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Case report

Swept-source optical coherence tomography angiography for choroidal neovascularization after bevacizumab and photodynamic therapy

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ABSTRACT

Purpose: To report the swept-source optical coherence tomography angiography (SS-OCTA) findings after bevacizumab anti-vascular endothelial growth factor (anti-VEGF) and full-fluence photodynamic therapy (PDT) for choroidal neovascularization.
Design: Case report.
Methods: An 87-year-old, Chinese male presented with a shadow and decreased vision to 20/160 in his left eye (OS). Clinical examination, color photographs, swept-source optical coherence tomography (SS-OCT), widefield dye-fluorescein angiography (FA) and SS-OCTA revealed an extrafoveal, subretinal choroidal neovascularization (CNV) in the superior macula. Bevacizumab anti-VEGF and full-fluence PDT was initiated.
Results: Initial imaging with conventional color photography and FA demonstrated a classic CNV with significant early hyperfluorescence and late leakage. SS-OCT demonstrated subretinal hyperreflective material, fluid and hemorrhage emanating from a subretinal, type 2 neovascularization (NV). SS-OCTA showed a mixed lesion with a type 2, subretinal component with segmentation above the retinal pigment epithelium (RPE) and a type 1, sub-RPE component below. Treatment with anti-VEGF and PDT led to immediate regression of the CNV. One month after treatment, SS-OCTA demonstrated significant resolution of the type, 2 subretinal component and decreased flow and size of the type 1 sub-RPE lesion.
Conclusion: We report the first SS-OCTA images of successfully treated extrafoveal NV after combination PDT and ant-VEGF therapy. Early treatment of extrafoveal NV may improve our ability to treat mixed type 1 and 2 NV before these neovascular complexes mature from repetitive anti-VEGF treatment.

1. Introduction

Choroidal neovascularization (CNV) remains one of the main vision-threatening complications of chorioretinal diseases including neovascular age-related macular degeneration (nAMD) [1]. The discovery of anti-vascular endothelial growth factor (VEGF) has revolutionized the management of nAMD and provided unprecedented gains in visual acuity since their development. Prior to anti-VEGF, photodynamic therapy with Verteporfin (PDT) was used to treat classic CNV (Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) investigations) [2], and more recently, PDT combined with anti-VEGF treatments including bevacizumab or ranibizumab have been utilized to successfully treat polypoidal choroidal vasculopathy (PCV) [3] and retinal angiomatous proliferation [4]. Although combination treatment remains effective, the immediate and long-term effects of PDT including the extent of choroidal vascular thrombosis and possible collateral choroidal damage has not been clearly imaged.

Conventional fluorescein angiography (FA) remains essential in the diagnosis of CNV, and the current gold standard for diagnosing and identifying the anatomical location of CNV includes combining optical coherence tomography (OCT) and FA together [5]. Spectral-domain OCT (SD-OCT) is an essential tool when monitoring the activity of nAMD at diagnosis and after intravitreal anti-VEGF treatment, but remains limited in its ability to completely resolve the entire extent of the neovascularization (NV) [6]. FA can clearly

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image the activity of NV based on leakage or staining but cannot image the true axial location, extent and size of the neovascularization due to its lack of depth resolution. Another significant limitation is that FA requires intravenous injection of dye and this invasive procedure may cause nausea, vomiting and rarely, anaphylaxis [7].

Optical coherence tomography angiography (OCTA) is a new imaging technique utilizing signal intensity decorrelation and/or phase properties to non-invasively measure the flow of red blood cells [8]. *En-face* OCTA can generate high-resolution images of CNV in several ophthalmic diseases including nAMD [9]. Herein, we provide the first swept-source OCTA (SS-OCTA) images of an extrafoveal, mixed type 1 (sub-retinal pigment epithelium, RPE) and type 2 (subretinal) NV membrane that was successfully treated with combined bevacizumab and PDT. Utilizing this novel imaging technique, we can identify and visualize each component of the NV and demonstrate the exact effects of treatment on the vascular network and surrounding choroidal circulation.

2. Case report

An 87-year-old, Chinese male presented with a shadow and decreased vision in his left eye (OS) for 1 day. He had previously undergone successful cataract surgery in both eyes (OU) and had a history of non-neovascular AMD OU. His best-corrected visual acuity (BCVA) was 20/40 in his right eye (OD) and 20/160 OS. Anterior examination was normal OU. Posterior evaluation OD demonstrated few soft drusen and OS revealed an extrafoveal CNV membrane with associated subretinal fluid and hemorrhage in the superior macula (Fig. 1). Conventional dye-FA showed a well demarcated, early intense hyperfluorescence with late leakage suspicious for a classic CNV or type 2 NV (Fig. 1). SD-OCT (Carl Zeiss Meditec, Dublin, CA) showed a linear collection of subretinal hyperreflective material (SHM) directly above the RPE line and significant intra- and subretinal fluid with a central foveal thickness (CFT) of 505-μm. *En-face* SS-OCTA with a central wavelength of 1050 nm and a speed of 100,000 A-scans per second (Investigational SS-OCTA Prototype; Carl Zeiss Meditec, Dublin, CA) demonstrated a large, tangled vascular network in the subretinal location with a connection to a deeper, sub-RPE vascular trunk (Fig. 2). Intravitreal bevacizumab was initiated and full-fluence PDT was performed 6 days after presentation. One month later, BCVA OS had significantly improved to 20/50. SD-OCT demonstrated a CFT of 228-μm and resolution of all SHM, intra- and subretinal fluid. Repeat SS-OCTA showed regression of the type 2 component and the type 1, vascular trunk remained present with a small decrease in size and flow signal. There was minimal loss of the surrounding choriocapillaris (Fig. 3).

3. Discussion

Recently, longitudinal spectral-domain OCTA follow-up of CNV from several diseases including nAMD showed the overall decrease in greatest linear dimension and area after anti-VEGF treatment [10], although type 1 NV may be more resistant [9]. In this current case, *en-face* SS-OCTA using an intensity and phase-based contrasting microangiography algorithm-(OMAG^{C}) with 100,000 A-scans per second, clearly demonstrated a vascular trunk of the extrafoveal type 1 NV and the type 2, “medusa-like” component [9], which was leaking into the subretinal space. We elected to use combination treatment with bevacizumab and PDT to target the type 2 component with anti-VEGF, and PDT to decrease the size and flow and prevent maturation of the extrafoveal, type 1 lesion. Successful combined treatment has been similarly observed in myopic classic CNV [11] and in PCV [3]. Type 1 NV has been shown to be quite extensive on OCTA and may represent a more chronic, mature neovascular complex resistant to repetitive anti-VEGF therapy [9,12]. Early treatment with combined anti-VEGF and PDT therapy may be more effective in pruning the type 2, subretinal component and controlling the type 1, sub-RPE vessels before abnormalization therefore possibly preventing future recurrence and need for continuous anti-VEGF injections.

The risk of chorioretinal atrophy after PDT remains a significant issue. It has been speculated based on conventional FA, which showed early hypoperfusion of the choroidal circulation, that PDT may damage the normal choroidal vascular network [11]. In this case, we did note that there was minimal collateral damage to the surrounding normal choriocapillaris. Even with presumed accurate identification of the NV membrane with conventional FA or indocyanine green angiography (ICGA), the size of the treatment area may still be overestimated due to borders of the lesion being obscured by dye leakage. SS-OCTA allows for a clear and objective identification of the extent of the lesion; and future use of OCTA when planning PDT treatment may be warranted to accurately identify the required treatment area especially due to its increased depth resolution compared to FA or ICGA.

Multimodal imaging with non-invasive tools such as SS-OCTA continue to improve our ability to identify CNV and its anatomy. The increased number of A-scans and longer wavelength with SS-OCTA compared to SD-OCTA potentially allows for better detailed

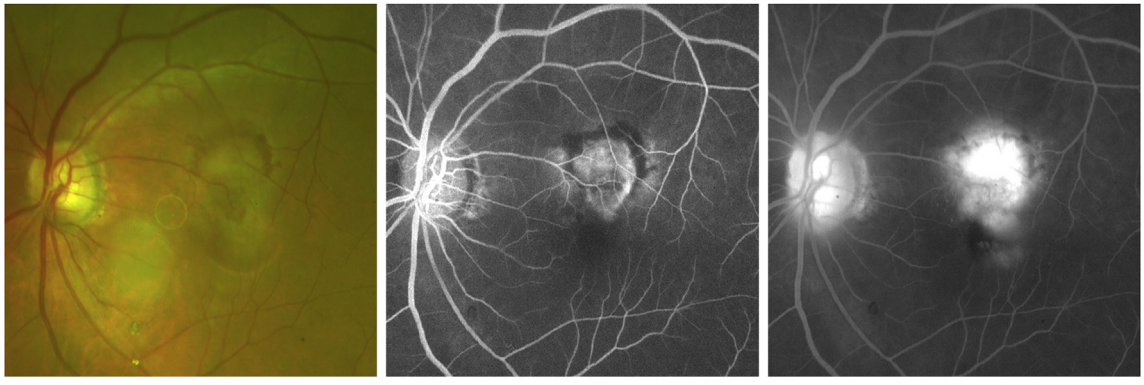

Fig. 1. Conventional imaging and fluorescein angiography of an 87-year-old male with a classic, type 2 choroidal neovascularization. Color fundus photo (**left panel**) and dye-fluorescein angiography (FA) (Optos, Marlborough, MA, USA) (**middle and right panel**) of the left eye demonstrated a gray, extrafoveal subretinal choroidal neovascular (CNV) membrane with associated subretinal fluid and hemorrhage in the superior macula (**left panel**). Conventional FA showed a well demarcated, early intense hyperfluorescence (middle panel) with late leakage (**right panel**) suspicious for a classic CNV or type 2 neovascularization.

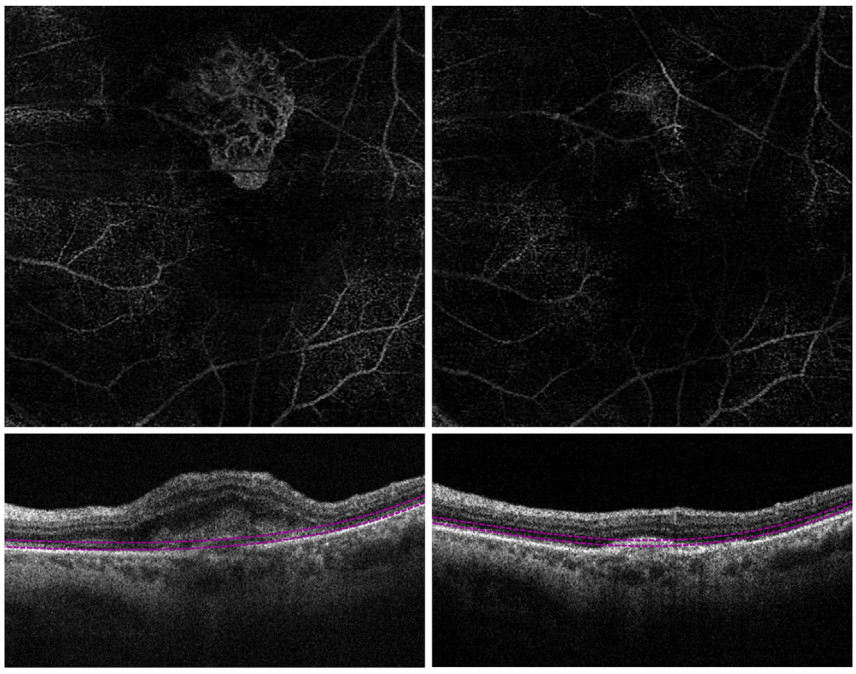

Fig. 2. Swept-source optical coherence tomography and angiography with subretinal segmentation of the CNV before and after treatment. *En-face* swept-source optical coherence tomographic angiography (Investigational SS-OCTA Prototype; Carl Zeiss Meditec, Dublin, CA) of the left macula segmented above the retinal pigment epithelium (RPE) and included the vascularized pigment epithelial detachment (PED) before treatment (**top left**) demonstrated a subretinal, tangled vascular network in a "medusa-like" pattern. Note the vascular projection artifact of the retinal vessels and capillaries at the level of the RPE. This type 2 neovascularization (NV) was clearly seen on the swept-source optical coherence tomography (SS-OCT) with a linear collection of subretinal hyperreflective material (SHM) directly above the RPE and significant intra- and subretinal fluid (**bottom left**). Intravitreal bevacizumab was initiated and full-fluence PDT was performed 6 days after presentation and one month later, *en-face* SS-OCTA showed regression of the type 2 NV component (**top right**), and SS-OCT demonstrated resolution of the SHM and flattening of the neovascular PED (**bottom right**).

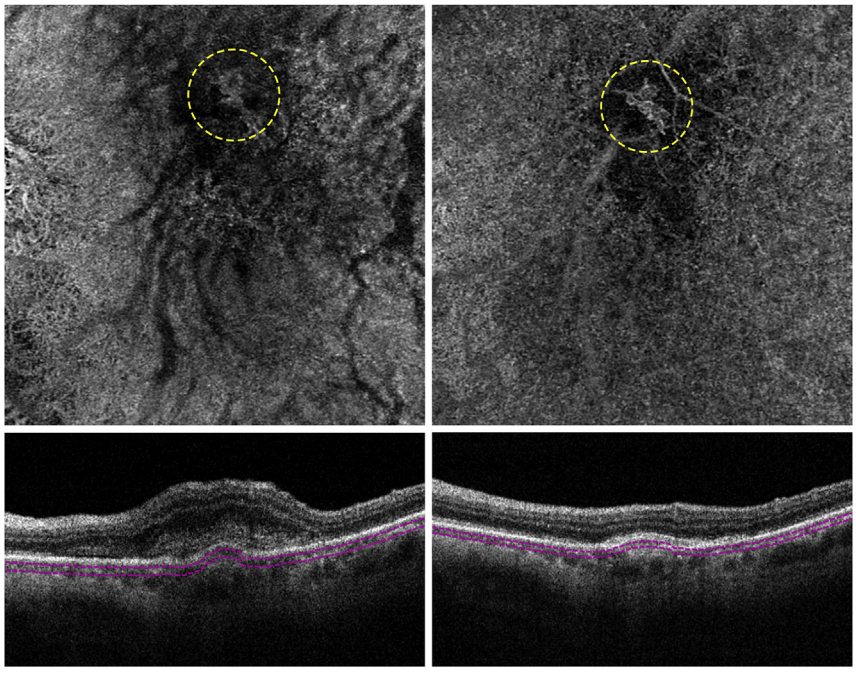

Fig. 3. Swept-source optical coherence tomography and angiography with sub-retinal pigment epithelium segmentation of the CNV before and after treatment. *En-face* swept-source optical coherence tomography and angiography (Investigational SS-OCTA Prototype; Carl Zeiss Meditec, Dublin, CA) segmented below the retinal pigment epithelium (RPE) of the vascularized pigment epithelial detachment showed a connection to a deeper, sub-RPE vascular trunk, which was the type 1 NV component (yellow dotted circle, **top left, bottom left**). After combination treatment, there was a small decrease in size and flow signal in the type 1, vascular trunk that remained in the vascularized PED (**top right, bottom right**), and minimal collateral loss of the surrounding choriocapillaris after PDT treatment.

visualization, penetration through subretinal fluid and exudative material and depth resolution of each neovascular component. Also, increasing the number of A-scans acquired per second provides for more averaging therefore increasing the signal to noise

ratio and quality of B-scan images. Although the current case is a single report limited to 1 month of follow-up, we demonstrate the first SS-OCTA images of successfully treated extrafoveal NV after combination PDT and ant-VEGF therapy and propose that this form of early treatment may improve our ability to treat type 1 NV before these neovascular complexes mature and abnormalize from repetitive anti-VEGF treatment. Future larger and long-term studies combining new imaging techniques such as swept-source OCTA with treatment planning and monitoring response to therapy may continue to improve our ability to treat CNV in nAMD.

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