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Differentiating Exudative Macular Degeneration and Polypoidal Choroidal Vasculopathy Using OCT B-Scan

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Purpose: Although polypoidal choroidal vasculopathy (PCV) is best diagnosed with indocyanine green angiography (ICGA), ICGA is often unavailable or not ordered. OCT is widely available, and OCT B-scan can visualize polypoidal lesions diagnostic of PCV as inverted U-shaped elevations of the retinal pigment epithelium (RPE) with heterogeneous reflectivity and sometimes ring-shaped lesions within the polypoidal lesion. This study aims to differentiate findings between eyes diagnosed with PCV or typical exudative age-related macular degeneration (AMD) using ICGA and then compares findings noted on the OCT B-scan line scan in each group.

Design: Retrospective, chart review.

Methods: Clinical features of eyes with PCV and typical exudative AMD were compared by using ICGA. Eyes with PCV were evaluated for inverted U-shaped polypoidal lesions, which are the main differentiating finding of PCV from typical exudative AMD. Data collected included presence of subretinal fluid (SRF), macular edema or intraretinal edema, subretinal hyperreflective material (SHRM), and retinal pigment epithelial detachment (RPED). These findings were evaluated in 2 parts: baseline and after 6 to 9 months of antiangiogenic therapy. Additionally, analysis was performed for the presence of polypoidal lesions before and after treatment.

Main Outcome Measures: Presence of inverted U-shaped lesions on OCT B-scan following treatment.

Results: A total of 112 eyes of 106 patients were included. A total of 69 eyes were diagnosed with PCV, and 43 eyes were diagnosed with typical exudative AMD. Compared with AMD eyes, PCV eyes had an increased prevalence of SRF at baseline and after 6 to 9 months of treatment, but the prevalence of macular edema, SHRM, and RPED was similar at baseline and at 6 to 9 months after treatment. In PCV eyes, the presence of visible polypoidal lesions decreased from 56.5% to 24.6% after treatment.

Conclusions: If PCV is suspected in an anti−vascular endothelial growth factor (VEGF)-resistant case of exudative AMD, in the absence of ICGA availability, it is important to look at the baseline OCT B-scan before therapy for evidence of polypoidal lesions. The characteristic inverted U-shaped elevation was present in more than half of PCV eyes on OCT B-scan at baseline but disappeared after antiangiogenic therapy in 56.4% of cases in which this was initially identified. Subretinal fluid was more prevalent in PCV eyes than non-PCV AMD eyes. *Ophthalmology Retina 2021;5:954-961 © 2021 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

See editorial on page 943.

The current standard of care for exudative age-related macular degeneration (AMD) is antiangiogenic therapy using injections of anti−vascular endothelial growth factor (VEGF) drugs. Despite dramatic improvements visually and anatomically in many cases, some eyes do not respond well to anti-VEGF agents and have persistent subretinal fluid (SRF) and bleeding despite anti-VEGF injections even with short intervals between injections (anti-VEGF resistance). Recently, a subtype of exudative AMD has been shown to have a higher prevalence of anti-VEGF resistance.[1-4] This phenotypic subtype is polypoidal choroidal vasculopathy (PCV),[5-7] which is characterized by polypoidal or subretinal aneurysmal lesions as part of the choroidal neovascularization, often associated with a branching vascular network (BVN). Because of anti-VEGF resistance, the diagnosis of PCV is important in managing exudative AMD, which is best diagnosed with indocyanine green angiography (ICGA).[8-10] However, ICGA is often not available or ordered in the usual evaluation of exudative AMD in most clinical centers.[5,11] OCT is readily available and commonly used in most clinical care situations, and the polypoidal lesions on OCT are visible as an inverted U-shaped elevation of the retinal pigment epithelium (RPE) with heterogeneous reflectivity, which can be correlated to the hyperfluorescent polypoidal lesions on ICGA.[9,10]

Alternative ways to image PCV without ICGA include fundus photographs, B-scan OCT, en face OCT, and OCT angiography (OCTA).[12-20] Fundus photographs can show a subretinal orange nodule consistent with a polypoidal lesion of PCV and, occasionally, the entire PCV complex with polypoidal lesions and the BVN visualized through the RPE. B-scan OCT can image the polypoidal lesions as a

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sharply peaked protrusion of the RPE with heterogeneous reflectivity, a notched or multi-lobulated retinal pigment epithelial detachment (RPED), a double line sign with a slight elevation of the RPE consistent with the BVN, and a hyperreflective ring within the polypoidal lesion on OCT (Fig 1).[9,10,14] En face OCT can image the vascular network and polypoidal lesions, although this is less sensitive than ICGA.[15-18] OCT angiography, which creates images based on blood flow through the subretinal vascular network, often shows the BVN well but is less sensitive in showing the polypoidal lesions, possibly due to decreased flow through the polypoidal lesions.[19,20]

The importance of making the diagnosis of the PCV subtype of exudative AMD is to identify this high-risk subgroup for anti-VEGF resistance[1-4] and to be prepared to consider therapeutic alternatives in these eyes. This PCV subtype has been shown to be responsive to alternative therapy, such as combination verteporfin photodynamic therapy (vPDT) with anti-VEGF injection.[11,21,22] The recent results of the EVEREST II study showed improved visual outcomes with significantly fewer injections for combination vPDT with ranibizumab injection as opposed to ranibizumab monotherapy.[21,22] The presence of the polypoidal lesions and the high rate of closure after vPDT may significantly affect future recurrence and persistent leakage.

This retrospective study was designed to study eyes with a definite diagnosis of PCV based on ICGA and to evaluate findings diagnostic of PCV based on B-scan OCT both before and after anti-VEGF therapy.

Methods

This study was a retrospective chart review of patients seen by the Retina Consultants of Hawaii and the Hawaii Macula and Retina Institute for management of PCV and exudative AMD from September 2007 to December 2019. The Western Institutional Review Board exempted this study from Institutional Review Board approval because of its retrospective design (#1-1202591-1). This study adhered to the policies set forth by the Health Insurance Portability and Accountability Act and the Declaration of Helsinki. All participants provided informed consent.

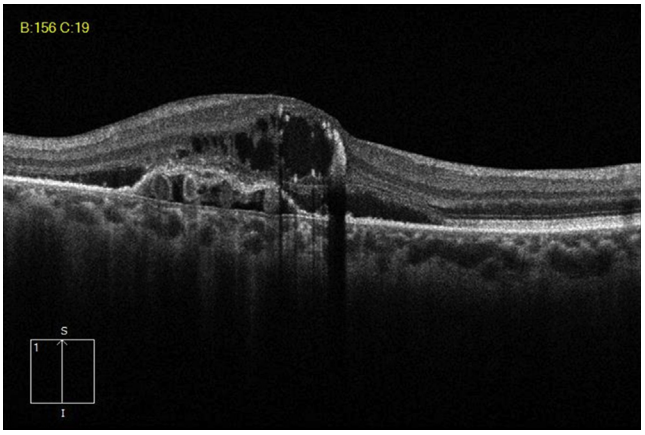

Figure 1. B-scan OCT showing retinal pigment epithelial detachment (RPED), subretinal fluid (SRF), and intraretinal edema associated with polypoidal choroidal vasculopathy (PCV). Note the 4 ring-shaped lesions beneath the retinal pigment epithelium (RPE) typical of PCV.

Patients were seen and diagnosed with PCV or exudative AMD by 4 retinal specialists at the Retina Consultants of Hawaii and the Hawaii Macula and Retina Institute. All patients underwent a baseline ophthalmic examination, including best-corrected visual acuity, slit-lamp examination, dilated fundus examination with a 90-diopter lens, OCT (Cirrus HD-OCT, Carl Zeiss Meditec), and ICGA using the scanning laser ophthalmoscope (Spectralis HRA+OCT, Heidelberg Engineering). All ICGA images used for the diagnosis of PCV were reviewed by one doctor specifically trained in the diagnosis of PCV. Data were collected retrospectively from medical records, and included basic demographics, fundus findings, affected eye, visual acuity, family history, prior ocular surgery or laser treatment, duration of disease, systemic medical history, date of onset, number of intravitreal anti-VEGF injections, and type of medications (bevacizumab, aflibercept, and ranibizumab).

For part 1 of the study, we evaluated eyes with PCV confirmed on ICGA and eyes without PCV confirmed on ICGA. The best images to evaluate for PCV on ICGA are those taken between 3 and 5 minutes after ICG dye injection, which is when the polypoidal lesions and complex are best visualized. The visualization of aneurysmal dilations or polypoidal vascular lesions with or without a BVN was used to make the diagnosis of PCV. OCT B-scan characteristics were evaluated using the standard spectral-domain OCT, as well as the OCT associated with the ICGA on the scanning laser ophthalmoscope, which allowed point-to-point localization of the lesion visualized on ICGA with the OCT B-scan characteristics at that exact location (Fig 2).[9,10]

OCT B-scan findings were collected at baseline for both the PCV group and the exudative AMD group. The OCT data at baseline were evaluated for SRF, height of SRF, macular edema, RPED, RPED height, subretinal hyperreflective material (SHRM), and BVN identified as a double line sign. Macular edema was defined as an increase in central foveal thickness. The double line sign is a shallow elevation of the RPE that correlates to the BVN of PCV.[15] The important data also collected included the most characteristic finding of PCV on B-scan OCT: the inverted U-shaped elevation of the RPE with heterogeneous reflectivity that is typical of the polypoidal lesions of PCV. This OCT diagnosis was confirmed on ICGA with point-to-point localization to the visible polypoidal lesions noted on ICGA.

For part 2 of the study, the OCT findings of the PCV eyes were evaluated for characteristic diagnostic findings on B-scan OCT both before treatment and after beginning treatment with intravitreal anti-VEGF medications for 6 to 9 months with a treat-and-extend approach. The OCT data included presence of SRF, maximal height of SRF, macular edema, retinal pigment epithelium detachment (RPED), maximal height of RPED, SHRM, BVN (double line sign),[11] and focal inverted U-shaped lesion consistent with a polypoidal or aneurysmal lesion. The B-scan diagnostic criteria for polypoidal aneurysmal lesion associated with PCV was a sharply peaked RPE protrusion with a rounded top and heterogeneous internal reflectivity. This lesion was often at the outer edge of a notched RPED, but could also be independent of RPED. These polypoidal lesions are often at the peripheral edge of a BVN. These lesions on B-scan OCT were correlated with the polypoidal lesion of PCV on the initial ICGA. Exclusion criteria included concomitant retinal diseases, including diabetic retinopathy, vascular occlusion, myopic degeneration, inflammatory disease, prior focal laser therapy or prior vPDT, major trauma, previous vitrectomy or intraocular surgery except for uncomplicated cataract surgery, and prior intravitreal steroid. For this anti-VEGF treatment analysis, all eyes were required to

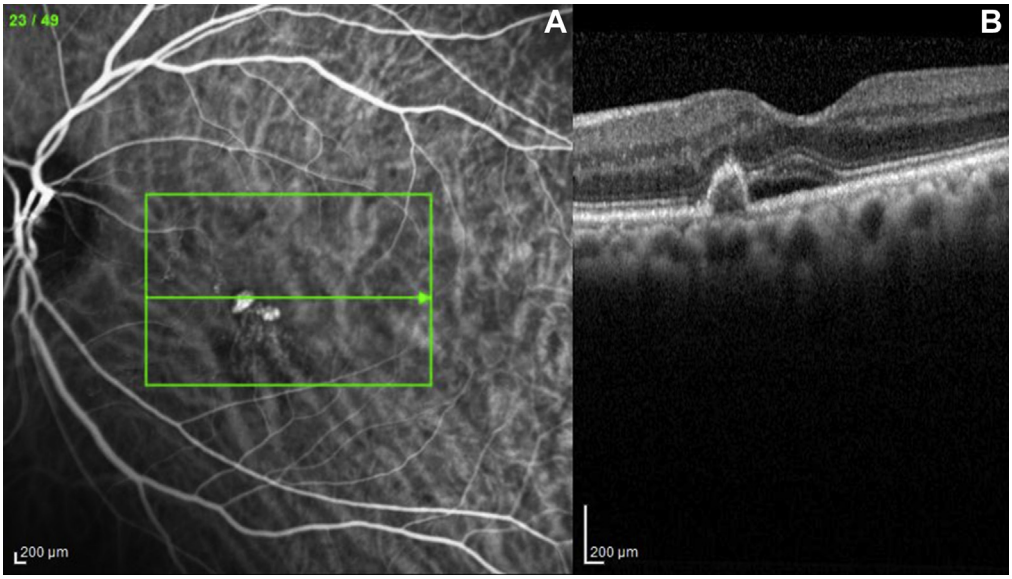

Figure 2. Point-to-point correlated indocyanine green angiogram **(A)** and B-scan OCT **(B)** showing polypoidal lesion as an inverted U-shaped elevation of the RPE with SRF.

have OCT images before treatment and follow-up OCT data 6 to 9 months after beginning treatment.

Analysis of OCT B-scans was performed using IBM SPSS Statistics for Windows version 24.0 (IBM Corp). Two-tailed, 2-sample unequal variance *t* tests were used to calculate the *P* value for SRF heights, RPED heights, and visual acuity data. A chi-square test was used to calculate the *P* value when comparing various categorical groups for analysis. A *P* value less than 0.05 was considered statistically significant.

Results

In this study, baseline and follow-up data (6–9 months) were collected for 112 eyes of 106 patients. The average age of patients in this data set was 75.9 years (52–96 years). There were 75 eyes of Asian patients, 30 eyes of White patients, 4 eyes of Pacific Islander patients, 1 eye of a Latino patient, 1 eye of a Black patient, and 1 eye of a mixed-race patient. A total of 64 patients were male, and 42 patients were female. Indocyanine green angiography revealed 69 eyes with PCV and 43 eyes with neovascular AMD.

Visual acuity data were converted to logarithm of the minimum angle of resolution (logMAR) scoring for analysis. The average logMAR for eyes with PCV at baseline was 0.608 (20/80 Snellen equivalent), and the average logMAR for eyes with AMD at baseline was 0.837 (20/125 Snellen equivalent). There was no significant difference between PCV and AMD visual acuity at baseline ($P = 0.055$). Polypoidal choroidal vasculopathy eyes had significantly better vision after treatment with an average logMAR of 0.455 (20/60 Snellen) that was significantly better than typical AMD eyes after treatment with an average logMAR of 0.729 (20/100 Snellen) ($P = 0.008$).

In part 1 of the study, the clinical characteristics of eyes with typical exudative AMD without PCV and eyes with PCV were compared at baseline (Table 1). Before treatment, eyes with PCV had SRF in 88.4% (61/69 eyes), macular edema in 43.5% (30/69 eyes), SHRM in 58.0% (40/69 eyes), RPED in 79.7% (55/69 eyes), and a branching retinal network (BVN) in 50.7% (35/69

Table 1. Baseline Characteristics on OCT between PCV and Typical Exudative AMD Eyes

	PCV			AMD			
	Present	*Absent*	*Percent (%)*	*Present*	*Absent*	*Percent (%)*	*P Value*
SRF	61	8	88.41%	29	14	67.44%	0.007
ME	30	39	43.48%	17	26	39.53%	0.681
SHRM	40	29	57.97%	27	16	62.79%	0.613
RPED	55	14	79.71%	32	11	74.42%	0.513
BVN	35	34	50.72%	0	43	0.00%	<0.001
Inverted U	39	30	56.52%	1	42	2.33%	<0.001
SRF height (µm)	156.2			131.1			0.291
RPED height (µm)	337			289.8			0.264

AMD = age-related macular degeneration; BVN = branching vascular network; ME = macular edema; PCV = polypoidal choroidal vasculopathy; RPED = retinal pigment epithelial detachment; SHRM = subretinal hyperreflective material; SRF = subretinal fluid.

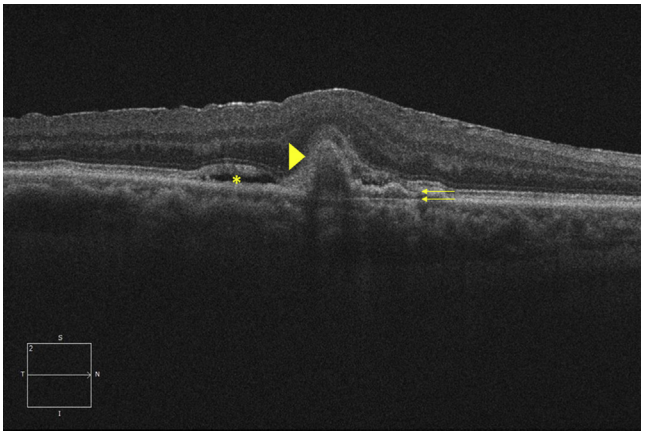

Figure 3. B-scan OCT showing inverted U-shaped elevation of the RPE (**arrowhead**) with adjacent double line sign characteristic of the branching vascular network (BVN) (**arrows**) and associated SRF (**asterisk**).

eyes). Before treatment, typical AMD eyes without PCV had SRF in 67.4% (29/43 eyes), macular edema in 39.5% (17/43 eyes), SHRM in 62.8% (27/43 eyes), RPED in 74.4% (32/43 eyes), and BVN in none (0/43 eyes). There were significantly more eyes with SRF in PCV eyes at baseline (61/69 eyes) than AMD eyes at baseline (29/43 eyes) ($P = 0.007$) (Figs 2–4). There was also a significantly higher presence of BVN between PCV eyes (35/69 eyes) and AMD eyes (0/43 eyes) ($P < 0.001$). At baseline, there was no significant difference in the prevalence of macular edema between PCV eyes (30/69 eyes) and typical AMD eyes (17/43 eyes) ($P = 0.681$), SHRM between PCV eyes (40/69 eyes) and typical AMD eyes (27/43 eyes) ($P = 0.613$), or RPED between PCV eyes (55/69 eyes) and AMD eyes (32/43 eyes) ($P = 0.513$). The average height of SRF at baseline was 156.2 μm for PCV eyes and 131.1 μm for typical AMD eyes. There was no significant difference in the height of SRF at baseline between PCV and AMD eyes ($P = 0.291$). The average height of RPED at baseline was 337.0 μm for PCV eyes and 289.8 μm for AMD eyes, with no significance between PCV and typical AMD eyes ($P = 0.264$).

In part 2 of the study, eyes were evaluated 6 to 9 months after initiating treatment with anti-VEGF intravitreal medications (Table 2). After treatment, eyes with PCV had SRF in 47.8% (33/69 eyes), macular edema in 26.1% (18/69 eyes), SHRM in 27.5% (19/69 eyes), RPED in 49.3% (34/69 eyes), and BVN or double line sign in 39.1% (27/69 eyes). After treatment, eyes with exudative AMD without PCV had SRF in 27.9% (12/43 eyes), macular edema in 27.9% (12/43 eyes), SHRM in 34.9% (15/43 eyes), and RPED in 62.8% (27/43 eyes); BVN was not present in any eye. There was a significant difference in the prevalence of SRF after treatment between eyes with PCV (33/69 eyes) and eyes with exudative AMD (12/43 eyes) ($P = 0.037$). There was also a significantly higher prevalence of BVN between PCV eyes (27/42 eyes) and AMD eyes (0/43 eyes) ($P < 0.001$). After treatment, there was no significant difference in the prevalence of macular edema between PCV eyes (18/69 eyes) and AMD eyes (12/43 eyes) ($P = 0.832$), the prevalence of SHRM between PCV eyes (19/69 eyes) and AMD eyes (15/43 eyes) ($P = 0.411$), or the prevalence of RPED between PCV eyes (34/69 eyes) and AMD eyes (27/43 eyes) ($P = 0.162$). The average height of SRF for PCV eyes after treatment was 105.1 μm and 88.2 μm for typical AMD eyes, with no significant difference ($P = 0.281$). The average height of RPED was 223.5 μm for PCV eyes after treatment and 255.3 μm for typical AMD eyes after treatment, which was not significantly different ($P = 0.406$).

B-scan OCT was evaluated for findings that would be diagnostic of PCV. The inverted U-shaped elevation of the RPE with heterogeneous reflectivity corresponding to a polypoidal lesion on ICGA is the most diagnostic finding of PCV on B-scan OCT. This was noted at baseline in 56.5% of PCV eyes (39/69 eyes) and in 2.3% (1/43 eyes) of eyes with typical AMD ($P < 0.001$). The sensitivity of the inverted U on OCT at baseline was 56.5%, the specificity was 97.7%, the positive predictive value was 97.5%, and the negative predictive value was 58.3%. After 6 to 9 months of treatment, the inverted U-shaped lesion was present in 24.6% of eyes with PCV (17/69 eyes) and resolved in the 1 eye with typical AMD after treatment ($P < 0.001$). The sensitivity of the inverted U-shaped lesion on OCT after treatment was 24.6%, the specificity was 100%, the positive predictive value was 100%, and the negative predictive value was 45.3%. This most characteristic finding of PCV decreased significantly after anti-VEGF treatment in PCV eyes, decreasing from 56.5% (39/69 eyes) to 24.6% (17/69 eyes) ($P < 0.001$). This represents a 56.4% decrease in visible PCV lesions after treatment (Fig 4).

The first 3 anti-VEGF treatments were recorded for each eye. Of the eyes diagnosed with PCV, 50.7% (35/69 eyes) received bevacizumab, 40.6% (28/69 eyes) received aflibercept, 7.2% (5/69

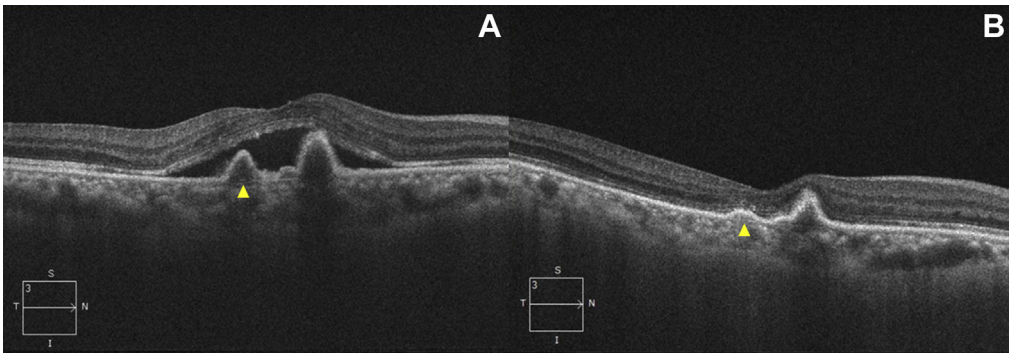

Figure 4. B-scan OCT findings before and after anti–vascular endothelial growth factor (VEGF) treatment. **A,** The initial inverted U-shaped elevation of the RPE typical of the polypoidal lesions, as well as SRF before treatment. **B,** After treatment there is loss of the inverted U-shaped elevation temporally and resolution of SRF.

Table 2. Post-treatment (6–9 Months) Findings on OCT between PCV and Typical Exudative AMD Eyes

	PCV			AMD			
	Present	*Absent*	*Percent (%)*	*Present*	*Absent*	*Percent (%)*	*P Value*
SRF	33	36	47.83%	12	31	27.91%	0.037
ME	18	51	26.09%	12	31	27.91%	0.832
SHRM	19	50	27.54%	15	28	34.88%	0.411
RPED	34	35	49.28%	27	16	62.79%	0.162
BVN	27	42	39.13%	0	43	0.00%	<0.001
Inverted U	17	52	24.64%	0	43	0.00%	<0.001
SRF height (μm)	105.1			88.2			0.281
RPED height (μm)	223.5			255.3			0.406

AMD = age-related macular degeneration; BVN = branching vascular network; ME = macular edema; PCV = polypoidal choroidal vasculopathy; RPED = retinal pigment epithelial detachment; SHRM = subretinal hyperreflective material; SRF = subretinal fluid.

eyes) received ranibizumab, and 7.2% (5/69 eyes) were treated with combination bevacizumab and dexamethasone. Eyes with AMD without PCV were treated with bevacizumab in 55.8% (24/43 eyes), 23.3% (10/43 eyes) aflibercept, and 23.3% (10/43 eyes) ranibizumab; no eyes received combination bevacizumab with dexamethasone. There were significantly more eyes treated with ranibizumab in AMD eyes (10/43 eyes) than PCV eyes (5/69 eyes) ($P = 0.016$). There was no significant difference in anti-VEGF use between PCV and typical AMD eyes for bevacizumab ($P = 0.600$), aflibercept ($P = 0.060$), or combination bevacizumab and dexamethasone ($P = 0.071$).

Discussion

Polypoidal choroidal vasculopathy is a subtype of exudative AMD that is characterized by subretinal neovascularization, which most often is located between the RPE and Bruch's membrane[8,9] and which has characteristic findings with dilated polypoidal lesions and a BVN. Recent studies using ICGA to screen all cases of exudative AMD shows a higher prevalence in all populations, including not only Asian populations but also White populations.[1,2,5,21] The diagnosis of PCV is often missed because ICGA was not available or not considered.[5] OCT is a widely used diagnostic test and available to most practices, and B-scan OCT is also a diagnostic test available and familiar to most practitioners.

On B-scan OCT, the polypoidal lesion under the RPE and above Bruch's membrane is seen as a sharply elevated RPE protrusion with heterogeneous reflectivity (inverted U-shaped elevation).[8,9] Correlation of this B-scan elevation with ICGA shows that these lesions correspond to the aneurysmal dilation characteristic of PCV. This finding was chosen because it is the main finding confirming a polypoidal lesion on B-scan OCT, which is the most commonly evaluated diagnostic study by most practitioners. Subsequent to this study, the Asia Pacific Ocular Imaging Group identified 2 other helpful parameters, including ring-shaped lesions beneath the RPE within the U-shaped RPE elevation, which is also characteristic of PCV (Fig 1) and en face OCT.[14] However, the ring-shaped lesion is not that common and en face OCT is not used by most practitioners. This study on inverted U-shaped lesions in PCV shows that it is highly specific for PCV but not that sensitive, because only 56.5% of eyes with PCV have this lesion, but this also means that PCV can be identified with high specificity with B-scan OCT without ICGA in more than half of PCV eyes. However, the low negative predictive value implies that absence of the inverted U-shaped lesion does not necessarily predict a patient not having PCV. The sensitivity of the inverted U-shaped lesion is further decreased after treatment.

The inverted U-shaped elevation of the RPE with heterogeneous reflectivity (Figs 2–4) is important to identify, because PCV lesions are more often anti-VEGF resistant, thus not responding as well to the usual anti-VEGF therapy injections.[1-4] In addition, according to the EVEREST II study, which showed that combined vPDT and ranibizumab showed improved vision with fewer injections over ranibizumab monotherapy, alternative primary therapy can be considered.[18-20] However, in this study the characteristic polypoidal lesion on OCT resolved in 56.4% (22/39 eyes) of cases after beginning anti-VEGF therapy for at least 6 months (Fig 4). Often, PCV is considered only after anti-VEGF resistance has been identified after prolonged anti-VEGF injections. This study shows that many cases do not show the characteristic lesions of PCV after treatment, so it is important to look back at the initial B-scan OCT scans before therapy to make the diagnosis of PCV on B-scan OCT.

The clinical characteristics of PCV and exudative AMD were also noted to be different in key findings on OCT. At baseline, there were significantly more eyes with SRF in PCV than in AMD (Fig 3). Subretinal fluid was noted in 88.4% of eyes with PCV compared with 67.4% in typical AMD. This compares similarly to the findings of Ozawa et al,[23] in which SRF was observed in 78% of eyes with PCV and 53% of eyes with exudative AMD.[23] In addition, there was more SRF in PCV eyes after treatment (47.8%) than in eyes with typical AMD (27.9%). This further supports the increased prevalence of anti-VEGF resistance in PCV compared with typical exudative AMD.[1-4,20] This study could not confirm any difference in the height of SRF, possibly due to the smaller sample size than in Ozawa et al's study.[23]

Anti-VEGF resistance is the most important clinical factor associated with PCV. Although initially thought to be mainly in Asian populations,[7] the prevalence of PCV using ICGA with the scanning laser ophthalmoscope (Spectralis HRA+OCT; Heidelberg Engineering) in White populations has been assessed at 20% in a population seen at the Duke Eye Center,[24] 24.5% in a predominantly White population seen in Brazil,[25] and 31.9% in a White population seen in Hawaii.[1] In addition, anti-VEGF resistance was noted to be significantly higher in PCV eyes in both Asian and White populations.[1] Because PCV is more common than initially thought in White populations and is frequent in Asian populations, the importance of making the diagnosis becomes more significant because it can affect patient care in a significant percentage of patients presenting with symptoms and findings of exudative AMD. The EVEREST II trial has shown that combination vPDT and ranibizumab has better vision results with less frequent injections than ranibizumab monontherapy.[11,21,22] Thus, combination vPDT and ranibizumab should be considered as an alternative in the primary management of exudative AMD with the PCV subtype. In addition, because most patients with exudative AMD are initially started on anti-VEGF monotherapy, many patients are evaluated for PCV once eyes have exhibited anti-VEGF resistance. If ICGA is not available, then B-scan OCT, which is readily available, can be useful in making the diagnosis of PCV. However, because the findings characteristic of PCV decrease after anti-VEGF therapy, this study shows the importance of going back and reviewing the pretreatment B-scan. The most common findings on B-scan OCT are the inverted U-shaped RPE protrusion with heterogeneous internal reflectivity, the notched RPED, and the multi-lobed RPED. In a study by Chaikitmongkol et al,[13] fundus photography and OCT alone were shown to have high specificity and sensitivity to make the diagnosis of PCV. These results are promising to make the diagnosis of PCV without ICGA with diagnosticians trained in the diagnosis of PCV, but are too optimistic for the usual practicing retina specialist unfamiliar with the diagnosis of PCV.

In the EVEREST II study, vPDT is based on the ICGA, which is used to determine the greatest linear dimension. For vPDT for PCV, the target spot size is limited to the area around the PC complex or just including a small 300-μm border around the PCV lesion on the ICGA.[21,22] Previously, when originally conceived for exudative AMD, vPDT was based on the fluorescein angiogram, and the area of leakage was targeted with an additional large 1000-μm border around the area of leakage. This resulted in a broader area of treatment to the macula than currently used for vPDT for PCV. In addition, with full fluence treatment in the EVEREST II trial, there were no cases of sudden vision loss after vPDT.[21,22] If PCV is recognized on initial evaluation or recognized later with anti-VEGF resistance, then combination vPDT and anti-VEGF injection provides a possible treatment option, which is not supported for typical exudative AMD.

Although ICGA remains the gold standard for diagnosing PCV, B-scan OCT, which is readily available, can help to make the diagnosis in many cases. The key findings are the sharply elevated inverted U-shaped RPE protrusion characteristic for the polypoidal lesions of the subretinal vascular complex (Figs 2–4). On imaging, the BVN is seen as the double line sign, which is a slight elevation of the RPE above Bruch's membrane (Fig 3). There is also more SRF associated with PCV than typical wet AMD (Figs 2–4). Another OCT-based imaging is en face OCT imaging. Although not as sensitive as ICGA, en face OCT can image the entire PCV complex in some cases and often can show the BVN and the outline of the polypoidal lesions.[15-18] OCTA using the proper boundaries to image the polypoidal lesions and the vascular complex is also useful to make the diagnosis of PCV and is particularly useful at imaging the BVN. The polypoidal lesions are not as well seen on OCTA, possibly due to decreased flow through the polypoidal lesions,[19,20] but new findings using structural OCT and cross-sectional OCTA together showed higher specificity and sensitivity.[19] However, as with ICGA, OCTA is not widely available in many clinics, which is why understanding the findings on B-scan OCT is important for the diagnosis of PCV in most clinics.

Although the goal of the study was not to compare different anti-VEGF agents, but to evaluate an important diagnostic marker for PCV, there was a difference between the 2 groups. In the typical AMD group, there were more ranibizumab-treated eyes. However, ranibizumab and aflibercept were shown to be equal in efficacy with regard to both anatomic and vision results for typical exudative AMD.[26] In PCV eyes there is good evidence to suggest that aflibercept has a significantly better effect on anatomic results, including decrease in SRF and macular edema than ranibizumab.[27,28] Aflibercept treatment was not statistically significantly different between the typical AMD and PCV groups in this study. In the PCV group, 52% of the eyes had resolved SRF after treatment, whereas in the PLANET study,[27] 77% of eyes had resolved fluid after 3 months of treatment. The difference is explained by the monthly treatment in the PLANET study and the use of only aflibercept in the PLANET study versus the varied treatments in this study and the treat-and-extend protocol in clinical practice usually starting with treatment every 5 to 6 weeks. In the typical AMD group, 72% had resolution of SRF, and 72% had resolution of SRF in the ranibizumab monotherapy group in the EVEREST II trial at month 12.[29]

Study Limitations

The limitations of this study are the retrospective nature of this study and the relatively small numbers of the study groups. However, this study was focused on the OCT findings of PCV, because B-scan OCT is widely available and has the ability to diagnose PCV before and after treatment. In addition, it confirmed the higher prevalence of SRF in eyes with PCV both before and after treatment.

Conclusions

One of the most important subtypes of exudative AMD is PCV, a subretinal network of blood vessels usually above Bruch's membrane and below the RPE associated with

polypoidal dilated lesions as part of the choroidal neovascularization. Although best diagnosed on ICGA as the gold standard, this diagnostic testing is not widely available. B-scan OCT is widely available, and cases can be identified on the basis of polypoidal lesions, which appear as a sharply peaked elevations of the RPE,[9,10,14] which correlates to the polypoidal lesions on ICGA. Because anti-VEGF resistance is more prevalent in eyes with PCV than typical AMD,[1-4] alternative therapies are being considered in this subgroup, which is more difficult to manage and treat. However, to make this diagnosis, this study shows that it is important to look at the pretreatment B-scan OCT before the beginning of anti-VEGF therapy, because the inverted U-shaped lesions decrease after treatment (Fig 4). Eyes with a poor response to anti-VEGF therapy often will be missed if the B-scan OCT is only evaluated after anti-VEGF therapy. The B-scan OCT can help guide therapy in eyes with exudative AMD by showing typical findings of PCV, which allows consideration of alternative therapy such as combination vPDT and anti-VEGF, helps to predict anti-VEGF resistance, and helps to understand which anti-VEGF therapy may have the best therapeutic response.

Footnotes and Disclosures

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Author Contributions:

Conception and design: Kokame, Omizo, Kokame, Yamane

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Abbreviations and Acronyms:
AMD = age-related macular degeneration; **BVN** = branching vascular network; **ICGA** = indocyanine green angiography; **logMAR** = logarithm of the minimum angle of resolution; **OCTA** = OCT angiography; **PCV** = polypoidal choroidal vasculopathy; **RPE** = retinal pigment epithelium; **RPED** = retinal pigment epithelial detachment; **SHRM** = subretinal hyperreflective material; **SRF** = subretinal fluid; **VEGF** = vascular endothelial growth factor; **vPDT** = verteporfin photodynamic therapy.

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Age-related macular degeneration, Anti-VEGF, OCT B-scan, OCT, Polypoidal choroidal vasculopathy.

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