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The Evaluation and Follow-up of Retinal Angiomatous Proliferation by Optical Coherence Tomography with Simultaneous Fluorescein Angiography and Indocyanine Green Angiography

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ORIGINAL ARTICLE

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The Evaluation and Follow-up of Retinal Angiomatous Proliferation by Optical Coherence Tomography with Simultaneous Fluorescein Angiography and Indocyanine Green Angiography

Abstract

Retinal angiomatous proliferation (RAP) is an intraretinal change resulting from retinal neovascularization. In advanced cases of RAP, retinal anastomosis occurs forming choroidal neovascularization (CNV), and differentiation from exudative age-related macular degeneration (AMD) becomes difficult. Treatment strategies differ between RAP and exudative AMD. We evaluated the combined use of optical coherence tomography (OCT) and simultaneous fundus fluorescein angiography (FFA) and indocyanine green angiography (ICG) in patients with RAP. In the early stages of the disease, the OCT was superior for determining the location of RAP lesions, follow-up evaluation of intraretinal edema during progression, and post-treatment evaluation after photocoagulation. In the advanced stage, OCT imaging was obscured by severe fibroplasia, and hemorrhage. In the late stages, simultaneous FFA and ICG helped with evaluation. Because some cases of RAP may progress into the advanced stage in a short period, combined findings from both OCT and simultaneous FFA and ICG are useful in providing a guide for the appropriate treatment.

Key Words

retinal angiomatous proliferation, optical coherence tomography, fluorescein angiography, indocyanine green angiography, Heidelberg Retina Angiograph, digital imaging, confocal scanning laser

Introduction

The concepts of exudative AMD have been broadened beyond the classic and occult types of CNV. In 1992, Hartnett, et al.[1] reported the presence of intraretinal neovascularization as an early change in patients with exudative AMD before progression to disciform cicatricial lesions. Neovascularization was present in the deep retinal layers[2] with retinal choroidal anastomosis (RCA),[3,4] which was referred to as a retinal angiomatous lesion. Subsequently, it was reported that neovascularization is not limited to the deep retinal layers and RCA is not an essential symptom, though observed in the end stage.[5] To distinguish RAP from exudative AMD, Yannuzzi et al. advocated the use of the term RAP[6] for the condition characterized by early manifestation of retinal neovascularization, occurrence of retinal-retinal anastomosis (RRA), extension of neovascularization into the subretinal space and RCA in the end stage. In RAP, extension and proliferation of intraretinal neovascularization leads to the onset of intraretinal edema. It is important to differentiate RAP from occult or classic CNV. In advanced cases, however, differentiating RAP from occult CNV is difficult using FFA,[7] and diagnostic imaging studies are essential for early diagnosis. In this study, we used OCT with simultaneous FFA and ICG and obtained useful information following the progression of RAP.

Methods

Three patients with RAP ranging from early to advanced underwent fundus photography and OCT-3000 (*Carl Zeiss, Germany*) imaging and simultaneous FFA and ICG[13,14] using a Heidelberg Retinal Angiograph (HRA) (*Heidelberg Engineering, Heidelberg, Germany*). The images were obtained after the injection of a 4-mL mixed solution of Fluorescite® (*Japan Alcon, Tokyo, Japan*) 300 mg/3 mL and Ophthagreen® for (*Santen ,Osaka, Japan*) 25 mg/mL. HRA imaging used software version 1.10, with the brightness/contrast, sharpen, and computing mean images programs.

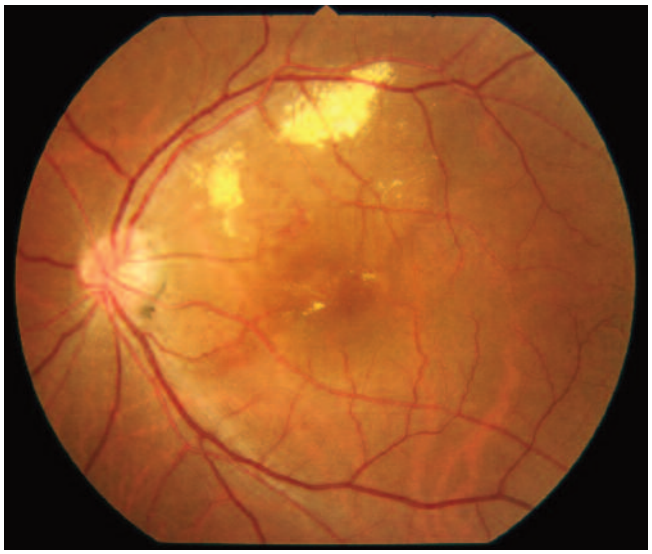

Figure 1: Case 1: stage I RAP. A round lesion with hard exudates.

Case 1: stage I RAP in a 53-year-old man. The right eye was normal. The left eye had hard exudates and circular lesions on the nasal side of the macular area (Figure 1). OCT showed intraretinal edema and an RPE detachment (Figure 2). In the early FFA, fluorescein staining indicated that intraretinal neovascularization was present (Figure 3a). With ICG, RAP was visualized as hot spots (Figure 3b). In the late FFA, fluorescein leakage from intraretinal neovascularization was seen (Figure 4a) and leakage of ICG from hot spots was observed (Figure 4b). Based on OCT and simultaneous FFA and ICG findings, the RAP was classified as stage I. Five weeks later, the RPE detachment had enlarged (Figure 5). OCT showed increased intraretinal edema and RPE detachment with expansion of the intraretinal RAP (Figure 6). Photocoagulation was applied to the hot spots, which was followed by scar formation and diffuse hard exudates (Figure 7). Follow-up OCT,

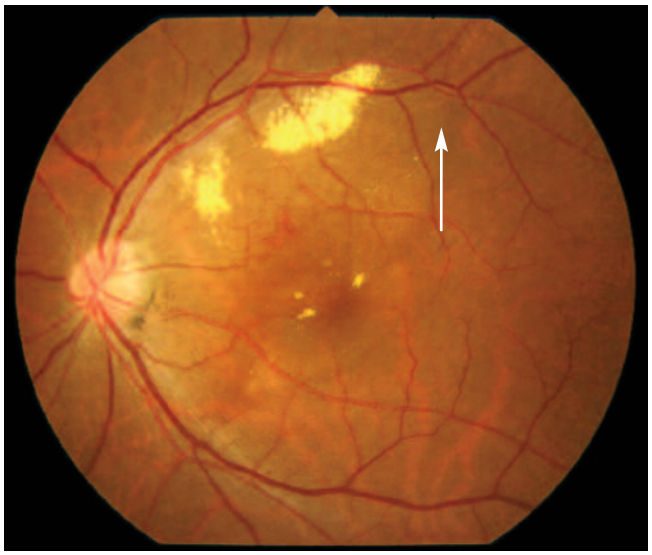

Figure 5: Case 1: stage I RAP five weeks later. The RPE detachment (arrow) has expanded.

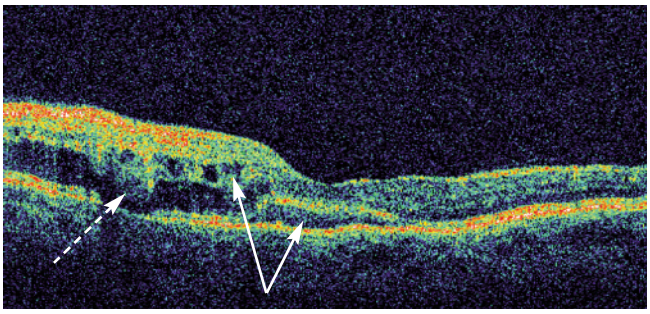

Figure 2: Case 1: stage I RAP (OCT). The arrow indicates intraretinal edema and RPE detachment. Waveform arrow indicates the focus of RAP.

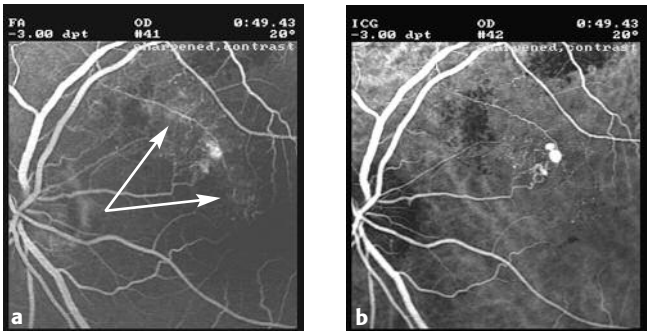

Figure 3: Case 1: stage I RAP (Early FFA/ICG). (a) Intraretinal neovascularization indicates fluorescein staining (arrow). (b) RRA is observed with ICG as a hot spot.

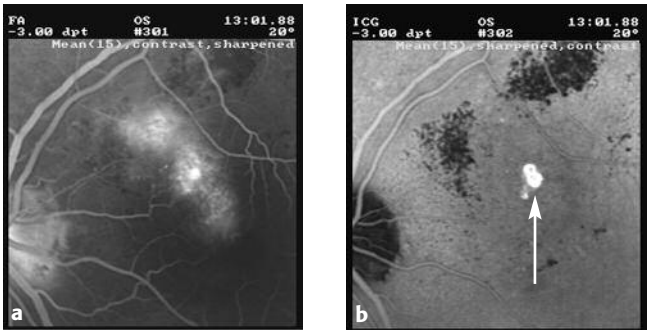

Figure 4: Case1: stage I RAP (FFA/ICG late phase). (a) Fluorescein leakage from intraretinal neovascularization. (b) ICG leakage (arrow) from the hot spot.

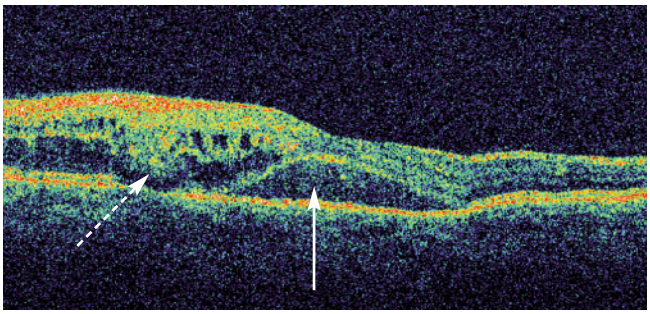

Figure 6: Case 1: stage I five weeks later (OCT). An enlarged RPE detachment (arrow), and the expansion of RRA (waveform arrow).

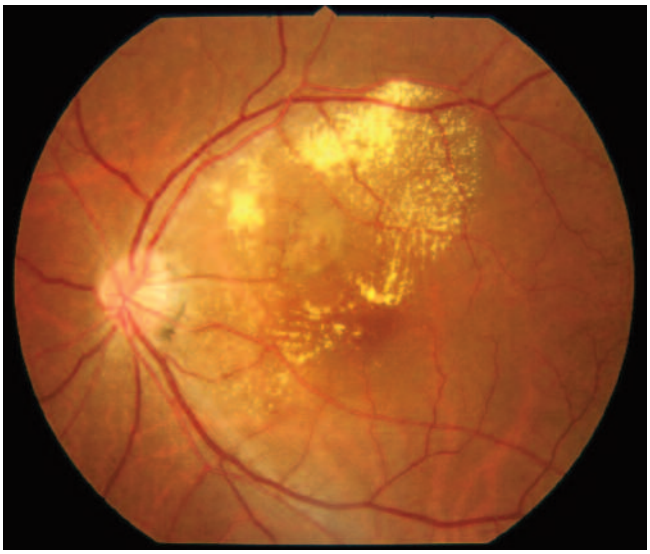

Figure 7: Case1: stage I RAP after photocoagulation. Scarring from hard exudates and retinal RAP.

performed six weeks later, showed reduced intraretinal edema and resolution of the RPE detachment but scarring was present (Figure 8). In the late FFA, the remaining tissue was stained due to intraretinal neovascularization, but ICG showed hypofluorescence of RAP and resolution of the hot spots (Figure 9).

Case 2: stage II RAP in a 65-year-old woman. The right eye had a minor intraretinal hemorrhage, multiple soft drusen, and hard exudates (Figure 10), while the left eye had cicatricial lesions. OCT of the right eye revealed cystoid edema and a high reflection within the area of the elevated RPE detachment (Figure 11). Early stage FFA two months earlier confirmed RRA (Figure 12a). In the late stage, the macular area showed granular hyperfluorescence (Figure 12b). Based on fundus photography, OCT, and FFA, the RAP was classified as stage II. The visual acuity

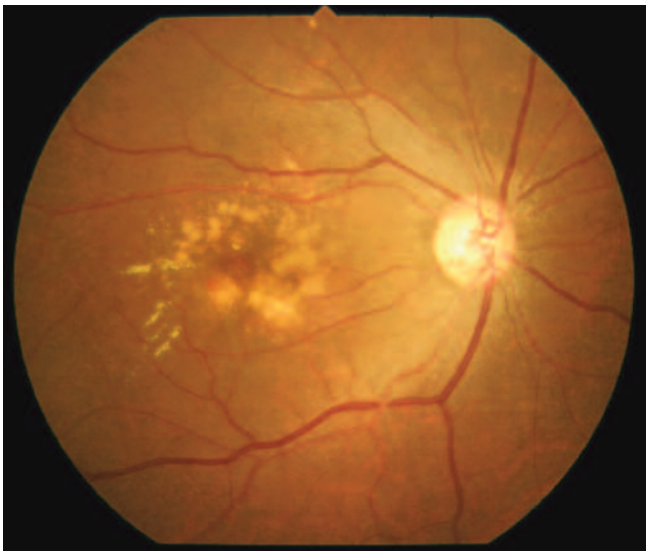

Figure 10: Case 2: stage 2 RAP. RAP soft drusen and hard exudates are seen in the macular area.

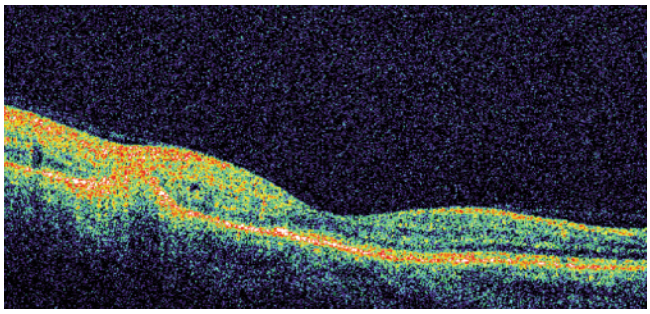

Figure 8: Case 1: stage I RAP after photocoagulation (OCT). The RRA has become a scar.

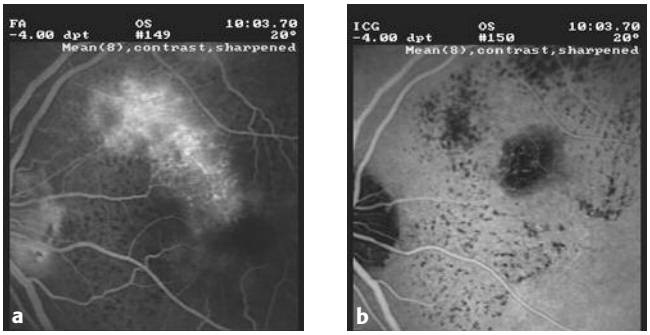

Figure 9: Case 1: stage I RAP after photocoagulation (FFA/ICG late phase). (a) Fluorescein staining. (b) The hot spot has resolved.

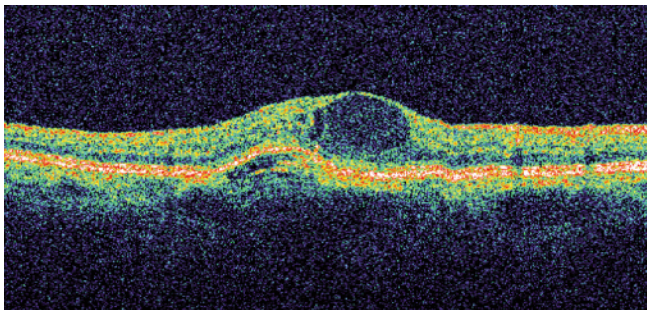

Figure 11: Case 2: stage II RAP (OCT). Protrusion of the RPE and cystoid edema.

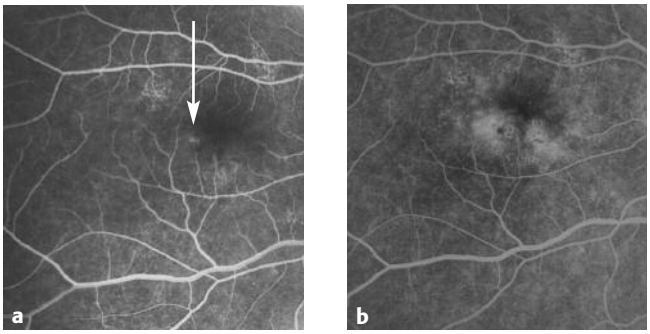

Figure 12: Case 2: stage II RAP 2 months previously (FA). (a) RRA (arrow) in the early stage (after 51 seconds). (b) Granular hyperfluorescence in the late stage (after 10 minutes).

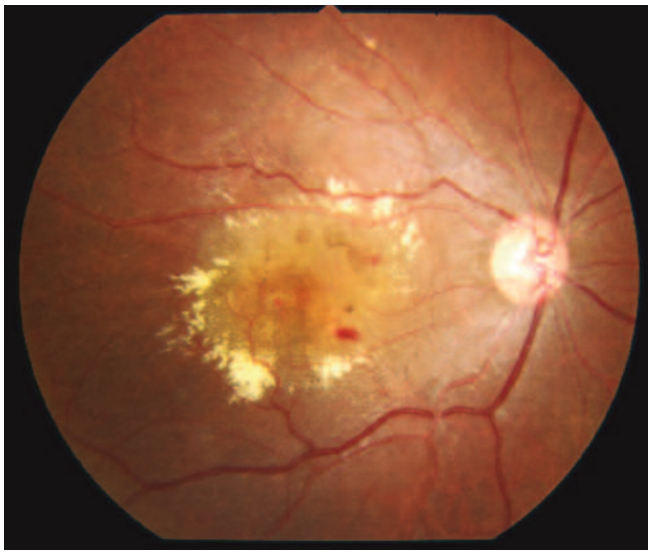

Figure 13: Case 2: stage II RAP eight months postoperatively. The lesion has increased.

of the fellow eye had decreased to counting fingers, and the patient underwent vitrectomy and triamcinolone acetonide infusion. Eight months after the surgery, the lesion had elarged with fibroplasia (Figure 13). OCT showed reduced cystoid edema, but irregular elevation of the RPE (Figures 14). Along with the cystoid macular edema (CME), FFA showed retinal neovascularization and ICG showed staining (Figure 15). One year postoperatively, the lesions had enlarged with increased intraretinal and subretinal hemorrhaging and severe fibroplasia (Figure 16). With the OCT, because of light attenuation due to the hemorrhaging and fibroplasia, the posterior portion was obscured (Figure 17). FFA showed CME (Figure 18a), ICG showed the RAP lesions as hot spots, but there was no RCA (Figure 18b).

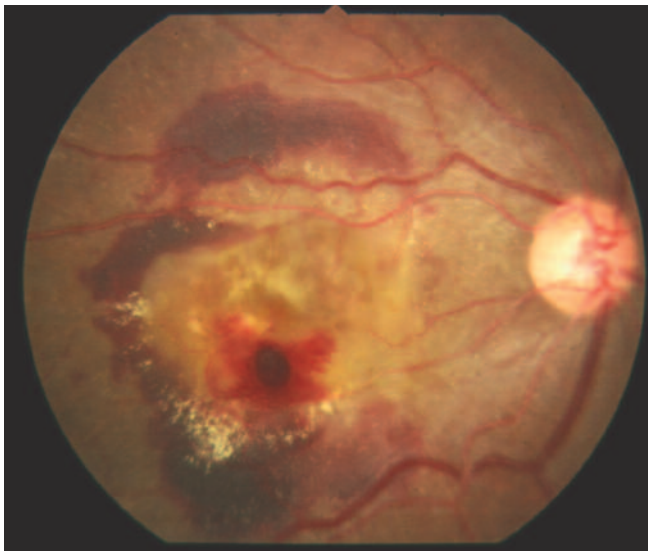

Figure 16: Case 2: stage II RAP one year after treatment. Preretinal and subretinal hemorrhaging and an enlarged lesion are seen.

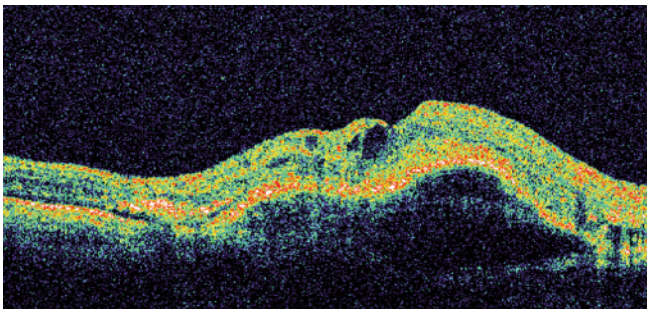

Figure 14: Case 2: stage II RAP eight months after treatment (OCT). RPE layer upheaved though cystoid edema inside the retina decreased.

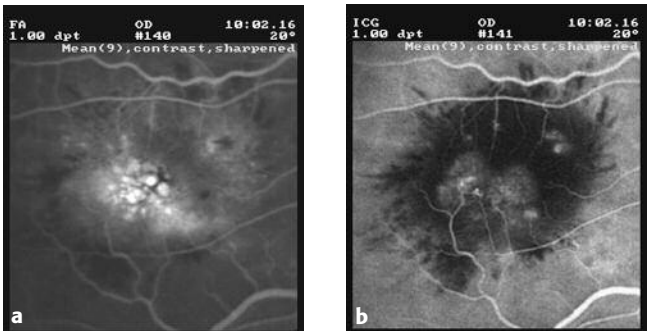

Figure 15: Case 2: stage II RAP eight months after treatment (FFA/ICG late phase). (a) CME (FFA) can be seen. (b) The neovascular membrane of retinal origin under the RPE (ICG).

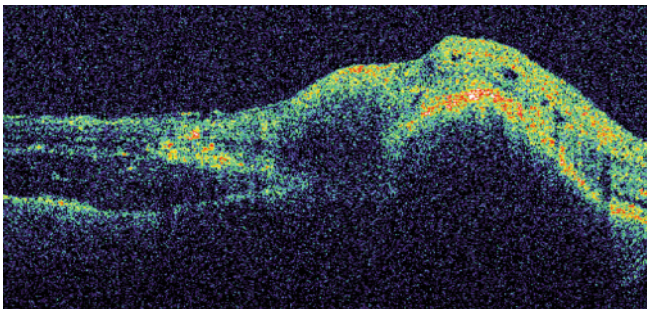

Figure 17: Case 2: stage II RAP one year after treatment (OCT). A portion of the retina and the RPE cannot be observed.

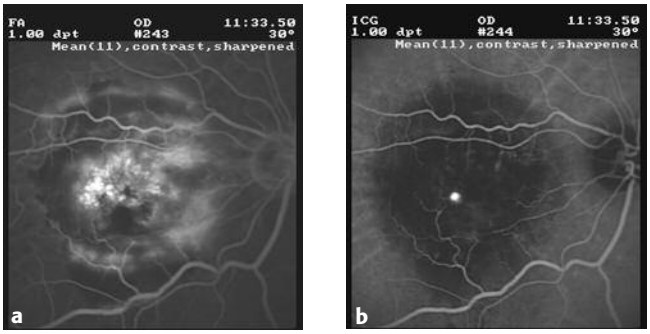

Figure 18: Case 2: stage II RAP one year after treatment (FFA/ICG late phase). (a) CME (FFA). (b) RAP is seen as a hot spot (ICG).

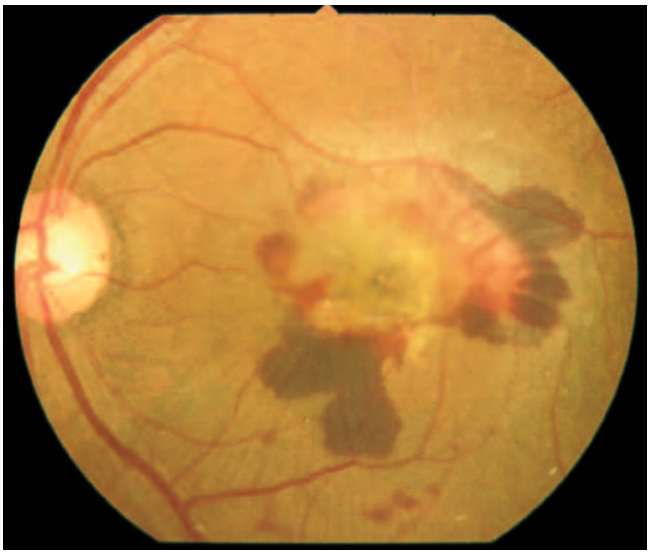

Figure 19: Case 3: stage III RAP. A lesion with a subretinal hemorrhage.

Case 3: stage III RAP in a 71-year-old man. The right eye was normal. The left eye had a circular lesion surrounded by a subretinal hemorrhage (Figure 19). OCT showed that the neovascularization extended into the subretinal space (Figure 20). The early FFA confirmed RRA, and ICG showed RCA (Figure 21). Two weeks later, OCT showed an enlarged RPE detachment, along with neovascularization growing under the RPE (Figure 22). Photodynamic therapy (PDT) was performed to suppress the RCA. One month later, the subretinal hemorrhage was found to have enlarged (Figure 23). With OCT, the RPE was increasingly elevated and the posterior portion was shadowed, making interpretation of findings difficult (Figure 24). In the early ICG, RRA was confirmed (Figure 25). Late stage ICG showed the CNV as hypofluorescence (Figure 26).

Discussion

OCT is an imaging modality that measures backscattered light from the boundaries of the deep tissues in-vivo with different refractive indices and provides information about the position and intensity of the reflection. A disadvantage of OCT, however, is that marked light absorption

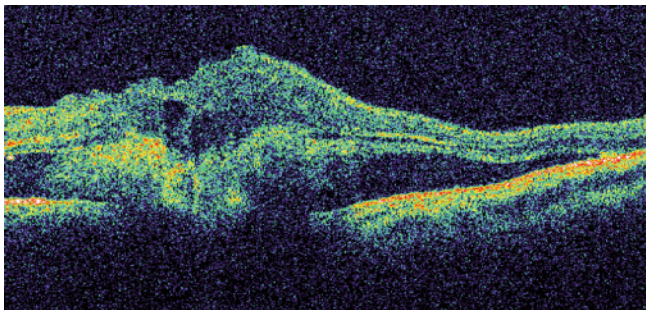

Figure 22: Case 3: stage III RAP five weeks later (OCT). Neovascularization of retinal origin protrudes through the RPE.

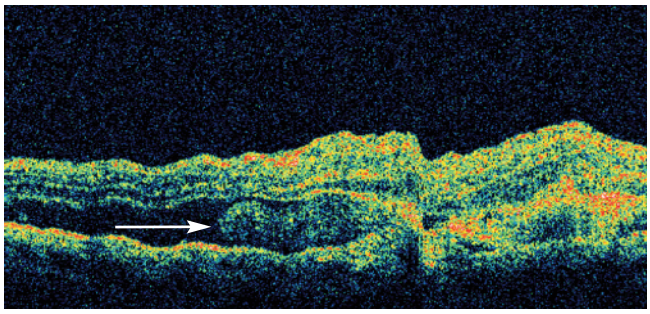

Figure 20: Case 3: stage III RAP (OCT). Neovascularization has invaded the subretinal space (arrow).

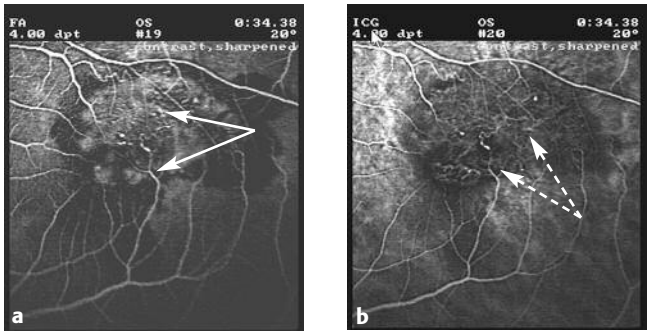

Figure 21: Case 3: stage III RAP (FFA/ICG early phase). (a) The arrow indicates RRA (FFA). (b) The waveform arrow indicates RCA (ICG).

obscures posterior visualization. In fact, the RPE produces a strong reflection, and thus combined use of FFA and ICG is required to obtain detailed information about the choroidal layer. Yannuzzi et al.[6] classified the disease into stages I, II, and III according to clinical findings and the patterns of progression. In the advanced stage of RAP, differentiation from occult CNV becomes difficult using only FFA. Unlike subretinal CNV with AMD, RAP involves retinal neovascularization and is resistant to laser therapy, and thus differentiation from AMD is important

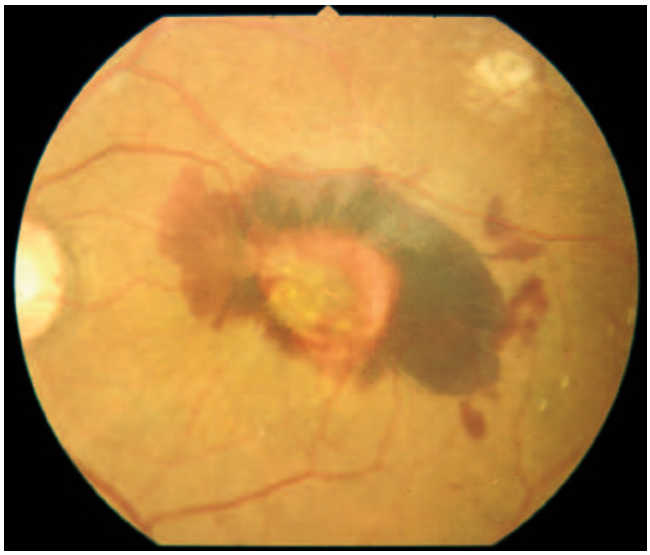

Figure 23: Case 3: stage III RAP 1 month after PDT. The subretinal hemorrhage has become more extensive.

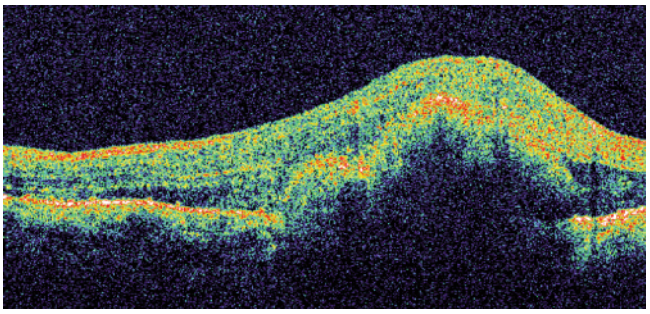

Figure 24: Case 3: stage III RAP one month after PDT (OCT). Outer layer from the protruding RPE cannot be observed.

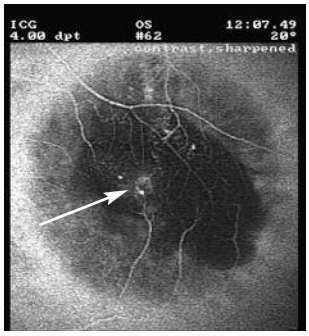

Figure 25: Case 3: stage III RAP one month after PDT (ICG early phases). The arrow indicates RRA.

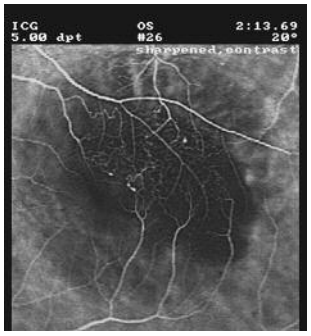

Figure 26: Case 3: stage III RAP one month after PDT (ICG late phase). Decreased activity of the CNV.

for establishing an appropriate treatment plan. For this reason, early assessment of intraretinal changes is essential. Diagnosis of RAP can be evaluated by OCT in the early stages, but in advanced cases when there is fibrin-laden exudation within the retina diagnostic imaging with both ICG and FFA is required to evaluate RCA and CNV.

The spectral domain systems that are currently under investigation with high-resolution imaging will offer greater promise for imaging RAP cases. However, in the meantime, it is useful to categorize the various components to the neovascularized process with our current imaging modalities. One point should be the current concept which is that the neovascularisation may not simply originate from the retina, but it may also, in some cases, originate from the choroid or develop simultaneously in the retina and choroid.

Conclusion

We used OCT and simultaneous FFA and ICG using an HRA in patients with RAP and determined the usefulness of these modalities for the evaluation and follow-up of RAP. OCT was useful in the early phase of the disease. In the advanced stage, however, anastomosis to CNV with fibroplasia and formation of cicatricial lesions led to attenuation of the backscattered light, and the OCT provided inadequate images of the inferior retina, the area beneath the RPE, or both, angiography using FFA and ICG were more useful. In the early stage, OCT was superior for locating RAP lesions, follow-up evaluation of intraretinal edema during progression, and post-treatment evaluation after photocoagulation for RPE detachment. In the late stage, however, simultaneous FFA and ICG were superior. RAP may progress to the advanced stage in a short period of time and the combined findings from OCT and simultaneous FFA and ICG are essential for early diagnosis and accurate evaluation to enable the early initiation of the appropriate treatment.

Editor's note: Dr Yannuzzi kindly evaluated this manuscript and broadly agreed with the findings and interpretation and commended the authors on their extensive illustrations.

References

1. Harnett 0ME, Weiter JJ, Gardts A. Classfication of retinal pigment epithelial detachments associated with drusen. *Graefes Arch Clin Exp Ophthalmol* 230:11-19, 1992.
2. Harnett ME, Weiter JJ, Staurenghi G et al. Deep retinal vascular anomalous complexes in advanced age-related macular degeneration. *Ophthalmology* 130:2042-2053, 1996.
3. Lakter JS, Yannuzzi LA, Schneider U et al. Retinal choroidal anastomoses and occult neovascularization in age-related macular degeneration. *Ophthalmology* 107:742-752, 2000.
4. Kuhn D, Meunier I, Soubtane G et al. Imaging of chorioretinal anastomoses in vascularized retinal pigment epithelium detachment. *Arch Ophthalmol* 113:1392-1398, 1995.
5. Lafaut BA. Aisenbrey S, Broecke CV et al. Clinicopathological correlation of deep retinal vascular anomalous complex in age related macular degeneration. *Br J Ophthalmol* 84:1269-1274, 2000.
6. Yannuzzi LA, Negrao S, Iida T et al. Retinal angiomatous proliferation in age-related macular degeneration. *Retina* 21:416-434, 2001.
7. Novotony HR, Alvis DL. A method of photographing fluorescence in circulating blood in human retina, *Circulation* 24, 82, 1961.