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Exudative perifoveal vascular anomalous complex (ePVAC) resembling lesion in a patient with adult-onset foveomacular vitelliform dystrophy

Serena Milan, Marco Rocco Pastore *, Andrea Gaggino, Silvia Rinaldi, Daniele Tognetto

Eye Clinic, Department of Medical Surgical Sciences and Health, University of Trieste, 34129, Trieste, Italy

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ABSTRACT

Purpose: to report a case of exudative perifoveal vascular anomalous complex (ePVAC) in a patient with adult-onset foveomacular vitelliform dystrophy.

Observations: A 71-year-old male presented with moderate vision loss in his left eye. His past medical and ocular history were unremarkable. The best-corrected visual acuity was 20/32. Fundus examination disclosed the presence of a perifoveal vascular abnormality, associated with a small egg-yolk lesion. Optical coherence tomography (OCT) scan passing through the perifoveal vascular abnormality seen on fundus, revealed a small round hyperreflective lesion located at the outer plexiform layer-inner nuclear layer, surrounded by intraretinal cysts. Fluorescein angiography displayed an isolated perifoveal aneurysmal lesion with minimal leakage. OCT angiography permitted to localize the lesion flow signal at the deep capillary plexus (DCP) and the avascular slab; choriocapillaris structure was unaffected; any retino-choroidal anastomosis was detected. A systemic workup was suggested to rule out any vascular diseases, and any abnormality was found. He was thus diagnosed with ePVAC. A stability of the clinical picture was demonstrated after 3 months of follow up.

Conclusion: ePVAC has recently been described to appear in association with other macular abnormalities, such as age-related macular degeneration and myopic macular degeneration. Our case firstly demonstrates an ePVAC lesion in an eye with adult-onset foveomacular vitelliform dystrophy. This observation highlights the importance of discerning between different vascular disorders of the macula, to offer the right treatment to the patient.

1. Introduction

Perifoveal Exudative Vascular Anomalous Complex (PEVAC) was first described by Querques and colleagues in 2011.[1] It was defined as a unilateral, perifoveal, isolated aneurysmal lesion occurring in otherwise healthy patients, typically associated with intraretinal exudation. It was initially characterized based on its OCT features, represented by a round hyperreflective lesion associated with intraretinal cystic spaces; the absence of any additional retinal or choroidal vascular abnormality on FA and ICGA was also required.[1] Lately, the observation of similar lesions presenting without any signs of exudation led to the conversion of the original acronym to ePVAC (exudative peri-foveal vascular anomalous complex) and nePVAC (nonexudative form of PVAC).[2]

As per the original definition, the exclusion of any concomitant ocular or systemic vascular disease was required for the diagnosis. Indeed, perifoveal retinal vascular lesions are generally detected in presence of systemic or ocular risk factors, such as hypertension, diabetic retinopathy, venous occlusion, inflammatory diseases, radiation retinopathy, and blood dyscrasias.[3] Macular telangiectasia (Mac-Tel) and retinal angiomatous proliferation (RAP) represent less frequent etiologies.

Nevertheless, subsequent clinical experience and multimodal imaging studies led to expand the spectrum of PVAC lesion.[3] It has been reported in association with other macular disease, including age-related macular degeneration, myopic maculopathy and pigment pachychoroid epitheliopathy.[3–5] Here, we report a case of ePVAC in a patient affected by adult-onset foveomacular vitelliform dystrophy (AOFVD).

2. Case report

A 71-year-old male was referred to the medical retina and imaging service of our department due to macular edema in his left eye (LE). He complained of blurry vision in the last 3 months. He was in good health and his past medical and ophthalmic history were uneventful. He denied

* Corresponding author. Eye Clinic, University of Trieste, Ospedale Maggiore, Piazza dell'Ospitale 1, 34129, Trieste, Italy.
E-mail addresses: serena.milan@studenti.units.it (S. Milan), marco.pastore@hotmail.it (M.R. Pastore), andrea.gaggio@gmail.com (A. Gaggino), silvia_rinaldi@hotmail.com (S. Rinaldi), tognetto@units.it (D. Tognetto).

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any previous or ongoing treatment.

On eye exam, the best-corrected visual acuity was 20/25 in the right eye (RE) and 20/32 in the LE. Intraocular pressure was 14 mmHg in both eyes. Slit lamp examination of the anterior segment was unremarkable.

Fundus examination in the RE fundus examination demonstrated two perifoveal, elevated, yellow lesions with internal hyperpigmentation, associated with some druplets (Fig. 1A, left). LE showed a translucent macular reflex for early extrafoveal epiretinal membrane and focal vitreomacular adhesion, associated with a small, elevated, yellowish foveal lesion surrounded by druplets. In addition, an aneurysmatic vessel dilatation supertemporal to the fovea was disclosed (Fig. 1A, right). Retinal vascular diameter was otherwise within normal limits and no sign of hypertension or vascular pathology was detected. Multimodal imaging was required. At autofluorescence examination the yellow lesions in both eyes appear hyperautofluorescence (Fig. 1B).

The optical coherence tomography (OCT) passing through the yellow lesions illustrated the presence of hyperreflective subretinal material with an underlying irregularly thickened retinal pigment epithelium (RPE) in both eyes (Fig. 1C). A scan passing through the vessel dilation revealed a round hyperreflective lesion with a horizontal diameter of 159 μm and a vertical diameter of 165 μm, containing irregular hyperreflective material localized between the outer plexiform layer (OPL) and the inner nuclear layer (INL), surrounded by intraretinal cystic spaces (Fig. 2A).

Both early fluorescein angiography (FA, Fig. 1C left) and early indocyanine green angiography (ICGA, Fig. 1D left) in LE revealed a corresponding well-defined round hyperfluorescent lesion, with a mild leakage in the late frames only on FA (Fig. 2C right). No other vascular abnormalities were present outside the area of the lesion with both dyes' examinations. The yellow lesions detected at fundus examination appeared as hypofluorescent spots at FA surrounded by a hyperfluorescent spoked ring on early frames; they showed central staining on late images without leakage (Fig. 2C). The multimodal imaging for these lesions was consistent with lipofuscin deposits.

OCT angiography (OCT-A) was assessed using Heidelberg Spectralis II OCT (Software Version 6.15, Heidelberg Engineering, Heidelberg Germany) (Fig. 3). An isolated aneurysmal abnormality with detectable flow was displayed both in the DCP and the avascular slab (Fig. 3C and D), associated with a rarefaction of retinal capillaries in the perilesional area. The presence of any anastomosis between the choriocapillaris and the retinal capillary plexuses was excluded and any choriocapillaris anomalous flow was visualized. Additional examination, including electrooculogram, were normal.

The presence of systemic hypertension and any vascular risk factor were excluded: blood tests were negative for hyperglycemia, hypercholesterolemia, blood dyscrasia, and inflammatory pathology.

The patient was thus diagnosed with AOFVD complicated by ePVAC.

Due to the described unresponsiveness of this pathology to antivascular endothelial growth factor (antiVEGF) treatment, and to the proximity of the lesion to the fovea, neither intravitreal injection nor laser photocoagulation was suggested.

The patient was followed up for three months, and a stability of the clinical picture was recorded (Fig. 2 B).

3. Discussion

In this article, a case of PEVAC in a patient affected by AOFVD is described.

PEVAC was first defined by Querques and colleagues as a unilateral, perifoveal, isolated, large aneurysmal lesion occurring in otherwise healthy patients, typically associated with intraretinal exudation.[1]

The presence of perifoveal retinal vascular abnormalities is typically

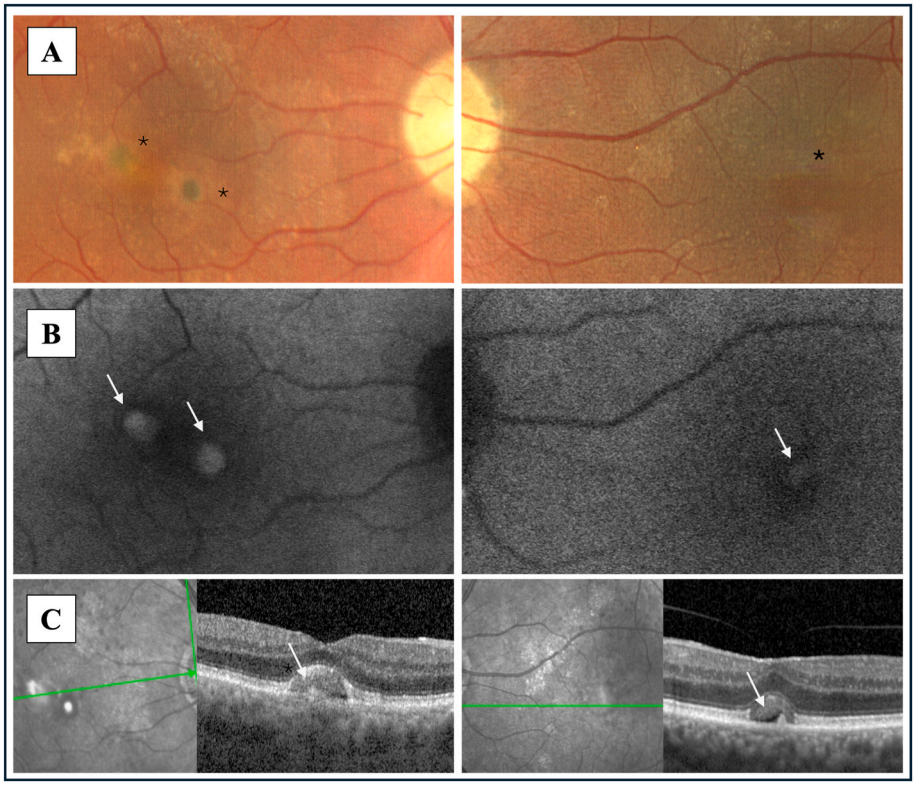

Fig. 1. Multimodal imaging of adult-onset foveomacular vitelliform dystrophy: retinography (A), autofluorescence (B) and optical coherence tomography (OCT) (C). Figures on the left refer to the right eye. In the right eye, two yellow perifoveal lesions with a pigmented center can be observed in the retinography (A, outlined by *), showing hyperautofluorescence (B, outlined by arrows). In the left eye, a PEVAC lesion is shown in the retinography (A, *) associated with a vitelliform lesion presenting hyperautofluorescence (B, arrow). Vitelliform lesions in both eyes were associated with the accumulation of hyperreflective subretinal material on OCT (C, outlined by arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

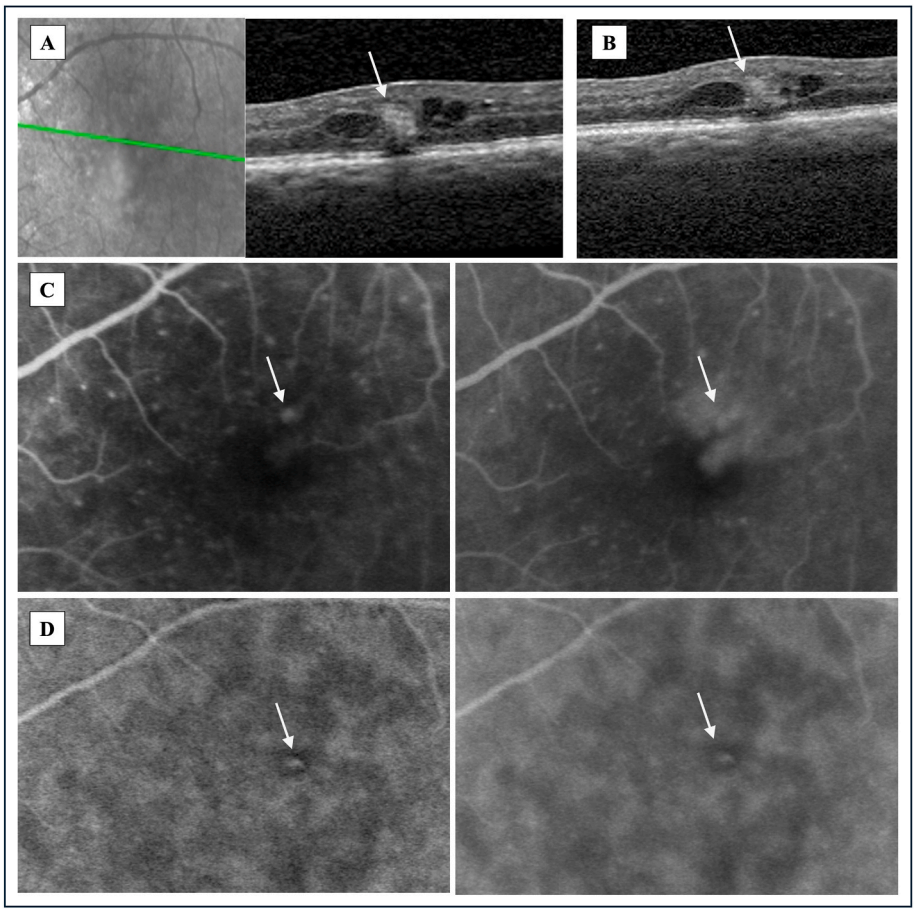

Fig. 2. Multimodal imaging of perifoveal exudative vascular anomalous complex in the left eye. The ePVAC lesion is outlined by arrows.Optical coherence tomography (OCT) at the diagnosis (A) shows a round hyperreflective lesion (arrow) containing irregular hyperreflective material localized between the outer plexiform layer and the inner nuclear layer, surrounded by intraretinal cystic spaces, consistent with ePVAC. Fluorescein angiography demonstrates a well-defined round hyperfluorescent lesion in the early frames (C, left), with a mild leakage in the late frames (C, right). Indocyanine green angiography shows a well-defined round hyperfluorescent lesion in the early (D, left) and late (D, right) frames. OCT at the last follow up demonstrates a stability of the clinical picture (B). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

related to an underlying systemic or ocular disease, such as hypertension, diabetic retinopathy, venous occlusion, inflammatory diseases, radiation retinopathy and blood dyscrasias.[3] In our case, multimodal imaging didn't disclose any associated retinal abnormality suggestive of these pathologies; moreover, a systemic work up permitted to exclude additional predisposing factors.

Type 1 macular telangiectasia (MacTel) represents a rare entity characterized by visible and exudative unilateral telangiectasia accompanied by multiple arteriolar, venular and capillary aneurysms, which weren't detected in our patient, who showed an isolated vessel dilation.[6]

Retinal angiomatous proliferation (RAP) is a form of perifoveal neovascularization occurring in AMD.[7]

The differential between PEVAC and stage 1 RAP may at times be challenging. In fact, it is characterized by a vascular proliferation deriving from the retina vascularization, particularly from the DCP. However, it is generally associated with very minimal fluid, and it typically tends to grow downwards towards the RPE. Moreover, its ICGA characteristics are clearly defined: it can be visualized as a hot spot in the mid frames with late-phase leakage. The retinal-retinal anastomosis becomes visible as a hairpin loop. We didn't observe any of the described features. In addition, RAP typically has an aggressive clinical course, while an indolent course was detected in our case, which is typical for PEVAC.[8]

Deep retinal age-related microvascular anomalies (DRAMAs) have been recently described as a type of DCP alterations occurring in association with AMD typical findings, such as soft drusen and intraretinal hyperreflective foci.[9]

The multimodal imaging features for the diagnosis of PEVAC have been described in several reports and our findings were consistent with the literature. On OCT, PEVAC looked like a round hyperreflective structure; the dark appearance of the lumen was less evident at presentation, as already previously described.[8] FA and ICGA disclosed a well-defined hyperfluorescent lesion; however, late leakage was evident only with the former exam. According to a multicentric cohort study on 18 PEVAC cases reported by Sacconi et al., the aneurysmal dilation of PEVAC can be localized at the DCP, superficial capillary plexus (SCP), or both, or in the DCP and the avascular slab. In addition, the perilesional area is characterized by a remarkable rarefaction of the retinal capillaries, whose significance is still unclear: it may constitute a true pathologic alteration, or a segmentation artifact linked to the intraretinal cysts.[3]

As per its original definition, PEVAC is tipically associated with intraretinal exudation.[1] In 2020, PEVAC cases presenting without any signs of exudation were described, ending with the modification of the original acronym: lesions are now classified based on the presence of exudation, in ePVAC (exudative peri-foveal vascular anomalous complex) and nePVAC (nonexudative form of PVAC).[2]

Moreover, PEVAC was originally described in otherwise healthy patients. However, its occurrence in association with AMD, diabetic retinopathy, myopia, pachychoroid pigment epitheliopathy was reported, leading to the recognition of the expanded spectrum of PEVAC lesion.[3–5]

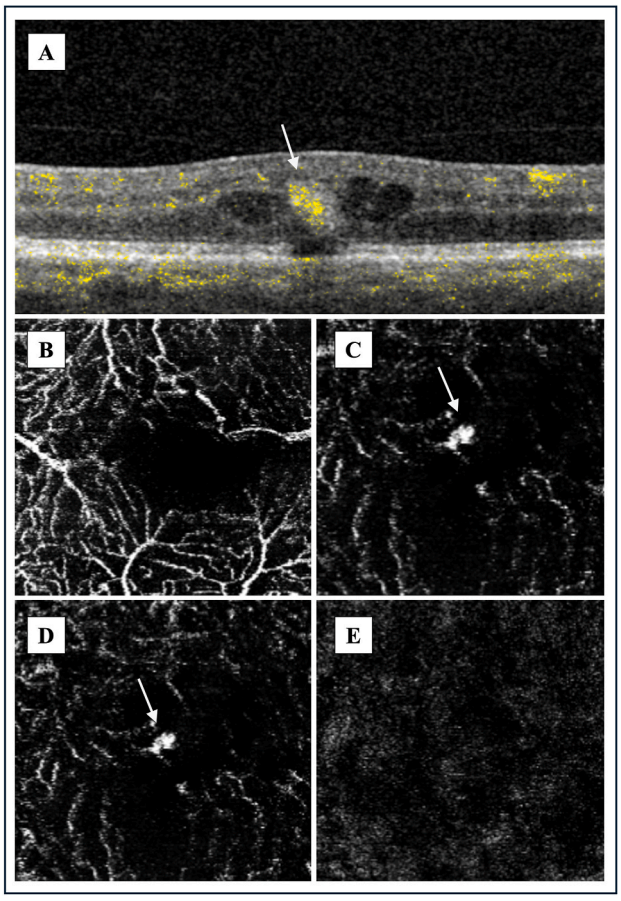

Fig. 3. Optical coherence tomography - angiography of perifoveal exudative vascular anomalous complex in the left eye. The lesion is outlined by arrows. The radial scan (A) shows a hyperreflective round intraretinal lesion with detectable flow, which can be localized at the level of the deep capillary plexus (C) and the avascular slab (D), associated with a rarefaction of retinal capillaries in the perilesional area. Any abnormality is detected in the superficial capillary plexus (B)and choriocapillaris slab (E).

Telangiectatic capillaries (TelCaps) represent another type of capillary macroaneurysms (>150 μm). They are usually observed in eyes affected by retinal vascular diseases, such as diabetes and vascular occlusion. They may cause chronic macular edema, causing them to often escape fundus, FA and OCT examination. Since their lumen contains lipids and stagnant blood, the diagnosis may be helped by ICGA, whose affinity for these materials may explain the very late staining. Their differentiation with PEVAC may be challenging since they may overlap with PEVAC resembling lesions, occurring in patients with vascular diseases.[10,11]

In our case, PEVAC occurred in an eye affected by AOFVD.

An AOFVD-related neovascularization had to be excluded. However, it typically arises from the choroid; our case presented any sign of choroidal neovascularization on OCT-A, FA, or ICGA.

In this retinal pattern dystrophy, pigment accumulates in the RPE in the foveal or perifoveal region in the form of a vitelliform yolk-like lesion. Studies with OCT-A illustrated a decrease in the blood flow at the SCP and DCP. It was speculated that the vitelliform material could determine the compression of blood vessels.[12]

The pathogenesis of PEVAC is still not well understood. Querques et al. and Sacconi et al. proposed a focal vasogenic mechanism triggered by gradual retinal endothelial cell degeneration.[8] The mechanical damage induced by the vitelliform material may have been the culprit in our case, determining progressive degeneration of the capillary endothelium leading to aneurysmatic dilatation of the perifoveal capillaries, namely PEVAC.

It must be stated that AOFMD is usually characterized by bilateral, subfoveal, monofocal lesions. However, the occurrence of multifocal lesions has already been described by previous authors, and a possible role of VMD2 gene was suggested.[13–16]

A correct differential diagnosis is critical since each entity is characterized by a different pathological substrate. Indeed, RAP represents a severe subtype of AMD, characterized by a rapid natural course and a high rate of recurrence; however, it is typically associated with prompt response to antiVEGF injections.[17,18] Choroidal neovascularization complicating AOFVD may be efficiently controlled with intravitreal therapy, however the prognosis is undermined by the progression of the vitelliform lesions.[19–21] At the onset, ePVAC typically presents with intraretinal cystic spaces, at times associated with hard exudates and hemorrhages.[22] According to the literature, ePVAC is typically unresponsive to antiVEGF therapy.[3]

However, it must be considered that this entity is generally not progressive. Although usually permanent, both the exudation and the PVAC lesion itself may display a spontaneous resolution over time..[4,19,23] Moreover, it generally determines only a moderate impact on vision.[4]

Successful cases of laser selective photocoagulation are reported in the literature.[23,24] Nevertheless, PVAC typically affects the perifoveal region, making laser treatment challenging. Due to its relatively limited exudation and its location close to the fovea, clinical monitoring was preferred in our case. The clinical picture remained stable after three months of follow up, supporting the diagnosis of ePVAC.

4. Conclusion

PEVAC may complicate eyes affected by AOFVD. This evidence broadens the possible associations of PEVAC, which was already described in concomitance with AMD,myopia and pigment pachychoroid epitheliopathy. This entity may manifest an indolent course and is usually characterized by unresponsiveness to antiVEGF treatment. It is imperative to outline a correct differential diagnosis when facing intraretinal exudation in patients affected by maculopathy, to schedule the correct management.

CRediT authorship contribution statement

Serena Milan: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Marco Rocco Pastore:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Andrea Gaggino:** Writing – review & editing. **Silvia Rinaldi:** Supervision. **Daniele Tognetto:** Supervision.

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.

Claim of priority

After conducting a literature review July 24, 2024 utilizing PubMed and Google Scholar using the key words (perifoneal exudative vascular anomalous complex, adult-onset foveomacular vitelliform dystrophy), we did not find any prior reports of perifoneal exudative vascular anomalous complex on patients affected by adult-onset foveomacular vitelliform dystrophy.

Authorship

All authors attest that they meet the current ICMJE criteria for

Authorship.

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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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References

1. Querques G, Kuhn D, Massamba N, Leveziel N, Querques L, Souied EH. Perifoveal exudative vascular anomalous complex. *J Fr Ophtalmol*. 2011 Oct;34(8):559.e1–559.e4. https://doi.org/10.1016/j.jfo.2011.03.002.
2. Sacconi R, Borrelli E, Sadda S, et al. Nonexudative perifoveal vascular anomalous complex: the subclinical stage of perifoveal exudative vascular anomalous complex? *Am J Ophthalmol*. 2020 Oct;218:59–67. https://doi.org/10.1016/j.ajo.2020.04.025.
3. Sacconi R, Freund KB, Yannuzzi LA, et al. The expanded spectrum of perifoveal exudative vascular anomalous complex. *Am J Ophthalmol*. 2017 Dec;184:137–146. https://doi.org/10.1016/j.ajo.2017.10.009.
4. Sacconi R, Borrelli E, Bandello F, Querques G. Perifoveal exudative vascular anomalous complex in a highly myopic eye. *Ther Adv Ophthalmol*. 2020 Sep 11;12, 2515841420947930. https://doi.org/10.1177/2515841420947930.
5. Herda N, Semoun O, Srour M, et al. Atypical case of perifoveal exudative vascular anomalous complex associated with pachychoroid pigment epitheliopathy. *Am J Ophthalmol Case Rep*. 2022 Aug 28;28, 101691. https://doi.org/10.1016/j.ajoc.2022.101691.
6. Yannuzzi LA, Bardal AM, Freund KB, Chen KJ, Eandi CM, Blodi B. Idiopathic macular telangiectasia. *Arch Ophthalmol*. 2006 Apr;124(4):450–460. https://doi.org/10.1001/archopht.124.4.450.
7. Yannuzzi LA, Negrão S, Iida T, et al. Retinal angiomatous proliferation in age-related macular degeneration. *Retina*. 2001;21(5):416–434. https://doi.org/10.1097/00006982-200110000-00003.
8. Jadnanansing AI, Martinez Ciriano JP, van Droogenbroeck J, Spielberg L, Vanhonsebrouck E. Perifoveal exudative vascular anomalous complex (PEVAC) resembling lesion in a patient with multiple myeloma. *Am J Ophthalmol Case Rep*. 2023 Jul 16;34, 101891. https://doi.org/10.1016/j.ajoc.2023.101891.
9. Berlin A, Cabral D, Chen L, et al. Histology of type 3 macular neovascularization and microvascular anomalies in treated age-related macular degeneration: a case study. *Ophthalmol Sci*. 2023 Feb 10;3(3), 100280. https://doi.org/10.1016/j.xops.2023.100280. PMID: 36970117; PMCID: PMC10033755.
10. De Oliveira MRV, Mota I, Higino TM, Ventura CV, Japiassú RM, Gantois M. Telangiectatic capillaries in retinal vascular occlusions: multimodal imaging in a case series. *J Vitreoretin Dis*. 2023 Feb 16;7(2):154–159. https://doi.org/10.1177/24741264221149295.
11. Dupas B, Castro-Farias D, Girmens JF, et al. Photocoagulation or sham laser in addition to conventional anti-VEGF therapy in macular edema associated with TelCaps due to diabetic macular edema or retinal vein occlusion (TalaDME): a study protocol for a multicentric, French, two-group, non-commercial, active-control, observer-masked, non-inferiority, randomized controlled clinical trial. *Trials*. 2024 Apr 22;25(1):273. https://doi.org/10.1186/s13063-024-07994-1.
12. Nipp GE, Lee T, Sarici K, Malek G, Hadziahmetovic M. Adult-onset foveomacular vitelliform dystrophy: epidemiology, pathophysiology, imaging, and prognosis. *Front Ophthalmol (Lausanne)*. 2023 Aug 10;3, 1237788. https://doi.org/10.3389/fopht.2023.1237788.
13. Renner AB, Tillack H, Kraus H, et al. Morphology and functional characteristics in adult vitelliform macular dystrophy. *Retina*. 2004 Dec;24(6):929–939. https://doi.org/10.1097/00006982-200412000-00014.
14. Chowers I, Tiosano L, Audo I, Grunin M, Boon CJ. Adult-onset foveomacular vitelliform dystrophy: a fresh perspective. *Prog Retin Eye Res*. 2015 Jul;47:64–85. https://doi.org/10.1016/j.preteyeres.2015.02.001. Epub 2015 Feb 11.
15. Krämer F, White K, Pauleikhoff D, et al. Mutations in the VMD2 gene are associated with juvenile-onset vitelliform macular dystrophy (Best disease) and adult vitelliform macular dystrophy but not age-related macular degeneration. *Eur J Hum Genet*. 2000;8:286–292. https://doi.org/10.1038/sj.ejhg.5200447.
16. Boon CJ, Klevering BJ, den Hollander AI, et al. Clinical and genetic heterogeneity in multifocal vitelliform dystrophy. *Arch Ophthalmol*. 2007 Aug;125(8):1100–1106. https://doi.org/10.1001/archopht.125.8.1100. PMID: 17698758.
17. Browning AC, O'Brien JM, Vieira RV, Gupta R, Nenova K. Intravitreal aflibercept for retinal angiomatous proliferation: results of a prospective case series at 96 weeks. *Ophthalmologica*. 2019;242(4):239–246. https://doi.org/10.1159/000500203.
18. Kramann CA, Schöpfer K, Lorenz K, Zwiener I, Stoffelns BM, Pfeiffer N. Intravitreal ranibizumab treatment of retinal angiomatous proliferation. *Acta Ophthalmol*. 2012 Aug;90(5):487–491. https://doi.org/10.1111/j.1755-3768.2010.01952.x.
19. Mimoun G, Caillaux V, Querques G, Roth(