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Mini Review

# Polypoidal Choroidal Vasculopathy: Management and Review of Literature

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## Abstract

Polypoidal choroidal vasculopathy (PCV) is a condition characterized by the presence of abnormal choroidal vascular network of vessels ending in an aneurysmal bulge with exudation under the retinal pigment epithelium (RPE) and neurosensory retina. The lesion has distinct clinical, epidemiologic and pathologic features that distinguish it from age related macular neovascularization. Although indocyanine angiography is the most diagnostic tool, the concurrent use of optical coherence tomography, fluorescein angiography and fundus autofluorescence increased sensitivity of detection and monitoring response to treatment. Different lines of treatment are currently available including anti vascular endothelial growth factor (anti VEGF) and photodynamic therapy.

***Keywords:*** *Polypoidal Choroidal Vasculopathy; Anti Vascular Endothelial Growth Factors; Photodynamic*

## Introduction

Polypoidal choroidal vasculopathy (PCV) is a condition characterized by the presence of inner choroidal vascular network of vessels ending in an aneurysmal bulge or outward projection. Exudation under the retinal pigment epithelium (RPE) and neurosensory retina is common secondary to leakage and bleeding from the peculiar choroidal vascular lesion [1].

Clinical studies suggest that the incidence of PCV is remarkably higher in blacks than in Asians and is lower in whites [2,3]. In Asians, there is a preponderance of men, unilateral involvement, and macular location of abnormal vessels [4]. Yannuzzi., *et al.* [5] described a predominance of women, bilateral involvement, and peripapillary location of PCV in white patients. The age of presentation is 50 to 65 years. In Sub-Saharan Africa Sudden visual loss was the commonest presentation. Bilateral disease occurred in about 70% of the cases. The main findings included breakthrough vitreous hemorrhage, subretinal orange lesions, and hemorrhagic RPE detachment with subretinal exudates and blood [6].

### Clinical presentation

Polypoidal choroidal vasculopathy is characterized by the presence of dilated, choroidal vascular channels ending in orange, bulging, polyp-like dilatations visible clinically as a reddish orange, spheroid, polyp-like structure. Associated features are recurrent subretinal hemorrhage and vitreous hemorrhage, relatively minimal fibrous scarring, absence of retinal vascular disease, pathologic myopia, and signs of intraocular inflammation [1]. Clinically, it is associated with chronic, multiple, recurrent serosanguinous detachments of the RPE and neurosensory retina (Figure 1) with remittent- relapsing course and good visual outcome. The pigment epithelial detachment (PED) associated with PCV does not necessarily involve central macula and does not form a fibrotic scar [1].

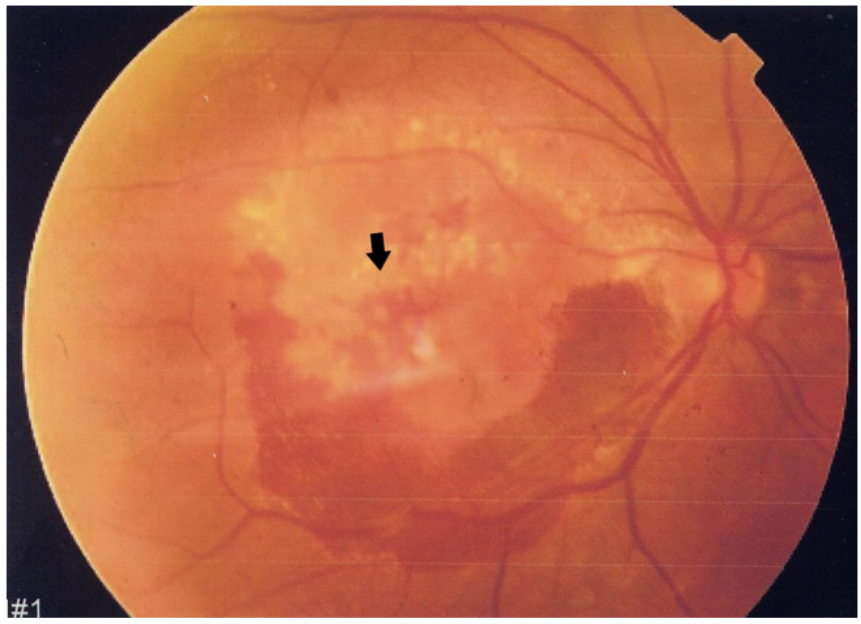


***Figure 1:*** *Colored fundus photography of the right eye showing red-orange nodules (arrow) at the center of macula and a large hemorrhagic sensory and pigment epithelial detachment along the lower macular arcade.*

If polypoidal lesions arises from the outer choroidal vessels. It appears larger in size and the diagnosis is easier on biomicroscopy, especially when the lesions are located beneath the atrophic RPE [7]. If it arises from the middle choroidal vessels it appears smaller with difficulty on clinical diagnosis and the only method of diagnosis is indocyanine angiography (ICG) [1].

The lesion is commonly located at the macula or the peripapillary regions [8]. With multiple recurrences, disciform scarring characteristic of end- stage age related macular degeneration is not commonly seen [9]. However, if spontaneous resolution of the acute serosanguineous complications occurs, signs of subretinal fibrosis, pigment epithelial hyperplasia, and atrophic degeneration may be seen [10].

Microrips of "RPE" and RPE tears may occur at the margin of the serosanguineous PED [11]. In their series, Uyama., *et al*. found that 50% of PCV eyes (14 eyes) had a favorable outcome. While in the remaining eyes the disorder persisted for a long time with occasional repeated bleeding and leakage, resulting in macular degeneration and visual loss [12].

Polypoidal choroidal vasculopathy may be associated with macular abnormalities such as sickle cell retinopathy [13], central serous chorioretinopathy [14], typical neovascular (type 1 or 2) age-related macular degeneration [15].

## Pathogenesis

Yuzawa, 2012 [16] classified PCV into two groups according to ICG, optical coherence tomography (OCT) and genetic testing into polypoidal CNV and PCV in the strict sense. Polypoidal CNV has feeder and draining vessels and points of focal dilatation representing

polypoidal lesions. They are thought to represent deformation of CNV under the RPE in age-related macular degeneration. PCV in the strict sense has no feeder or draining vessels with points of deformation representing the polyps. It is characterized histopathologically by arteriosclerosis. It is thought to be due to choroidal vessel abnormalities [16].

## Diagnosis

### Indocyanine angiography

Polypoidal choroidal vasculopathy is best diagnosed with ICG because the longer wavelengths used in this imaging system penetrates more deeply. The higher transmission of infrared light and the strong intravascular retention of the ICG molecule allow better resolution of the choroidal vasculature [17].

Larger vessels of the PCV network is filled in early stages of the angiogram with surrounding area of hypofluorescence. Polyps are easily identifiable within the choroid. The polypoidal structures correspond to the reddish orange lesions visible on biomicroscopy. In the late phase of angiogram, the area surrounding the lesion becomes hyperfluorescent and the center of the lesion demonstrates hypofluorescence. In the very late stages, the dye disappears from the lesions "washout phenomenon". However, if polypoidal lesions are leaking, it remains hyperfluorescent throughout the late phases of the angiogram [18].

### Optical coherence tomography "OCT"

Optical coherence tomography "OCT" imaging often shows reddish-orange nodules as a sharp protrusion of RPE with inner moderate reflectivity. Polypoidal lesions are located between the Bruch membrane and the RPE [19].

Tsujikawa A [20] found that 55% of eyes with PCV had serous or hemorrhagic PEDs. The PED had a tomographic notch in 57% of eyes with PCV (Figure 2), most of which corresponded in location with polypoidal lesions by ICG. Most polypoidal lesions (65%) were observed at the margin of the PEDs and adherent to the RPE (Figure 2 and 3), and some were seen inside the PED (24%). Some polypoidal lesions, which were adherent to the RPE in the serous PED, appeared to be detached from the Bruch membrane and the choroid. As leakage from the polypoidal lesions increased, the fluid from the polypoidal lesions would infiltrate under the polypoidal lesions, resulting in detachment of the lesions.

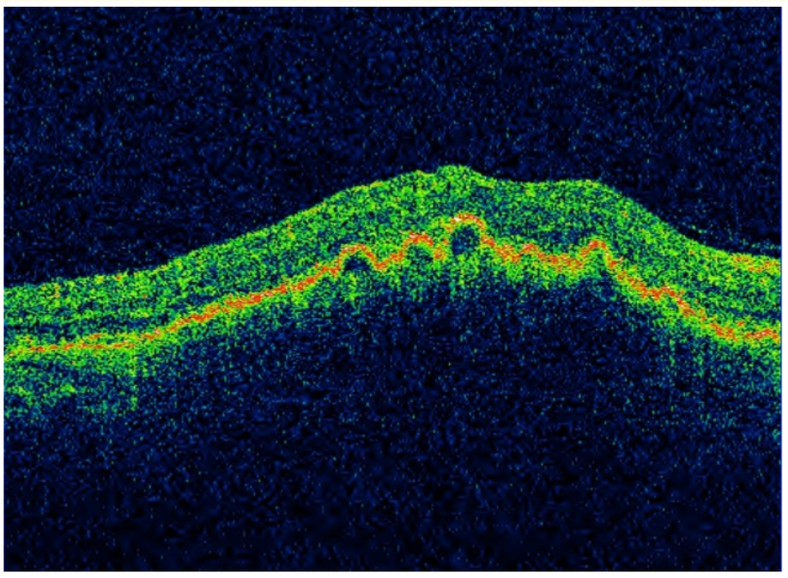

***Figure 2:*** *Optical Coherence Tomography "OCT" Scan showing large pigment epithelial detachment "PED" with evident notching. The cavity shows polypoidal lesions as moderately reflective tissue adherent to retinal pigment epithelium (RPE).*

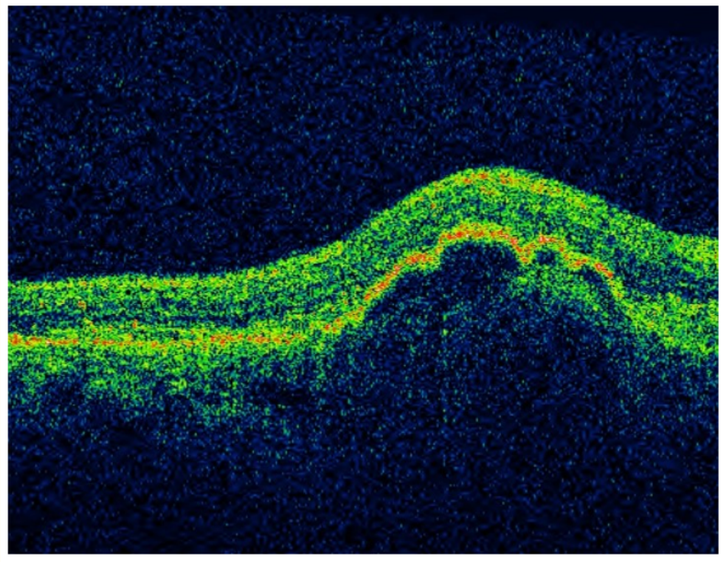

***Figure 3:*** *Optical Coherence Tomography "OCT" Scan showing polypoidal lesion as moderate reflectivity adherent to retinal pigment epithelium "RPE" with overlying notch. Fluid within pigment epithelial detachment "PED" is seen beneath polypoidal lesion. Haemorrhage is seen in subretinal space. Bruch membrane and choroid are not clearly seen at bottom of PED because of shadowing effect.*

High resolution OCT with segmentation techniques such as "c scans" allowed the description of signs peculiar to PCV such as ''hematocrit sign'' which represent separation of blood into its corpuscular and serous components. Bola sign describes the appearance of the abnormal vascular choroidal network along its entirety [21].

### Fluorescein angiography

Fluorescein angiography (FA) is not valuable in the diagnosis of PCV. Pigment in the fundus, particularly in RPE mask the inner choroid. In addition, serosanguineous complications in recently diagnosed patients may further mask the features of the polypoidal choroidal vascular abnormalities. However, in Some patients, large polypoidal choroidal vascular components, aneurysmal or polypoidal lesions with overlying atrophy of the pigment epithelium can be imaged but not along the whole course of the vascular network (Figure 4) [21].

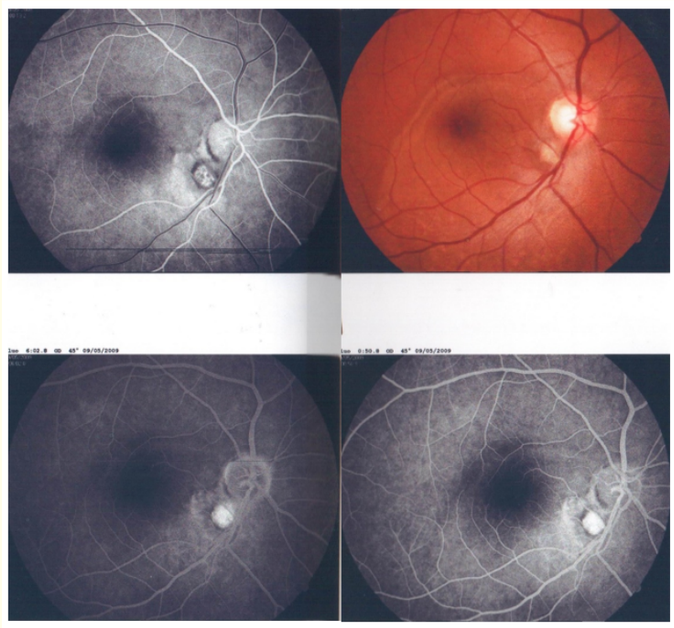

***Figure 4:*** *Peripapillary PCV. Top left: colored fundus photography showing neuro-sensory detachment extending between the macula and disc with Lower temporal peripapillary slightly elevated yellowish lesion. Top right: early phase of fluorescein angiography showing juxtapapillary hyperfluorescent patch with granular appearance. Bottom left: increased hypoflourescence with dye leakage. Bottom right; late phase of angiogram showing blurred margin of the lesion with preserved lobular appearance.*

### Fundus autofluorescence

In eyes with PCV, the polypoidal lesions and the branching choroidal vascular networks affect the RPE and induce peculiar fundus autofluorescence findings. Compared to patients with typical neovascular AMD, widespread RPE damage was more frequently observed in the patients with PCV, both in the affected eyes and in the unaffected fellow eyes [22].

### Treatment

The criteria for selecting a treatment modality depends on the location of the polyps. Extrafoveal polyps can be treated with thermal laser. While photodynamic therapy" PDT" or transpupillary thermotherapy "TTT" may be reserved for peripapillary and subfoveal polyps depending on the affordability of the patient [23].

### Photocoagulation

Photocoagulation is recommended only if it is feasible to treat the entire polypoidal lesion. Yuzawa,. *et al.* reported that 54% of eyes undergoing laser photocoagulation of only the polypoidal component, showed decreased visual acuity because of recurrent or persistent exudation and/or classic choroidal neovascularization or, alternatively, because of atrophy at the fovea [24]. Reports of laser photocoagulation to feeder vessels of polypoidal lesions have been reported [25].

### Photodynamic therapy

Several studies have reported the efficacy of PDT using verteporfin in the treatment of patients with subfoveal PCV. Because thermal laser causes retinal damage, direct targeting to choroidal vessels using verteporfin is theoretically preferable. Visual stabilization or improvement was achieved in 80% of the patients over an average follow up period of one year [26-29]. Photodynamic therapy is more effective for PCV than for neovascular age-related macular degeneration [30]. Complications of PDT include; subretinal haemorrhage [31], recurrent bullous detachment and chorioretinal anastomosis [32], recurrence or the development of new polypoidal Lesions [21].

### Intravitreal injection

It has been suggested that vascular endothelial growth factor (VEGF) may have a similar role in PCV as it does in choroidal neovascularization (CNV) owing to marked increases in VEGF concentration in aqueous humor and histologic examination in active PCV eyes. However, VEGF concentration is still significantly lower in PCV than in neovascular age related macular degeneration [33].

Short-term results reported by Lee., *et al*. indicate that intravitreal bevacizumab (1.25 mg) alone or in combination with PDT is well tolerated and associated with improvement in best corrected visual acuity and reduced angiographic leakage in most patients. Intravitreal bevacizumab was repeated at 6-week intervals until the regression of active lesion was detected on fluorescein angiography [34].

Gomi., *et al*. reported that intravitreal injection of bevacizumab may reduce the fluid from PCV but seems to be ineffective for diminishing its choroidal vascular changes. These results suggest that polypoidal dilation of choroidal vessels in PCV may not depend on VEGF to the same extent as ''normal'' age-related neovascularization [35].

Intravitreal injections of bevacizumab and ranibizumab appear to have similar effects in stabilizing of visual acuity, macular edema, and regression of polypoidal complex in PCV eyes over the short term [36].

With prolonged use of ranibizumab, diminution of biological effects adversely affects long-term efficacy. One possible mechanism of diminution is tachyphylaxis, (phenomena causing reduced drug efficacy by repeated administration) [37]. A possible countermeasure for tachyphylaxis is introduction of a drug with a different mechanism of action. Aflibercept (Eylea; Regeneron, Tarrytown, PA, USA and Bayer HealthCare, Berlin, Germany)) is a recombinant fusion protein, which binds all isomers of the VEGF-A family and placental growth factor.

It has higher binding affinity for VEGF and was shown to be clinically equivalent to Ranibizumab [38]. Switching therapy to aflibercept is effective for patients with PCV who develop tachyphylaxis to ranibizumab [39].

### Combined therapy

PDT was more effective than anti-VEGF in achieving regression of polyps [40] while Anti-VEGF therapy significantly reduced central retinal thickness compared with PDT at 3 months [41].

Repeated PDT sessions may induce subretinal haemorrhage and ischemic damage to choroidal tissue, explaining the loss of improvement in visual acuity in the PDT monotherapy. Combined intravitreal injection and photodynamic therapy for polypoidal choroidal vasculopathy reduce the risk for post PDT subretinal haemorrhage, maintained long term visual acuity outcome and reduced the exudation with no significant difference in central retinal thickness reduction [42-44].

## Conclusion

The progression and visual outcome of PCV is favorable than in age related macular degeneration due to the lower incidence of subretinal fibrosis and disciform scarring. However, the overall visual outcome of PCV is relatively poor if untreated. Neither PDT monotherapy nor anti-VEGF monotherapy is the best option for the treatment of PCV although each has distinct advantages over the other. Therefore, combination therapy may allow for more comprehensive treatment.

## Conflict of Interest

I have no proprietary interest in any material or method mentioned.

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## Informed Consent

All images are taken with permission from Mansoura Ophthalmic Center, Vitreoretinal imaging unit. Patients have given their consent for their images and other clinical information to be reported in the current work.

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