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Long-term follow-up of perifoveal exudative vascular anomalous complex treated with intravitreal injections of anti-vascular endothelial growth factor and thermal laser photocoagulation

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ABSTRACT

Purpose: To describe the long-term follow-up of a patient with perifoveal exudative vascular anomalous complex (PEVAC) treated initially with intravitreal injections of anti-vascular endothelial growth factor (VEGF) followed by focal thermal laser photocoagulation.

Observations: A 78 years-old man presented with large, soft drusen in both eyes. Optical coherence tomography and fluorescein angiography revealed the presence of PEVAC in the left eye. The patient was in good general health with no history of diabetes and had no signs of other retinal vascular disease. During the follow-up, the intraretinal fluid accumulation progressively increased and the best-corrected visual acuity (BCVA) dropped from 20/20 to 20/30 over a period of 33 months. As the intraretinal fluid continued to increase and BCVA further decreased to 20/50 despite two intravitreal injections of anti-VEGF, the patient underwent focal thermal laser photocoagulation with a reduction in intraretinal fluid observed 1 month later. Two months after laser, the BCVA increased to 20/25 with complete reabsorption of the intraretinal fluid. Ten months after laser, the BCVA remained stable at 20/25 with no recurrence of intraretinal fluid.

Conclusions and Importance: This case illustrates that a PEVAC lesion may remain non-exudative for an extended period of time, but when exudation develops, anti-VEGF therapy may be ineffective requiring the use of thermal laser photocoagulation.

1. Introduction

Perifoveal exudative vascular anomalous complex (PEVAC) is a rare disorder with an uncertain etiology, which is characterized by retinal vascular abnormalities in the perifoveal region.[1] It is defined by the presence of a unilateral, isolated, perifoveal aneurysm that has been reported in subjects with no relevant personal or familial medical history or in patients with macular diseases including age-related macular degeneration (AMD) and myopic macular degeneration.[2,3] Considering the rarity of this condition, the appropriate management of exudation secondary to PEVAC is not well-established. In this report we describe the extended follow-up of a patient with PEVAC, initially without exudation, who subsequently developed exudation and was treated with intravitreal injections of anti-vascular endothelial growth factor (VEGF) followed by focal thermal laser photocoagulation.

2. Case report

A 78 year-old man was referred to the Doheny-UCLA Eye Center for evaluation of age-related macular degeneration. The patient was in good general health with no history of diabetes or hypertension. Best-corrected visual acuity (BCVA) was 20/20 in the both eyes. On slit-lamp examination, no abnormalities were found in the anterior chamber and intraocular pressure was 14 mmHg in both eyes. Fundus examination revealed the presence of large, soft drusen in both eyes (Fig. 1A–D). The left eye (LE) also showed an isolated aneurysmal lesion immediately nasal to the fovea, accompanied by small hemorrhages. Patient had no other signs of retinal vascular disease. In the LE, spectral

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domain optical coherence tomography (OCT) revealed the presence of drusen and a single oval hyporeflective lesion at the level of outer nuclear layer, outer plexiform layer and inner nuclear layer without subretinal or intraretinal fluid (Fig. 1F). As the patient had good vision, no symptoms, and no exudation, the lesion was followed. Although no exudation was observed by 6 months, intraretinal fluid was evident by 19 months, but the patient remained asymptomatic. However, over the next year, the fluid progressively increased and BCVA dropped to 20/30 by 33 months. Fluorescein angiography at this time revealed the hyperfluorescent aneurysmal lesion with pooling of the dye in the intraretinal cystoid spaces (Fig. 2). The aneurysmal lesion was not evident by OCT angiography (not shown). As the vision was decreasing and the patient was complaining of visual, after informed consent, the was patient treated with two intravitreal injections of aflibercept (Eylea, Regeneron-Bayer HealthCare). After two months, despite therapy, the intraretinal fluid increased with an associated decrease in BCVA to 20/50. After further discussion and informed consent, the patient underwent focal thermal laser photocoagulation (2 spots, 50 μm, 50 ms, 50 mW). One month later the intraretinal fluid was slightly reduced, and after two months, the BCVA increased to 20/25 with a complete reabsorption of the intraretinal fluid. 10 months after focal laser, the BCVA remained stable at 20/25 with no recurrence of intraretinal fluid (see Fig. 3).

3. Discussion

First reported in 2011, PEVAC has been described as a condition characterized by an isolated large perifoveal aneurysm, in the absence of retinal vascular or inflammatory diseases.[1] In a recent study, it was shown that PEVAC occurred in healthy patients with coincident macular disease, such as AMD or my myopic macular degeneration.[2,3] Two reports also described PEVAC in patients with diabetes mellitus but without evident diabetic retinopathy.[4,5]

Herein, we describe the extended follow-up of a patient with PEVAC treated unsuccessfully with intravitreal anti-VEGF injections, with resolution of exudation after focal thermal laser photocoagulation. In this case, the patient also manifested an extended period of time where the aneurysmal lesion was apparent without exudation and/or visual impairment, before the cystoid macular edema first appeared. In a recent study, this phase was described as the pre-exudative stage of PEVAC or non-exudative perifoveal vascular anomalous complex (nePVAC).[6]

Distinguishing a PEVAC lesion from other mimicking disorders is essential for appropriate follow-up and management. In particular, PEVAC lesions should be differentiated from type 1 macular telangiectasia, nascent type 3 lesions and isolated diabetic retinal macroaneurysms.[2] The absence of other telangiectatic retinal vascular alterations and macular pigment abnormalities on fundus autofluorescence can aid in excluding type 1 macular telangiectasia. Nascent type 3 macular neovascularization (MNV) typically progress with a downgrowth of vessels from the deep capillary plexus to the retinal pigment epithelium/sub-retinal pigment epithelium space — which was not observed during the course of follow-up in our case.[7] Type 3 MNV is particularly important to distinguish as this lesion typically responds very well to anti-VEGF therapy. Diabetes could be ruled out as an explanation in our case as our patient was in good general health with no history of diabetes.

With regards to treatment, patients with retinal arteriolar macroaneurysms are generally thought to have a favorable visual prognosis, even without treatment. In contrast, PEVAC lesions, despite essentially

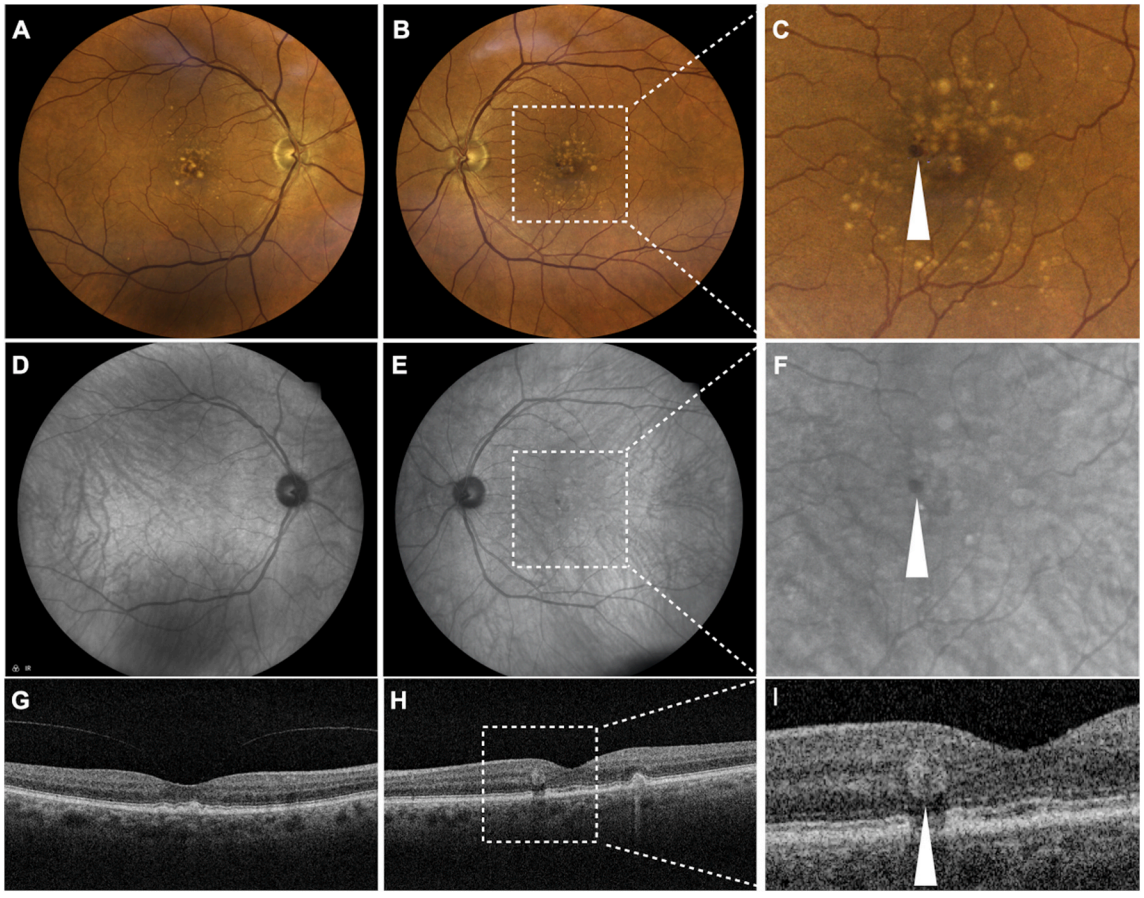

Fig. 1. Multimodal imaging at baseline. Fundus color photography (A, B and C), infrared reflectance (C, D and E) and optical coherence tomography (F, G and H) showing drusen and an isolated aneurysmal lesion nasal to the fovea in the left eye (white arrowhead).

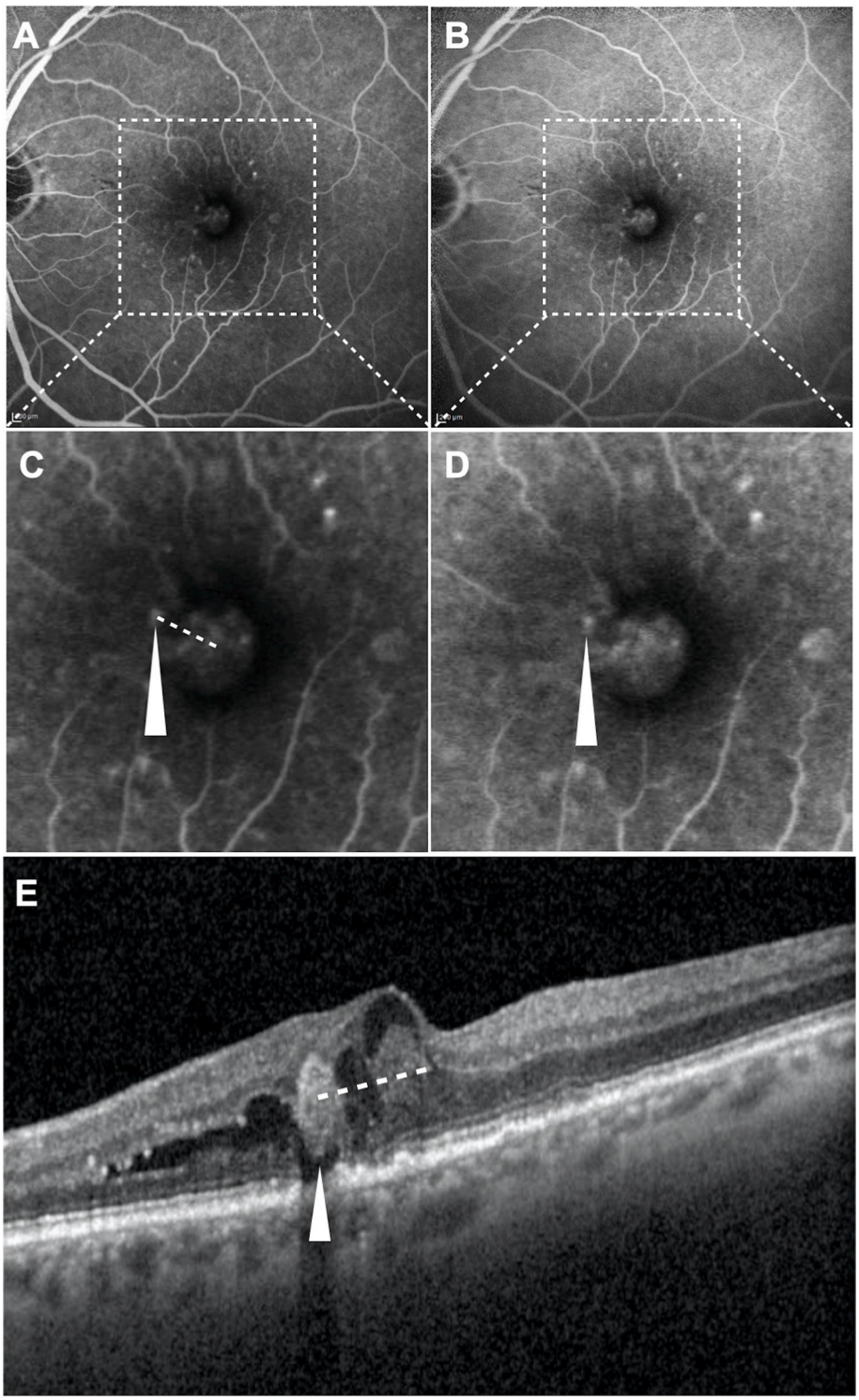

Fig. 2. Multimodal imaging at month 33. Fluorescein angiography in the early phase (A and C) showing retinal pigment epithelial defects with an isolated aneurysmal lesion nasal to the fovea (white arrowhead) and pooling of the dye in the late phase (B and D). Optical coherence tomography (E) displaying the oval aneurysmal lesion with adjacent exudation. White dotted lines indicate the distance between the center of the aneurysmal lesion and the foveal center which measured approximately 819 μm.

being macroaneurysnal lesions associated with the capillary circulation appear to have a poorer visual outcome despite various treatments.[6] Consistent with previously reported cases, our patient did not show any functional or anatomical improvements after intravitreal anti-VEGF therapy. In fact, Zhang et al.[4] reported the case of a patient with PEVAC that underwent two injections of anti-VEGF resulting in an increase in macular edema, hard exudates and hemorrhages. Mrejen et al.[3] described positive anatomic and functional results in a patient treated with 13 injections of anti-VEGF therapy. However, the improvement did not occur immediately after the injections but after several months of follow-up. Siedlecki et al.[8] presented a case of lamellar macular hole associated with PEVAC and suggested a questionable role for anti-VEGF injections due to spontaneous fluctuation in edema during follow-up. Our case would appear to support the general lack of enthusiasm for anti-VEGF therapy as a treatment for PEVAC. In contrast, focal thermal laser photocoagulation, which has been shown to be an effective treatment for macular edema associated with microaneurysms in other contexts (e.g. diabetic retinopathy), was also effective for the larger PEVAC aneurysmal lesion in our case. Mrejen et al.[3] also described a case of PEVAC which did not respond to intravitreal ranibizumab, but

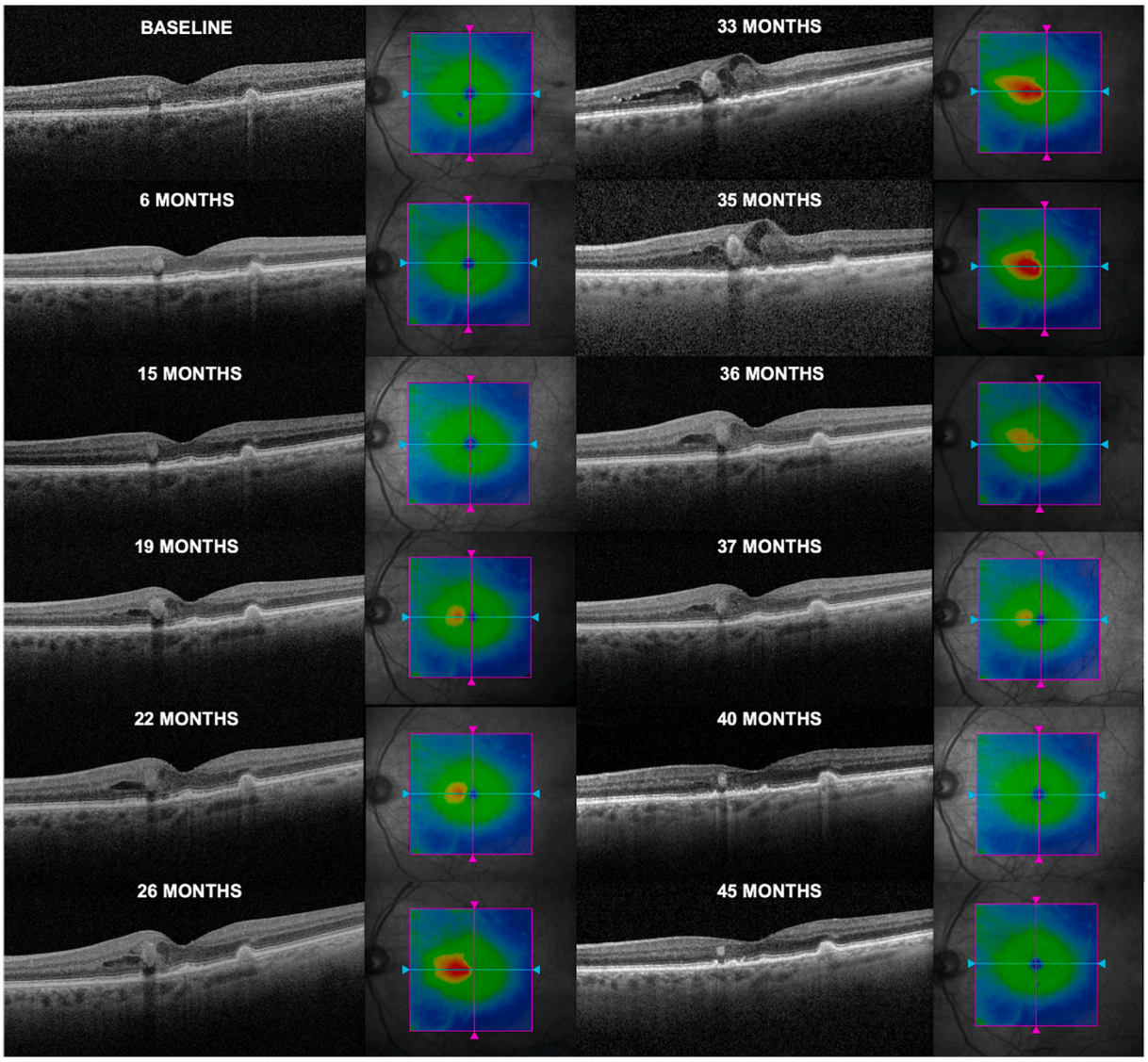

Fig. 3. Optical coherence tomography during follow-up. Optical coherence tomography with the thickness map showing the progressive increase of exudation adjacent to the oval aneurysmal lesion nasally during follow-up. Intravitreal injections of anti-vascular endothelial growth factor were administered at month 33 and 34, with reduction in edema after thermal laser photocoagulation at month 35.

was subsequently treated with focal thermal laser photocoagulation and demonstrated improvement in BCVA. However, a recurrence in exudation occurred 7 months later and a second session of laser photocoagulation was required. In contrast, after a single session of laser in our case, the core of the perifoveal aneurysm lesion became more homogeneously and intensely hyperreflective, with associated sustained (>10 months) resolution of macular edema and no visible laser scar.

In conclusion, PEVAC lesions may be initially nonexudative and asymptomatic, but may develop exudation with extended follow-up. When exudation develops, it may not be responsive to anti-VEGF therapy, but may respond to focal thermal laser photocoagulation.

4. Patient consent

The patient consented to publication of the case in writing. This report does not contain any personal identifying information.

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Authorship

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

Declaration of competing interest

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