GENERAL REVIEW

POLYPOIDAL CHOROIDAL VASCULOPATHY, DIAGNOSIS AND MANAGEMENT

COPPENS G., SPIELBERG L., LEYS A.

ABSTRACT

Polypoidal Choroidal Vasculopathy (PCV) was first identified in 1985. Initially considered to be rare, PCV is currently frequently diagnosed in patients of African and Asian descent. In Caucasians, PCV counts for 10% of cases of AMD, and for up to 85% of patients with hemorrhagic or exudative retinal pigment epithelial detachment. Although the clinical presentation can be suggestive, extensive investigation with the indispensable indocyanine green angiography, is required for confirmation of PCV. Treatment has to be considered in active disease threatening the macula. Photodynamic therapy with Verteporfin is required for closure of PCV complexes. Anti-VEGF treatment reduces associated macular edema.

KEYWORDS

Polypoidal choroidal vasculopathy (PCV), serohemorrhagic pigment epithelium detachments (PED), age-related macular degeneration (AMD), central serous choroidopathy (CSC), optical coherence tomography (OCT), fluorescein angiography (FA), indocyanine green angiography (ICGA), thermal laser therapy, photodynamic therapy standard fluence rate /reduced fluence rate (PDT SFR/RFR), anti-vascular endothelial growth factor intravitreal injections (anti-VEGF IVT)

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Polypoidal Choroidal Vasculopathy (PCV) was first identified as a specific disease entity in 1985 (1). Recurrent serohemorrhagic retinal pigment epithelial detachments (PED) are pathognomonic for the disease. However, PCV can also manifest as age-related macular degeneration (AMD) or mimic central serous choroidopathy (CSC) (2-7). Occasionally, PCV is observed in eyes with tilted disk syndrome and high myopia with staphyloma (8). Despite 25 years of clinical experience with PCV, and the existence of diagnostic criteria, which have been available since 2005 (9), it remains controversial as to whether PCV represents a subtype of neovascular AMD or an independent disease (3, 10-13). PCV and AMD share common genetic factors and environmental risk factors such as smoking, but the natural history, the visual prognosis and the response to treatment differ greatly (3). PCV tends to occur at a younger age (between 50 and 65 years of age), is more prevalent in pigmented races, is not associated with drusen and often presents with serosanguinous maculopathy or hemorrhagic PED (3). PCV is initially bilaterally in 10 to 25% of patients (3, 10, 13) and the majority of patients who initially present with unilateral disease subsequently develop bilateral lesions (14). Histopathologic observations of PCV describe saccular, dilated, thin-walled vessels with a large lumen located under the retinal pigment epithelium (RPE) (15).

Although initially considered to be a rare condition, PCV is currently frequently identified in patients of African and Asian descent. The reported prevalence ranges from 22 to 55% of newly diagnosed AMD and exudative AMD in these population groups (3, 13, 16). In contrast, PCV was identified in 4 to 10% of cases

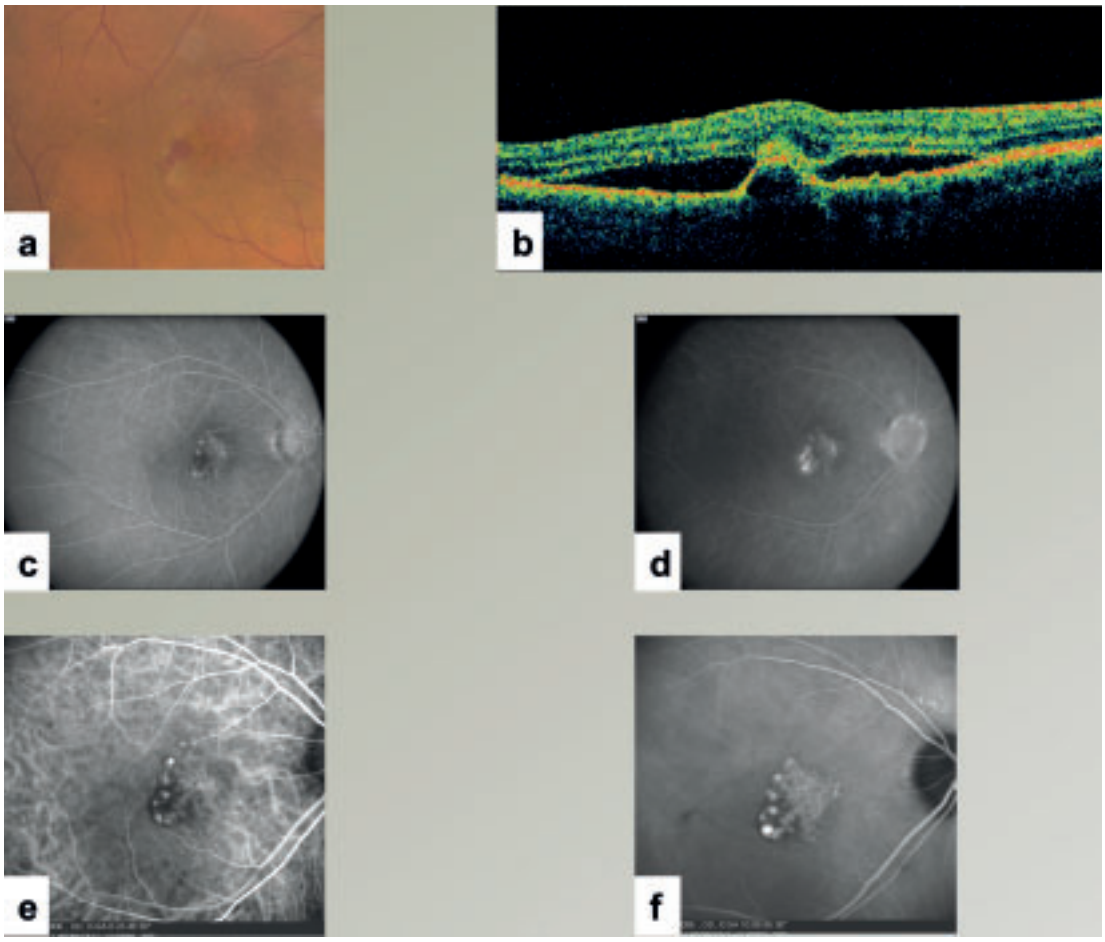

Fig. 1: Caucasian male patient, age 61, with visual loss in the right eye since 7 months. Funduscopy shows macular elevation and blood (a). A macular horizontal section of spectral OCT (Cirrus) shows a subretinal lesion with steep dome-like elevation suggestive of an active empty polyp with associated neurosensory detachment and macular edema (b). Fluorescein angiography shows in the early phase a maculopathy with a subretinal vascular net and grape-like dilations at the temporal border (c) and in the late phase leakage and pooling of dye temporally (d). Indocyanine green angiography shows in the early phase a subretinal abnormal vascular net and a cluster of large polyps at the temporal border (e). The late phase shows hyperfluorescence of the net and pooling of dye in the dilated polyps (f) .
Visual acuity was 20/60 and returned to 20/25 after two sessions of photodynamic therapy and remained stable during the 3-year follow-up.

of AMD (3, 10), and in up to 85% of patients with hemorrhagic or exudative PED in Caucasians (4). In Caucasians, the patients are predominantly female; in Asian populations, males are more commonly affected (14).

Although the clinical presentation of papillomacular, macular or midperipheral orange-red lesions with exudative or hemorrhagic complications (Fig 1, Fig 2) is highly suggestive for PCV, extensive investigation is required to make a definitive diagnosis. Fluorescein angiography (FA) and optical coherence tomography (OCT) are useful diagnostic and differential diagnostic tools (17), and indocyanine green angiography (ICGA) is the gold standard for the ultimate confirmation of PCV. On OCT, PCV is characterized by a higher incidence of PED, greater PED height, and less intraretinal edema than eyes with exudative AMD (17) (Fig

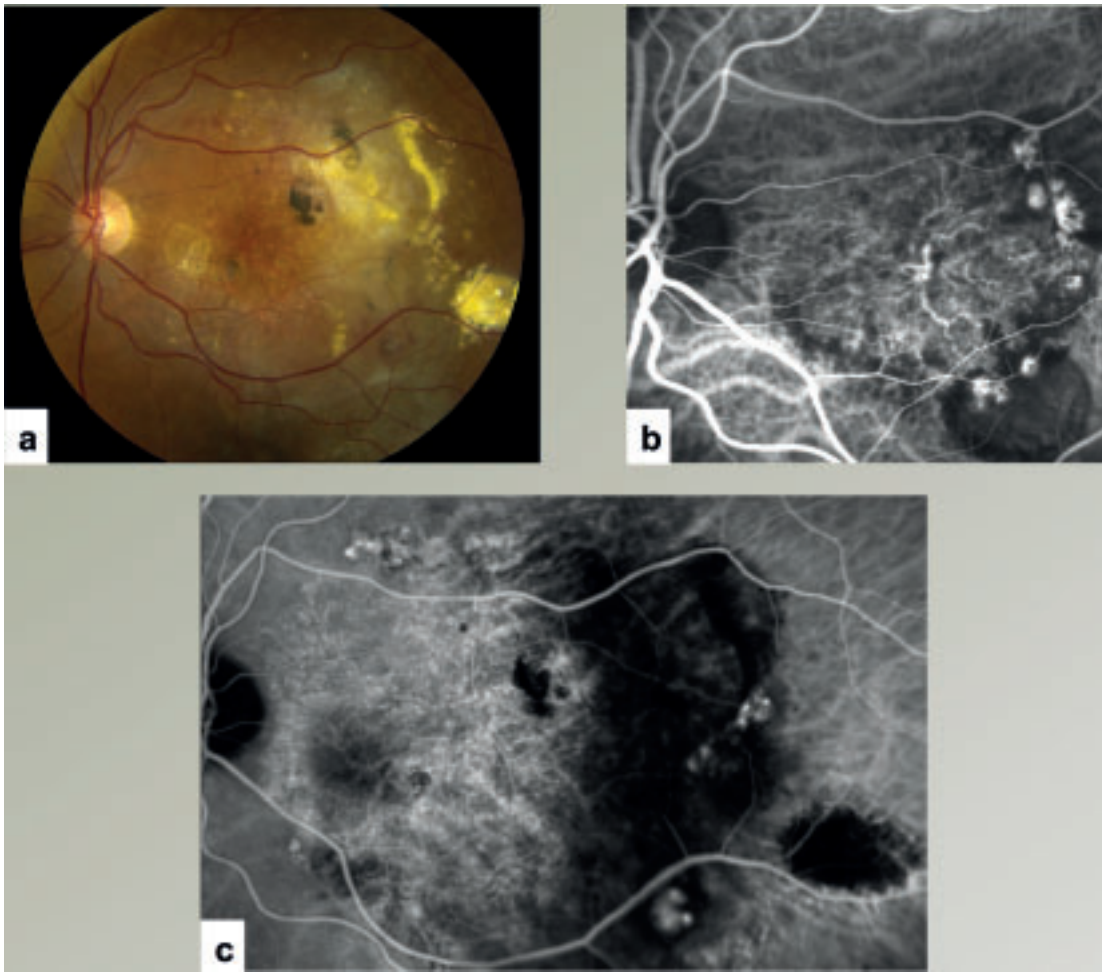

Fig. 2: Caucasian female patient, age 60, history of bilateral visual loss at age 53 and diagnosis of PCV. The left eye was recently treated with ranibizumab injections because of increasing exudative lesions and edema temporal of the macula (a). ICGA at age 53 shows a large subretinal vascular net and polyps at the temporal border and a serous pigmentepithelial detachment at the temporoinferior border (b). ICGA at age 60 shows an enlarged lesion with macular atrophic changes, few polyps in the papillomacular and macular region and numerous active polyps temporally with massive exudative detachment (c).
VA remained 20/25 during follow-up, but the central scotoma enlarged.

1b). A branching vascular network on ICGA, even without identification of polyps, and/or recurrent hemorrhagic and/or serous PED, makes diagnosis of PCV probable (3, 9). Definite criteria for PCV, according to the Japanese Study Group of PCV, are protruding elevated orange-red lesions observed by fundus examination and/or polypoidal vascular lesions at the border of a vascular network seen on ICGA (9) (Fig 1). The polyps are difficult to identify on FA, as they are under the RPE. On ICGA, however, the polyps are clearly visible as single or multiple vascular aneurysms with a diameter of 100 to 500 μm which fill after a short delay and remain hyperfluorescent until the late phases (18). The lesions can be juxtapapillary or macular. In early ICGA images, juxtapapillary lesions show a radial arching pattern, and the vascular channels may be interconnected by smaller spanning branches at the lesion's edge

(19). In macular lesions, the vascular network often arises in the macula and follows an oval distribution (19). The choroidal vessels in the network are dilated and irregular (18). The area surrounding the choroidal vascular network is hypofluorescent during early phases of ICGA (Fig 2b). In the late-phase ICGA, there is often a reversal of this pattern: the area surrounding the polypoidal lesion hyperfluoresces and the center becomes hypofluorescent. In very late phases, ICGA displays disappearance of the fluorescence (washout) in non-leaking lesions (15). PCV can run a benign course with mildly active lesions that spare the macular function and remain undetected. These lesions can often greatly expand without fibrous scarring and with relatively spared vision (Fig 2). However, if left untreated, half of the patients with PCV experience persistent leakage or repeated bleeding and suffer a poor visual outcome (20). Poor prognostic signs are the development of a cluster of grape-like polypoidal dilatations observed on ICGA and intra-polyp pulsations.
Treatment of PCV must be considered in patients with active PCV threatening the macula. The most frequently employed treatment options include photodynamic therapy with Verteporfin (PDT), and/or intravitreal injections with anti-VEGF antibodies. Occasionally, lasercoagulation for extramacular lesions, or vitrectomy for hemorrhagic events, can be considered.

The one-year results of a prospective interventional study with PDT in 22 eyes are encouraging (21). One year after PDT for PCV with serosanguinous maculopathy, stable or improved visual acuity (VA) was achieved in 95% cases, a complete absence of leakage on FA in 91% and total regression of the polyps visible on ICGA in 95% of eyes. Subsequently, numerous reports (22) and our own experience (Fig 2) have confirmed that PDT is efficacious for treating PCV, and one-year as well as long-term results have shown greater benefit of PDT for PCV than for AMD-associated CNV (16, 23, 24). A better pre-treatment VA and a smaller pre-treatment greatest linear dimension (GLD) are significantly beneficial for a better VA at 12 months after PDT for PCV (25). Since a better VA and a smaller GLD likely indicate early stages of disease, it is reasonable to assume that early treatment results in a better prognosis. However, after 12 months of follow-up, the visual prognosis apparently deteriorates, as a result of recurrence of PCV activity (6, 26, 27). ICGA studies after PDT have shown that the branching vascular networks do not regress and thus allow the recurrence of polypoidal lesions (28). Further, the adjunctive use of intravitreal triamcinolone acetonide during PDT does not appear to result in additional benefit (29).

Anti-VEGF injections have been applied for PCV in monotherapy and in association with PDT (30, 31). Intravitreal bevacizumab appears to stabilize vision and reduce the incidence of exudative retinal detachment in PCV. However, intravitreal bevacizumab monotherapy shows limited effectiveness in causing regression of the polypoidal lesions on ICGA, while PDT appears to be useful for treating these lesions (32). Interestingly, it has been shown that neovascular AMD that is refractory to anti-VEGF may harbor PCV (33). Modifications in therapeutic protocols may be indicated in order to improve visual outcomes in this population

The 6-months results of intravitreal ranibizumab monotherapy for PCV in the PEARL study showed similar results: stabilization of vision, a 17% chance of VA improvement of 3 lines or more and reduced macular edema, subretinal blood and fluid. However, branching choroidal vessels and polypoidal lesions on ICGA persisted (34). Recently, the EVEREST trial compared PDT alone (21 eyes) versus ranibizumab alone (21 eyes) versus combination therapy (18 eyes) for PCV (35). Patients in all groups gained vision, but the combination group achieved the greatest gain. Treatment with PDT in monotherapy or combined with ranibizumab showed, on ICGA, a much higher rate of anatomic closure of PCV complexes, than with ranibizumab alone.

In part due to the recently improved diagnostic techniques of OCT and ICGA, PCV is currently more frequently identified than before. Consequently, greater general knowledge of available treatment options, indications for treatment, and expected results would be beneficial. Based on recent studies, lasercoagulation or PDT is required for closure of PCV complexes, and anti-VEGF treatment is useful to reduce PCV-associated macular edema.

KEY MESSAGES

Polypoidal Choroidal Vasculopathy presents clinically and on FA with serohemorrhagic PED or as mimicking AMD or CSC. Polyps are visible on OCT as steep, domelike elevations. On ICGA, polyps, an interconnecting vascular network and PEDs are seen. Anatomic closure of PCV complexes requires lasercoagulation or PDT. Intravitreal anti-VEGF treatment can reduce macular edema. However, recurrences are common.

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Address for correspondence
Dr Greet Coppens
Department of Ophthalmology
University Hospitals
Kapucijnenvoer, 33, 3000 Leuven BELGIUM
E-mail: greetcoppens@hotmail.com