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Polypoidal choroidal vasculopathy in Caucasians

Received: 10 January 2000
Revised: 30 March 2000
Accepted: 16 May 2000

Presented in part at the 4th International Symposium on Indocyanine Green Angiography, Baden-Baden, Germany, 10 September 1999; in part at EVER99, Palma, Spain, 8 October 1999; and at Macula 2000, New York City, USA, 14 January 2000

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Abstract Purpose: To study the prevalence of polypoidal choroidal vasculopathy (PCV) in Caucasian patients with occult choroidal neovascularization (CNV); to study the clinical spectrum of PCV in Caucasians and the outcome after laser photocoagulation of such lesions. **Methods:** (1) A consecutive series of 374 eyes of Caucasian patients at least 58 years old, presenting occult CNV, presumed to have age-related macular degeneration (AMD) on fluorescein angiography (FA) were further characterized by indocyanine green angiography (ICGA) to determine the frequency of PCV. (2) The funduscopy, FA and ICGA findings in a cohort of 36 Caucasian patients with PCV were analyzed. (3) The outcome after laser photocoagulation was studied in 14 PCV eyes with a minimum follow-up of 6 months. **Results:** (1) Fourteen of 374 eyes (4%) presenting occult CNV in patients at least 58 years old were diag-

nosed as PCV by means of ICG-A. (2) A polypoidal lesion was found in the macula in 22 of 45 PCV eyes, in the peripapillary area in 16 of 45, under the temporal vascular arcade in 6 of 45 and in the midperiphery in 6 of 45. Large or soft drusen were observed in 15 of 45 eyes with PCV. (3) Regression of fundus signs without persisting polyps 6 months after laser photocoagulation was obtained in 5 of 5 treated peripapillary lesions but in only 5 of 9 treated macular or arcade lesions. **Conclusion:** Polypoidal choroidal vasculopathy is not rare in Caucasian patients presenting with occult choroidal neovascularization. The fundus abnormalities seen in such eyes overlap with the typical manifestations of AMD. Whereas the prognosis after photocoagulation of peripapillary polypoidal lesions appears to be relatively good, it is more guarded for macular or arcade lesions.

Introduction

In 1985, Stern and colleagues reported the cases of three middle-aged black American women suffering from multiple, recurrent, serosanguinous retinal pigment epithelial detachments (PED) [14, 22]. Fluorescein angiography (FA) showed either focal or diffuse leakage suggestive of choroidal neovascularization (CNV). These complications resolved and recurred, sometimes associated with subretinal hemorrhages or even vitreous hemorrhages. The complete resolution of the lesions pro-

duced retinal pigment epithelial mottling and chorioretinal scars. The cause of the clinical findings remained unclear. The course did not resemble any known disease, and a variant of CNV was suggested. Yannuzzi et al. [24] and Kleiner et al. [9] reported series of similar cases in 1990 and termed the entity respectively "idiopathic polypoidal choroidal vasculopathy" and "posterior uveal bleeding syndrome". In these early reports, the majority of the patients were black women in the sixth decade of life. They had recurrent serosanguinous retinal pigment epithelial and neurosensory retinal detachment often as-

sociated with prominent lipid exudate deposition. Most patients did not have soft drusen or other characteristics of age-related macular degeneration (AMD). Despite recurrent leakage and bleeding, many did not develop disciform scars and retained useful vision. The original vascular anomaly was visualized by indocyanine green angiography (ICGA) and optical coherence tomography as a network of branching vessels terminating in aneurysmal enlargements that protruded anteriorly [8, 20].

Early reports emphasized the peripapillary location, and the lesions were considered to be intrachoroidal [9, 14, 20, 22, 24]. More recently, similar anomalies have been reported in elderly Caucasians and Japanese, often solely within the macula [13, 19, 23, 25, 27], more rarely in the fundus periphery [26]. This disorder was termed polypoidal choroidal vasculopathy (PCV) [27] and even polypoidal choroidal neovascularization [23]. It was suggested that the vascular abnormality is a variant of choroidal neovascularization with significant differences from AMD in demographic risk profile, natural course and visual prognosis [23, 25, 27].

This study aims to identify the frequency of PCV in Caucasian patients presenting with occult choroidal neovascularization, to show that the fundus manifestations of PCV largely overlap with those of AMD and to report preliminary outcome of laser photocoagulation of such lesions.

Methods

Patient population

Group 1. A consecutive series of 374 eyes with characteristics of occult CNV on FA in patients at least 58 years old from the Ghent University Hospital were retrospectively studied to define the type of lesion found by ICGA and to determine the frequency of PCV in this patient population.

Group 2. Retrospective study of a cohort of 36 Caucasian patients with PCV collected from the patient pools of four Belgian university eye clinics. Patients younger than 58 years were not excluded. All patients defined as PCV from group 1 were included herein. We studied the clinical presentation of PCV in this cohort, namely the location of the polypoidal lesion, its association with a net of vessels in the early phase of ICGA and a plaque in the late phase, the frequency of associated findings such as PED, lipid exudates and retinal or subretinal hemorrhages, and the kind of lesions observed in the fellow eyes.

Group 3. Retrospective study of the outcome after laser photocoagulation of the PCV eyes studied in group 2, for which a follow-up of at least 6 months was available.

Ophthalmologic examination

All patients underwent a standard clinical ophthalmological examination, including fundus photography, FA and ICGA. ICGA was obtained with a conventional fundus camera and the last photos were taken at least 30 min after intravenous injection of the dye or later, when a negative pattern of choroidal veins was not obtained after 30 min.

Definition/interpretation of ICGA findings

A “plaque” and “hot spot” were defined following Guyer et al. [3, 5]: a plaque is a more or less well delineated hyperfluorescent region larger than one disc area in the late phase; a hot spot is a hyperfluorescent area smaller than one disc area in the late phase. A lesion was considered “marginal” when it overlapped with the margin of a PED, “distant” when there was no contact at all and “inside” when the lesion was entirely located within the boundary of the PED.

A “polypoidal lesion” was defined when one or more focal vascular dilations in the inner choroid were already visualized in the early phase of ICGA: either a “polyp” when a single lesion was seen or a “cluster” when multiple polyps were observed lying closely together. The presence of an associated net of dilated vessels was not considered necessary. Groups of polyps more than one disc diameter distant from one another were considered as separate clusters when no connecting net was identified. The lesion was defined as “macular”, “peripapillary”, “arcade” or “mid-peripheral” when respectively the polyp or the majority of the cluster was located in the macula, within one disc diameter of the disc edge, under the temporal vascular arcade (within one disc diameter of the temporal retinal vein outside the peripapillary area) or outside the posterior pole. “Extensive scarring” was defined as an area of retinal pigmentary changes with or without subretinal fibrosis with a diameter of at least 5 disc diameters.

Laser procedure

Laser photocoagulation was considered when a polypoidal lesion was extrafoveal in a symptomatic patient. The technique used corresponded to the treatment practice of the Macular Photocoagulation Study [12], but was guided by ICGA findings.

Statistics

Statistical analysis was performed with the Mann-Whitney test (nonparametric test, unpaired groups; GraphPad Prism 2.0) to find out whether different manifestations of PCV tended to appear in different age ranges.

Results

Group 1

Fourteen eyes (4%) of the 374 eyes presenting occult CNV in patients minimally 58-years-old were diagnosed as PCV by means of ICGA. Nine of the 374 eyes (2%) had transient choroidal hyperfluorescence and were considered to have chronic central serous chorioretinopathy. The remaining 351 eyes had straightforward AMD, 254 eyes without and 97 with a PED. In 3 of the 97 eyes with a PED (3%) the serous part of the PED was hyperfluorescent in the late phase of ICGA (Fig. 1).

Group 2

Thirty-six Caucasian patients with PCV were included in group 2: 17 males and 19 females (Table 1). Fourteen patients had strictly unilateral fundus lesions, bi-

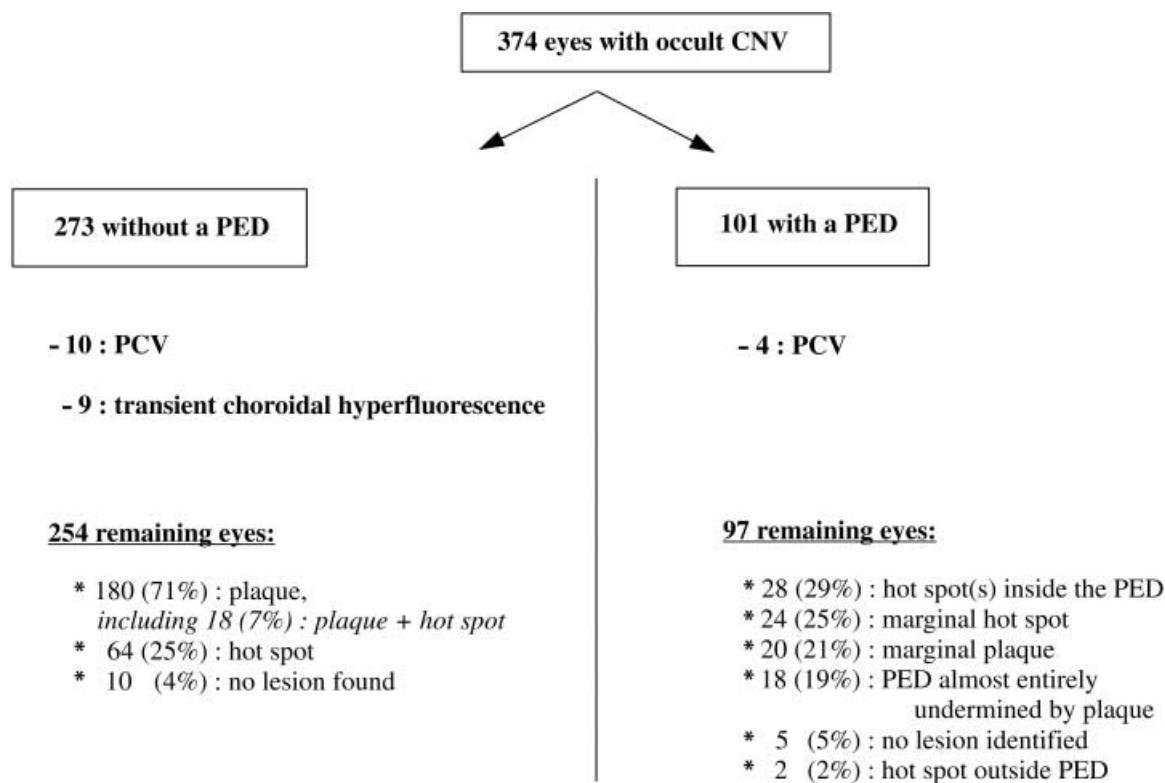


Fig. 1 Group 1: Schematic representation of ICGA findings in 374 eyes with occult CNV

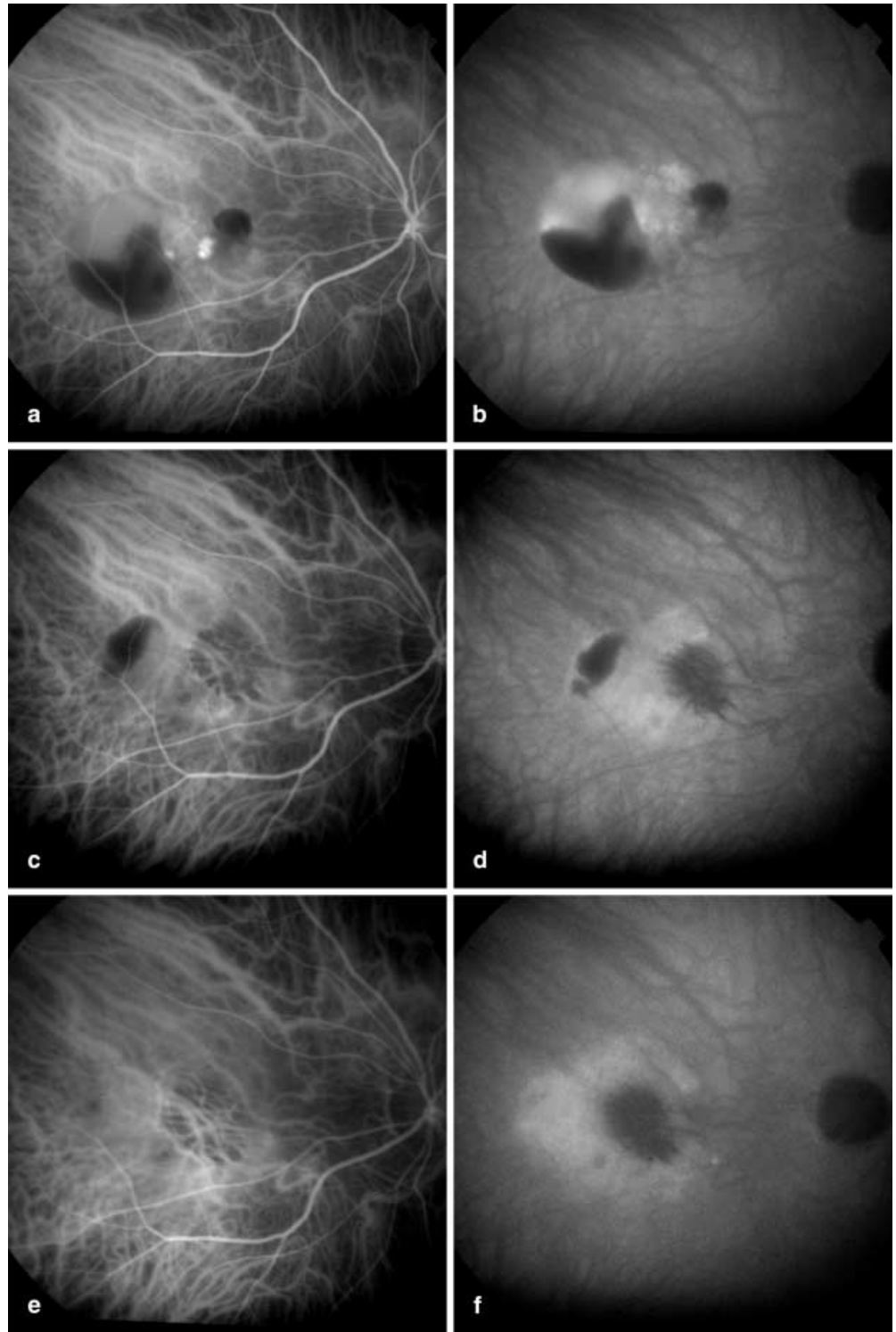
Table 1 Group 2: Summary of demographic data for the subgroups. No statistically significant differences in age range were identified

Subgroup	Proportion	Age (years)	
		Range	Mean
36 patients with PCV			
17 males	47%	46–87	63
19 females	53%	46–90	71
14 strictly unilateral fundus lesions	39%	46–87	64
9 bilateral polypoidal lesions	25%	46–77	68
13 unilateral polypoidal lesions, but bilateral fundus lesions	36%	54–90	70
45 eyes with PCV			
22 macula	49%	46–87	64
16 peripapillary area	36%	46–90	70
6 temporal vascular arcade	13%	52–87	72
6 midperiphery	13%	62–87	73
15 large or soft drusen	33%	62–87	71
8 multiple polypoidal lesions	18%	46–87	68

lateral PCV was identified in 9 patients and in 13 patients PCV was identified in only one eye but in the fellow eye fundusoscopic or angiographic abnormalities were observed in the absence of identifiable polyps. In one of these 13 fellow eyes a vitreous hemorrhage and a hemorrhagic retinal detachment were seen. In 7 of 13 eyes a small (one-third to two-thirds disc diameter), well-delineated area of retinal pigmentary changes was

found on FA: extrafoveal (3 eyes), juxtafoveal (1 eye), peripapillary (1 eye) and under the temporal arcade (2 eyes). In none of these 13 eyes was a hot spot or plaque associated with the pigmentary changes, but in one eye an unassociated peripapillary plaque was seen. A larger area of macular retinal pigmentary changes was observed in four fellow eyes; it was associated with a plaque lesion in three eyes and with mild atrophy in

Fig. 2 **A** Early venous phase and **B** late venous phase ICGA of a 56-year-old man. A cluster with associated net is seen in the early phase; the polyps persist in the late phase by staining of their wall. The sero-hemorrhagic PED becomes hyperfluorescent in the late phase. **C** Early venous phase and **D** late venous phase ICGA 6 months after treatment. The sero-hemorrhagic PED has disappeared; a subretinal hemorrhage persists. Polypoidal elements are not found, but a plaque appears temporal to the photocoagulation scar. **E** Early venous phase and **F** late phase ICGA 12 months later. The exudative fundus manifestations have disappeared. Polyps are not identified but the plaque has slightly enlarged

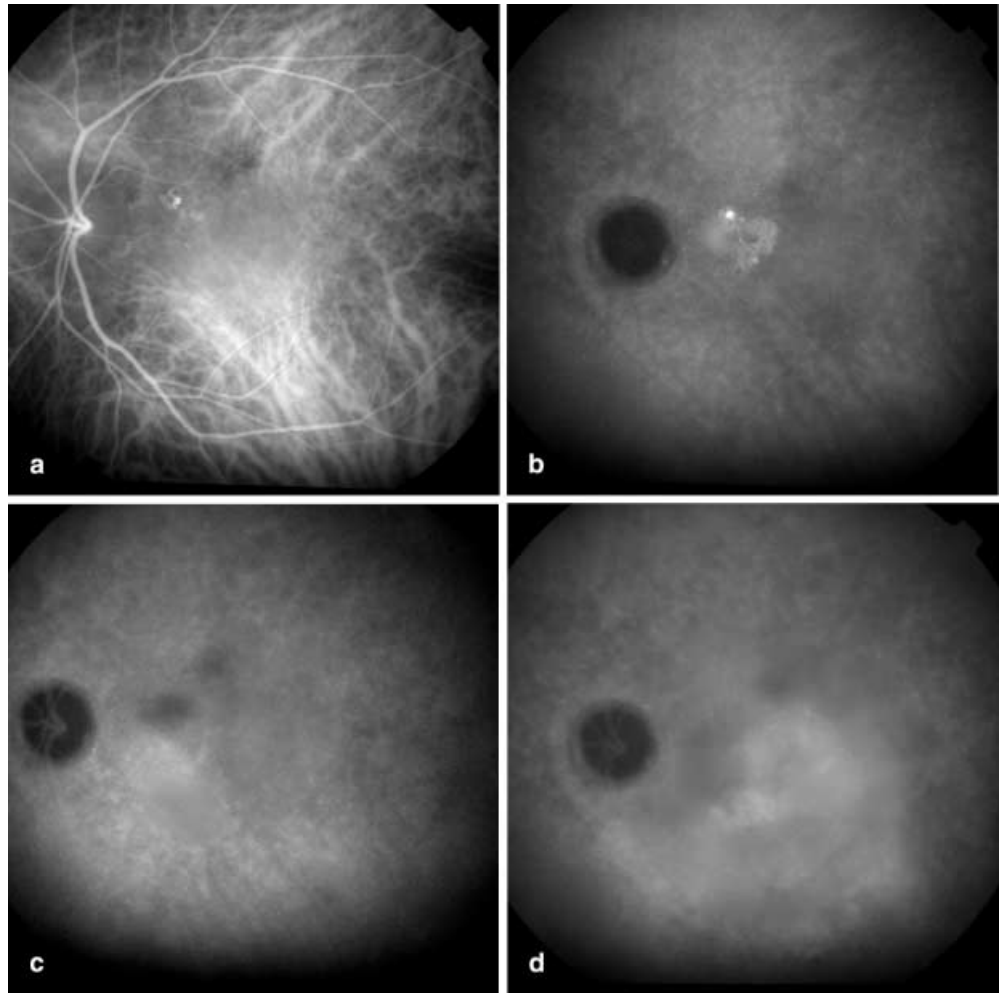


one. In a last fellow eye, no abnormalities were found on either funduscopy or FA but in the midvenous phase (10–20 min) two focal vascular dilatations appeared on ICGA, one macular and one in the nasal midperiphery; these disappeared in the late phase (30 min). Signifi-

cant differences in the age ranges of these subgroups were not found.

Polypoidal vessels were situated in the macula in 22 of 45 eyes (Figs. 2, 3), in the peripapillary area in 16 of 45 eyes, under the temporal vascular arcade in 6 of 45

Fig. 3 **A** Early venous phase and **B** late venous phase ICGA of a 64-year-old man. A polyp is seen embedded in a vascular net in the early venous phase and persists in the late phase as part of a plaque. The lesion was photocoagulated. **C** Late phase ICGA, 6 months after treatment. The exudative changes have increased, and a serous pigment epithelial detachment has appeared. An ill-defined plaque is seen inferior to the laser scar, which was photocoagulated. **D** Late phase ICGA, 12 months after initial treatment. The exudative manifestations and serous pigment epithelial detachment persist, a new large plaque is observed that undermines the fovea



eyes and in the midperiphery in 6 of 45 eyes (Fig. 4). Confer Table 1. The age ranges were not significantly different. Multiple polypoidal lesions were found in 8 of 45 eyes. Seven of these 8 presented bilateral PCV and 7 of 8 presented extensive scarring. Two eyes had two macular clusters, two eyes a macular and an arcade cluster, one eye a macular and a midperipheral cluster, one eye a peripapillary and a midperipheral cluster and one eye had two midperipheral clusters. Ten eyes of 7 patients showed extensive scarring; 4 of 7 had angiographically proven bilateral PCV but a fifth patient also likely suffered from bilateral PCV as the fellow eye presented a vitreous hemorrhage and a hemorrhagic retinal detachment.

A cluster of polyps was identified in 19 of 22 macular lesions, 10 of 16 peripapillary lesions, 3 of 6 arcade lesions and 6 of 6 midperipheral lesions, while a single polyp was found in respectively 3 of 22, 6 of 16, 3 of 6 and 0 of 6 (Table 2). An associated net with the cluster of polyps could be traced in only 6 of 19 macular clus-

ters, 1 of 10 peripapillary clusters, 2 of 3 arcade clusters and in none of the midperipheral clusters. A plaque was visualized in 15 of 22 macular lesions, 6 of 16 peripapillary lesions, 3 of 6 arcade lesions and 2 of 6 midperipheral lesions.

The presence of large drusen, an associated PED, macular lipid exudation, subretinal or intraretinal hemorrhages and extensive chorioretinal scarring is elaborated in Table 2 for the various locations of the polyps. Large or soft drusen were seen in 15 of 45 eyes with PCV (33%; Fig. 4) and in 3 fellow eyes. At least one PED was present in 20 of 45 eyes with PCV (44%). In 7 of 14 eyes with a serous or serohemorrhagic PED (50%) the serous part of the pigment epithelial detachment became hyperfluorescent in the late phase of the indocyanine green angiogram (Fig. 2).

Group 3

Fourteen treated polyps had a minimum follow-up of 6 months: 7 macular, 5 peripapillary and 2 arcade lesions.

Fig. 4 **A** Early venous phase and **B** late venous phase ICGA of the superonasal mid-periphery of the left eye in a 62-year-old woman. A midperipheral cluster of polyps is seen, an associated net is not observed but a plaque appears in the late phase. **C** Late phase ICGA of fellow eye: peripapillary polyps and a macular plaque without polyps are found. **D** Late phase of left eye, peripapillary polyps are seen as well as masking of choroidal fluorescence by subconfluent large drusen

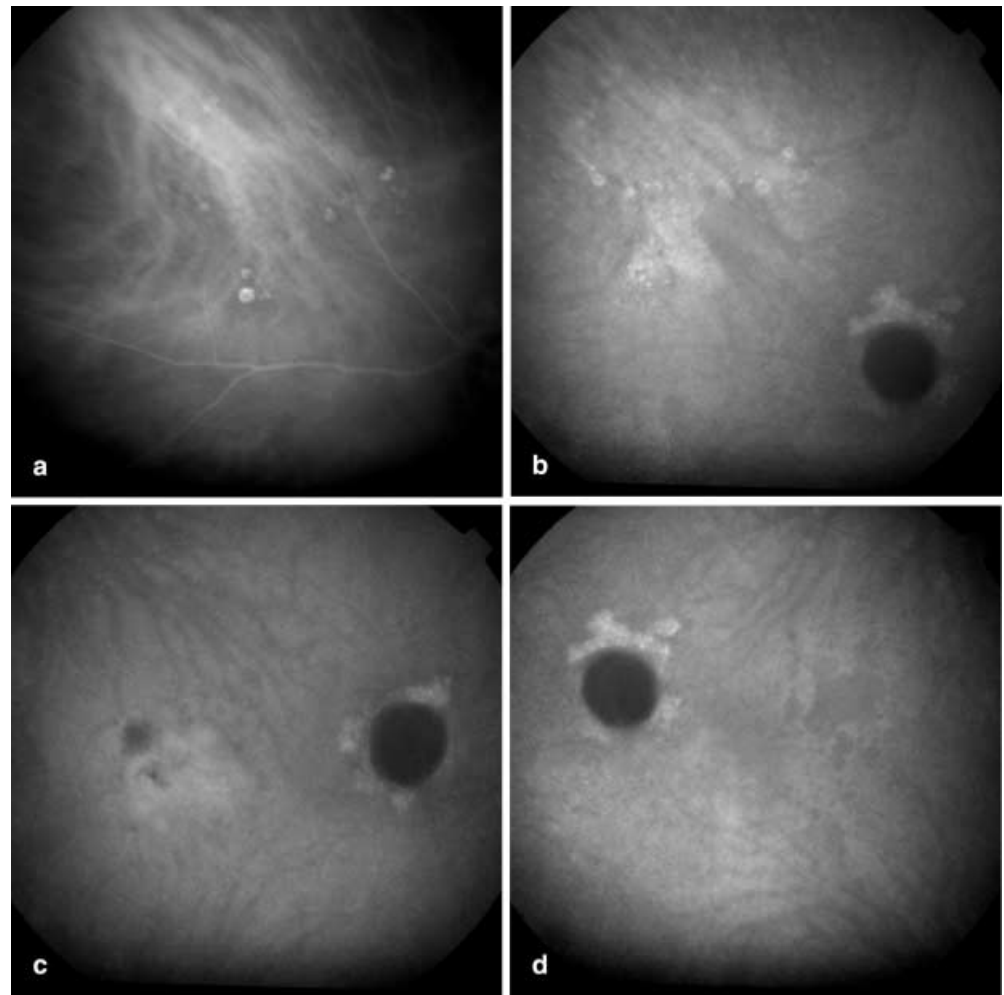


Table 2 Group 2: ICGA characteristics and associated fundus findings summarized for the four different locations of polyps: macular, peripapillary, arcade and midperiphery

Site of lesion	ICGA characteristics			Associated fundus findings				
	Cluster	Associated net	Plaque	Large drusen	PED	Lipid exudates	Hemorrhages	Extensive scarring
Macular (<i>n</i> =22)	19 (86%)	6 (27%)	15 (68%)	6 (27%)	9 (41%)	10 (49%)	11 (50%)	5 (23%)
Peripapillary (<i>n</i> =16)	10 (63%)	1 (6%)	6 (38%)	6 (38%)	4 (25%)	7 (44%)	9 (56%)	1 (6%)
Arcade (<i>n</i> =6)	3	2	3	1	4	3	5	3
Midperiphery (<i>n</i> =6)	6	0	2	5	5	1	3	4

Regression of fundus signs without persisting polyps was found in all 5 peripapillary lesions 6 months after treatment. In two, however, a new neighboring cluster developed 1 year later, that became symptomatic about 2 years after the initial treatment. A longer follow-up was not available for the other eyes. Regression of fundus signs without persisting polyps was obtained in 5 of 9 eyes with either macular or arcade lesions after 6 months, but in 2 eyes a plaque persisted (Fig. 2). The

condition stabilized in two eyes and had worsened in two others. A plaque without persisting polyps (Fig. 3) was identified. One year after treatment, the macular exudation had worsened in these latter four eyes. ICGA indicated a growing plaque in each eye, associated with a new polyp in only one eye. The original polyps had disappeared.

Discussion

Polypoidal choroidal vasculopathy is not a rare diagnosis in Caucasians, as 4% of a consecutive series of eyes with occult CNV were found to have PCV. This disorder was often not recognized in Caucasians [4, 18] until better descriptions became available [20, 23, 25, 27]. Our observed frequency (4%) is close to the 6% (10/149) observed by Yannuzzi et al. [27] in their series, after excluding non-Caucasians. Their methodology was rather similar, since they studied a consecutive series of symptomatic patients with exudative maculopathy due to presumed neovascularized AMD. In 2% of eyes from this study, multizonal transient choroidal hyperfluorescence was observed. These eyes were considered to have exudative maculopathy due to chronic central serous chorioretinopathy mimicking occult CNV on FA [4, 11, 16, 21]. The remaining eyes were considered to have straightforward AMD. The frequency of plaques and hot spots in eyes without a PED was similar to those found in other studies; it was somewhat different, however, in eyes with a PED. Whereas Guyer et al. [3] found plaques in 62% of eyes with a PED, we only observed plaques in 40% and hot spots in 56% of such eyes. In about half of the latter eyes the hot spot(s) were entirely within the PED. This type of lesion can be considered to represent a deep retinal vascular anomalous complex [6, 7] or a chorioretinal anastomosis [10], as in many cases a retinal vessel was typically suspected to dip into the lesion on FA. Kuhn et al. [10] identified chorioretinal anastomoses in 27% of a consecutive series of 186 eyes with PED, which is very close to the 29% we have observed in this series.

Polypoidal choroidal vasculopathy is best visualized or even solely recognized by ICGA. The essential finding is a focally dilated vessel stemming from the choroidal circulation. When the lesion is small it looks rather like an aneurysm, when larger it really appears like a polyp. While others [20, 25, 27] have considered the presence of an associated net of dilated vessels in the early phase of ICGA necessary to make a proper diagnosis of PCV, we found such vessels in only 9 of 45 eyes with typical polyps. A plaque, often much larger than the area occupied by the polyps, appeared in 26 of 45 eyes. Conventional ICGA is not able to show capillaries of neovascular membranes in the early phase, but their presence is indirectly demonstrated by the visualization of a plaque in the late phase. Similarly, the polyps are likely to be connected by a capillary net, which can be seen only indirectly in the late phase as a plaque. The polyp(s) may leak some indocyanine green and be visible as a hot spot in the late phase or they may disappear. The smaller polyp(s) may easily be overlooked in the late phase, especially when a plaque appears, while the larger ones remain visible because the staining of their wall contrasts with a less hyperfluorescent lumen. The

presumed association of PCV with central serous chorioretinopathy (L.A. Yannuzzi and A.C. Bird, personal communication) does not appear likely, since transient choroidal hyperfluorescence was not seen in the 45 eyes with PCV.

The PCV lesions were located predominantly in the macula, somewhat less frequently in the peripapillary area and much less commonly under the temporal vascular arcade and in the midperiphery. The age ranges overlapped; significant differences were not found. The great majority of macular lesions were clusters, whereas single polyps were found somewhat more frequently around the disc. Large or soft drusen were observed in 33% of eyes with PCV and in 11% of fellow eyes in this study. When only patients above 54 years old are considered the frequencies change to 39% (15/38) and 14% (3/22) respectively. Yannuzzi et al. [27] found large drusen in 17% of fellow eyes, all in patients above 54 years of age, but did not describe the frequency of drusen in the affected eye. A PED was found in 44% of PCV eyes. Half of the serous or serohemorrhagic PED in PCV became hyperfluorescent in the late phase of ICGA, whereas this late hyperfluorescence was observed in only 3% of serous or serohemorrhagic PED in the absence of PCV. This indicates greater permeability of the vascular abnormality in PCV than in other types of occult CNV in PED.

As both the location of the lesions and the nature of the associated fundus lesions are similar to those in exudative AMD, one may even speculate that polypoidal choroidal vasculopathy represents a peculiar variant of exudative AMD in Caucasians that cannot be recognized by FA alone. Clinicopathological correlations will be instrumental in clarifying this point.

It has been suggested that PCV can be effectively treated with ICGA-guided laser photocoagulation of polypoidal lesions [1, 14, 15, 24, 27]. Indeed, a short-term beneficial effect was obtained in all five peripapillary lesions. The response to photocoagulation appeared to be less beneficial for macular or arcade lesions, as exudative signs persisted or worsened in four of nine patients treated. A plaque persisted in these four eyes without identifiable polyps. Uyama et al. [23] also reported a possibly less favorable outcome after laser photocoagulation in Japanese patients.

In conclusion, there certainly seem to be demographic differences between idiopathic polypoidal vasculopathy, described in middle-aged black American female patients, and AMD, which is rare in that population [9, 14, 15, 17, 22, 24]. Such differences are not so clear at all for polypoidal choroidal vasculopathy or polypoidal CNV in Caucasians. They tend to be older when presenting PCV, an entity identified in 4% of presumed occult CNV. Soft drusen, a hallmark of AMD, are found in 33% of these eyes apart from retinal pigmentary changes, which is also characteristically observed in AMD. Is the natural course different? Since follow-up studies are not

yet available for either Caucasian or Japanese patients with PCV, this question cannot be answered. The ultimate prognosis does not appear good, however, as many patients in this study suffered from poor visual function. Whether this vasculopathy responds better to laser pho-

tocoagulation than does CNV in AMD has also not been established. The outcome of laser photocoagulation is more guarded for macular or arcade lesions than for peripapillary lesions.

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