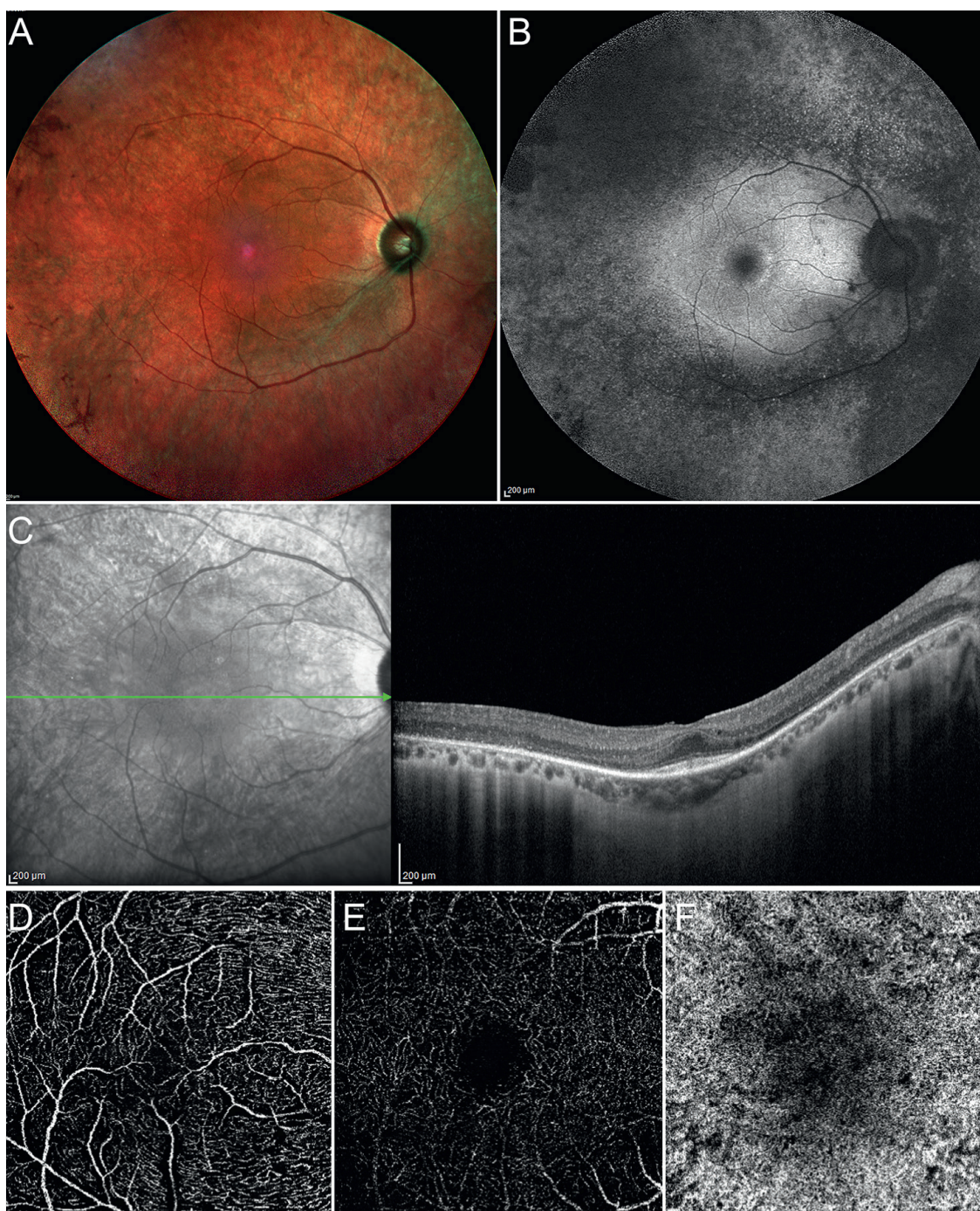
Figure 1.
Multimodal retinal imaging in RP. Confocal multicolor image (A) shows changes in the peripheral pigment with some bone spicule, attenuated retinal vasculature, and central pigment rarefaction. FAF image (B) shows extensive peripheral hypoautofluorescent signal, the perifoveal hyperautofluorescent Robson-Holder ring, and the preserved central physiological hypoautofluorescence. Structural OCT (C) shows the disappearance of the peripheral outer retinal bands, with preservation limited to the foveal region. Moreover, OCT shows myopic signs, such as the increased curvature of the eye and thin choroid. OCTA shows preserved SCP (D), markedly altered DCP (E) with some projections artifacts, and increased CC flow voids (F).

also of the inner retina [12]. Previous studies showed either thickening or thinning of inner retinal layers, and no consensus has been reached regarding the precise inner retinal changes occurring in RP yet [10, 12, 13]. It is likely to hypothesize that inner retinal involvement may vary as different phenotypic profiles of different RP subgroups. On the other side, all the studies agreed on correlating the inner retinal

status with central retina function [10, 12–17]. Moreover, cystoid macular edema is a common structural OCT finding, occurring in approximately 10–50% of cases. The pathogenesis is still poorly understood; the current hypotheses include the breakdown of the inner blood-retinal barrier, the dysfunction of RPE pumps, the macular Müller cells impairment, possible autoimmune-related phenomena, and vitreomacular anomalies and traction [18, 19]. Other structural OCT-described findings include vitreoretinal interface alterations, epiretinal membrane, and macular hole [20]. Moreover, hyperreflective foci have been described in RP, correlating their number with the severity of the disease and the rate of progression [21, 22].

It is known that choroidal perfusion is impaired in RP; OCT-based imaging modalities may offer a detailed detection of choroidal features, improving the diagnostic workup of RP patients [23–26]. The choroid is not simply thinner than controls; a recent study highlighted how quantitative-based approaches can unveil specific RP choroidal patterns, characterized by different baseline features as well as the rate of progression. By combining the measure of choroidal thickness, Sattler layer thickness, Haller layer thickness, and choroidal vascularity index (CVI), it was possible to find three different RP choroidal patterns [27]. Pattern 1 is characterized by normal-appearing choroid, whereas Pattern 2 shows reduced Haller and Sattler layers. Moreover, Pattern 3 is characterized by reduced Haller and Sattler layers and choroidal caverns [27]. Pattern 1 was associated with better visual acuity and imaging parameters, and lower progression. Pattern 3 showed the worst baseline conditions and the fastest progression. Pattern 2 showed intermediate characteristics, since the morpho-functional status resulted worse than Pattern 1, although the 1-year progression resulted in unremarkable.

OCTA provided noninvasive evidence both of intraretinal and choroidal perfusion impairment in RP. Indeed, intraretinal vascular network impairment has been clearly shown by OCTA, together with degenerative changes occurring at the level of the choriocapillaris [28–31]. DCP represents the most altered plexus, as usually occurs almost in all retinal diseases. The main reason is related to the fact that DCP is a low-pressure network, thus earlier suffering from perfusion reductions associated with the disease-related pathological changes [1]. Hence, DCP alterations can be considered very sensitive to disease-related degenerative processes, although poorly specific. The use of quantitative OCTA metrics allowed us to distinguish two different RP vascular patterns, the first one characterized by better perfusion status and lower amount of vascular network disorganization, associated with lower progression and better visual outcome, than the second RP vascular pattern [32]. Vascular changes in RP occur as a consequence of progressive retinal homeostasis loss. However, the overall improvement of quantitative imaging techniques will allow us to better categorize different RP subtypes, also optimizing the diagnostic workup for future clinical trials.

3. Stargardt disease

STGD is one of the most common IRD associated with both recessive and dominant autosomal transmittance. Most of the patients show pathogenic variants of *ABCA4* gene, whose transmission is autosomal recessively inherited, while the remaining ones have autosomal dominant transmission mainly involving *PROM1* gene or *EVLOV4* [33–35]. The clinical presentation is usually characterized by bilateral central vision loss due to the macular involvement and fundoscopy-detectable
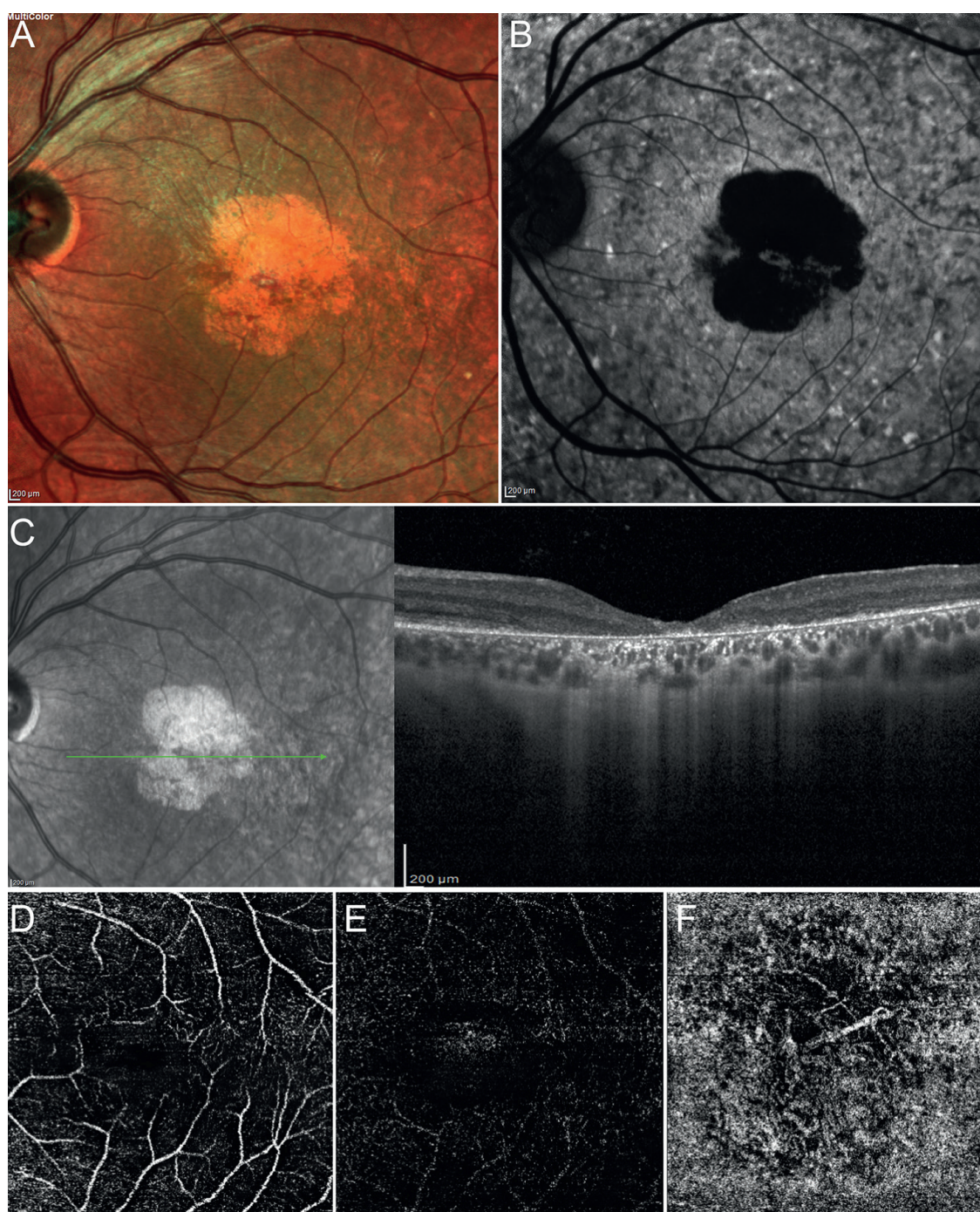
Figure 2.
Multimodal retinal imaging in STGD. Confocal multicolor image (A) shows hypopigmentation interesting the entire macular region. FAF image (B) confirms the presence of complete macular atrophy, with a thin line of partially preserved autofluorescent signal, together with sparse hyper- and hypoautofluorescence flecks over the entire posterior pole. Structural OCT (C) shows the complete disappearance of the central outer retinal bands, with choroidal hypertransmission and evident thinning of inner retinal layers. OCTA shows rarefied SCP (D), almost absent DCP (E) with some projections artifacts, and disappeared central CC with exposure of choroidal vessels, associated with markedly altered CC in the rest of the posterior pole (F).

flecks, namely sparse lipofuscin accumulations localized within the posterior pole and outside the vascular arcades. Age presentation follows two main peaks; the first is around 20 years of age with a more severe progression and worse prognosis, while the second one is around 40 years of age, typically presenting in a milder form [36]. A complete noninvasive multimodal retinal imaging STGD case is shown in **Figure 2**.

FAF examination is extremely useful in monitoring STGD progression by delineating atrophic regions, typically presenting as a central hypoautofluorescent area surrounded by a hyperautofluorescent ring [37, 38]. It is important to deeply assess two different sources of hypoautofluorescent signals. In particular, FAF can discriminate definitely decreased autofluorescence (DDAF), defined as a signal more than 90% black in Ref. to the optic nerve head, and questionably decreased autofluorescence (QDAF), defined as a signal included between 50% and 90% of reference black [39]. If DDAF corresponds to complete retinal atrophy, DDAF is more associated with the activity of the disease and the expansion of the atrophic margins. Near-infrared autofluorescence (NIR-AF) is a noninvasive modality focused on the assessment of melanin distribution. It is useful to describe the composition of flecks, which may disclose melanin content over lipofuscin, as well as to clearly detect the sparing of the fovea [40, 41]. If STGD has been mainly considered central dystrophy, the introduction of ultra-wide-field approaches expanded the knowledge regarding peripheral retinal involvement. In particular, different ultra-wide-field FAF patterns have been described, including Type I showing only central alterations without peripheral FAF changes; Type II is characterized by central atrophy and peripheral flecks; Type III presenting macular atrophy, peripheral FAF changes secondary to flecks, and progressively increasing extension of peripheral atrophy, further subclassified as IIIa, IIIb, and IIIc [42]. The peripheral extension of STGD-related alterations significantly correlated with the amount of central morpho-functional involvement, thus configurating completely different STGD phenotypes [43].

OCT is a mandatory investigation in STGD. Flecks are categorized into five different types (A, B, C, D, and E), based on their localization and their stage [44, 45]. In particular, Type A flecks resulted limited to the outer photoreceptors segment. Type B flecks showed protrusions through the interface of the inner photoreceptors segment. Type C flecks protrude up to the lower margin of the outer nuclear layer. Type D flecks lesions were characterized much more involved the thickness of the outer nuclear layer. Type E lesions appeared as drusen-like lesions. Structural OCT provides highly detailed pictures of the amount of outer and inner retinal degeneration, and of the number of hyperreflective foci [46–49]. The outer retinal bands are completely absent in the central part of the retina when atrophic changes occur, with typical choroidal hypertransmission. As previously described for RP, also in STGD it was possible to detect different clinically relevant choroidal patterns. In particular, Pattern 1 had a normal-appearing choroid, whereas Pattern 2 was characterized by alterations of Sattler or Haller choroidal layers. Pattern 3 showed significant alterations in both of the Sattler and Haller choroidal layers, whereas Pattern 4 was characterized by significant alterations in both of the Sattler and Haller choroidal layers and choroidal caverns [50]. The higher the choroidal pattern, the worse result of morpho-functional retinal status [50]. Moreover, choroidal patterns significantly correlated with the rate of STGD progression, resulting in the fastest in the Pattern 4 subtypes [50].

OCTA highlighted the significant vascular involvement of the intraretinal vascular network in STGD, showing a relationship between the amount of vascular impairment and both visual function, FAF, and structural OCT alterations [51–53]. In particular, DCP results highly altered already in early STGD stages, whereas the alterations at the level of the SCP occurs in later stages. The contribution of OCTA was improved by quantitative metrics segregating two different vascular patterns of STGD eyes [54]. Remarkably, the prevalence of foveal sparing was similar between the two OCTA subgroups, suggesting that the pathogenesis of foveal involvement might be even more complex, showing vascular supply impairment as a minor

pathogenic element [54]. In addition, OCTA provided further support to the hypothesis of greater choriocapillaris involvement in STGD, compared with geographic atrophy secondary to age-related macular degeneration, providing the basis for a reliable differential diagnosis [55].

4. Best vitelliform macular dystrophy

Best vitelliform macular dystrophy (BVMD) is a rare IRD caused by dominant variants in the *BEST1* gene, encoding for the bestrophin-1 protein, a RPE chloride channel [56]. The typical clinical presentation is a central yellowish vitelliform or egg-yolk-like lesion, made by lipofuscin and photoreceptors' outer segment remnants [56]. The classic BVMD classification includes different stages. Stage I (subclinical) is characterized by the absence of biomicroscopic fundus abnormalities. Stage II (vitelliform) shows the typical egg yolk subretinal macular lesion. Stage III (pseudohypopyon) is characterized by partial fluid reabsorption in the upper part of the lesion and persistence of the yellowish subretinal deposition in the lower part. Stage IV (vitelliruptive) shows the reabsorption and breakdown of the material, giving a "scrambled egg" appearance. Stage V (atrophic/fibrotic) is complicated by the development of chorioretinal atrophy or macular neovascularization [57]. A complete noninvasive multimodal retinal imaging BVMD Stage IV case is shown in **Figure 3**.

FAF showed no alterations in the subclinical stage. Conversely, the vitelliform stage is characterized by a well-defined hyperautofluorescent alteration. The FAF signal progressively decreased passing through the pseudohypopyon stage, up to the vitelliruptive stage. Stage five is characterized by decreased FAF signal due to RPE atrophy [58]. However, BVMD-FAF appearance may be characterized by quite heterogeneous presentations, including classic, hyperautofluorescent, hypoautofluorescent, patchy, multifocal, and spoke-like patterns [59]. NIR-AF remarkably contributed to provide the pathognomonic sign of the subclinical BVMD stage, namely the presence of a central well-defined area of NIR-AF decrease [60]. The relationship between FAF assessment and retinal functionality is very close, making FAF a mandatory diagnostic tool for BVMD [61].

Regarding OCT findings, the subclinical stage may show only thickening of the interdigitation zone of cones and RPE in about 40% of cases [60]. The vitelliform stage is characterized by a dome-shaped subretinal hyperreflective lesion, which leaves space for the progressively increasing subretinal fluid hyporeflective signal occurring as pseudohypopyon and vitelliruptive stages proceed. The advanced stage shows either outer retinal atrophy or hyperreflective neovascular scar [62]. The presence of subretinal fluid is associated with worse visual acuity and retinal sensitivity values, compared with the persistence of vitelliform material [63–65]. Moreover, OCT was able to describe a clinically relevant outer retinal finding, namely the optically preserved islet in the context of the vitelliform accumulation, corresponding with EZ integrity and good macular function; its disappearance causes a remarkable decrease of visual acuity and retinal sensitivity [66, 67]. A high number of hyperreflective foci correlated with disease severity and progression rate also in BVMD [68]. Focal choroidal excavation is a frequent finding in BVMD, occurring in correspondence with a significant choroidal thinning [69, 70].

OCTA contributed by detecting a progressively increasing vascular impairment as the BVMD stages progress [71]. In the subclinical stage, OCTA was allowed to describe an early sign of choriocapillaris impairment, represented by central
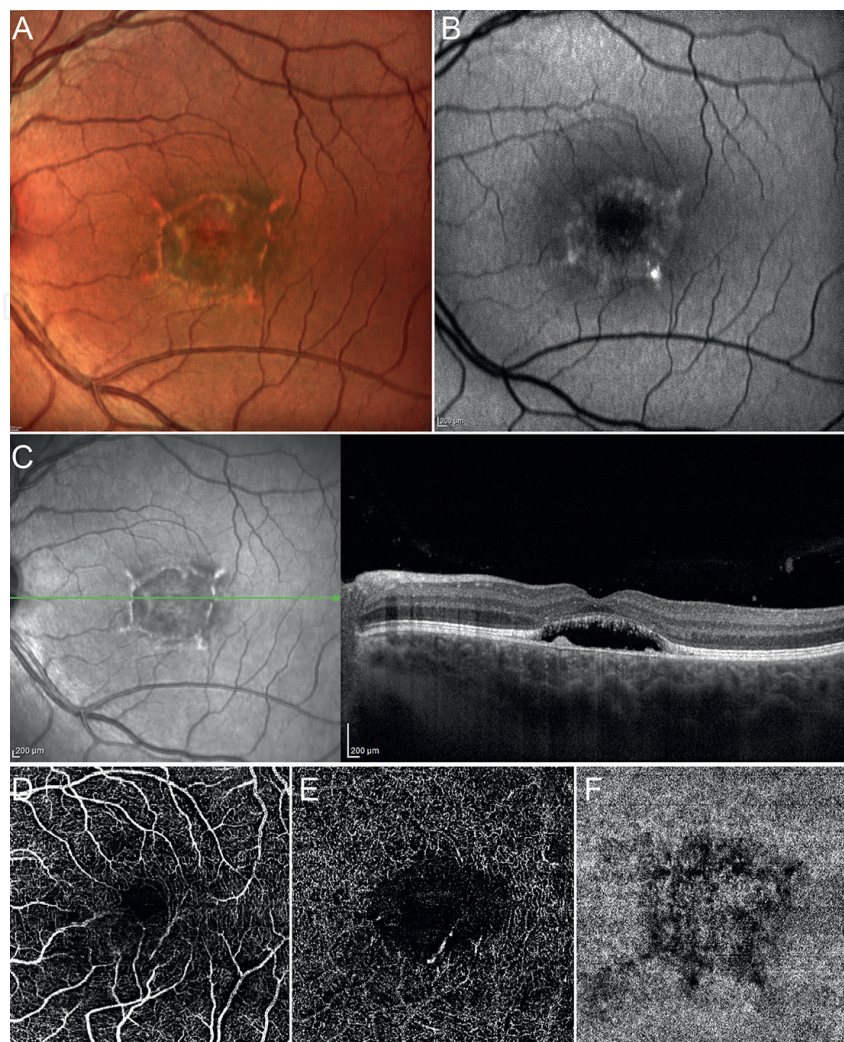
Figure 3.
Multimodal retinal imaging in BVMD. Confocal multicolor image (A) shows a scrumble egg appearance, which is suggestive of Stage IV vitelliruptive BVMD stage. FAF image (B) shows central alterations of the autofluorescent signal, either with hyper- or hypoautofluorescent changes. Structural OCT (C) shows the subretinal fluid corresponding with the vitelliform material in progressive reabsorption. OCTA shows almost preserved SCP (D), altered DCP with some alterations secondary to possible segmentation artifacts (E), and central CC alterations, probably related to the masking effect of the above localized subretinal fluid (F).

increased choriocapillaris flow voids [60]. In clinical stages, DCP first, followed by SCP, resulted altered in BVMD. However, the biggest OCTA contribution is regarding the radical change of macular neovascularization prevalence in BVMD. Indeed, before OCTA the prevalence of macular neovascularization was estimated at around 2–9% of cases [72]. After OCTA, the prevalence increases up to 65% of eyes [73, 74]. BVMD is characterized by two different macular neovascularization subtypes on OCTA: exudative and non-exudative. Exudative macular neovascularization is rare, more typical of Stages II and III, whereas non-exudative macular neovascularization develops very commonly in the advanced IV and V Stages [73]. Unfortunately, OCTA is less useful in evaluating the status of the choriocapillaris, since affected by the masking effect of the vitelliform material. Conversely, as expected, choriocapillaris is markedly impaired in advanced stages. Although the increased choriocapillaris flow voids detected in the subclinical stage may suggest that CC is effectively impaired in BVMD, further technological improvements are warranted to assess the choriocapillaris involvement in early BVMD stages.

5. Pigmented paravenous retinochoroidal atrophy

PPCRA is a rare chorioretinal atrophy characterized by perivenous aggregations of pigment clumps associated with peripapillary and radial zones of RPE atrophy following the course of retinal veins, usually bilateral and symmetric [75]. The etiopathogenesis of PPCRA is still unknown, and it is considered sporadic in most cases [76]. Patients are frequently asymptomatic, and the diagnosis is based on the typical fundus appearance. The natural history of the disease may be either nonprogressive or slowly progressive [75, 76]. In this chapter, we included PPCRA since many previous reports showed a familiar transmission of the disease, thus justifying the hypothesis of a genetic origin [77–82]. Interestingly, PPCRA has been also associated
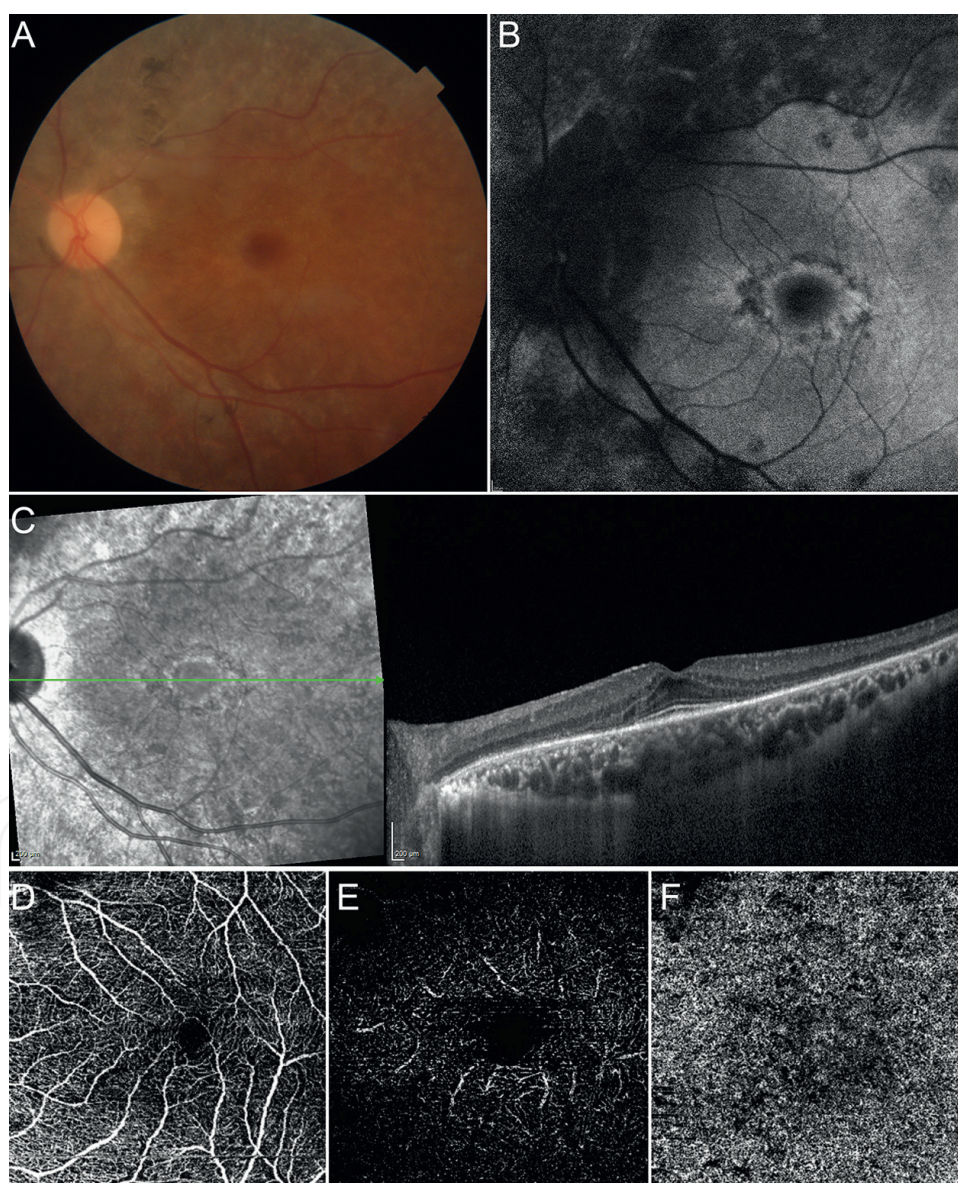

Figure 4.
Multimodal retinal imaging in PPCRA. Fundus image (A) shows evident hypopigmentation following the course of the vascular arcades, together with sparse alterations of the macular pigment. FAF image (B) confirms both the perivascular and the central alterations, detected as mainly hypoautofluorescent signals. Structural OCT (C) shows the disappearance of the peripheral outer retinal bands and some focal alterations localized at the level of the inner retina. OCTA shows almost preserved SCP (D), strongly altered DCP with many projection artifacts (E), and markedly altered CC (F).

with pathogenic variants of *CRB1* gene [83]. The typical onset occurs between 10 and 67 years of age [84]. However, this time might be underestimated by the fact that PPCRA is usually asymptomatic, thus representing an incidental finding during routine ophthalmologic examinations. When present, the most common symptoms are mild visual loss, although visual acuity is usually preserved, reduction of the peripheral visual field and nyctalopia [84]. PPCRA has been classified into three categories based on the distribution of pigmentary changes: (I) "paravenous" type, distinguished by characteristic chorioretinal atrophy with pigment clumping that is geographically connected; (II) "focal" type, characterized by isolated chorioretinal atrophy with pigment clumping; (III) "confluent" type showing chorioretinal atrophy with diffuse bone spicules [76]. A complete noninvasive multimodal retinal imaging PPCRA case is shown in **Figure 4**.

FAF imaging is characterized by continuous hypoautofluorescent signal along the large retinal veins, surrounded by linear hyperautofluorescent signal extending to the periphery [76]. As expected, FAF alterations are different when considering the "paravenous", "focal", or "confluent" types.

OCT shows severe disruption of the RPE and outer retinal layers, usually associated with choroidal thinning, which may sometimes be the only pathological modification detected in PPCRA [76]. Moreover, OCTA may be normal in the early stages of the disease [85]. However, significant changes in deep capillary plexus and choriocapillaris have been recently described in a cohort of 12 patients affected by PPCRA [86]. The scientific interest in PPCRA is growing and noninvasive retinal imaging will undoubtedly provide clinically relevant data in the next future.

6. Pattern dystrophies

This paragraph is focused on pattern dystrophies in an attempt to offer a complete overview of OCT findings in IRD. However, in this case, the available literature is poor because of the rarity of these conditions, and in many cases, OCTA studies are completely absent.

Pattern dystrophies are a group of very rare autosomal dominant macular diseases characterized by very heterogeneous patterns of retinal pigment depositions and outer retinal alterations. Although a definite classification is still absent, pattern dystrophies are usually divided into five different categories: (I) Adult-onset foveomacular vitelliform dystrophy (AFVD); (II) Butterfly-shaped pigment dystrophy (BPD); (III) Reticular dystrophy; (IV) Multifocal Pattern Dystrophy Simulating Stargardt Disease (MPDSSD); and (V) Fundus pulverulentus [87]. However, especially looking at *PRPH2* gene variants, the clinical manifestations of pattern dystrophies may be extremely variable. In many cases, pattern dystrophies are caused by pathogenic variants of *PRPH2* gene, although other genes have been described as involved in the pathogenesis of these rare conditions. A complete noninvasive multimodal retinal imaging case diagnosed as pattern dystrophy associated with *PRPH2* gene variants is shown in **Figure 5**.

AFVD probably represents the most common pattern dystrophy, closely resembling BVMD, however is characterized by later onset, usually at 40–60 years of age. The clinical presentation is characterized by round, bilateral, symmetrical, grayish-yellow, lesions within the macular area. Visual acuity is usually preserved, and electrophysiology is within normal limits. Pathogenic variants are associated with *BEST1*, *PRPH2,* or *IMPG1* genes [88, 89]. FAF is characterized by hyperautofluorescent
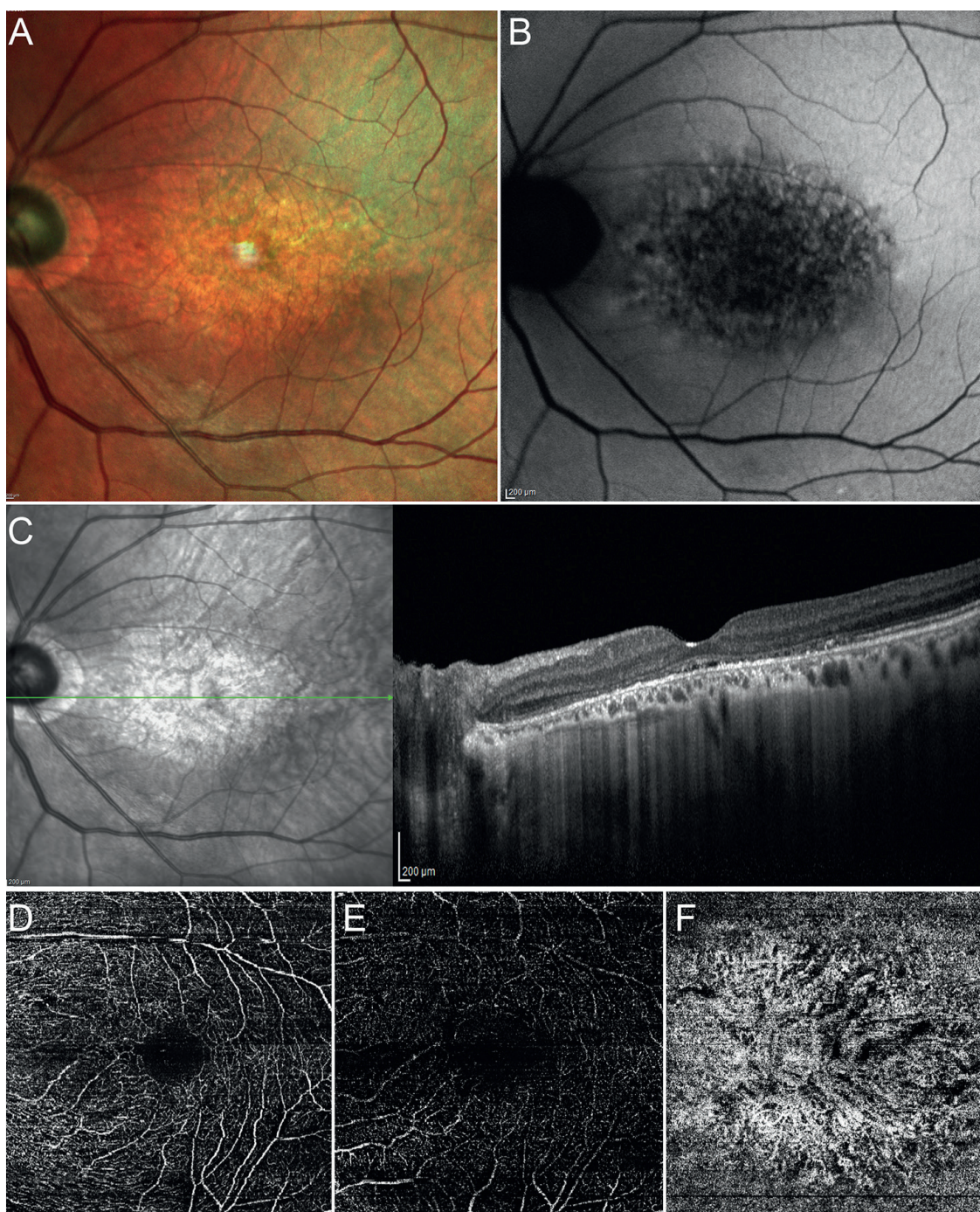
Figure 5.
Multimodal retinal imaging in PRPH2 gene-related pattern dystrophy. Confocal multicolor image (A) shows almost complete central retina atrophy. FAF image (B) confirms this finding, detecting a central mainly hypoautofluorescent signal. Structural OCT (C) shows disappeared or markedly attenuated outer retinal bands and inner retinal layers thinning. OCTA shows partially altered SCP with some segmentation and motion artifacts (D), strongly altered DCP with many projection artifacts (E), and absent central CC with exposure of choroidal vessels (F).

macular lesion in the vitelliform stage; changes in FAF signals follow the progressive degeneration of the outer retina. Structural OCT shows the presence of a subretinal vitelliform lesion very similar to the vitelliform stage of BVMD. Vitelliruptive, as well as atrophic stages, can be detected also in AFVD. The clinical course of AFVD is usually more benign than BVMD. OCTA detects flow deficits especially interesting the DCP; neovascular complications can be well-reconstructed [90].

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BPD has an onset around 20–40 years of age and is characterized by bilateral accumulation of yellowish or pigmented material in a butterfly wings-like pattern at the level of the RPE; visual acuity is usually good [91]. These butterfly-like pigment changes, corresponding both to hyper- and hypoautofluorescent signals on FAF, are well-detected on structural OCT, with heterogeneous patterns of outer retinal band alterations [92]. To the best of our knowledge, no OCTA studies are available for BPD.

Reticular dystrophy is characterized by a RPE network of hyperpigmentation, resembling a fishing net, extending from the macula in all directions, with sparing of the retinal periphery in early stages. In advanced stages, this network is complicated by atrophy [92, 93].

MPDSSD shows flecks-like alterations sparse within the entire posterior pole, with atrophic changes detected in the later stages of the disease. Flecks are often localized around the vascular arcades. Fundus appearance and OCT are very similar to STGD, and the differential diagnosis is mainly based on the detection of the autosomal dominant mechanism of inheritance [94].

Fundus pulverulentus is the rarest of all pattern dystrophies and is characterized by a granular appearance with coarse and punctiform mottling of the macular RPE. The clinical presentation is quite similar to age-related macular degeneration, leading to possible diagnostic delays [95]. Choroidal neovascularization has been described as a possible complication [96].

7. Final remarks

In this chapter, the most relevant OCT and OCTA findings in IRD have been described. Although several steps forward have been performed, especially looking at the most frequent IRD types, further prospective studies are needed to provide a definite categorization of each IRD and to improve the knowledge regarding the pathogenesis and the patterns of progression. Moreover, it should always be taken into account that OCT and OCTA are prone to imaging artifacts. These can be categorized as patient-related, technology-related, and disease-related artifacts [1]. Patient-related artifacts are mainly related to patients' fixation and collaboration, leading to many artifacts, including motion and blinking artifacts. Technology-related artifacts are related to the current limitation of the post-processing algorithm in carefully segmenting images and detecting signals, thus leading to biases, such as projection and segmentation artifacts. Disease-related artifacts are secondary to the disease-related alterations affecting the retinal structures, potentially masking or altering the detection of the signals. In brief, the higher are both fixation instability and pathological modifications of retinal structures, the higher will be the artifacts affecting the quality and the interpretation of OCT and OCTA images. This is particularly true for IRD, since in most of the cases, the retinal structures are remarkably impaired, and the visual function of the patients is strongly compromised. For these reasons, from one side both expert and nonexpert ophthalmologists should be familiar with imaging artifacts, to avoid misinterpretation of the findings. On the other end, further technological improvements are warranted to make noninvasive retinal imaging even more reliable for performing the diagnostic workup of IRD patients.

8. Conclusions

In conclusion, we provided an updated overview regarding the retinal imaging characteristics of RP, STGD, BVMD, and PPCRA, highlighting how heterogeneous can

be the clinical spectrum and how useful the contribution of OCT and OCTA diagnostic techniques. Moreover, we provided a brief updated description of current imaging findings in pattern dystrophies. The advances in knowledge regarding the above-described as well as all the other IRD are mandatory to reach the high level of information required to develop useful treatments. In addition, the proper use of imaging techniques is fundamental to optimize the selection of patients for potential clinical trials, allowing the categorization of clinically different diseases' subgroups, and for the monitoring of treatments' effect on the course of the disease. Moreover, the even larger employment of artificial intelligence-based diagnostic approaches will undoubtedly benefit from the improvements of quantitative multimodal retinal imaging approaches, which are able to provide a very high amount of detailed, objective, and easily reproducible data. However, especially looking at very rare IRD types, further studies are warranted to collect more cases and to provide more data regarding the imaging characteristics of these diseases. The future of IRD management is promising, and noninvasive retinal imaging technologies will further contribute to improve the ophthalmologic diagnostic workup and, consequently, the quality of life of IRD patients.

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