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Peripapillary retinal neovascularization and vitreous hemorrhage secondary to peripapillary pachychoroid syndrome

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ABSTRACT

Purpose: To report a case of peripapillary pachychoroid syndrome (PPS) complicated with peripapillary retinal neovascularization causing vitreous hemorrhage.

Observation: A 42-year-old man, with a history of a visual loss of the right eye (RE) for 4 years, presented for ophthalmological examination. Best-corrected visual acuity was «counting fingers» in the RE and 20/25 in the left eye. Fundus examination showed irregular pattern of hypopigmentation of the retinal pigmented epithelium in both eyes with retinal neovessels in the peripapillary region of the RE. Swept-source optical coherence tomography demonstrated a central serous pigment epithelial detachment with intraretinal cysts and serous retinal detachment in the nasal macula extending from the temporal disc margin in the RE. Fluorescein angiography showed multiple areas of hyperfluorescence without clear distinction of retinal neovessels. Indocyanine green angiography showed patches of choroidal hyperpermeability predominant in the peripapillary region in both eyes. Optical coherence tomography angiography provided a good visualization of the papillary and retinal neovessels without signs of choroidal neovascularization. Two months after initial examination, the patient presented with vitreous hemorrhage associated to juxtapapillary preretinal hemorrhage in the RE. After vitreous injections of bevacizumab, we observed a total resolution of the vitreous hemorrhage a partial decrease of the intraretinal and subretinal fluid.

Conclusions and importance: We report an unusual case of peripapillary retinal neovascularization and vitreous hemorrhage complicating a PPS. OCTA was useful to detect retinal neovessels and peripapillary retinal and choriocapillaris hypoperfusion, supporting the understanding of the pathogenic mechanism of neovascularization in PPS.

1. Introduction

Pachychoroid has been recently described as a phenotype which is thought to be related to a spectrum of diseases, the «pachychoroid spectrum».[1] These pachychoroid-related diseases are not simply referring to a thick choroid, which is not necessarily a pathologic condition, but to detailed functional and structural ocular changes of a pathologic state.[2,3] Pachychoroid disease (PD) is a phenotype characterized by a thinning of the choriocapillaris and Sattler' s layer overlying dilated choroidal vessels in Haller's layer (pachyvessels), choroidal hyperpermeability demonstrated by indocyanine green angiography, associated with progressive retinal pigment epithelium dysfunction and neovascularization.[4,5] Although the etiology of pachychoroid disease remains controversial, several related disorders have been identified. The pachychoroid spectrum includes: central serous chorioretinopathy (CSC), pachychoroid pigment epitheliopathy (PPE), pachychoroid neovasculopathy (PNV), polypoidal choroidal vasculopathy or aneurysmal type 1 neovascularization (PCV/AT1), focal choroidal excavation (FCE), and peripapillary pachychoroid syndrome (PPS). PPS was described by Phasukkijwatana et al., in 2018 as a novel variant of PD that involves the peripapillary region, with a thicker choroid surrounding the optic nerve that could develop nasal macular subretinal fluid (SRF) and intraretinal fluid (IRF) and occasional optic nerve head edema.[6] Montero Hernández et al. reported a novel entity within PD, describing a case of peripapillary type 1 choroidal neovascularization (CNV), associated to a PPS, called peripapillary pachychoroid neovasculopathy (PPN).[7] However,

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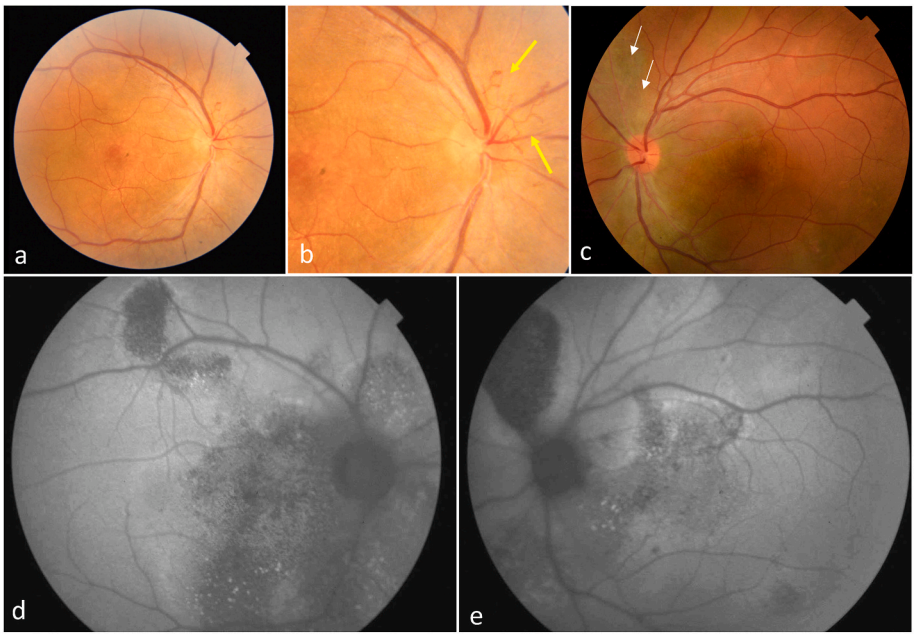

Fig. 1. (a,b) Fundus photographs of the right eye (RE) showing irregular pattern of hypopigmentation of the retinal pigmented epithelium. Retinal neovessels were seen in the nasal part around the optic disc (yellow arrows). (c) Fundus photography of the left eye (LE) showing hypopigmentation of the retinal pigmented epithelium appearing as bundles in the peripapillary region (white arrows). (d) Fundus autofluorescence of the RE illustrates areas of hypoautofluorescent peripapillary atrophy and large areas of peripapillary mottled autofluorescence, like gravity descending tracts. (e) Fundus autofluorescence of the LE illustrates areas of hypoautofluorescent atrophy and of mottled autofluorescence in the peripapillary region. Hyperautofluorescent patches were seen superior to the macular area. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

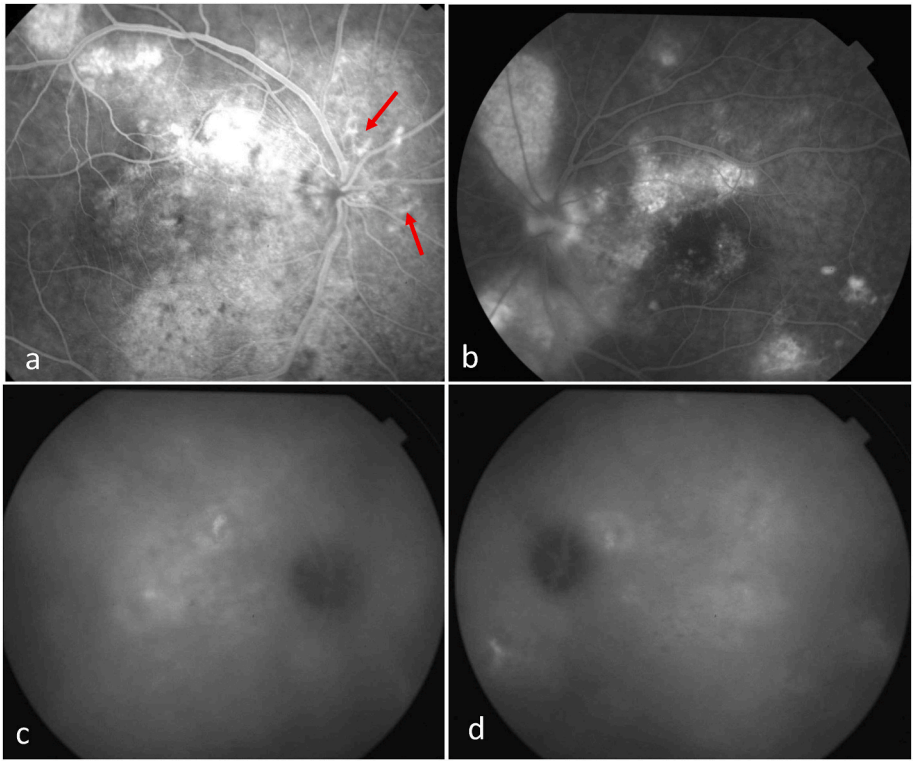

Fig. 2. (a) Mid-phase fluorescein angiography of the right eye (RE) illustrates speckled hyperfluorescent window defects around the optic disc and in the superior part of the macular area. The retinal neovessels adjacent to the optic disc (red arrows) are barely distinguished. (b) Late-phase fluorescein angiography of the left (LE) eye illustrates speckled hyperfluorescent window defects around the optic disc and in the superior part of the macular area. Mild optic disc leakage is observed. (c) Late-phase indocyanine green angiography of the RE shows multifocal patches of choroidal hyperpermeability in the peripapillary region. (d) Late-phase indocyanine green angiography of the LE shows multifocal patches of choroidal hyperpermeability in the peripapillary region. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

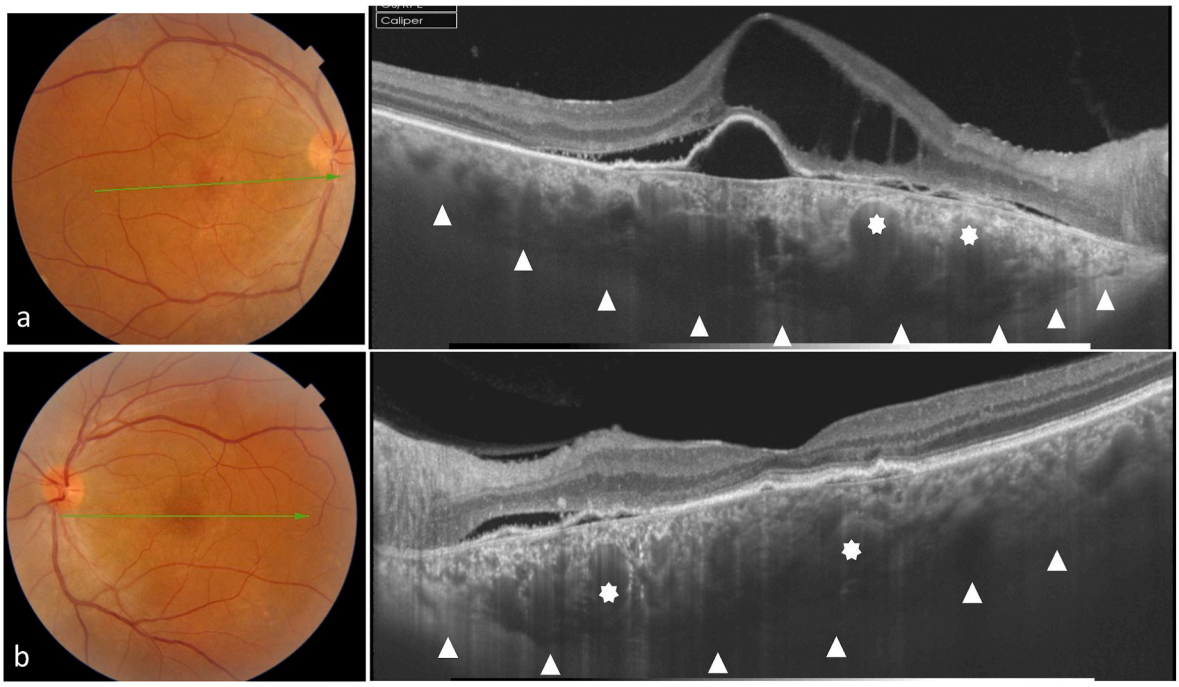

Fig. 3. (a) Swept-source optical coherence tomography of the right eye demonstrates a central serous pigment epithelial detachment with intraretinal cysts and serous retinal detachment in the nasal macula extending from the temporal disc margin. Note the chronic aspect the macular edema with large cystoid spaces, disruption of the ellipsoid layer and the presence of hyperreflective granular layer in the anterior and posterior borders of the SRD, explaining the photoreceptors damage and the important visual impairment. Note also the thickened nasal macular choroid (outlined by arrowheads) associated with pachyvessels (asterisks) and thinning of the overlying choriocapillaris. (b) Swept-source optical coherence tomography of the left eye demonstrates a flat irregular pigment epithelial detachment associated to a serous retinal detachement in the temporal side of the optic disc. The nasal macular choroid (outlined by arrowheads) was also thickened, associated with pachyvessels (asterisks) and thinning of the overlying choriocapillaris.

no retinal nor papillary neovascularization have been observed in previously reported cases of PPS.

The purpose of our report is to describe a case of PPS complicated with peripapillary retinal NV causing vitreous hemorrhage and to present its aspects on multimodal imaging, with the aim of better understanding of retinal neovascularization development in PD.

2. Case report

A 42-year-old man, with a history of a visual loss of the right eye (RE) since 4 years treated with oral steroids during 3 weeks, presented for a routine ocular examination. The patient did not report any systemic medical history.

Best-corrected visual acuity was «counting fingers» in the RE and 20/25 in the left eye (LE). The patient had a low hyperopia of +1,50 D in both eyes with an axial length of 22,61 mm in the RE and 22,70 mm in the LE. Slit-lamp examination did not show any evidence of intraocular inflammation. Fundus examination showed irregular pattern of hypopigmentation of the retinal pigmented epithelium in both eyes, appearing as bundles in the peripapillary region (Fig. 1 a-c). Besides, retinal neovessels were seen in the nasal part around the optic disc of the RE. Fundus autofluorescence demonstrated areas of hypoautofluorescent peripapillary atrophy and large areas of peripapillary mottled autofluorescence, like gravity descending tracts in both eyes (Fig. 1 d,e). Hyperautofluorescent patches were seen superior to the macular area in the LE.

Early and mid-phase fluorescein angiography (FA) showed speckled hyperfluorescent window defects around the optic disc and in the superior part of the macular area in both eyes (Fig. 2 a,b). No clear distinction of the peripapillary retinal neovessels was seen on FA, but areas of leakage in the late phase were observed in the nasal region adjacent to the optic disc of the RE. No peripheral retinal ischemia was found on FA. Late-phase indocyanine green angiography showed multifocal patches of choroidal hyperpermeability predominant in the peripapillary region in both eyes (Fig. 2 c,d).

Swept-source optical coherence tomography (SS-OCT) demonstrated a central serous pigment epithelial detachment (PED) with intraretinal cysts and serous retinal detachment (SRD) in the nasal macula extending from the temporal disc margin in the RE (Fig. 3a). This was also associated to a flat irregular PED in the maculo-papillary area. In the LE, SS-OCT showed a flat irregular PED associated to a SRD in the temporal side of the optic disc (Fig. 3b). The choroid was thicker with more dilated large choroidal vessels on the nasal side compared with the temporal side of the macula, with a thinning of the overlying choriocapillaris in both eyes. The choroidal thickness was measured in the nasal 1,5 mm (550 μm in the RE and 490 μm in the LE), subfoveal (575 μm in the RE and 548 μm in the LE) and temporal 1,5 mm locations (389 μm in the RE and 390 μm in the LE).

Optical coherence tomography angiography (OCTA) provided a good visualization of the peripapillary retinal neovessels adjacent to hypoperfused areas on the superficial retinal capillary plexus of the RE (Fig. 4). On the choriocapillaris layer, OCTA confirmed the absence of choroidal neovascularization and revealed dark areas corresponding to SRD and PED in both eyes and to flow voids in the peripapillary region (Figs. 4 and 5). The diagnosis of bilateral PPS associated to retinal neovascularization in the RE was made. Initial observation without treatment was considered as a first line management option. Two months after initial examination, the patient presented with a sudden vision loss of the RE. Ophthalmological examination showed moderate diffuse vitreous hemorrhage with juxtapapillary preretinal hemorrhage. The patient received one intravitreal injection of bevacizumab in the RE, with a total resolution of vitreous hemorrhage and persistence of retinal neovessels, intraretinal and subretinal fluid (Fig. 6 a-j). Peripheral FA did not show additional retinal abnormalities (Fig. 7). Follow-up after 3 additional monthly intravitreal injections was marked by absence of hemorrhage recurrence and partial improvement of macular edema and

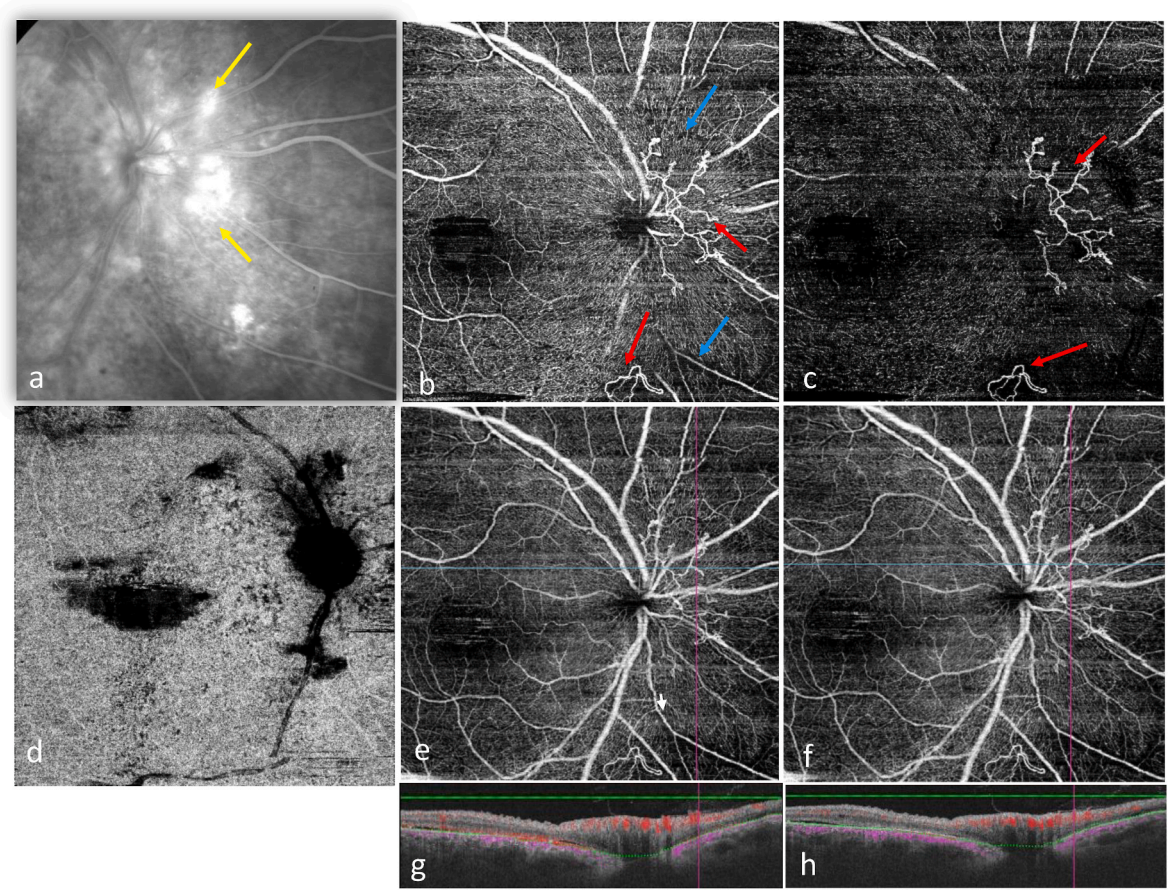

Fig. 4. Late-phase fluorescein angiography and optical coherence tomography angiography (OCTA) of the right eye. (a) Late-phase fluorescein angiography shows areas of leakage in the nasal region adjacent to the optic disc (yellow arrows) corresponding to retinal neovessels, associated to mild leakage of the optic disc. (b,c,d) OCTA illustrates peripapillary neovessels and in the inferior to the optic disc (red arrows) in the superficial capillary plexus (b) and their projection on the deep capillary plexus (c). Note some hyporperfused capillary areas around the neovessels (blue arrows). The choriocapillaris layer (d) shows dark areas corresponding to mask effect of intraretinal and subretinal fluid and to flow voids in the peripapillary region, without signs of choroidal neovascularization. (e,f) OCTA images and corresponding OCT B-scan images with flow overlay (g and h respectively) demonstrate intraretinal flow partially extended to the vitreous (white arrows) corresponding to the retinal neovessels. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

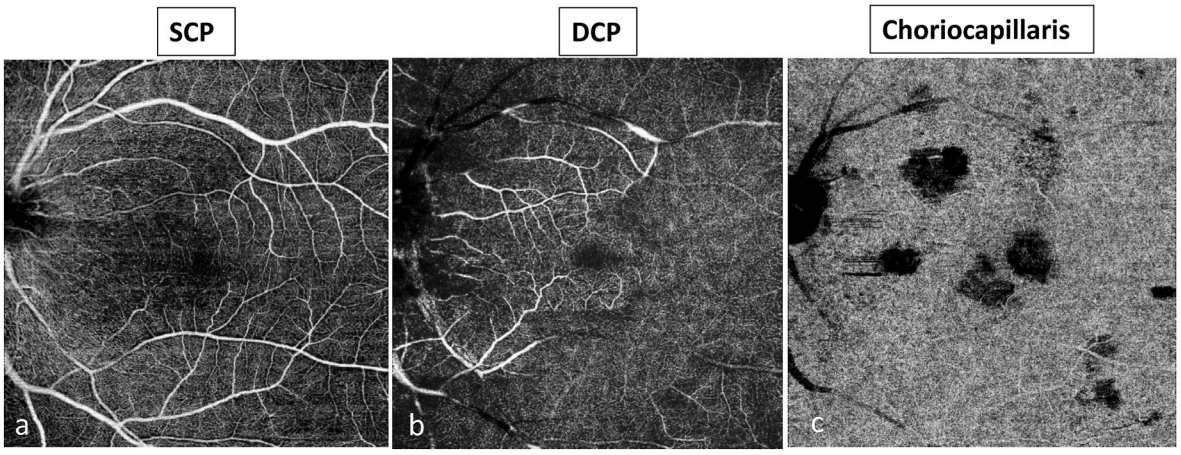

Fig. 5. Optical coherence tomography angiography of the left eye is normal in the superficial (a) and deep capillary plexus (b) and shows dark areas of shadowing effect on the choriocapillaris layer (c).

subretinal fluid.

Informed consent for publication of clinical details and clinical images was obtained from the patient.

3. Discussion

The PD, a new group of diseases, constitutes a common pathogenic process, which is a sustained, focal or diffuse increase in choroidal

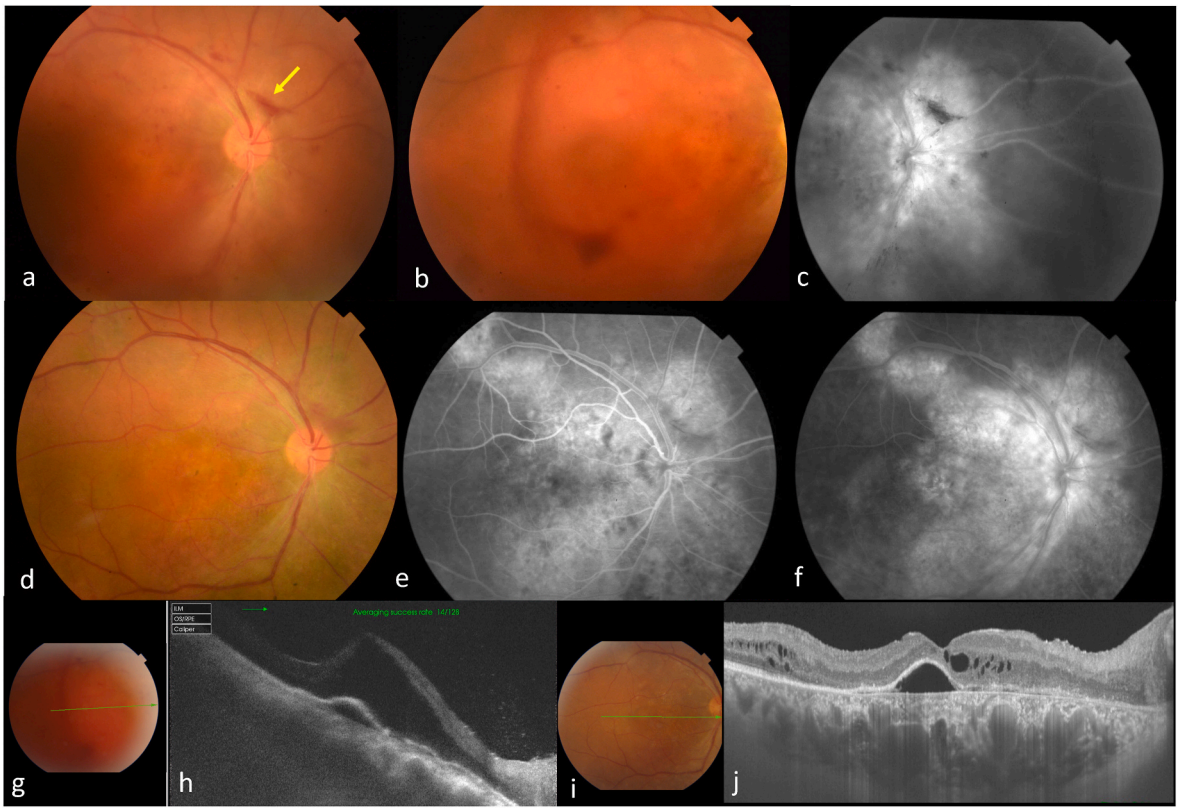

Fig. 6. Vitreous hemorrhage in the right eye and its imaging before and one month after intravitreal bevacizumab injection. (a,b) Fundus photographs showing diffuse vitreous hemorrhage with peripapillary retinal hemorrhage (yellow arrow). (c) Fluorescein angiography illustrates peripapillary leakage with mask effect of retinal hemorrhage. (d,e,f) Fundus photography (d) and fluorescein angiography at the mid (e) and late-phase (f) one month after intravitreal bevacizumab injection demonstrate improvement of vitreous and retinal hemorrhage. (g,h,i,j) Fundus photography and optical coherence tomography before (g,h) and after intravitreal injections (i,j). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

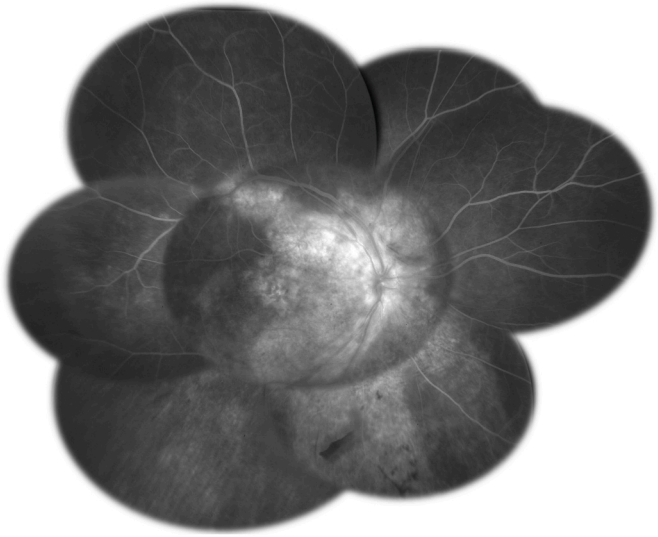

Fig. 7. Fluorescein angiography of the right eye showing normal peripheral retina.

thickness over 300 μm.[8] However, choroidal thickness, even though frequently observed on OCT, is not the determining factor in the disease. Abnormally thickened choroid may be found in healthy eyes and is considered as "pachychoroid" or "uncomplicated pachychoroid".[7] In PD, subfoveal choroidal thickness may be normal but it is increased focally in extrafoveal areas. This may explain the heterogeneous phenotypes of PD.[2]

The inner choroidal attenuation, of the choriocapillaris and intermediate caliber vessels within Sattler's layer in areas overlying abnormally dilated Haller's layer vessel is a key pathophysiologic mechanism for characteristic morphologic changes in PD.[5]

A uniform classification system based on this choroidal dysfunction gave rise to PD, including CSC, PPE, PNV, PCV/AT1, FCE, and PPS. But, as they represent different manifestations of a common pathogenic process, progression from one disorder to another are frequently observed.[5]

PPS is a new subgroup described in the PD. The initial study as well as subsequent studies described the defining features of PPS including peripapillary IRF and SRF associated with significant choroidal thickening in the nasal macula compared to the temporal macula in other PD.[6,9] The frontiers may be hard to distinct between CSC and PPS as seen in our patient, mainly because of the presence of sub and intraretinal fluid in the foveal region of the RE. In fact, PPS has common features with chronic CSC, such as pigment epitheliopathy, focal retinal pigment epithelium and external limiting membrane alterations with gravitational tracks, pachyvessels and multifocal hyperpermeability on ICGA, and, in some cases, the presence of serous PED and SRD.[3] However, in PPS, all these features are found mainly around the optic disc with a maximum of choroidal thickness in the nasal macula side, with a decrease towards the temporal side. Additionally, even though patients are often men, they are typically older than those with CSC. Besides, patients demonstrated choroidal folds, short axial length with hyperopia and crowded optic disc with mild late disc leakage on FA. Most of these features were found in our patient, but the frontiers are hard to distinct between CSC and PPS particularly in this case. In fact, the choroid was thickened nasally but also subfoveally with intra and subretinal fluid

which can also be consistent with CSC. But in another hand, most of retinal and pigmentary changes were located in the peripapillary region suggesting PPS.

In our patient, we observed juxtapapillary retinal neovascularization well visualized on fundus photographs, FA and especially on OCTA without signs of CNV. CNV may develop in PD, such as in CSC with secondary CNV, FCE with secondary CNV, PCN, and PCV/AT1. The mechanism of CNV (type 1 or type 2) in PD is yet unknown. However, it is thought that the attenuation of the inner choroid caused by the pachyvessels and/or chronic mechanical disruption of Bruch's membrane may induce local ischemia ischemia causing vascular endothelial growth factor (VEGF) expression and progression of choroidal neovessels.[10–12] In PPS, only one case of type 1 CNV has been reported and authors described this new entity as peripapillary pachychoroid neovasculopathy.[7]

However, in this observation, we found an atypical development of peripapillary and retinal neovessels in a case or PPS. OCTA was a useful tool to detect retinal neovessels which can be hard to differentiate from leaking points or window defects on FA. The vitreous hemorrhage is probably secondary to the retinal neovessels as a juxtapapillary preretinal hemorrhage has also occurred in the retinal neovessels area. Others causes of vitreous hemorrhage such as ocular trauma, posterior vitreous detachment, retinal tears and proliferative retinopathy have been ruled out. This finding is atypical et has not been described in PPS. However, some atypical cases of CSC with retinal neovascularization have been reported, especially in case of systemic corticosteroids use, as seen in our patient.[13,14] In fact, the use of systemic corticosteroids in chronic CSC can exacerbate the condition, leading to unusual findings including acute bullous retinal detachment, subretinal fibrin, subretinal fibrosis, hard exudates, and even retinal neovascularization.[15–17] As PPS and CSC have common pathogenic process, we can hypothesize that systemic corticosteroids must be avoided in PPS also, but no evidence of relationship between corticosteroid therapy and PPS has been clarified. The mechanism by which PPS might predispose to peripapillary retinal neovascularization is the compartment syndrome caused by a thicker choroid responsible of the optic nerve head ischemia, as it was reported in some cases of nonarteritic anterior ischemic optic neuropathy.[18] Besides, in some cases of PPS, optic disc edema with late leakage on FA was observed, as seen in our patient. Also, from an anatomical point of view, the circle of Zinn-Haller (a cilioretinal anastomotic vascular complex), is formed by arteriolar branches from the choroid, perfusing the prelaminar optic nerve fibres.[19] Thus, we hypothesize that in PPS, choriocapillaris ischemia around the optic disc may also induce the production of pro-angiogenic factors and the growth of retinal juxtapapillary neovessels. Another hypothesis is that a chronic SRD can cause retinal ischemia and growth of retinal neovessels.

Recent treatment evaluations in PPS have been reported. Xu et al. analyzed long-term anatomic and visual outcomes of patients with PPS. They compared observed patients to those that received treatment with anti-VEGF or photodynamic therapy.[9] Overall, there was no visual benefit in the treated group. However, subfoveal retinal and choroidal thickness decreased after anti-VEGF therapy at final follow-up. Thus, they recommend treatment only in patients with subfoveal SRF. In our patient, visual impairment was related to chronic macular IRF, SRF and foveal PED. Recently, a pilot study investigated the anatomical and functional results in eyes with PPS undergoing PDT.[20] Authors found a significant improvement in retinal anatomy and in visual acuity. However, no control untreated group was compared. Some recent reports described a reduction of peripapillary intraretinal fluid after treatment with topical prednisolone for 4 weeks, a novel finding which can raise questions about relationship between steroids and PD.[21] Larger prospective studies regarding treatment are needed to determine the treatment strategy in PPS.

To the best of our knowledge, this is the first report of peripapillary retinal neovascularization and vitreous hemorrhage in PPS. Peripapillary retinal and choriocapillaris hypoperfusion seen on OCTA support the understanding of the pathogenic mechanism of neovascularization in PD, as this feature can be explained by a choriocapillaris ischemia around the optic disc.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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