



## Atypical case of perifoveal exudative vascular anomalous complex associated with pachychoroid pigment epitheliopathy

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### ABSTRACT

**Purpose:** To report an unusual association of a perifoveal exudative vascular anomalous complex (PEVAC) and a bilateral pachychoroid pigment epitheliopathy (PPE), which responded positively to anti-vascular endothelial growth factor (VEGF) intravitreal injections (IVI).

**Observations:** A 44 year-old man with no significant medical or ocular history, complained of unilateral blurred vision in his right eye (RE) over several months. On examination, best corrected visual acuity (BCVA) was 75 letters in the RE and 85 in the left eye (LE). Fundus examination in the RE showed a large perifoveal aneurysmal lesion with a macular thickening, small hemorrhages and linear hard exudates accumulation, associated with multifocal retinal pigment epithelium (RPE) changes in the posterior pole of both eyes. Optical coherence tomography of the RE showed the PEVAC as a large round retinal capillary aneurysm with surrounding intraretinal fluid, associated with serous and drusenoid RPE elevations in both eyes, consistent with PPE. Subfoveal choroidal thickness was more than 500 μm in both eyes, with several dilated choroidal veins. Fluorescein angiography showed, in the RE, the hyperfluorescent aneurysmal lesion with late leakage, associated with scattered hyperfluorescent areas in the posterior pole of both eyes. Indocyanine green angiography showed, in the RE, the same hyperfluorescent lesion but without leakage, associated with areas of choroidal hyperpermeability in both eyes. After 2 anti-VEGF IVI in the RE, good functional and anatomical improvement was observed. After 10 months of follow-up, there was no evidence of new exudation. BCVA remained stable and RPE abnormalities remained unchanged.

**Conclusion and importance:** We describe an atypical case of PEVAC associated with PPE, which responded positively to anti-VEGF therapy. To our knowledge, this is the first report of a patient presenting PEVAC and diseases of the pachychoroid spectrum. Further studies, assessing the choroid in PEVAC, are required to investigate the hypothetical relationship between these 2 entities and the efficiency of anti-VEGF therapy.

### 1. Introduction

Perifoveal exudative vascular anomalous complex (PEVAC) is a recently described uncommon macular disorder, characterized by the presence of a large, unilateral and isolated perifoveal aneurysm, in otherwise healthy patients.<sup>1</sup> It is typically unresponsive to anti-vascular endothelial growth factor (VEGF) therapy.<sup>1,2</sup>

Pachychoroid pigment epitheliopathy (PPE) is a recently described condition characterized by retinal pigment epithelium (RPE) changes, which occur in the posterior pole, over regions of choroidal thickening.

It is considered as a « forme fruste » of central serous chorioretinopathy (CSC).<sup>3</sup>

The purpose of this article is to describe an unusual association of a PEVAC and a PPE in a healthy young man. The aneurysmal lesion was unilateral, large, solitary and had an early and complete response to anti-VEGF IVI.

### 2. Case report

A 44 year-old man with no significant medical or ocular history, was

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referred to our department for the management of intraretinal fluid in his right eye (RE), with complaints of unilateral blurred vision over several months. The patient had never been treated with corticosteroids. He did not show type A behavior. His family medical history was not relevant. On examination, best corrected visual acuity (BCVA) was 75 letters in the RE and 85 in the left eye (LE) using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. The results of anterior segment examination were unremarkable. Fundus examination in the RE, showed a large aneurysmal lesion at the temporal margin of the fovea associated with a macular thickening, small hemorrhages and linear hard exudates accumulation. There were also reduced fundus tessellation and multifocal hyper- and hypopigmented RPE changes in the posterior pole of both eyes (Fig. 1A and B). Fundus autofluorescence (FAF) imaging (Spectralis HRA-OCT Heidelberg Engineering, Heidelberg, Germany) in the RE, showed the aneurysm as a hypoautofluorescent lesion, along with scattered areas of hyper- and hypoautofluorescence in the posterior pole in both eyes (Fig. 1C and D). Structural spectral domain optical coherence tomography (Spectralis HRA-OCT Heidelberg Engineering, Heidelberg, Germany) of the RE, showed a large round retinal capillary aneurysm with a hyperreflective wall and a variably reflective lumen, with a posterior shadowing. It was located between the outer nuclear layer and the ganglion cell layer. It measured 340  $\mu\text{m}$  in its largest diameter and was located less than 700  $\mu\text{m}$  from the center of the fovea. There was surrounding intraretinal fluid with cystic spaces in the inner and outer nuclear layers, extending under the fovea, and intraretinal hyperreflective dots corresponding to the hard exudates seen on fundus. No signs of choroidal neovascularization (CNV) were detected. There were also serous and drusenoid RPE elevations corresponding to RPE changes noted clinically in both eyes. Central foveal thickness (CFT) was 333  $\mu\text{m}$  in the RE, and 262  $\mu\text{m}$  in the LE. Subfoveal choroidal thickness as measured by Enhanced depth imaging-Optical coherence tomography (EDI-OCT) was 510  $\mu\text{m}$  in the RE and 515  $\mu\text{m}$  in the LE, with several dilated choroidal veins noted below the areas of RPE changes (Fig. 2).

Fluorescein angiography (Spectralis HRA-OCT Heidelberg Engineering, Heidelberg, Germany) showed the aneurysm as an early well-defined hyperfluorescent lesion increasing in size with late leakage. There were also, early scattered hyperfluorescent areas in the posterior pole of both eyes, with no leakage, corresponding to RPE changes seen clinically. There were no other retinal vascular abnormalities in the central or in the peripheral parts of the retina, and no signs of CNV (Fig. 3). Indocyanine green angiography (Spectralis HRA-OCT Heidelberg Engineering, Heidelberg, Germany) showed in the RE the same

well-defined hyperfluorescent lesion, identified by fluorescein angiography (FA) but without leakage in the late frames. There was also choroidal hyperpermeability, which was prominent beneath the RPE changes noted clinically in both eyes (Fig. 3).

Systemic work-up ruled out diseases possibly associated with aneurysms such as diabetes, systemic hypertension, blood dyscrasias and inflammatory diseases. The diagnosis of PEVAC was then proposed.

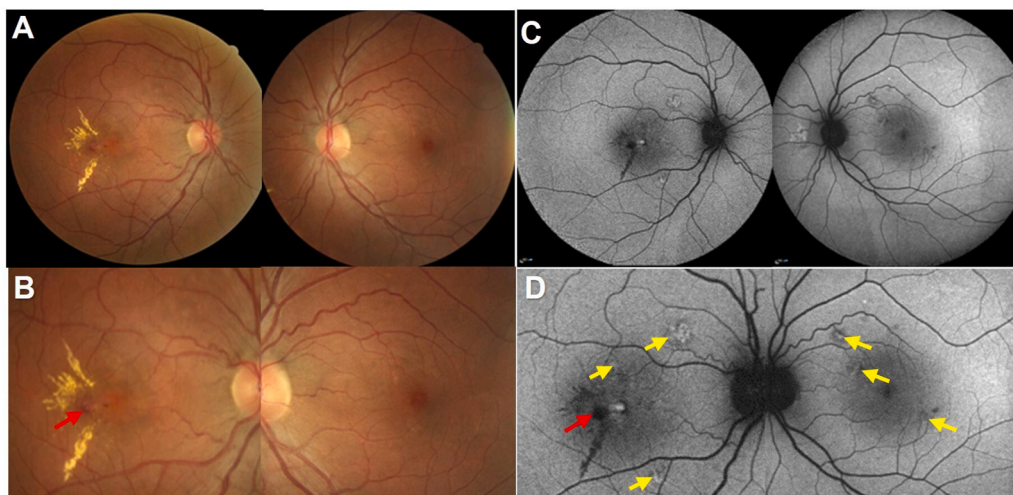
Considering the exudative nature of the aneurysm with the disturbance of vision and the close proximity to the foveal center, we decided not to treat by laser photocoagulation but with a single IVI of Aflibercept (0.05 ml/2 mg). One month after the first injection, BCVA improved to 80 letters. Optical coherence tomography (OCT) showed a decrease of both the aneurysm and the intraretinal fluid with a decrease of CFT from 333 to 252  $\mu\text{m}$ . As the response was positive but not complete, we decided to perform a second Aflibercept IVI. One month later, BCVA was 85 letters. On OCT, the aneurysm was uniformly reflective and had a diameter of 220  $\mu\text{m}$  along with a complete resolution of intraretinal fluid. CFT was 242  $\mu\text{m}$  (Fig. 4). We then decided to stop the injections and to follow the patient closely.

Optical coherence tomography angiography (OCT-A) was performed with AngioVue RTVue XR Avanti (Optovue, Fremont, California, USA) with a scanning area of  $3 \times 3$  mm centered on the fovea, 1 month after the second Aflibercept IVI. There was no flow signal corresponding to the involuted aneurysmal lesion. Rarefaction of retinal capillaries was observed in the perianeurysmal area in both the superficial and the deep plexuses. No microvascular dilations suggestive of telangiectasia were detected. No anomalous flow signal in the outer retina or choriocapillaris was present (Fig. 5).

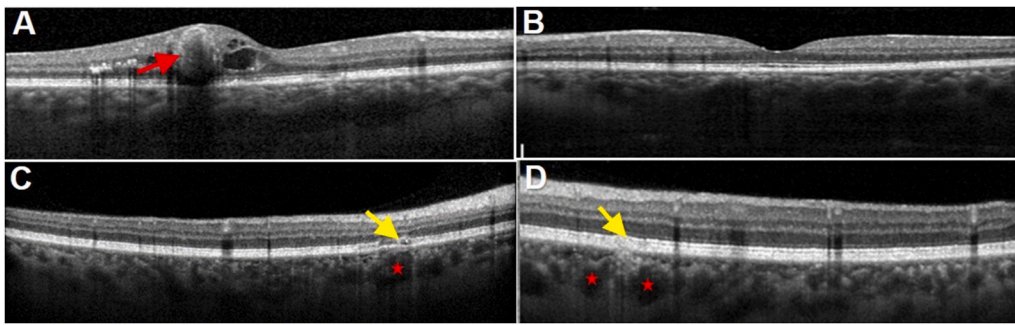
The patient was followed closely for 10 months with serial multimodal imaging. During this time, he experienced no evidence of new exudation. BCVA remained stable. RPE abnormalities remained unchanged compared to the initial examination (Fig. 6).

### 3. Discussion

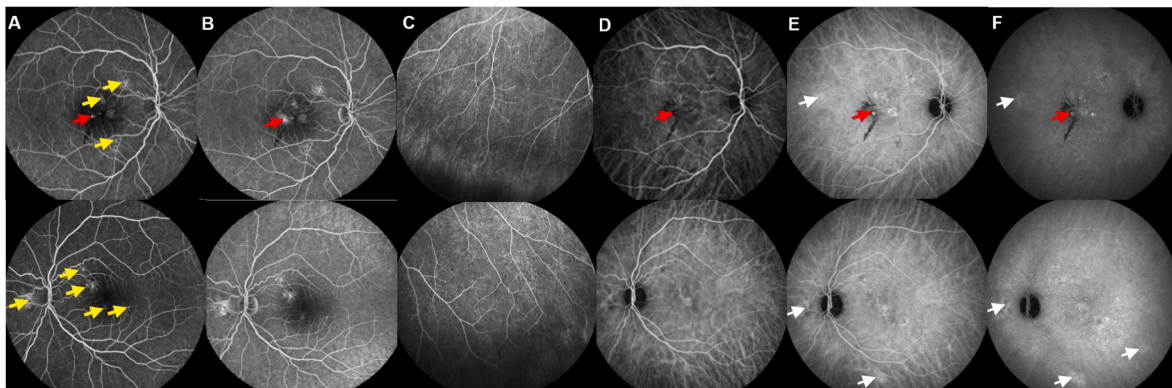
Perifoveal retinal vascular abnormalities (PRVA) are usually secondary to inflammatory diseases or retinal vascular occlusive disorders such as retinal vein occlusion, diabetic retinopathy, hypertensive retinopathy and blood dyscrasias.<sup>1</sup> PRVA were also reported in a peculiar form of age-related macular degeneration (AMD) namely type 3 neovascularization.<sup>4</sup> This condition is characterized by intraretinal neovascularization and is typically associated with a downward growth towards the RPE with progressive exudation.<sup>5</sup> PRVA may also develop in



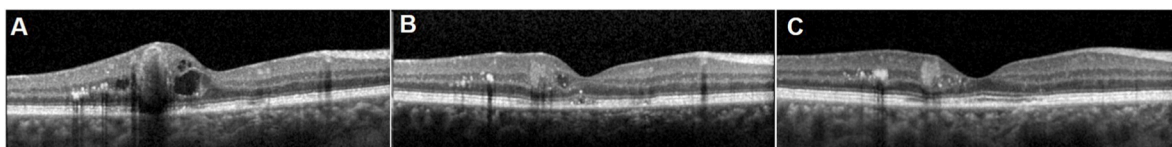
**Fig. 1.** Fundus color photograph (A, B: Enlarged view) and FAF (C, D: Enlarged view). Fundus color photograph of the RE shows a large perifoveal aneurysmal lesion (red arrow), accompanied by macular thickening, small hemorrhages and linear hard exudates accumulation. RPE changes in both eyes are better seen on FAF (yellow arrows). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



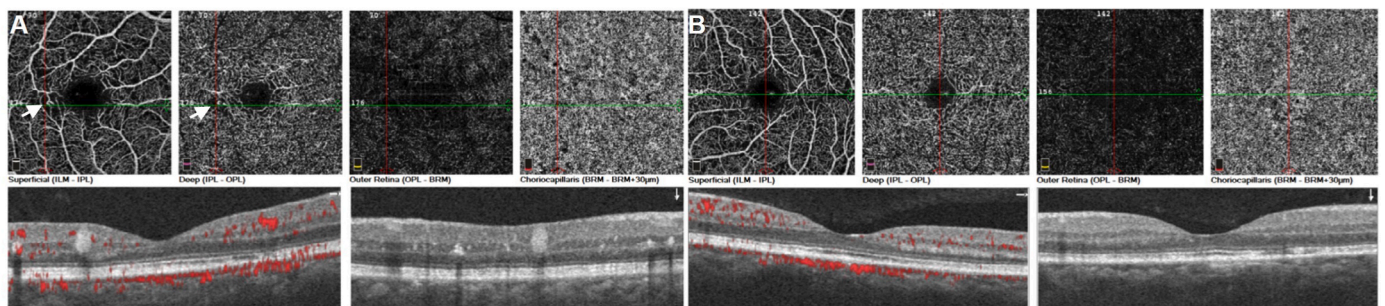
**Fig. 2.** EDI-OCT scans of both eyes (A and B: foveal scans in the RE and the LE respectively, C and D: scans passing through the RPE changes seen on fundus examination and FAF in the RE and the LE respectively). EDI-OCT shows in the RE, a large round intraretinal lesion with a hyperreflective wall and a variably reflective lumen (red arrow), surrounded by intraretinal cystic spaces. Dilated choroidal veins (red stars) are noted below RPE changes (yellow arrows) in both eyes. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



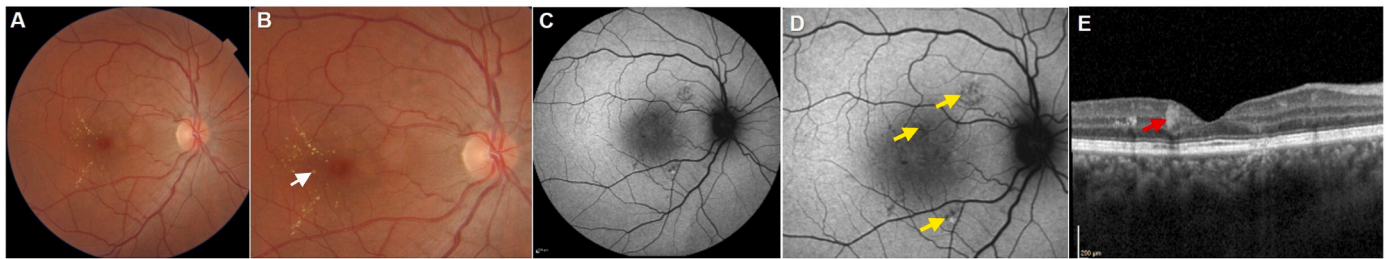
**Fig. 3.** Fluorescein angiography (A, early phase; B, late phase; C, Peripheral retina) and indocyanine green angiography (D, early phase; E intermediate phase; F late phase), in the RE (top) and LE (bottom). Angiographic examination reveals the aneurysm in the RE as a well-defined hyperfluorescent lesion with leakage on FA and no leakage on ICGA (red arrow). On FA, there are also, scattered hyperfluorescent areas in the posterior pole of both eyes, with no leakage, corresponding to RPE changes (yellow arrows). ICGA shows areas of choroidal hyperpermeability in the intermediate and late phases in both eyes (white arrows). There are no other retinal vascular abnormalities on FA in the peripheral part of the retina. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 4.** Structural spectral domain OCT of the RE during follow-up. OCT at baseline (A).OCT 1 month after the first Afibercept IVI (B) showing a decrease of both the aneurysm and the intraretinal fluid. OCT 1 month after the second Afibercept IVI (C) showing the aneurysm uniformly reflective with a complete resolution of intraretinal fluid.



**Fig. 5.** OCT-A (A, Right eye; B, Left eye). OCT-A shows in the RE, a rarefaction of retinal capillaries in the perianeurysmal area in both the superficial and deep capillary plexuses (White arrows) but no flow signal corresponding to the involuted aneurysmal lesion. No microvascular abnormalities and no anomalous flow signal in the outer retina or choriocapillaris are detected.



**Fig. 6.** Fundus color photograph (A, B: Enlarged view), FAF (C, D: Enlarged view) and structural OCT (E) of the RE at 10 months follow-up. Fundus color photograph shows the aneurysm involuted to a smaller yellow-white nodular lesion (white arrow). There is no retinal thickening but persistent fine lipid deposits. The OCT shows that the remaining lesion left after closure is 190  $\mu\text{m}$  in diameter and has a uniformly hyperreflective character (red arrow). There is no intraretinal exudation. RPE abnormalities better seen on FAF remain unchanged (yellow arrows). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

type 1 idiopathic macular telangiectasia. This intraretinal microangiopathy is predominantly unilateral and is characterized by the presence of telangiectasias in the juxtafoveal area with multiple capillary, venular and arteriolar aneurysms. These microvascular abnormalities affect both the superficial and the deep capillary plexuses. Some patients show patchy capillary ischaemia on FA. Type 1 idiopathic macular telangiectasia is associated with cystoid intraretinal fluid and lipid deposition,<sup>6</sup> and it typically responds to anti-VEGF treatment.<sup>7</sup>

In 2011, Querques et al. first described a new peculiar clinical entity, namely “Perifoveal exudative vascular anomalous complex”. PEVAC is defined as a large solitary perifoveal aneurysm, in the absence of retinal vascular or inflammatory diseases.<sup>1</sup> It affects both young adults and aged subjects, but the latter more frequently. It is frequently unilateral and typically unifocal, but two lesions were found in the same eye in some patients.<sup>2,8</sup> Recently, Vigo et al. described a bilateral and multifocal case of PEVAC.<sup>9</sup> The pathogenesis of the disease remains unclear, although PEVAC may be classified in the spectrum of idiopathic PRVA.<sup>2</sup>

We present the case of a young and otherwise healthy patient with a PEVAC. A systemic work-up was done to exclude diseases possibly associated with aneurysms such as diabetes, systemic hypertension, blood dyscrasias and inflammatory diseases. Concerning the possibility of type 3 neovascularization, the patient was not in the AMD age range. With structural OCT, the aneurysm displayed a different morphology versus type 3 neovascularization. On OCT-A, no anomalous flow signal was present in the

outer retina and the choriocapillaris. During follow-up, the lesion remained confined to the retinal layers. There was no evidence of downward growth towards the RPE and the outer retinal layers remained preserved. The case of our patient could be confused with type 1 idiopathic macular telangiectasia, because there are some similarities with this condition (age and clinical presentation). However, there are significant differences. PEVAC is characterized by an isolated and well-defined aneurysmal lesion with no adjacent telangiectasia or other capillary aneurysms, on FA, indocyanine green angiography (ICGA) and OCTA while type 1 idiopathic macular telangiectasia typically features multiple capillary, venular, and arteriolar aneurysms with patchy capillary ischaemia on FA. Our patient had signs of PPE which can go on to develop type 1 neovascularization, without necessarily developing CSC.<sup>10</sup> This diagnosis could be possible in our patient. However, with multimodal imaging, this diagnosis was excluded because the aneurysm displayed a different morphology versus type 1 neovascularization and during follow-up, the lesion remained confined to the retinal layers.

In the three largest series published to date, no association has been described between PEVAC and diseases of the pachychoroid spectrum.<sup>2,8,11</sup> Sacconi et al. have analyzed the clinical characteristics of 15 cases of PEVAC from 4 retina referral centers worldwide. In their study, PEVAC was found in patients with coincident AMD and myopia.<sup>2</sup> Kim et al. showed also concomitant AMD among their patients.<sup>11</sup> In our patient, we did not evidence any sign of AMD or myopia. Mrejen et al. reported one case of RPE changes associated with PEVAC in their study

but the pachychoroid spectrum diseases were not mentioned. The choroidal thickness and the presence of pachyvessels on structural OCT were not reported.<sup>8</sup> Furthermore, Battista et al. reported microvascular retinal alterations in eyes with chronic CSC by OCTA consisting of telangiectasias, vascular rarefactions and enlargement of foveal avascular zone (FAZ). Although CSC is known to represent a choroidal disorder, retinal vascular alterations may be present in these eyes.<sup>12</sup> However, no retinal capillary aneurysms, similar to our case, were reported in this study and the microvascular retinal alterations were reported only in chronic CSC. The other diseases of the pachychoroid spectrum were not mentioned.

In the three largest series published to date, PEVAC lesions were found unresponsive to anti-VEGF therapy.<sup>2,8,11</sup> Sacconi et al. reported no differences in BCVA and CFT between patients receiving anti-VEGF therapy and those without any treatment.<sup>2</sup> Kim et al. also described no improvement after anti-VEGF therapy in two patients.<sup>11</sup> In Mrejen et al. study, resolution of exudation was achieved in 2 patients, one after focal laser photocoagulation and one after 13 anti-VEGF IVI.<sup>8</sup> In addition, Sacconi et al. reported that the PEVAC displayed a stable clinical course, with no significant improvement or worsening in functional and anatomical outcomes, with or without intravitreal anti-VEGF therapy.<sup>2</sup>

In our patient, anti-VEGF therapy led to a significant functional and anatomical improvement after 2 IVI. After 10 months of follow-up, no worsening was observed. This unusual response to anti-VEGF therapy is not described in the literature. It may encourage to keep anti-VEGF IVI as a therapeutic option for PEVAC cases. It may also hypothesize a possible link with the association of PEVAC and PPE and may suggest a possible role of the choroid in PEVAC pathogenesis. However, this association may be coincidental with no link between these two entities. Whether or not, the association of the PEVAC with the PPE is related to a better response to anti-VEGF therapy can not be asserted as it is the first time, such association is reported. Further studies, assessing the choroid in PEVAC, are required to investigate this relationship and the effect of anti-VEGF therapy.

#### 4. Conclusion

We describe an atypical case of PEVAC associated with PPE, which responded positively to anti-VEGF therapy. To our knowledge, this is the first report of a patient presenting PEVAC and diseases of the pachychoroid spectrum. Further studies, assessing the choroid in PEVAC, are required to investigate the hypothetical relationship between these 2 entities and the efficiency of anti-VEGF therapy.

#### Patient consent

The patient consented to the publication of the case.

## Disclosures

The authors report no financial grants, or any other supports relevant to this study.

## Authorship

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

## Declaration of competing interest

The following authors have no financial disclosures associated with this publication: NH, OS, MS, FA, MB, VC, DC, SYC, GQ, EHS.

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