Pigment Epithelial Detachment in Polypoidal Choroidal Vasculopathy

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• PURPOSE: To study the morphological features of serosanguineous pigment epithelial detachments (PEDs) with accompanying polypoidal lesions in eyes with polypoidal choroidal vasculopathy (PCV).
• DESIGN: Retrospective observational case series.
• METHODS: For this observational case study, we retrospectively reviewed 93 consecutive eyes of 85 patients with PCV. The lesions in eyes with PCV were examined with indocyanine green angiography (IA) and optical coherence tomography (OCT).
• RESULTS: Of 93 eyes with PCV, 51 eyes (55%) had serous or hemorrhagic PEDs. Of these 51 eyes, a notch in the PED was found in 27 eyes (53%) by angiography, most of which showed polypoidal lesions by IA that corresponded in location to the notch observed by angiography. Polypoidal lesions were detected outside the PED in one eye (2%), at the margin of the PED in 33 eyes (65%), and inside the PED in 12 eyes (24%). OCT revealed that PED had a notch observed tomographically in 29 eyes (57%), most of which corresponded in location to polypoidal lesions seen by IA. In eight eyes, polypoidal lesions, which were adherent to the inner surface of the serous PED, appeared to be detached from the Bruch membrane and the choroid.
• CONCLUSIONS: Polypoidal lesions are located at the margin of PED and make a notch in the accompanying PED that is visible by angiography and tomographically. When the polypoidal lesions have increased exudate, the fluid from the lesions infiltrates under the polypoidal lesions themselves, which results in the lesions detaching from the Bruch membrane and appearing to be located inside the PED. (Am J Ophthalmol 2007; 143:102–111. © 2007 by Elsevier Inc. All rights reserved.)

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TO DATE, THE PATHOGENESIS OF POLYPOIDAL CHOroidal vasculopathy (PCV) is not fully understood,[1] but it reportedly originated in an abnormality of inner choroidal vessels.[2–5] PCV is characterized by a branching vascular network terminating in polypoidal lesions.[3–10] However, large serosanguineous pigment epithelial detachments (PEDs) are another clinical characteristic of PCV.[2–9,11–13] Ahuja and associates[12] have reported that 34 of 40 eyes with large serosanguineous PEDs in the absence of drusen showed polypoidal lesions by indocyanine green angiography (IA), and many of these lesions were located immediately adjacent to the PEDs. Because photocoagulation of polypoidal lesions often results in resolution of the associated PEDs,[14] Spaide and associates[3] have reported that the hemorrhagic and serous PED arises from leakage from the polypoidal lesions.

Because most lesion components in eyes with PCV are located under the retinal pigment epithelium (RPE),[3,6] IA is essential to diagnose and examine the extent of the disease.[3–5,8–10,15] Because only a small number of histological reports of PCV are available,[16–24] the location of the abnormal vessels in PCV is still controversial.[1] Recently, cross-sectional examinations with optical coherence tomography (OCT) have clarified the pathophysiology of various macular diseases.[25] In OCT scans, serous PEDs appear as dome-shaped elevations of RPE with no or minor inner reflectivity.[25,26] Reddish-orange nodules in eyes with PCV show a sharp protrusion of RPE and an inner structure with moderate reflectivity.[27,28] However, to date, limited information is available on the structures of serous PED with polypoidal lesions in eyes with PCV.[28,29]

In this study, we investigated serous or hemorrhagic PEDs with polypoidal lesions in eyes with PCV angiographically and cross-sectionally. On the basis of our findings, we report on the process by which serous

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TABLE. Relationship in Location Between Polypoidal Lesions and PED

Location of Polypoidal Lesions	Angiographic Notch Present (n = 27)		Angiographic Notch Absent (n = 24)
	Polypoidal Lesions Corresponded in Location With Notch (n = 23)	Polypoidal Lesions Did Not Correspond in Location With Notch (n = 4)	
Outside PED (n = 1)	0	0	1
At the margin of PED (n = 33)	18	4	11
Within PED (n = 12)	5	0	7
Undetermined (n = 5)	0	0	5

PED = pigment epithelial detachment.

PED is formed from the leakage of the polypoidal lesions.

METHODS

FOR THIS OBSERVATIONAL CASE STUDY, WE RETROSPECtively reviewed 93 consecutive eyes of 85 patients with PCV who visited the Macular Service in Kyoto University Hospital, Kyoto, Japan, for the first time from April 2004 to October 2005. All patients underwent comprehensive ophthalmologic examination, including best-corrected visual acuity, intraocular pressure, indirect ophthalmoscopy, slit-lamp biomicroscopy with contact lens, and OCT examination. Two types of OCT (Stratus OCT3000, Carl Zeiss, Dublin, California, USA; and OCT ophthalmoscope C7, Nidek, Gamagori, Japan) were used. After fundus photographs were taken, fluorescein angiography and IA were performed in each patient with a confocal laser scanning system (HRA-2, Heidelberg Engineering, Dossenheim, Germany; and SLO, Rodenstock Instruments, Munich, Germany). For this retrospective study, institutional review board and ethics committee approval were not required.

The diagnosis of PCV was based on IA, which shows a branching vascular network terminating in polypoidal swelling. The polypoidal lesion may be a single polyp or a cluster of multiple polyps. In most cases, reddish-orange nodules that were observed under ophthalmoscopic examination corresponded to polypoidal lesions seen by IA. Eyes with other macular abnormalities (that is, age-related macular degeneration [AMD], pathologic myopia, idiopathic choroidal neovascularization [CNV], presumed ocular hisoplasmosis, angioid streaks, and other secondary CNV) were excluded from the study.

RESULTS

IN THE CURRENT STUDY, WE EXAMINED 93 EYES OF 85 patients (56 men and 29 women), ranging in age from 49 to 93 years (71.4 ± 8.7 years). All patients were Japanese. The visual acuity of eyes with PCV ranged from hand motion to 20/15 (median 20/50). In all eyes, IA showed polypoidal lesions, most of which were connecting to a branching vascular network. In 92 eyes (99%), reddish-orange nodules were seen by ophthalmoscopic examination; many of these nodules corresponded to the polypoidal lesions seen by IA. Polypoidal lesions were located in the peripapillary in four eyes (4%), in the macula in 88 eyes (95%), and in the periphery in one eye (1%).

Of 93 eyes with PCV, 51 (55%) showed PED (serous PED in 46 eyes, hemorrhagic PED in five eyes) by angiography, most of which were also obvious by ophthalmoscopic examination. Although many PEDs seen in eyes with PCV were oval or round, some also had a notch at their margin. Of the 51 eyes with PED, a notch was found in 27 eyes (53%) by fluorescein angiography and IA (Table). Twenty-three eyes (45%) showed polypoidal lesions by IA that corresponded in location with a notch observed by angiography (Figure 1). Of the 51 eyes with PED, the relationship in location between the polypoidal lesions and the PED was obvious by IA in 46 eyes. Polypoidal lesions were detected outside the PED in one eye (2%), at the margin of the PED in 33 eyes (65%), and within the PED in 12 eyes (24%) (Figure 2).

With OCT, the morphologic feature of the PED could be evaluated in eyes with PCV. OCT often showed a notch at the inner surface of the PED. Of 51 eyes with PED, a notch was observed by OCT in 29 eyes (57%), most of which corresponded in location with polypoidal lesions seen by IA (Figures 3 to 5). In a hemorrhagic PED, intense reflectivity was seen at the inner surface of the PED, with no reflectivity within or under the PED. However, the inner structure of the serous PED in eyes with PCV could often be examined with the use of OCT. In serous PED, as the fluid within the PED showed minor or no reflectivity, the reflectivity of the Bruch membrane and choriocapillaris was often clearly detected beneath the fluid within the PED. Polypoidal lesions, which demonstrated moderate reflectivity, were often seen at the margin of or in the PEDs. In eight eyes, polypoidal lesions that were adherent to the inner surface of the PED appeared to

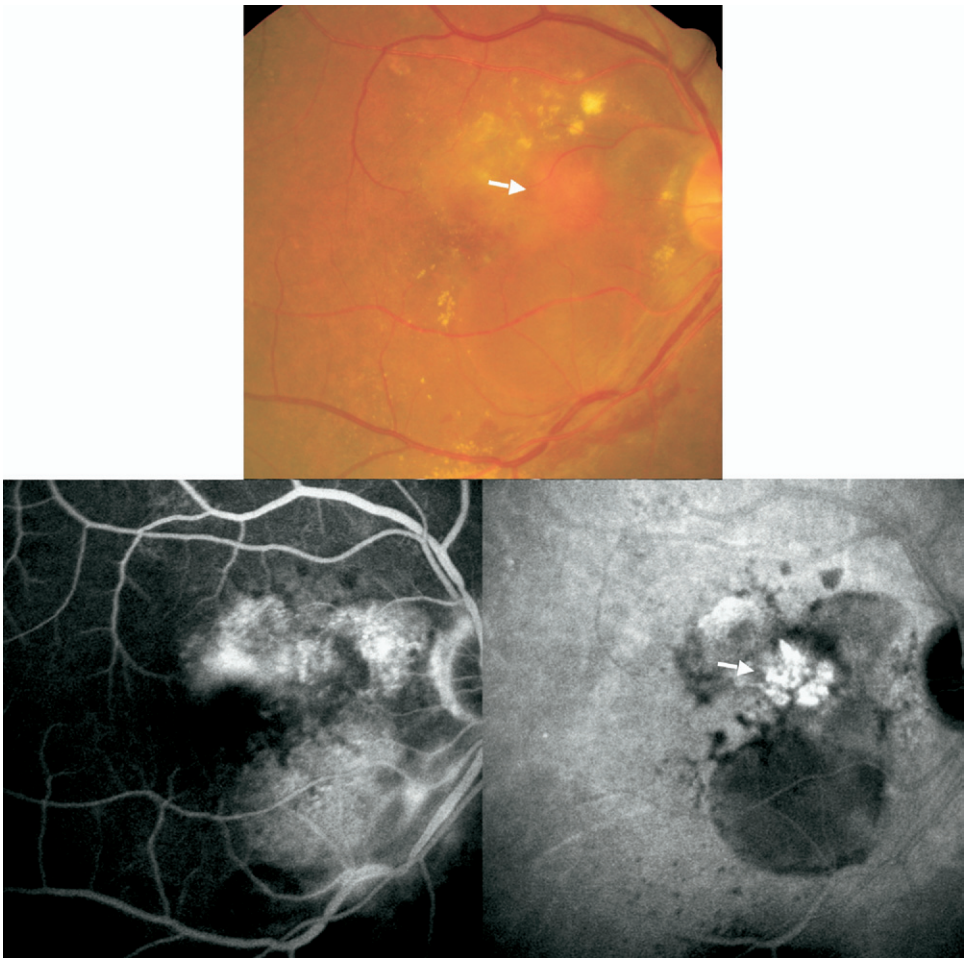

FIGURE 1. Serous pigment epithelial detachment (PED) with notch at its margin in polypoidal choroidal vasculopathy (PCV). (Top) Funduscopic examination shows large serous PED with reddish-orange nodule (arrow). (Bottom left) Serous PED with notch shows hyperfluorescence by fluorescein angiography. (Bottom right) Indocyanine green angiography (IA) revealed polypoidal lesions (arrow) corresponding in location to notch in PED.

be detached from the Bruch membrane and the choriocapillaris (Figures 3 to 6).

A 66-year-old man was referred to our clinic with a three-month history of decreased visual acuity in the right eye. At the initial visit, his visual acuity was 20/100 in his right eye and 20/20 in his left eye. Funduscopic examination of the left eye revealed serous retinal detachment with a reddish-orange nodule in the posterior pole (Figure 6). OCT imaging showed a subfoveal polypoidal lesion with serous retinal detachment. Serous PED could not be seen with any other examination. One month later, his right eye developed a serous PED of 1.5 disk diameter. IA revealed a branching vascular network terminating in two polypoidal lesions, which were located at the margin of the serous PED. OCT imaging showed a polypoidal lesion adherent to the inner surface of the PED, where it appeared to be detached from the Bruch membrane and the choriocapillaris.

DISCUSSION

PCV IS CHARACTERIZED BY A BRANCHING VASCULAR NETwork terminating in polypoidal lesions[3–10] and is often accompanied by serous or hemorrhagic PEDs.[2–9,11–13] In our patients, 55% of eyes with PCV had PED observed by angiography. Although many PEDs in eyes with PCV appear oval or round by angiography,[7,9] they often have a notch at the margin. In eyes with AMD, Gass[30] previously reported that a notched border of large serous PED is an important biomicroscopic and fluorescein angiographic sign of hidden CNV. In our patients, 53% of eyes with PCV and PED showed a notch by angiography. Moreover, 85% of eyes with an angiographically visible notch demonstrated polypoidal lesions by IA, which corresponded in location to the notch seen angiographically. Similar to eyes with AMD, an angiographically visible notch in large serous PED would be an important feature of polypoidal

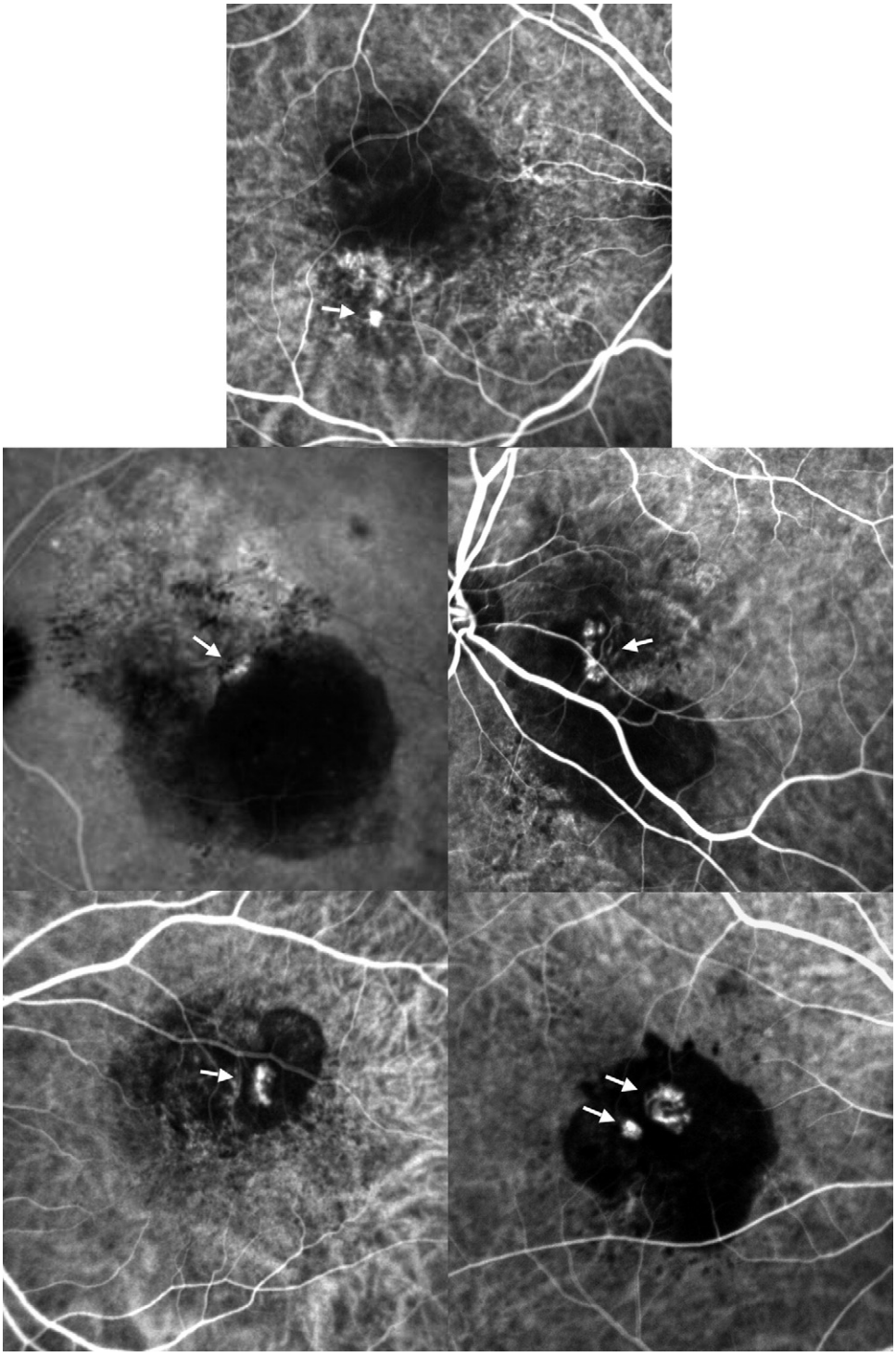

FIGURE 2. Relationship between serous pigment epithelial detachment (PED) and polypoidal lesions in polypoidal choroidal vasculopathy (PCV). Serous PEDs show hypofluorescence by indocyanine green angiography (IA). Polypoidal lesions (arrows) are located outside (Top row), at margin (Middle row), or inside PED (Bottom row).

lesions in PCV. However, the location of CNV (polypoidal lesion) in the associated PED would be different. Gass[30] reported that most hidden CNVs were located outside the area of the serous PED. In the current study, polypoidal lesions were often detected at the margin of the PED (65%), and some were seen inside the PED (24%).

In a recent report with OCT, Sato and associates[26] have shown that eyes with AMD may have a dome-shaped PED with an optically empty space and adjacent small PED.

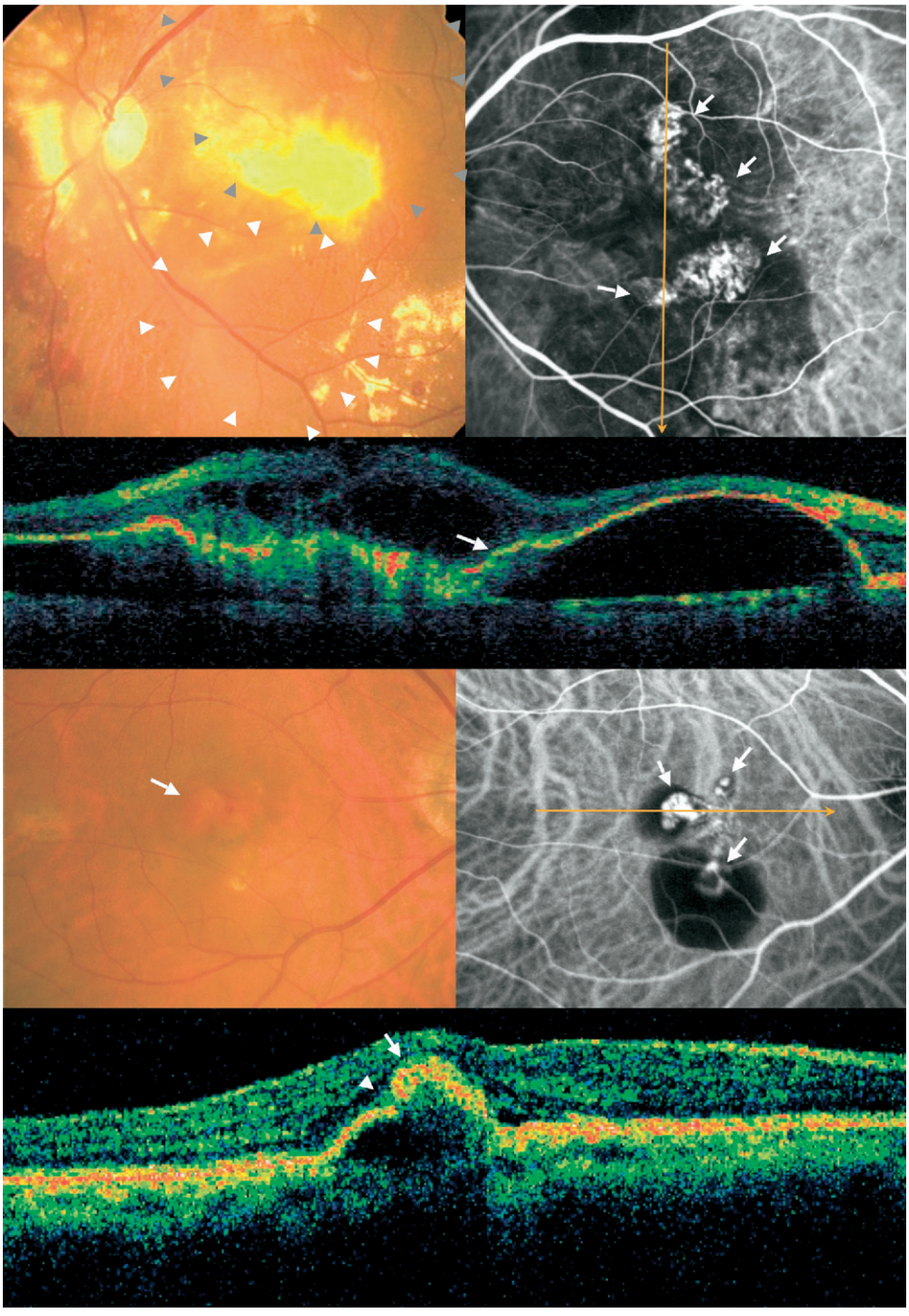

FIGURE 3. Polypoidal lesions detached from the Bruch membrane and choroid in polypoidal choroidal vasculopathy (PCV). (Top row, left) Fundus photograph of a 93-year-old man with PCV shows two large serous pigment epithelial detachments (PEDs) (arrowheads) with subretinal hemorrhage and hard exudate. (Top row, right) Indocyanine green angiography (IA) demonstrates polypoidal lesions (arrows) between two PEDs. Serous PEDs show hypofluorescence by IA. Sectional image of PEDs and polypoidal lesions is made along orange line with optical coherence tomography (OCT). (Second row) Scan shows polypoidal lesion with moderate reflectivity adherent to retinal pigment epithelium (RPE) (arrow). Fluid in PED is seen beneath polypoidal lesion. Reflectivity of the Bruch membrane and choroid is clearly seen at bottom of PED. (Third row, left) Fundus photograph of a 65-year-old man with PCV shows reddish-orange nodules (arrow). (Third row, right) IA disclosed polypoidal lesions (arrows) with two small PEDs. (Bottom row) OCT scan along orange line shows polypoidal lesion (arrow) with moderate reflectivity protruding to neurosensory retina. Notch is visible at inner surface of PED (arrowhead). Protruded polypoidal lesion appears detached from the Bruch membrane and choroid. Fluid in PED is visible beneath polypoidal lesion.

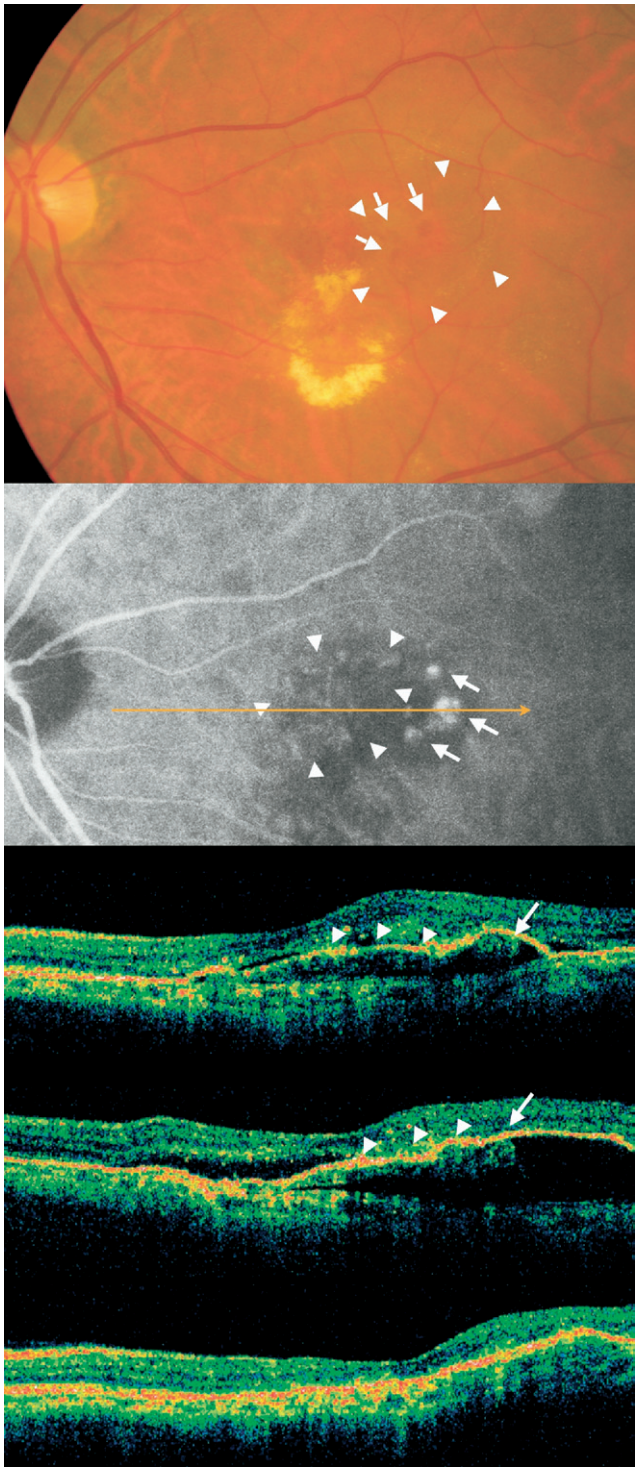

FIGURE 4. A 67-year-old man with polypoidal choroidal vasculopathy (PCV) with gradually decreasing visual acuity in left eye (20/200 left eye). (Top) Funduscopic examination shows reddish-orange nodules (arrows) with shallow serous pigment epithelial detachment (PED) (arrowheads). (Second) Indocyanine green angiography (IA) reveals branching vascular network (arrowheads) terminating in polypoidal lesions (arrows) with shallow PED. Scanned images with optical coherence tomography (OCT) are taken along orange line. (Third) OCT image shows moderate reflectivity of branching vascular network (arrowheads) connecting to polypoidal lesion (arrow), which appears adherent to retinal pigment epithelium (RPE). (Fourth) One month later, exudative change from polypoidal lesion has increased. OCT image shows branching vascular network (arrowheads) connecting to polypoidal lesion (arrow), which is adherent to inner surface of PED and detached from the Bruch membrane and choroid. (Bottom) Patient underwent photodynamic therapy in left eye. One month after treatment, fluid in PED has diminished.

The authors called the V-shaped depression between the two PEDs a tomographic notch. They found that the inner structure of the smaller PED showed some reflectivity, which corresponded to type 1 CNV.[26] In the current study, the PED had a tomographic notch in 57% of eyes with PCV, most of which corresponded in location with polypoidal lesions by IA. Most polypoidal lesions were observed at the margin of the PEDs and adherent to the RPE. In serous PEDs, the reflectivity of the Bruch membrane and choriocapillaris was often clearly detected beneath the fluid within the PED, which showed minor or no reflectivity.[25] In the current study, 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.

It is generally thought that PCV is a vascular abnormality of the inner choroid.[2–5] However, the location of the polypoidal lesions and a branching vascular network is still controversial.[1] Some histological examinations of surgical specimens from eyes with PCV showed that dilated venules and arterioles under the Bruch membrane are the primary lesion of PCV and are observed as polypoidal lesions by IA.[22] However, many other eyes with PCV that were examined histologically showed fibrovascular tissue located within the Bruch membrane,[16,17,19–21,23] while several eyes exhibited secondary CNV in the subretinal space.[16,18,21,23,24] MacCumber and associates[16] histologically examined an enucleated eye with multiple recurrent serosanguineous retinal pigment epithelial detachment syndrome and found extensive fibrovascular proliferation in the subretinal space and within the Bruch membrane. Lafaut and associates[19] reported that histological examination of submacular tissue removed from an eye with PCV showed several aneurysmal dilations located directly under diffuse drusen within a sub-RPE, the intra-Bruch fibrovascular membrane. In fact, a specimen obtained under direct visualization during macular translocation surgery by Terasaki and associates[21] showed the fibrovascular membrane with thin-walled vessels, which corresponded with the reddish-orange nodule, was located under the basement membrane of RPE and the elastic fiber layer of the Bruch membrane. The authors concluded that the vascular com-

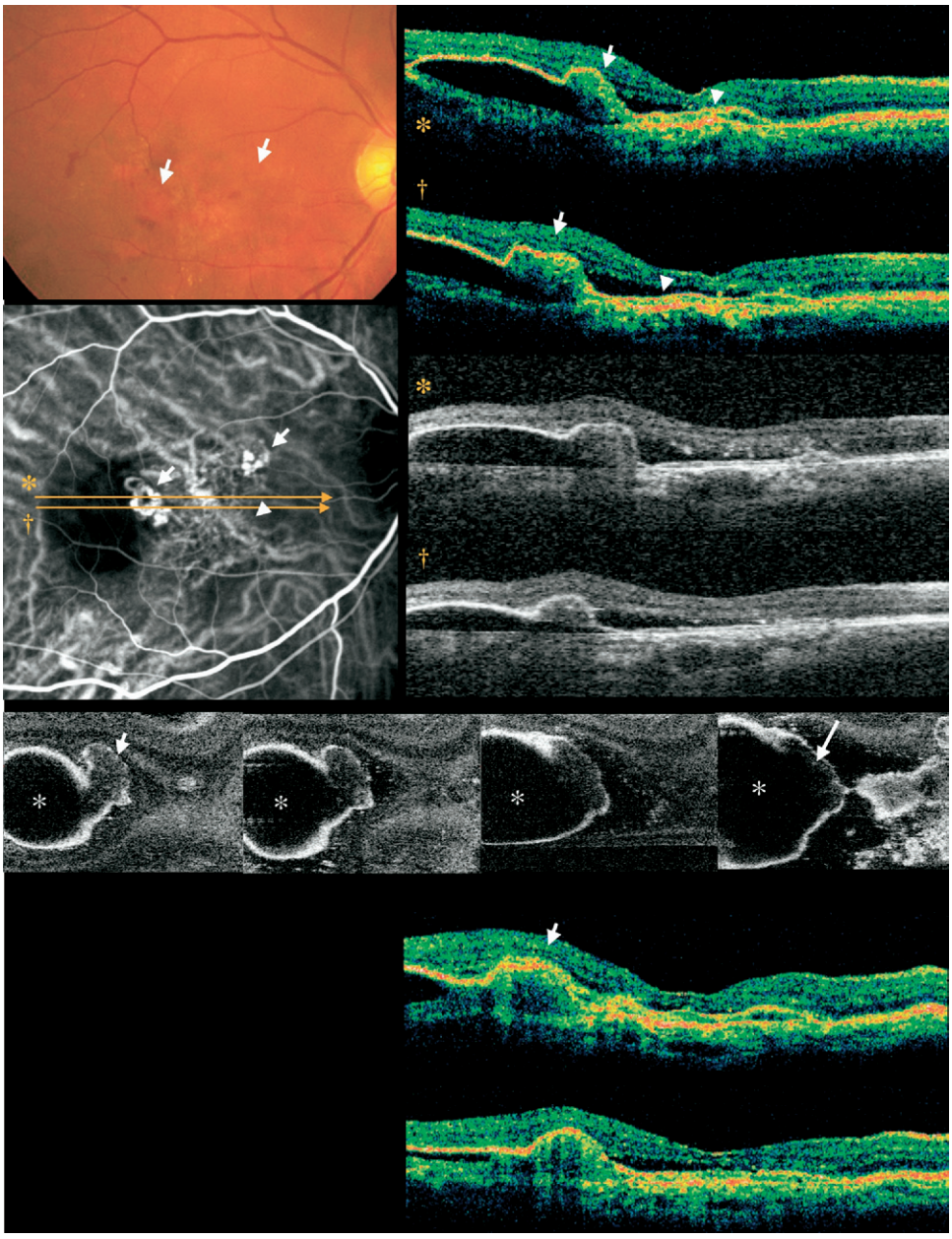

FIGURE 5. A 75-year-old man with polypoidal choroidal vasculopathy (PCV) with decreased visual acuity in right eye (20/60 right eye). (Top row, left) Funduscopic examination shows two reddish-orange nodules (arrows) with serous pigment epithelial detachment (PED). (Second row, left) Indocyanine green angiography (IA) reveals branching vascular network (arrowhead) terminating in polypoidal lesions (arrows). Temporal polypoidal lesion accompanies serous PED. Scanned images with optical coherence tomography (OCT) are taken along orange lines (* and †). (Top row, right) OCT3000 images show branching vascular network (arrowheads) terminating in polypoidal lesion (arrows). Polypoidal lesion, which is adherent to inner surface of PED, appears detached from the Bruch membrane. (Second row, right) B-scan images with OCT ophthalmoscope C7 demonstrate similar anatomical feature. (Third row) Sequence of C-scan images of PED and polypoidal lesion is seen from anterior (left) to posterior (right). Images are obtained with OCT ophthalmoscope C7. Although fluid in PED (asterisk) shows no reflectivity, polypoidal lesion (arrow) beside PED shows moderately intense reflectivity. Polypoidal lesion is detached from bottom of PED. No reflectivity (long arrow) is detected under polypoidal lesion. (Fourth row) Two months after initial visit, exudative change was reduced, and PED was diminished. Detached polypoidal lesion (arrow) has reattached to the Bruch membrane and choroid. (Bottom row) Patient underwent photodynamic therapy to right eye. One month after treatment, fluid in PED has almost disappeared.

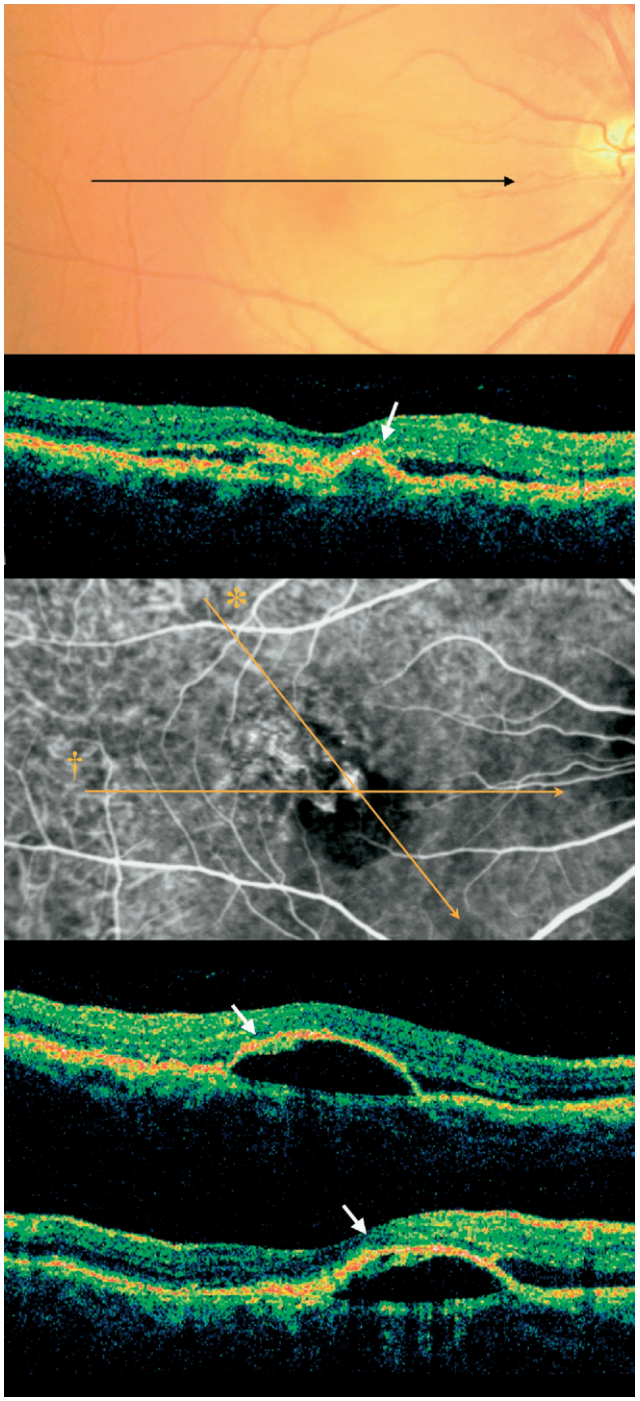

FIGURE 6. A 66-year-old man with three-month history of decreased visual acuity in right eye referred to our clinic. At initial visit, his visual acuity was 20/100 right eye and 20/20 left eye. (First image) Funduscopic examination of left eye reveals retinal detachment with reddish-orange nodule in posterior pole. (Second image) Scanned image with optical coherence tomography (OCT) along black line shows polypoidal lesion (arrow) with serous retinal detachment. One month later, his right eye developed serous pigment epithelial detachment (PED). (Third image) Indocyanine green angiography (IA) reveals branching vascular network terminating in two polypoidal lesions, which are located at margin of PED. (Fourth image) OCT images taken along orange lines (* and †) show polypoidal lesion (arrow) of moderate intensity adherent to inner surface of PED, which appears detached from the Bruch membrane and choroid.

ponents of the polypoidal lesions were CNV that was located in the intra-Bruch space.[21]

OCT imaging often showed reddish-orange nodules as a sharp protrusion of RPE with inner moderate reflectivity.[27–29] On the basis of this finding, Iijima and associates[28] reported that polypoidal lesions were situated beneath the Bruch membrane. From similar OCT findings, however, Otsuji and associates[27] reported that polypoidal lesions were located between the Bruch membrane and the RPE. Both reports were based on OCT1 images. In the current study, however, sectional images with OCT3 and OCT ophthalmoscope C7 clearly showed the morphologic feature of PED and polypoidal lesions in eyes with PCV. Polypoidal lesions were often detected at the margin of or within the PED.[13] In some cases, polypoidal lesions, which were adherent to the RPE in the serous PED, appeared to be detached from the Bruch membrane and choriocapillaris. Previous histological examinations showed that serous PED is formed by the accumulation of the fluid within the Bruch membrane, and that RPE with its basement membrane is separated from resultant layers of the Bruch membrane and the choroid.[31,32] Our findings in the current study suggested that polypoidal lesions were located in the Bruch membrane, consistent with most reports of histological examination.[16,17,19–21,23]

Figure 7 shows the process by which PED develops from leakage of polypoidal lesions in eyes with PCV. A branching vascular network that has infiltrated into the Bruch membrane terminates in polypoidal lesions.[16,17,19–21,23] When the exudate of the polypoidal lesions increases, the fluid accumulates within the Bruch membrane, resulting in a serous PED.[3] Polypoidal lesions are located at the margin of PED[3] and form a notch seen by angiography[30] and tomographically.[26] When the exudative change of polypoidal lesions further increases, the fluid infiltrates even under the lesions. A polypoidal lesion becomes detached from the Bruch membrane and appears to be located inside the PED. Previously, Fernandes and associates[13] reported that the hot spot was located at the margin of the PED in 11 eyes with PCV and near the center in just 1 of 12 eyes. In eyes with polypoidal lesion with active exudative change, however, polypoidal lesions were located inside the PED.

It is possible that the incidence of polypoidal lesions that detach from the Bruch membrane and choriocapillaris is underestimated. In some PEDs, the reflectivity of polypoidal lesions is so intensive or the fluid in the PED is so turbid that the reflectivity of the Bruch membrane and choriocapillaris beneath the polypoidal lesion cannot be detected clearly.[27–29] In the current study, polypoidal lesions were determined to be detached only when the

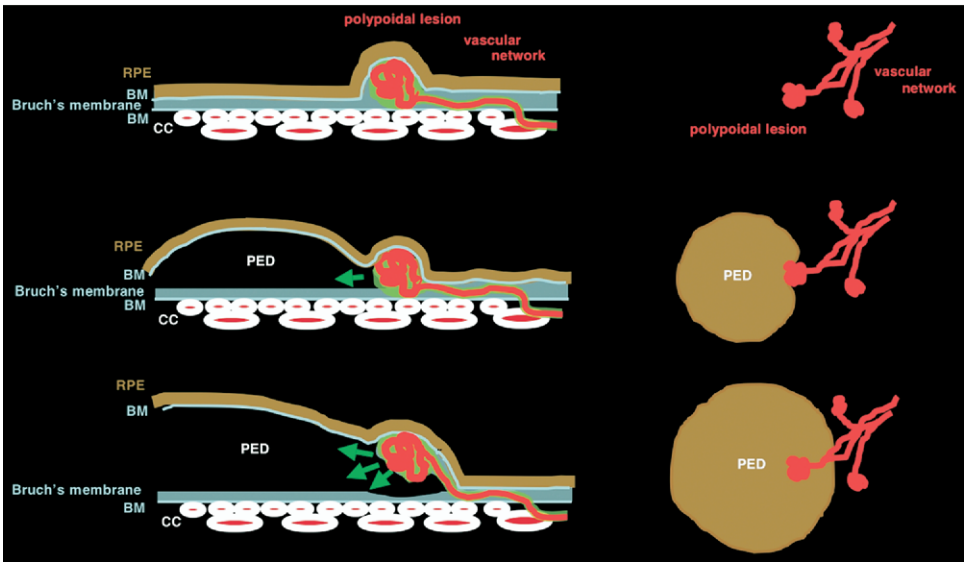

FIGURE 7. Illustration showing development of pigment epithelial detachment (PED) from exudate of polypoidal lesion in polypoidal choroidal vasculopathy (PCV) changes. (Top) Branching vascular network that infiltrates into the Bruch membrane terminates in polypoidal lesion. (Middle) When exudate of polypoidal lesion increases, fluid from polypoidal lesion accumulates in the Bruch membrane, resulting in serous PED. Polypoidal lesion located at margin of PED appears as notch by angiography and tomography. (Bottom) When exudate of polypoidal lesion further increases, fluid from lesion infiltrates under the polypoidal lesion. Polypoidal lesion then detaches from the Bruch membrane and choroid. Funduscopically, polypoidal lesion appears to be located within PED. BM = basement membrane; CC = choriocapillaris; RPE = retinal pigment epithelium.

reflectivity of the Bruch membrane and choriocapillaris beneath the polypoidal lesion was clearly seen. In addition, why polypoidal lesions are adherent to the RPE and not to the Bruch membrane was unclear. In the current study, no eye showed polypoidal lesions adherent to the Bruch membrane and detached from the RPE in a serous PED. When fluid in the PED is turbid, however, the underlying polypoidal lesion may not be detected with IA or OCT. Therefore, we cannot deny completely the possibility that some polypoidal lesions are adherent to the Bruch membrane at the bottom of the PED. Our findings do suggest that the detachment of the polypoidal lesion from the Bruch membrane and choroid is one process in the development of large serosanguineous PED in eyes with PCV.

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Biosketch

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