Progressive resolution of exudation from perifoveal vascular anomalous complex: A possible role of diclofenac therapy?

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ABSTRACT

Purpose: To report a case of progressive resolution of exudation in a patient affected by perifoveal vascular anomalous complex (PVAC) undergoing topical diclofenac therapy.

Observations: A 74-year-old man presented to our department with visual decrease in his right eye lasting six months. Lack of clinical history of arterial hypertension, diabetes, or any other systemic or local vasculopathy, together with retinal multimodal imaging, led to the diagnosis of exudative (e)PVAC. Serial spectral-domain optical coherence tomography (SD-OCT) examinations documented a resolution of intraretinal exudation after one-month topical diclofenac therapy.

Conclusion and Importance: Initiation of topical diclofenac was associated with resolution of exudation, therefore we hypothesize its potential role in the treatment of ePVAC.

1. Introduction

Perifoveal vascular anomalous complex (PVAC) is a perifoveal, unilateral, usually unifocal, less frequently multiple, large aneurysmal lesion associated with surrounding microvascular changes in an otherwise healthy patient. This condition was first described by Querques and associates as PEVAC.1

Lesions occurring in PVAC disease are usually not progressive and cause a moderate impact on vision, with visual decline and metamorphopsia caused by intraretinal exudation associated with the large aneurysmal lesions. Recently, it has been suggested to differentiate two forms of this condition: a non-exudative (nePVAC) and an exudative one (ePVAC), being the first the preclinical stage of the latter.2

Exudative PVAC is usually unresponsive to intravitreal anti-vascular endothelial growth factor (VEGF) injections, but spontaneous resolution of intraretinal cystic spaces without any treatment has been reported.1,3 Focal laser photocoagulation was also described as an effective treatment.3

In this report, we present the case of a patient with who was treated with one-month topical diclofenac therapy at another medical center and demonstrated a resolution of exudation. The possible role of diclofenac topical therapy in this case is discussed.

2. Case report

A 74-year-old man presented to the Medical Retina and Imaging Unit of San Raffaele Hospital (Milan, Italy) complaining of a visual decrease in his right eye (RE) lasting six months.

He was initially referred to another center, where he was evaluated with spectral domain-optical coherence tomography (SD-OCT) which showed the presence of perifoveal intraretinal cysts in the nasal macula in his RE. (Fig. 1a). No angiographic tests (fluorescein angiography, FA, or OCT angiography, OCTA) were performed by ophthalmologists of this center at first consultation. Four months later from baseline, repeated SD-OCT showed an increase in intraretinal cysts. (Fig. 1b).

Given the increase of intraretinal fluid, the patient was advised to start on topical diclofenac 0.1% drops twice a day for one month. Five months later from baseline, FA was performed (Fig. 1d), which, together with SD-OCT findings (Fig. 1c) led to the diagnosis of ePVAC. Interestingly, FA revealed a lack of perfusion of the large aneurysmal lesion associated with surrounding microvascular changes. However, due to the persistence of rare perifoveal intraretinal cysts and rare hard
Early (left) and late phases (right) reveal a lack of perfusion of the large aneurysmal lesion associated with surrounding microvascular changes. ePVAC: exudative perifoveal vascular complex.

1a) Baseline structural OCT showing perifoveal intraretinal cysts in the nasal macula of right eye. 1b) Structural OCT performed four-months later showing an increase in intraretinal cysts. 1c) Structural OCT performed five months later from baseline, after one-month topical non steroidal anti-inflammatory drug. Early (left) and late phases (right) reveal a lack of perfusion of the large aneurysmal lesion associated with surrounding microvascular changes. ePVAC: exudative perifoveal vascular complex. NSAID: non steroidal anti-inflammatory drug.

1d) Fluorescein angiography (FA) performed five months later (White rectangle) Corresponding magnification of rare intraretinal cysts and hard exudates. 200 µm. 

Fig. 1. Multimodal imaging of ePVAC in right eye at baseline and at follow-up examinations (from another center).

3. Discussion

Although multimodal imaging has provided a better understanding of many retinal diseases, nowadays PVAC pathogenesis remains still unclear. Different hypotheses have been proposed.

PVAC may be consequence of focal endothelial cell injury, in patients not affected by other vascular or inflammatory disease. Therefore, an increased endothelial damage may lead to exudation and progression from nePVAC to ePVAC. Both perifoveal aneurysm and perilesional capillaries rarefaction seem to result from pericytes loss, in particular from breakdown of pericytes’ basement membrane by matrix metalloproteinase-9. Thus, PVAC genesis would be not regulated by VEGF, but by the imbalance between a reduced wall strength and an increased wall tension, in accordance with Laplace’s law. Notably, perilesional microvascular rarefaction has been associated to an impaired angiogenesis and local ageing.

A glial cell–driven genesis, secondary to Müller cells necrosis, has been postulated to explain a case of concomitant PVAC and lamellar hole-associated epiretinal proliferation.

In addition, PVAC could be a response to anatomical variation, in particular to prepapillary arterio-arterial loop, in chronic slow flow retinopathy.

In this report, we present the case of a patient with PVAC who was treated with topical non-steroidal anti-inflammatory (NSAID) therapy and demonstrated a progressive resolution of exudation.

NSAIDs are one of the most common prescribed class of medications. Management of pseudophakic cystoid macular edema, post-operative pain after refractive surgery, allergic conjunctivitis, and prevention of miosis during intraocular surgery are some of on-label ophthalmological clinical uses of topical NSAIDs. As off-label medications, NSAID have been shown to be beneficial in the treatment of diabetic retinopathy, ocular tumors, post-retinal vein occlusion, and neovascular age-related macular degeneration.

NSAIDs inhibit expression of cyclooxygenase (COX) enzymes isoforms (COX-1, COX-2) and their products, namely prostaglandins (PGs) and thromboxanes (TXs). Normally, PGs acts as vasodilating agents, so that their inhibition causes blood-retina barrier disruption, leukocyte migration, and therefore inflammation and edema. Increasing evidence suggests that NSAIDs might also prove efficient as anti-angiogenic drugs. Recent clinical and experimental studies have demonstrated that COX-2 promotes angiogenesis. Interestingly, Chang et al. demonstrated a positive correlation between known angiogenic regulatory genes (VEGF, Ang2, Flt-1, Tie2) and COX-2 over-expression. Thus,
COX-2 pathway might induce anti-angiogenic genes' expression, such as Ang2 and Tie2. NSAIDs impact on angiogenic cascade could explain the supposed beneficial effect of topical diclofenac in reducing our case of exudative perifoveal vascular aneurysm complex.

Interestingly, topical NSAIDs together with topical steroids may lead to long-term resolution of cystoid macular edema secondary to...
idiopathic macular telangiectasia type 1.17

However, given the fact that there is no definitive evidence proving beyond doubt the role of diclofenac in reducing macular edema, including exudation from PVAC, there is clearly a possibility that the reduction in intraretinal exudation in our case was not related to any therapeutic effect of diclofenac, but rather occurred as a coincident event.

Patient consent

The patient provided written informed consent for publication of this case report and any accompanying images.

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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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