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Case Study

Retinal Angiomatous Proliferation - OCTA-Based Diagnosis and Staging

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Abstract

Retinal angiomatous proliferation (RAP) or type 3 neovascularization is a bilateral disease that occurs in 15 - 20% of newly diagnosed cases of exudative age-related macular degeneration. New diagnostic modalities can help in early diagnosis of RAP. This case series is aimed to help clinicians in interpretation of the results of optical coherence tomography angiography in patients suspected of RAP.

Keywords: *Retinal Angiomatous Proliferation; Age-Related Macular Degeneration (AMD); Imaging Systems; Optical Coherence Tomography (OCT)*

Abbreviations

AMD: Age-Related Macular Degeneration; exAMD: Exudative Age-Related Macular Degeneration; IFL: Intense, Transverse Flow Lesion; NV 3: Type 3 Neovascularization; OCT: Optical Coherence Tomography; OCTA: Optical Coherence Tomography Angiography; PED: Pigment Epithelium Detachment; RAP: Retinal Angiomatous Proliferation; FA: Fluorescein Angiography; ICGA: Indocyanine Green Angiography

Introduction

Retinal angiomatous proliferation (RAP) or type 3 neovascularization (NV 3) is a bilateral disease that occurs in 15 to 20% of newly diagnosed exudative age-related macular degeneration (exAMD) cases. Yannuzzi., *et al*. in their work highlighted the need for rapid diagnosis and treatment [1,2]. The risk of conversion to the active form of the disease in the fellow eye is higher than in any other classical presentation of exAMD. Fellow eye involvement occurs, on average, 15 months after initial diagnosis [2].

New diagnostic modalities force change in the clinical practice. Introduction of the optical coherence tomography angiography (OCTA) enabled a non-invasive visualization of retinal vasculature. When compared to the traditional methods of examination - fluorescein angiography (FA) and indocyanine green angiography (ICGA) it is less time consuming, in most cases it does not require mydriasis. It is also safer as it does not require any intravenous dye.

The image of retinal vessels in OCTA is captured via recording of blood flow in the vessels, when blood velocity is above the OCTA threshold. Additionally, this movement can be tracked on the classical OCT B-scans and evaluated in a 3-dimensional structure, which is not possible in FA and ICGA.

Materials and Methods

An investigator-initiated, single-center, prospective, real-world evidence case series has been chosen as a part of study (participants from control group) registered in ClinicalTrials.gov (https://clinicaltrials.gov/) with the number: NCT03889860 and conducted at the Department of Ophthalmology, Wroclaw Medical University with cooperation of Department of Optics and Photonics, Wroclaw University of Science and Technology, Poland.

All patients underwent a complete ophthalmological examination including slit-lamp biomicroscopy, fundoscopy and tonometry as well as OCT of posterior pole with OptovueRTVue OCT. In the follow-up period, additionally to the standard ophthalmological examination, the OCTA was performed and the fluorescein angiography results revised.

Results and Observations

We present 6 patients (10 eyes) diagnosed with RAP, based on the OCTA examination results. All of presented cases were referred to our department only for the OCTA examination, being diagnosed earlier with exAMD type 1.

In the OCTA images, in each patient's superficial capillary plexus, one of the retinal arteries heading to the macular region, disappeared suddenly- as if it was "cut-off" from the rest of vasculature. There was also a local decrease in vessel density (Figure 1 and 2). Similar vessel configuration was present in the deep capillary plexus, although less prominent and more difficult to visualize (Figure 1). Both superficial and deep capillary slab revealed the existence of the "hairpin loop" of retino-retinal anastomosis. In the retinal pigment epithelium slab (segmented by the OCT software) the high intensity spot has been recorded that easily can be missed as it is similar to the common artefacts in this region (Figure 1 and 2). Choroidal layer also revealed high intensity spot. In two cases it was surrounded by characteristic "halo", which was previously associated with disease activity (marker of activity in choroidal neovascularization type 1 and 2 (Figure 2). In two cases the vascularized PED was found (Figure 1 and 2). While observing the intensity of movement on the OCT B-scans, all of the aforementioned features appeared to be linked together. This observation was confirmed in the 3-dimensional visualization (Table 1 and Figure 1). Additionally, in the close proximity of the intense, transverse flow lesion (IFL) there was a presence of the sub- and intraretinal fluid, pigment epithelium detachment (PED) and soft drusen (Figure 1). Distortion of normal retinal layers in the OCT B-scan surrounded the IFL and was associated with retinal pigment epithelium changes.

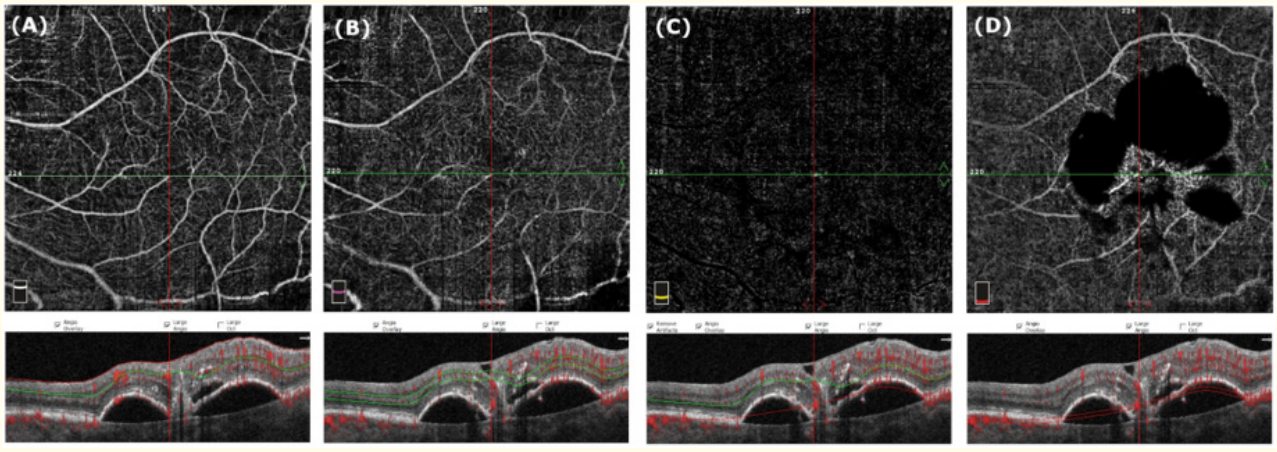

Figure 1: *Overview of OCTA findings in the correlation with increased transverse flow signal combined with intra- and subretinal fluid, distortion of retinal layers in OCT B-scans (A) and (B) respectively superficial and deep retinal plexus slab with the "cut off" vessel, (C) RPE slab with high-intensity micro spot with "halo", (D) choriocapillaris slab with vascularized PED.*

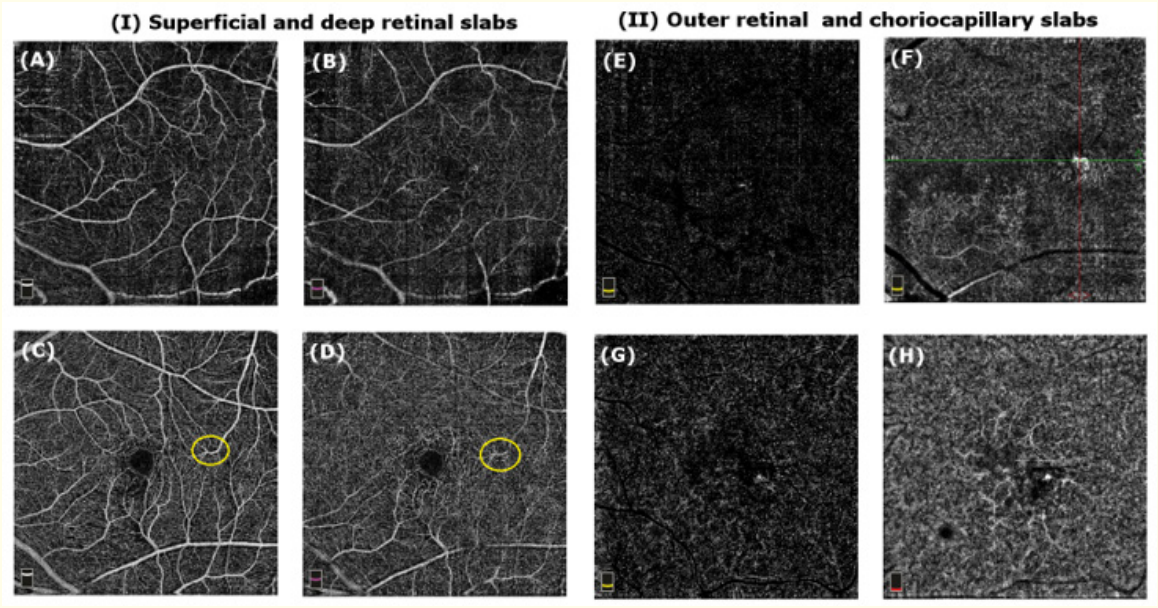

Figure 2: *Summary of OCTA findings: (A) and (B) -"cut off" sign of the vessel heading toward the macula respectively in the superficial and deep retinal slab, (C) and (D) - decrease of regional vessels density (marked by yellow ellipse) that corresponds with outer retinal changes in the OCT B-scans, respectively in superficial and deep slabs, (E) and (G) - high-intensity micro spot with "halo" in the outer retinal slab, (F) - vascularized PED in the outer retinal slab corrected for PED architecture from manufacturer settings, (H) - high-intensity spot with "halo" in the choriocapillaris slab.*

	Eye	Superficial plexus	Deep plexus	RPE layer	Choroidal layer	OCTA B scan	OCT B scan
Patient 1	OD	"Cut-off" vessel	"Cut-off" vessel	Artefacts	High-intensity spot	↑ Transverse retinal flow †	Intraretinal fluid, distortion of retinal layers, soft drusen
	OS	↓ Regional vessels density	↓ Regional vessels density	Normal	Normal	Normal	Soft drusen
Patient 2	OD	↓ Regional vessels density	↓ Regional vessels density	Artefacts	Medium-intensity micro spot	↑ Transverse retinal flow †	Intraretinal fluid, soft drusen
	OS	"Cut-off" vessel	"Cut-off" vessel	High-intensity micro spot with "halo"	Artefacts from superficial plexus with vascularized PED	↑ Transverse retinal flow †	Intra- and subretinal fluid, vascularized PED, distortion of retinal layers, soft drusen
Patient 3	OD	"Cut-off" vessel, tortuosity	"Cut-off" vessel	High-intensity spot with "halo"	High-intensity spot	↑ Transverse retinal flow †	Intra- and subretinal fluid, distortion of retinal layers, soft drusen

	OS	↓ Regional vessels density	↓ Regional vessels density	Artefacts	Medium-intensity micro spot	↑ Transverse retinal flow †	Intraretinal fluid, soft drusen
Patient 4	OD	↓ Regional vessels density	↓ Regional vessels density	Normal	Normal	Normal	Soft drusen
	OS	"Cut-off" vessel, tortuosity	"Cut-off" vessel	High-intensity spot	High-intensity micro spot with "halo"	↑ Transverse retinal flow †	Intra- and subretinal fluid, PED, distortion of retinal layers, soft drusen
Patient 5	OD	↓ Regional vessels density, "cut-off" vessel	Artefacts from superficial plexus	High-intensity spot with "halo"	High-intensity spot with "halo"	↑ Transverse retinal flow †	Intra- and subretinal fluid, PED, distortion of retinal layers, soft drusen
	OS	"Cut-off" vessel, ↓ regional vessels density, tortuosity	↓ Regional vessels density	Artefacts	Artefacts from superficial plexus	↑ Transverse retinal flow †	Soft drusen
Patient 6	OD	↓ Regional vessels density	↓ Regional vessels density	Normal	Normal	↑ Transverse retinal flow†	Distortion of retinal layers, soft drusen
	OS	↓ Regional vessels density	↓ Regional vessels density, near "hairpin loop"	High-intensity spot (vascularised PED)	Local decrease in flow signal near PED	↑ Transverse retinal flow†	PED, distortion of retinal layers, soft drusen

Table 1: *Summary of Optical Coherence Tomography Angiography findings In patients with retinal angiomatous proliferation.*

†: Localized near the hyperreflective intraretinal lesion that disturbs the normal architecture of retinal layers.

Interestingly, in two patients the eye not diagnosed with RAP displayed subtle changes in superficial and deep capillary plexus perfusion - a decrease in signal strength (Figure 2). This changes were associated with soft drusen and otherwise healthy looking retina.

Discussion

According to the previously described scale, RAP can be diagnosed in a classical manner using the 2001 Yannuzzi., *et al.* staging or the OCT B-scan-based classification by Su., *et al.* in 2016 (Table 2) [1-3]. We propose to include the OCTA findings in the OCT-based staging described by Su., *et al.* Taking into account findings described by Martins., *et al.* in 2017 about the contralateral eye to the one with RAP, we wish to underline the importance of close observation of the eyes that show decreased/loose local vessels density in the superficial and/or deep capillary plexus [4]. There are only few published papers on RAP changes in the OCTA examination and most of them retrospective, small sample studies focused mostly on treatment outcomes rather than a proper definite diagnosis. Other available papers are focused on the changes in fluorescein angiography combined with indocyanine green angiography.

There is an additional factor that could be further investigated and incorporated in diagnosis of RAP, namely the localized RPE atrophy. In a recent paper Jae., *et al.* present additional finding in diagnosis and prediction of RAP treatment. In that study involving 184 eyes with type 3 neovascularization diagnosed using methods established by Nagiel., *et al.* [5] and OCT was used for identification of lesion. The eyes were treated with anti-VEGF and followed for 37.6 ± 18.8 months. The authors observed a development of localized RPE atrophy in 13% of cases. The reactivation rate after 3 loading doses of anti-VEGEF was significantly lower in the atrophy group (58.3.%) compared to the group without RPE atrophy (85%) ($p = 0.004$). Additionally, the BCVA significantly better in the atrophy group [6].

Yannuzzi., *et al.* 2001 Clinical-based staging		Su., *et al.* 2016 OCT-based staging		OCTA- based staging	
				Pre	Contralateral RAP, ↓ regional vessels density, soft drusen
		Pre	Punctate hyperreflective foci in the outer retina	I	↑ Transverse retinal flow near foci in the outer retina
I	Small intraretinal hemorrhages, retino-retinal anastomosis	1	Larger intraretinal hyperreflective foci, CME, without outer retinal disruption	II	Larger intraretinal lesion with transverse retinal flow, intraretinal fluid
II	Growth of the retinal vessels into the subretinal space	2	Outer retinal disruption, CME	III	High-intensity micro spot with "halo" in RPE or choroid layer associated with CME
III	CNV, appearance of a vascularized PED	3	vascularised drusenoid/serous PED, CME	IV	Vascularised PED

Table 2: *Summary of existing classifications and proposed modification based on OCTA.*

Conclusion

OCTA can successfully add important information for early diagnosis of RAP. This imaging modality can serve as an valuable aid for a retina specialist at tertiary referral centre as well as for an comprehensive ophthalmologist.

Conflict of Interests

None.

Funding Sources

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