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# Optical Coherence Tomography as an Alternative for Diagnosing Polypoidal Choroidal Vasculopathy in Developing Countries

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**Abstract:** *Introduction:* Polypoidal choroidal vasculopathy (PCV) is a variant of neovascular age-related macular degeneration (nAMD). In clinical practice, PCV is frequently differentiated from nAMD or other retinal diseases using imaging modalities like optical coherence tomography, especially in ophthalmology clinics and hospitals which do not have access to indocyanine green angiography (ICGA), the gold standard in diagnosing PCV. As such, definite diagnosis of PCV is not possible in some cases and the actual prevalence of PCV remains unknown. *Case series presentation:* We have described a report of four patients without significant past medical history who presented with acute central or paracentral scotoma caused by PCV. Our approach to diagnosing PCV relied on the clinical manifestations of fundus fluorescein angiography (FFA) and spectral domain optical coherence tomography imaging (SS-OCT). *Conclusion:* In the absence of ICGA and OCT angiography in developing countries, it is essential to distinguish PCV from other retinal diseases, especially neovascular age-related macular degeneration as the treatment and prognosis of PCV differs from that of other retinal diseases. We believe that the key features observed in FFA and SS-OCT can potentially be equivalent to the findings on ICGA in accurate diagnosis of PCV, which is essential in tailoring patient treatment plans, set expectations, and find more effective and precise solutions.

**Keywords:** Occult Peripapillary Choroidal Neovascular Membrane, Polypoidal Choroidal Vasculopathy, Anti-VEGF, Age-Related Macular Degeneration, Type 1 Neovascularization

## 1. Introduction

Polypoidal choroidal vasculopathy (PCV) is a major cause of visual disability. It is considered a variant of type 1 neovascularization within the neovascular age-related macular degeneration (nAMD) spectrum. PCV is clinically characterized by serosanguinous exudative maculopathy, orange nodules associated with recurrent retinal pigment epithelial detachment (PED), serous exudation, and hemorrhage in multiple retinal layers observed predominantly in the peripapillary area [1-3]. PCV is highly prevalent in Asian populations with 25% to 50% of nAMD cases in these populations believed to be of the PCV subtype. The prevalence of PCV among white people, reportedly ranges between 10% and 20% [1, 2, 4].

However, the actual prevalence rate of PCV remains unclear, as it is quite challenging to diagnose PCV solely based on fundus photography, the imaging of choice in most population-based epidemiological studies [1, 5]. Additionally, since the invasive and time-consuming indocyanine green angiography (ICGA) method, which is

considered the gold standard for PCV diagnosis [5] may not be available in all ophthalmology hospitals, and in the absence of OCT angiography in developing countries, more accessible imaging modalities like spectral domain optical coherent topography (SD-OCT) and fundus fluorescein angiography (FFA) have successfully been used to effectively distinguish PCV from nAMD or other retinal diseases.

## 2. Patients and Methods

Case series presentation and analysis.

### *2.1. Clinical Case 1*

A 51-year-old female presented with a 15-day history of left eye paracentral scotoma. She has no significant past medical history and previously had good vision in both eyes with prescription.

Ophthalmic examination showed; Snellen Chart best-corrected visual acuity 20/20 on her right eye and 20/300 on her left eye. Intraocular pressure was normal in both eyes (14 and 15 mmHg, respectively).

Nothing remarkable was found on anterior segment biomicroscopy. Fundus examination of the right eye revealed clear media, with a healthy optic disc head, as well as no morphological or vascular abnormalities on retina or macula. The left eye showed a yellowish zone of roughly 7-disc areas (DA) involving the fovea and spreading from the temporal border of the optic disc head to the inferior temporal arcade. Additionally, a subretinal peripapillary orange round elevation with a central hemorrhage surrounded with multiple confluent intraretinal 50 to 100 µm white-yellowish ill-defined border spots were seen (Figure 1).

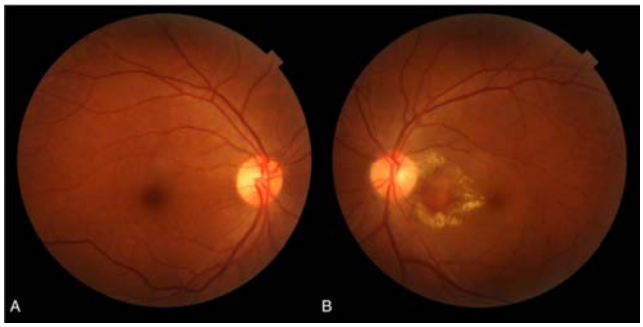


***Figure 1.*** *A) Right eye with clear media, healthy optic disc head, no morphological abnormalities on retina or macula. B) Subretinal peripapillary orange round elevation with a central hemorrhage surrounded with multiple confluent intraretinal 50 to 100 µm white-yellowish ill-defined border spots.*

Fundus fluorescein angiography (Spectralis FFA; Heidelberg Engineering, Heidelberg, Germany) of the left eye was performed to evaluate and characterize the lesion. Images revealed a hypo fluorescence zone secondary to blockage suggesting subretinal hemorrhage. Late stippled hyper fluorescence images showed ill-defined borders with increasing size and intensity, corresponding to a leakage pattern (Figure 2).

SS-OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany) evaluation of the left macula revealed subretinal and intraretinal fluid, hyperreflective elements in the external retina layers, and a "thumb-like protrusion" pigmented epithelium detachment (PED) (Figure 3). Based on these findings, the patient was diagnosed with peripapillary PCV and treated with one monthly intraocular injections of 2 mg aflibercept (Wetlia ®, Bayer) until reach a three doses scheme.

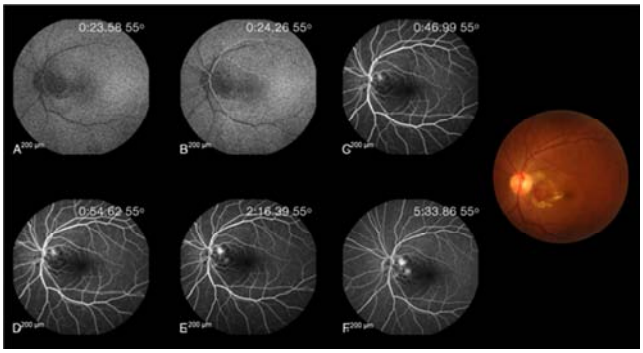


***Figure 2.*** *A-B) Hypo fluorescence zone secondary to blockage by subretinal hemorrhage. C-F) Two stippled hyper fluorescence images with ill-defined borders increase in size and intensity, associated with a leakage pattern.*

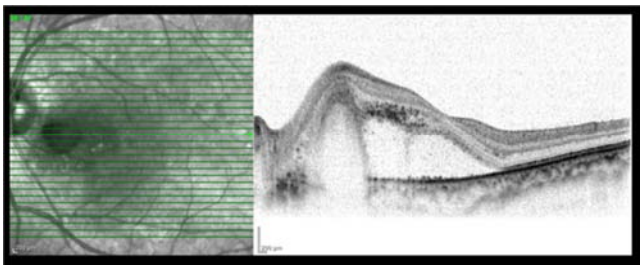

***Figure 3.*** *Subretinal fluid, hyperreflective material in the external retina layers, and a "thumb-like protrusion" pigmented epithelium detachment (PED).*

### *2.2. Clinical Case 2*

An 87-year-old man presented to the emergency department with rapid gradual visual loss of the right eye over 5 days of evolution. His past medical history was positive for well-controlled diabetes mellitus type 2 and essential hypertension. The patient did not have any positive history for ophthalmological diseases.

Ophthalmic examination showed best-corrected visual acuity of and 20/50 in his left eye. He perceived only hand movement with his right eye. Intraocular pressure was within the normal range in both eyes (12- and 13-mm Hg in the right and left eyes, respectively).

On anterior segment biomicroscopy, the presence of nuclear cataracts in both eyes was the only remarkable finding. Funduscopic examination of the right eye revealed mild opacification of the media due to cataract. The vitreous was optically empty and the optic disc head looked healthy. A central elevation of the macula involving the fovea with subretinal hemorrhage of approximately 6 DA was seen. No

relevant data were found on examination of the left eye (Figure 4).

FFA of the right eye showed a hypo fluorescent zone secondary to blockage by subretinal hemorrhage, without any late hyper fluorescence area (Figure 5).

SD-OCT of the right eye showed a large hyporeflective elevation and a "thumb-like protrusion" PED with a double-layer sign due to the presence of subretinal fluid and disruption of the external retinal layers (Figure 6). Based on clinical manifestation and OCT findings, the patient was diagnosed with PCV, and was treated with three intraocular injections of 2 mg aflibercept, one every month.

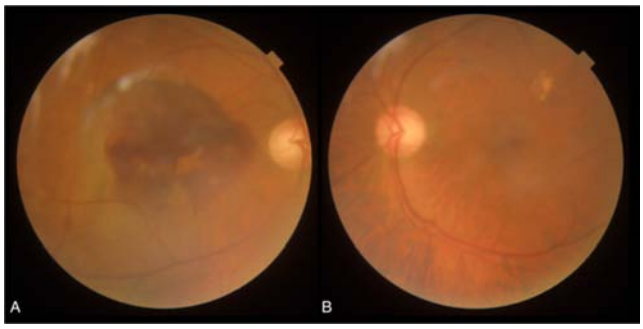


***Figure 4.*** *A) Right eye with clear vitreous, healthy optic disc head, macular elevation due to subretinal hemorrhage involving the fovea. B) Left eye with optically empty vitreous, healthy optic disc head, only the presence of soft drusen supero-temporal to fovea.*

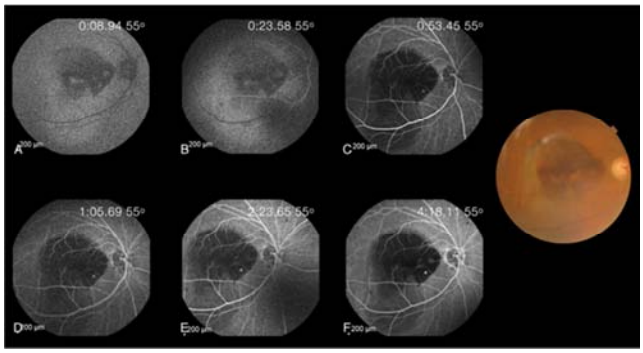

***Figure 5.*** *A-F) Hypo fluorescence zone secondary to blockage by subretinal hemorrhage.*

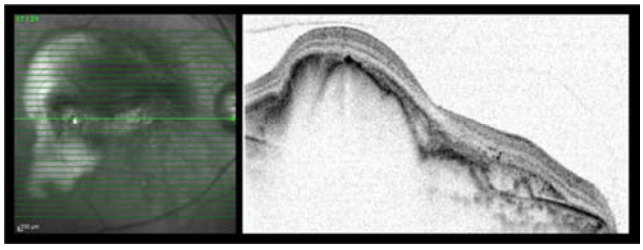

***Figure 6.*** *Subretinal fluid, disruption of the external retina layers, and a 'thumb-like protrusion' PED associated with the double–layer sign.*

### *2.3. Clinical Case 3*

A 60-year-old woman presented to our institute with gradual loss of vision over 1 month. No relevant past medical history was reported.

Ophthalmic examination showed best-corrected visual acuity (BCVA) of hand movement in the right eye and 20/25 in the left eye. Intraocular pressure and anterior segment biomicroscopy were unremarkable.

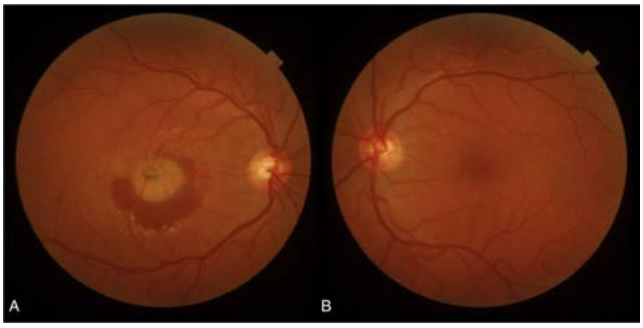


***Figure 7.*** *A) Right eye with clear vitreous, normal optic disc head, macular elevation with tortuous vessels and subretinal hemorrhage. B) Left eye with clear media, healthy optic disc head, with no abnormalities of the retina.*

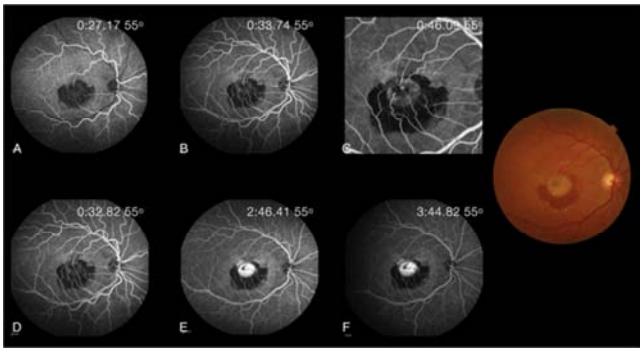

***Figure 8.*** *A-C) Hypo fluorescence zone secondary to blockage by subretinal hemorrhage associated with tortuous vessels at the center of the macula. D-F) A pronounced hyperfluorescent image with poorly defined borders increasing in size and intensity.*

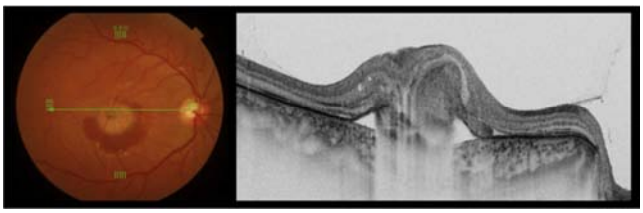

***Figure 9.*** *Elevation of the fovea with subretinal and intraretinal fluid, combined with disorganization of the external retinal layers with the double-layer sign.*

Funduscopic examination of the right eye revealed clear media and normal optic disc head. Central elevation of the macula with tortuous vessels and an incomplete ring of subretinal hemorrhage surrounded by hard exudates extending about 5 DA were also observed. The fundoscopy of the left eye was unremarkable (Figure 7).

FFA of the right eye showed hypo fluorescence zone secondary to blockage by subretinal hemorrhage at the center of the macula. Late hyper fluorescence revealed poorly defined borders with increasing size and intensity, corresponding to a leakage pattern (Figure 8).

SD-OCT of the right eye showed hyperreflective elevation of the fovea, presence of subretinal and intraretinal fluid, disruption of the external retinal layers, and the double-layer

sign (Figure 9). Considering the clinical manifestations and multi-imaging analysis, the patient was diagnosed with PCV; therefore, owing to the family's low wage income, we prescribed two doses of 2 mg aflibercept, one every month.

### *2.4. Clinical Case 4*

A 53-year-old symptomatic woman presented with a right eye visual loss lasting for 2 months. Medical past history at the moment of presentation was unremarkable.

Ophthalmic examination showed; best-corrected visual acuity of 20/300 on the right eye and 20/20 on the left eye. Anterior segment biomicroscopy and intraocular pressure were normal.

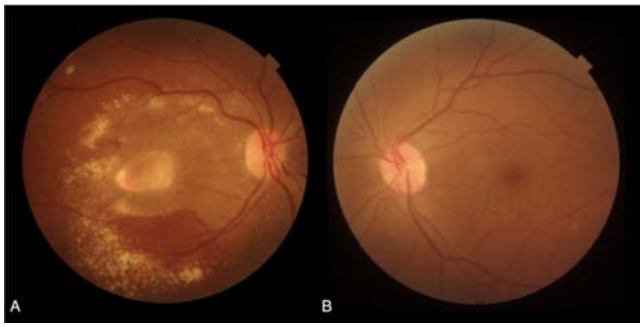


***Figure 10.*** *A) Right eye with central macular elevation, surrounded by fluid, hard exudation, and a subretinal hemorrhage. B) Healthy left eye fundoscopy.*

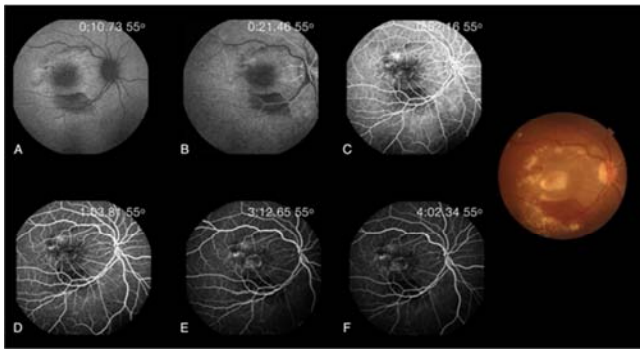


***Figure 11.*** *Hypo fluorescence zone secondary to blockage by subretinal hemorrhage, and a leakage pattern supero-temporal to fovea and an accumulation at the macula's center.*

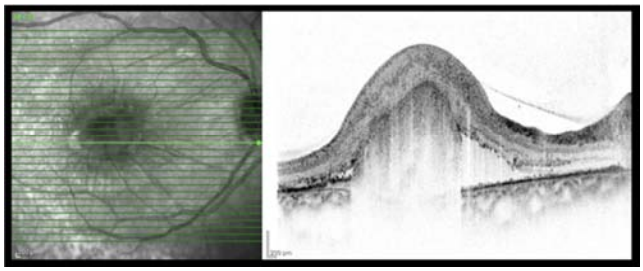

***Figure 12.*** *Subretinal fluid and hard exudates around a sharp PED in association with the double-layer sign.*

Fundus examination of the right eye showed a healthy optic disc head, and a central macular elevation extending 1 DA at the center of the fovea surrounded by subretinal fluid and lipid deposits with a subretinal hemorrhage at the level of the temporal inferior arcade. Left eye´s fundoscopy didn´t show any pathological sign (Figure 10). FFA of the right eye showed a hypo fluorescence zone secondary to blockage by subretinal hemorrhage inferior to the fovea. Afterward, an hyperfluorescent image supero-temporal to fovea appeared with ill borders increasing in intensity, accompanied with a dye accumulation at the center of the fovea (Figure 11). OCT of the right eye is presented with loss of foveal depression due to a big PED surrounded by subretinal fluid and lipid depositions and a double layer sign at the border of the PED (Figure 12). The patient was diagnosed with PCV, based on the clinical presentation and multi-analysis results; therefore, the patient underwent one monthly intraocular injections of 0.5 mg ranibizumab (Lucentis ®, Novartis), for three times.

## 3. Discussion

Accurate prevalence of PCV remains unclear due to challenges in diagnosing this entity based on clinical and funduscopic examinations. There aren't records of PCV prevalence in the Hispanic population but reports in the white and Asian populations showed a prevalence of 11% and 22% to 62%, respectively [6]. Furthermore, the limitation on the availability of ICGA diagnostic procedure in ophthalmology clinics and hospitals further exacerbates this problem, as the diagnosis of PCV and differentiating it from other retinal diseases, especially nAMD, is mainly made through alternative imaging modalities.

There are two sets of well-established diagnostic criteria for PCV: the one proposed by the Japanese Study Group for PCV and the criteria outlined in the EVEREST study. According to the Japanese Study Group, definite or probable diagnosis of PCV is possible based on findings from funduscopic examination, ICGA, or both. Definite diagnosis is made by observing elevated orange-red lesions on funduscopic examination and/or characteristic polypoidal lesions on ICGA, and probable PCV is diagnosed by the presence of a branching vascular network (BVN) seen on ICGA, or recurrent and/or serous PED. The EVEREST criteria (based on confocal scanning laser ophthalmoscopy) are based on the appearance of focal hyperfluorescent lesions ICGA within 6 minutes after the injection of green indocyanine and at least one of the following: BVN or hypo fluorescent halo on ICGA, pulsatility on dynamic ICGA, nodular appearance on stereoscopic ICGA, orange subretinal nodule on color photograph, or associated massive submacular hemorrhage (>4 DA in size) [1-4].

The clinical presentation of a peripapillary or foveal subretinal orange nodule suggests PCV, and ophthalmologists should ensure that this condition is considered in the differential diagnoses for subretinal nodules in all patients to provide appropriate approach. Patients with PCV may present with varying degrees of visual impairment due to serous or hemorrhagic maculopathy. One important feature to help discriminate PCV from nAMD is that in nAMD if serosanguineous or hemorrhagic maculopathy is present in one eye, the fellow

eye usually demonstrates at least some signs of early nAMD [1]. If soft drusen is not observed in the fellow eye, as in our patients, the diagnosis is more likely to be PCV or other diseases rather than nAMD.

Nonetheless, clinical findings should be complemented with imaging studies to attain a definitive diagnosis. According to the Japanese Study Group and the EVEREST Study criteria, ICGA is the gold standard and a definite diagnosis of PCV cannot be made without observing the relevant findings on ICGA.

Neither ICGA nor OCT angiography equipment are available in our hospital; therefore, we had to rely on FFA and SD-OCT findings to study and characterize the lesions in this visual devastating chorioretinal pathology. In cases where PCV is considered as a differential diagnosis, FFA and SD-OCT should be performed as initial evaluations. Although PCV lesions appear as stippled hyper fluorescence, simulating occult choroidal neovascularization on FFA [1], these findings are not as useful in determining the changes due to PCV changes, as they are for other forms of neovascularization. Nevertheless, the extent of the lesion, particularly in the presence of large PEDs, predicts the prognosis of the disease by determining leakage from BVN, which is a sign of activity [1, 5, 7]. On the other hand, SD-OCT provides information on various characteristic features that correspond to histopathological changes, which can be beneficial in the diagnosis of PCV. Multiple combinations of OCT features reportedly have high sensitivity and specificity for PCV. According to De Salvo et al. the presence of ≥3/4 OCT signs such as multiple PEDs, sharp PED peak, PED notch, and rounded subretinal RPE hyporeflective area has a sensitivity and specificity of more than 90% [2, 5, 8, 9]. Liu et al. reported a sensitivity and specificity of 85% when at least 2/3 features such as PED, double-layer sign, and thump-like protrusion are identified. Similar positive results were seen for our patients, where their clinical presentations and SD-OCT features such as multiple PEDs, thump-like protrusion, and a rounded RPE hyporeflective area suggested the most likely diagnosis being idiopathic PCV [7].

The goal of treatment is to achieve the best possible visual acuity with the least treatment burden for the patient. The EVEREST-II and PLANET studies demonstrated that anti-VEGF therapy provides excellent functional visual results one year after treatment and is considered as an acceptable initial treatment option. The PLANET study suggests PCV to be initially treated with three monthly injections of aflibercept [4].

There are some major limitations in this case study. First, we did not follow-up our patients for at least a year to identify possible recurrences. Second, due to the economic burden on our patients we did not follow the treatment protocol suggested by the PLANET study (three initial monthly aflibercept injections followed by bimonthly injections) or monitored monthly if following pro re nata (PRN, “as needed”) treatment protocol in case of active disease and discontinued the treatment prematurely, which might have resulted in less than favorable results. Third, the diagnoses were not confirmed by the gold standard method, ICGA.

In summary, it is crucial to differentiate PCV from other retinal diseases and typical nAMD as the treatment and prognosis for PCV is different than those for other retinal diseases. In this study, we showed that SD-OCT can be used as an effective diagnostic tool for PCV and can potentially be considered as equivalent to ICGA in terms of diagnostic accuracy; however, OCT angiography findings has given new insights in the diagnosis and approach in this entity [10-13].

Since there is a wide range of treatment options available that have been demonstrated efficacy and safety [14] for patients with PCV (e.g., focal laser photocoagulation, verteporfin photodynamic therapy, intravitreal aflibercept anti-VEGF therapy, and various combinations of these therapies) compared to those with typical nAMD (where the cornerstone for treatment has been intravitreal anti-VEGF therapy), appropriate diagnosis and treatment approaches would help tailor patients' treatment, set expectations, and find more effective and precise solutions [15].

# 4. Conclusion

In developing countries, it is often not possible to acquire expensive and sophisticated equipment to carry out more advanced studies consisting of angiogram by spectral domain optical coherence tomography, but ancillary studies such as fluorescein angiography and indocyanine green properly performed and interpreted continue to be very valuable and decisive in the diagnosis and treatment of this entity.

# List of Abbreviations

PCV, polypoidal choroidal vasculopathy; nAMD, neovascular age-related macular degeneration; SD-OCT, spectral domain optical coherence tomography; ICGA, indocyanine green angiography; PED, pigment epithelial detachment; DA, disc areas; FFA, fundus fluorescein angiography; anti-VEGF, anti-vascular endothelial growth factor.

# Declarations

### *Ethics Approval and Consent to Participate*

This consecutive eye study report adhered to the tenets of the Declaration of Helsinki, received full ethical approval from the Research Ethics Committees, and was approved by the Institutional Review Board and the Teaching Department of the institution enrolled (no reference number is provided for consecutive studies by this institution). Written informed consent in accordance with the institutional guidelines was obtained from all the patients.

### *Consent for Publication*

Obtained

### *Data Availability*

The photos and composite figures to support the findings of this study may be released upon written application to the Photographic laboratory and Clinical Archives department at Institute of Ophthalmology Fundacíon Conde de Valenciana (Non-profit Organization), Chimalpopoca 14, Colonia Obrera, Mexico City. Mexico. Zip code 06800, and from the Corresponding Author upon request.

### *Conflicts of Interest*

The authors declare that they have no competing interests.

### *Author's Contribution*

My self and all named co-authors take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

## Acknowledgements

We express our deep appreciation to the technical staff of the participant institution, Retina Service at the Institute of Ophthalmology, Fundacion Conde de Valenciana, Mexico City, Mexico.

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