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Optical Coherence Tomography Angiography Of Pathological Myopia Sourced and Idiopathic Choroidal Neovascularization With Follow-Up

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Abstract: To observe optical coherence tomography angiography (OCTA) images during follow-up of choroidal neovascularization (CNV) caused by pathological myopia (PM) or idiopathy and discuss OCTA's clinical applications

Patients with CNV caused by PM or idiopathic CNV (ICNV) were recruited prospectively from the Department of Ophthalmology, West China Hospital from March 2015 to June 2015. Intravitreal injections of Ranibizumab were conducted on all patients and repeated treatments were performed based on examinations of follow-up. Patients received OCTA the first week after injection, together with measurements of best-corrected visual acuity (BCVA) and central macular thickness (CMT). Subsequent follow-up was done once a month.

About 10 eyes of 10 patients were included in this study and mean age was (46.20 ± 10.15) years old. Around 6 (60%) were females and the other 4 (40%) were males and 5 were diagnosed with PM and 5 were ICNV. Mean follow-up was (7.82 ± 2.47) weeks. Except 4 (40%) patients got only 1 injection, 5 (50%) received two injections, and 1 (10%) patient got 4 (once every two weeks) due to his treatment-resistant lesion. Endpoint date of this study was on 25th June, 2015. Mean baseline BCVA was (0.81 ± 0.45) logarithm of minimal angle resolution (logMAR) and increased significantly to (0.50 ± 0.40) at last follow-up ($P = 0.005$). Average CMT of baseline was (276.90 ± 69.73) um and decreased to (249.70 ± 53.37) um at final follow-up with the statistical significance ($P = 0.008$). OCTA demonstrated details of reduction of CNV size and vessel density simultaneously.

OCTA could demonstrate the valid CNV form having advantages of rapid, noninvasive and repeatable. Combination of OCTA and other examinations had a promising future of clinical application on ocular neovascularization diseases. Further studies with larger sample size and longer follow-up are necessary and more advanced OCTA is being expected.

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Abbreviations: AMD = age-related macular degeneration, BCVA = best-corrected visual acuity, CMT = central macular thickness, CNV = choroidal neovascularization, FFA = fluorescein fundus angiography, ICNV = idiopathic choroidal neovascularization, LogMAR = logarithm of minimal angle resolution, OCT = optical coherence tomography angiography, OCTA = optical coherence tomography angiography, PM = pathological myopia, VEGF = vascular endothelial growth factor.

INTRODUCTION

Choroidal neovascularization (CNV) is a severe retinal and choroidal lesion resulting in vision loss or even blindness due to subretinal or intraretinal fluid, hemorrhage and ultimately the scar.[1,2] The main cause of CNV is neovascular age-related macular degeneration (AMD), mainly affecting elder patients.[1,3] Pathological myopia (PM) occupies the majority proportion of non-AMD CNV with the rate of 5% to 11% among its population.[1] Other less common sources include angioid streaks, multifocal choroiditis, punctate inner choroidopathy, presumed ocular histoplasmosis syndrome, and trauma.[1–4] Idiopathic CNV (ICNV) is defined as CNV without obvious signs of above reasons, influencing about 17% of CNV patients.[5] Although these CNVs show a relative more favorable natural course than AMD sourced,[5] permanent visual impairment and repeated recurrences might occur, from which patients suffer for a life time. Intravitreal injection of antivascular endothelial growth factor (VEGF) agents has been proved to be effective and safe in recent years for a variety of CNV.

Fluorescein fundus angiography (FFA) is the gold criteria of CNV with the dye distributing in retinal vessels directly. Nevertheless, rare side-effects such as nausea and even anaphylaxis limit the application of FFA and it is relatively contradicted on patients with heart or renal dysfunction. Furthermore, FFA is time-consuming especially in rushed hospitals, bringing about inconvenience on both doctors and patients to some extent.

The newly developed optical coherence tomography angiography (OCTA) could cover some of deficiencies of FFA through its noninvasive and rapid process. OCTA provides the imaging of en-face retinal and choroidal vasculature by detecting erythrocytes flowing in blood vessels with time.[6] The meantime OCT B-scan demonstrates direct comparisons between the structure and angiograms on the same cross-section. Split-spectrum amplitude decorrelation angiography (SSADA) algorithm was applied to improve the signal-to-noise for faster acquisition time and better images.[7,8] Motion correction was used by conducting two orthogonal imaging to adjust patients' movements.[7,9] In this study, we visualized the PM and idiopathic sourced CNV changes qualitatively by OCTA during patients' follow-up.

MATERIALS AND METHODS

Study Design

Our prospective case series recruited patients with ICNV or CNV caused by PM from Department of Ophthalmology, West

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China Hospital from March 2015 to June 2015. This study complied with requirements of the Declaration of Helsinki and was approved by Ethics Committee of West China Hospital. Informed consent was obtained from all included patients. Inclusion criteria contained: (1). Patients diagnosed with CNV caused by PM or ICNV, (2). Patients were treatment-naïve or had recurrent CNV with the last treatment 6 months before. Exclusion criteria were: (1). opaque refractive medium interfering imaging such as severe cataract or vitreous hemorrhage, (2). large amount of fundus hemorrhage caused by CNV preventing the incidence light from penetrating the retina.

Patients undertook a thorough ophthalmic examination at baseline including best-corrected visual acuity (BCVA) test, intraocular pressure measurement, dilated fundus examination by indirect ophthalmoscope and color fundus photography. BCVA was converted to logarithm of minimal angle resolution (logMAR). All CNV was confirmed by FFA. A single intravitreal injection of Ranibizumab (Lucentis; Genentech, Inc, South San Francisco, CA) was conducted on all patients. Extra treatments would be added if persistent hemorrhage or increase of the fluid was detected during follow-up.

Optical Coherence Tomography Angiography

OCTA was conducted by RTVue XR Avanti with Angio-Vue (Optovue Inc.,Fremont, CA) at 70,000 A-scans per second containing 304 × 304 A-scans in about 2.6 seconds. 3 × 3-mm scanning area focused on the macular was acquired using SSADA technique and if the former showed no exact CNV or incomplete CNV borders, a 6 × 6-mm scan was necessary for the entire CNV. Each of them consisted of two orthogonal images for motion correction. About 10-mm length B-scan and retinal map were achieved in the meantime to get the data of central macular thickness (CMT).

Outcomes and Follow-Up

Patients were followed up a week and a month after their injections, and then monthly follow-up was conducted subsequently. Main outcomes were BCVA and CMT. OCTA was repeated on them compared with changes of BCVA and CMT, combined with fundus photography and OCT B-scan.

Statistical Analysis

Statistical analysis was performed by SPSS (version 19.0 Inc., Chicago). Changes of BCVA and OCT were compared with baseline using Wilcoxon test. *P* values less than 0.05 were regarded as statistically significant.

RESULTS

Baseline Characteristics

General characteristics of patients were listed in Table 1. About 10 eyes from 10 patients were included in this study and mean age was (46.20 ± 10.15) years old. Around 6 (60%) of them were females and the other 4 (40%) were males. Also 5 (50%) were diagnosed with PM and 5 (50%) were ICNV and 2 (20%) patients had obvious intraretinal fluid and 4 (40%) had subretinal fluid. Mean follow-up was (7.82 ± 2.47) weeks. Except 4 (40%) patients got only 1 injection, 5 (50%) received two injections and 1 (10%) patient got 4 (once every two weeks) due to his treatment-resistant lesion. Around 2 (20%) of 10 patients had CNV recurred and both received intravitreal Ranibizumab more than half a year ago. Mean injections of this study was 1.80 ± 0.92. Detailed information of these 10 patients was demonstrated in Table 2 with their data of BCVA and CMT.

TABLE 1. Patient Characteristics and Demographics

	Patients Diagnosed with CNV (n = 10)
Age (year)	46.20 ± 10.15
Sex	
Male	4
Female	6
Cause of CNV	
PM	5
Idiopathy	5
Follow-up time (week)	7.82 ± 2.47
No. of injections (n)	
1	4
2	5
4	1
Newly diagnosed CNV	8
Recurrent CNV	2
Edema found by OCT	
Intraretinal fluid	2
Subretinal fluid	4
None	4

CNV = choroidal neovascularization, OCT = optical coherence tomography.

Changes or Best-Corrected Visual Acuity and Central Macular Thickness Table 3 gave BCVA of included patients in each follow-up. Mean baseline BCVA of 10 patients was (0.81 ± 0.45) logMAR. After treatments, it improved to (0.68 ± 0.43) significantly ($P = 0.028$) at 1 week and (0.51 ± 0.40) at 1 month ($P = 0.005$). BCVA became (0.50 ± 0.40) at last follow-up, indicating significant increase (($P = 0.005$). Follow-up data of CMT was shown in Table 4. CMT of baseline was (276.90 ± 69.73) um. It decreased to (254.60 ± 58.31) um and (257.4 ± 62.14) um at 1 week and 1 month, respectively. The result showed significant difference at 1-week follow-up ($P = 0.006$), turning out to be not statistically significant at 1 month compared to baseline ($P = 0.037$). At final visit, CMT declined to (249.70 ± 53.37) um, which was statistically significant ($P = 0.008$).

TWO SELECTED CASE REPORTS

Case Report 1

A 52-year-old female complaint of vision loss and metamorphopsia of her right eye. She was diagnosed with CNV caused by PM in her right eye. At baseline, she had a BCVA of 0.6 logMAR and CMT of 334 um. OCT B-scan, OCTA, fundus photography, and FFA were conducted on her affected right eye before treatment (Figure 1). She received intravitreal injection of Ranibizumab (0.5 mg/0.05 ml). A week later, BCVA was 0.3logMAR and CMT reduced to 276 um. OCTA demonstrated obvious reduction of the size and vessel density; however, the feeder blood remained almost unchanged. 1 month later, her BCVA returned to 0.4 and CMT increased to 359 um. OCTA showed reoccurrence of CNV, remarkable intraretinal fluid accumulated according to correlated B-scan and hemorrhagic persisted on fundus photography and. Then she received a

TABLE 2. Detailed Information of Included Patients

No. of Patient	Sex/ Age	Eye	Cause of CNV	Treatment	No. of Injections	Follow-up (wk)	Visual Acuity			Central foveal thickness,um		
							Baseline	End of follow-up	Change in VA, lines	Baseline	End of follow-up	Change in CMT,um
1	F/42	Right	Idiopathy	Ranibizumab	1	11.6	0.52	0.22	+3	299	256	−43
2	F/48	Right	Idiopathy		1	5.2	0.70	0.15	+6	213	194	−19
3	F/52	Left	PM		2	12.0	0.40	0.30	+1	365	332	−33
4	F/21	Right	Idiopathy		2	7.7	1.0	0.7	+1	215	212	−3
5	M/51	Right	PM		1	5.0	0.40	0.22	+2	225	223	−2
6	M/58	Right	PM		2	8.1	1.70	1.40	+1	343	248	−95
7	F/41	Right	Idiopathy		2	6.0	1.0	0.40	+6	166	168	+2
8	M/50	Left	PM		1	6.2	0.40	0.30	+1	263	256	−7
9	F/52	Right	PM		2	7.2	0.60	0.30	+3	334	326	−8
10	M/47	Right	Idiopathy		4	9.2	1.39	1.00	+3	346	282	−64

CMT = central macular thickness, CNV = choroidal neovascularization, PM = pathological myopia, VA = visual acuity.

second injection of Ranibizumab. After a week, improvement was found again and CMT was 268 um. Peripheral blood vessels occlusion was presented on OCTA. After 1 month of the second injection, CMT was 326 um due to repeated intraretinal fluid accumulation. She felt remission of metamorphopsia and her BCVA was 0.3logMAR with hemorrhagic having decreased. OCTA showed a reduction of CNV in size and vessel density compared to baseline. All follow-up images were presented in Figure 2. Additional treatments may be necessary for her if hemorrhagic recurs or expanding of the CNV indicated by OCTA.

Case Report 2

A 47-year-old male patient was diagnosed with ICNV in his right eye 2 years ago and had his lesion stable after treated by intravitreal injection of Ranibizumab. Around 3 months ago, his vision deteriorated rapidly and BCVA was only 1.39 logMAR. FFA and OCTA revealed recurrence of ICNV on his right eye (Figure 3) and CMT was 346 um based on OCT B-scan. Considering his long course of disease and severe condition, he received injections of Ranibizumab every two weeks with a double dose (1.0 mg). At a week after his first injection, his BCVA was stable and CMT reduced to 302 um. After two injections (1 month later), BCVA recovered slightly to 1.00 and CMT was 297 um. OCTA showed improvement of CNV compared with baseline image. Then another two injections were performed on his right eye biweekly. At week 6 and 8, OCTA remained almost unchanged and no obvious hemorrhage was found on fundus photography. BCVA was finally 1.00 logMAR and CMT was 282 um. All follow-up images were presented in Figure 4.

DISCUSSION

We conducted a prospective case series to explore the efficacy of OCTA imaging on CNV patients' follow-up. As OCTA has been applied in some institutions, several studies were carried out to research the value of OCTA in a variety of ocular diseases, most of which were cross-sectional studies or case reports. To the best of our knowledge, several studies have reported OCTA images of CNV arising from neovascular AMD, but CNV related to PM or idiopathic was seldom observed.

FFA is still the primary examination when patients are suspected with CNV by showing the form and function of CNV directly with dye flow and leakage. Traditional OCT-B scan demonstrates the structure of retinal and choroidal layers, mainly observing hemorrhage and fluid with different signal strengths; however, authentic images of CNV could not be revealed and tended to be confused with similar tissues, for example, the drusen.[9,10] In consideration of some side-effects such as nausea, vomiting and even anaphylaxis caused by contrast agents and limitations of structural OCT, the advanced OCTA compensates part of their shortage and provides vessels' arrangement of CNV through the technique SSADA, which distinguishes CNV with other structures by detecting flowing red blood cells.[11]

This study combined OCTA images with some quantitative parameters such as BCVA and CMT at each follow-up. In total, the reduced of size and vessel density of CNV accompanied increase of BCVA and decrease of CMT. Correlated OCT-B scan showed the relief of intraretinal or subretinal fluid and hemorrhage was absorbed when observing dilated fundus.

TABLE 3. Follow-up of Best-Corrected Visual Acuity

		1 week		1 month		End of Follow-up	
No. of Patient	**Baseline**	**BCVA**	***P* value**	**BCVA**	***P* value**	**BCVA**	***P* value**
1	0.52	0.40		0.22		0.22	
2	0.70	0.30		0.22		0.15	
3	0.40	0.40		0.30		0.30	
4	1.0	1.00		0.70		0.7	
5	0.40	0.40		0.30		0.22	
6	1.70	1.40	0.028	1.40	0.005	1.40	0.005
7	1.0	0.70		0.40		0.40	
8	0.40	0.40		0.30		0.30	
9	0.60	0.40		0.30		0.30	
10	1.39	1.39		1.00		1.00	
Mean	0.81 ± 0.45	0.68 ± 0.43		0.51 ± 0.40		0.50 ± 0.40	

BCVA = best corrected visual acuity.

Nevertheless, only 4 of 10 patients had their CNV stable after first treatment. Around 5 received two injections and 1 patient got 4 injections (once every two weeks) due to his resistant lesion. Among recurrent patients, improvement of BCVA and CMT could be found and OCT-B scan implied lessen of hemorrhage and edema. OCTA detected the persistent central trunk of CNV in spite of the reduction of its size. Similar images were reached by Kuehlewein et al[7,12] with unchanged feeder vessels. Previous studies speculated that these feeder vessels were hard to be eliminated by anti-VEGF agents on account of the protection from pericytes, while endothelial cells of other vessels were exposed to targeting drugs.[13] This point was not observed by other equipments or examinations, manifesting some advantages of OCTA.

Images of OCTA were automatically divided into four layers: superficial, deep, outer retina, and choroid capillaries. As the outer retina appears to be short of blood supply in normal patients, additional neovascularization is typical and prominent under the avasular background.[14] In addition, CNV on the layer of choroid capillaries was surrounded by an area with insufficient blood vessels, contrary to normal patients with adequate capillaries. Because hypoxia and ischemia might be responsible for the happening of CNV, our findings could be explained by possible CNV pathogenesis. Coscas et al[15] has observed the loss of choriocapillaris of AMD patients in their study and raised some benefits of OCTA compared to time-consuming and invasive indocyanine green angiography.

The application of OCTA remained to be restricted to patients without rapid eye movements.[7,9] Although motion correction was performed, frequent blink and shift of eyes led to difficulties for two orthogonal pictures merging into an intact one.[16] Images of incoordinate patients turned out to be distorted and no value for guidance and reference. Moreover, great amount of hemorrhage prevented the beam from penetrating through the retina, covering the existence of CNV and brought about challenges when finding the source of hemorrhage. de Carlo et al[6] conducted a diagnostic test to judge the efficacy of OCTA, with the sensitivity of 50% and specificity 91%. Around 3 of their false-negative cases were because of subretinal hemorrhage. In this study, we excluded these patients to achieve better and more precise images without disturbance of blood leakage.

TABLE 4. Follow-up of Central Macular Thickness

		1 week, um		1-month, um		End of Follow-up, um	
Patient No.	**Baseline, um**	**CMT**	***P* value**	**CMT**	***P* value**	**CMT**	**P value**
1	299	292		278		256	
2	213	194		202		194	
3	365	350		336		332	
4	215	201		201		212	
5	225	218		220		223	
6	343	287	0.006	264	0.037	248	0.008
7	166	163		165		168	
8	263	263		252		256	
9	334	276		359		326	
10	346	302		297		282	
Mean	276.90 ± 69.73	254.60 ± 58.31		257.4 ± 62.14		249.70 ± 53.37	

CMT = central macular thickness.

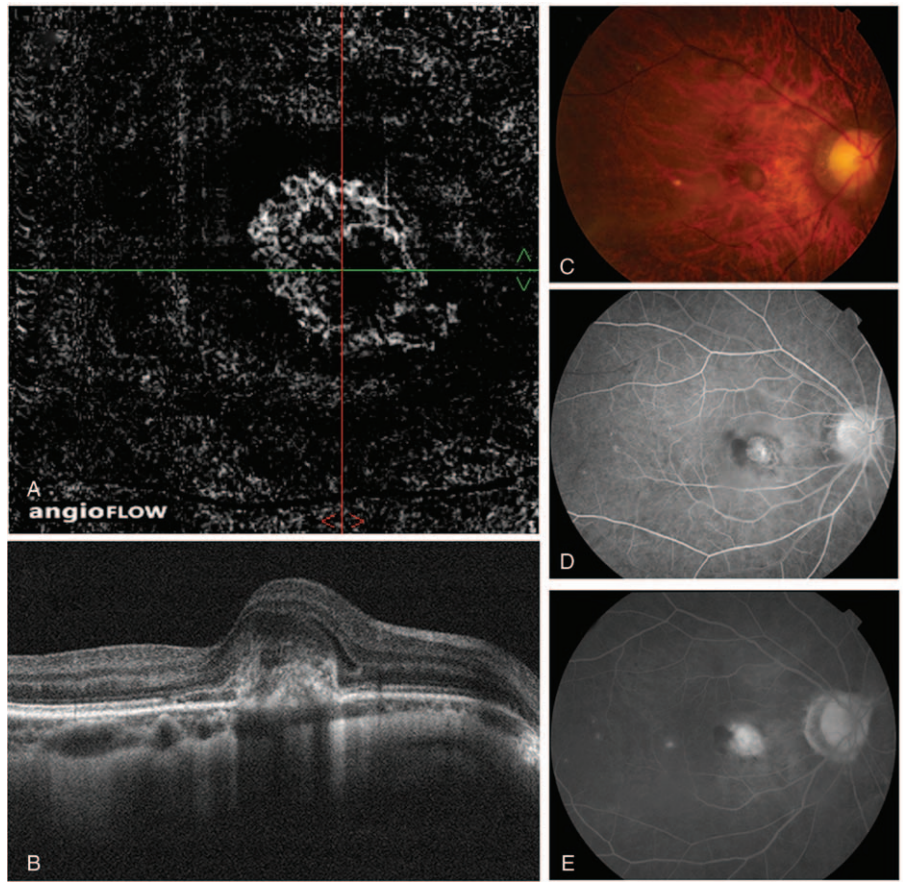

FIGURE 1. Choroidal neovascularization (CNV) caused by pathological myopia (PM). (A) Optical coherence tomography angiography (OCTA) of the right eye of a 52-year-old woman diagnosed with CNV caused by PM. Obvious neovascular image demonstrated on the outer retinal layer. (B) Correlated OCT-B scan showed intraretinal and subretinal hemorrhage related to CNV with discontinuous retinal pigment epithelium. (C) Color photography with hemorrhage on the posterior of ocular fundus. (D) Early phase of fluorescein fundus angiography (FFA) showed the appearance of hyperfluorescent lesion. (E) Late-phase of FFA indicated persistent leakage from CNV with adjacent hemorrhage blocking the fluorescein. CNV = choroidal neovascularisation, FFA = fluorescein fundus angiography, OCTA = optical coherence tomography angiography, PM = pathological myopia.

For PM patients, we faced several difficulties when we captured images from them, which are necessary to be specified. First, many lesions could be observed on PM's ocular fundus, such as lacquer cracks, RPE atrophy, and retinoschisis, which may disturb the appearance of CNV. Second, patients with severe RPE atrophy bare a poor fixation, having difficulty to cooperate our examinations. Third, the axial length of PM eye balls is relative long and impacts the accuracy of layer divided by OCTA automatically. These features of PM lead to increasing obstacles for both examiners and patients.

This study has several limitations. First, only 10 patients were included in this study. Small sample size restricted the validity and feasibility of the conclusion to be applied. Second, the follow-up period was short and long-time efficacy of OCTA observing CNV changes after treatment remained ambiguous in this study. Trials with longer follow-up are necessary to confirm further practical effects of OCTA. Third, the OCTA had its internal limitations. Segmentation of retinal and choroid capillaries automatically was not precise and sometimes delineated the CNV together with upper or lower layers by mistake.[6] Software with the function of adjusting the CNV area manually or more accurate automatic delineating is demanded for clinical use. The largest range of observing the ocular fundus is 9×9 mm and locates mainly on the posterior pole. Images of peripheral fundus are hard to be gained and it is quite impossible for patients to move their eyes because a stable fixation point is necessary for two orthogonal scans. Images with high quality are hard to acquire if patients are unable to maintain their eyes and heads' position. Eye movement is the main problem in the process of obtaining satisfactory pictures. Therefore, the technique with faster scanning speed and larger observing size is desirable in subsequent research.

In conclusion, OCTA presented the detailed CNV form with the technique SSADA and had advantages of rapid, noninvasive and repeatable. Images of OCTA were almost consistent with increase of BCVA and decrease of CMT. Besides, additional information which might not be found by other examinations could be provided based on OCTA, such as the size and vessel density of CNV. OCTA shows a promising future in clinical application. Further studies with larger sample size and longer follow-up are necessary to explore the value of OCTA and more advanced OCTA is being expected to compensate for current shortages.

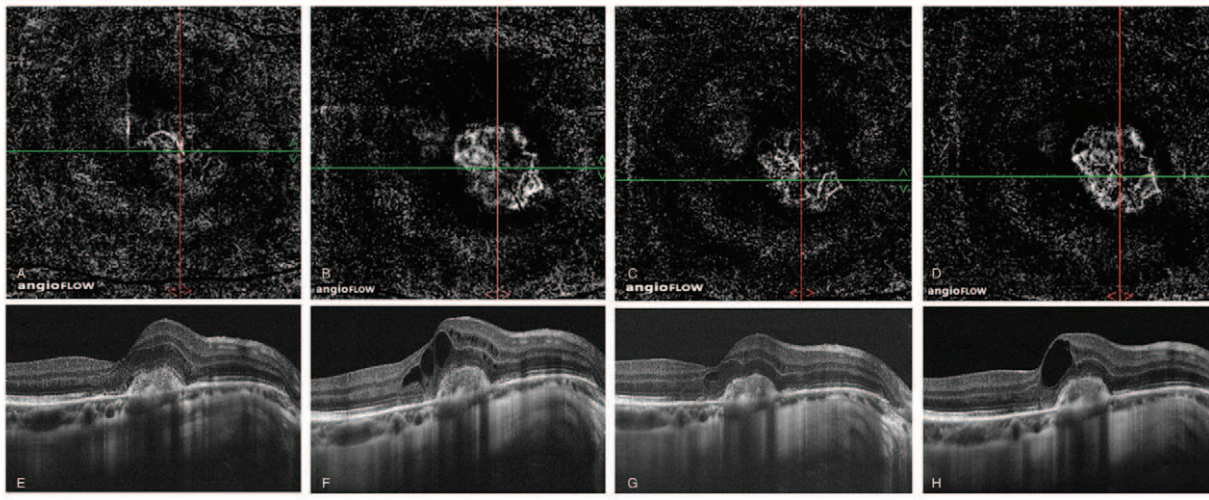

FIGURE 2. Follow-up of optical coherence tomography angiography (OCTA) images of the patient in Figure 1. (A) and (E). At a week after the first injection of Ranibizumab, apparent reduction of size and vessel density was demonstrated on OCTA and OCT-B scan pointed out decrease of the hemorrhage, but the feeder vessel was almost unaffected. (B) and (F) At a month after the first injection, neovascularization recurred with intraretinal fluid accumulating according to B scan. (E) and (G) At a week after the second injection, CNV network contracts and fluid was absorbed to some degree. (D) and (H) A month after the second injection, CNV recurred again with intraretinal fluid. CNV = choroidal neovascularisation, OCTA = optical coherence tomography angiography.

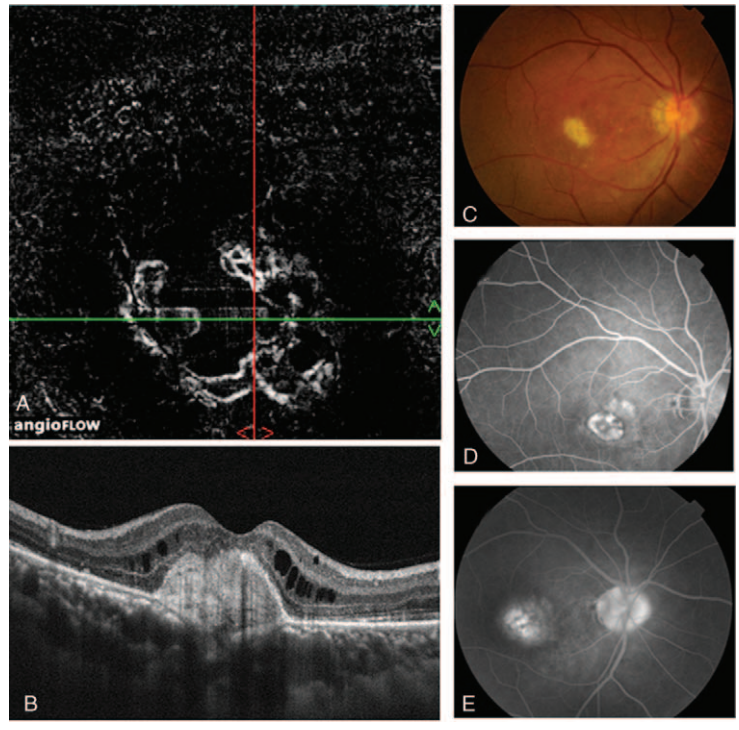

FIGURE 3. Images of a 47-year-old man with a history of idiopathic choroidal neovascularization (ICNV) for two years in his right eye. He had his ICNV recurred. (A) An area of CNV provided by optical coherence tomography angiography (OCTA). (B) Stale hemorrhage and cystic macular edema on OCT-B scan. (C) Color photography showing scar of the original lesion and spotted hemorrhage. (D) Early phase of fluorescein fundus angiography (FFA) showing hyperfluorescein with hemorrhage covering on the side. (E) Late-phase of FFA demonstrating expanding or the leakage. CNV = choroidal neovascularisation, FFA = fluorescein fundus angiography, ICNV = idiopathic idiopathic choroidal neovascularization (ICNV), OCTA = optical coherence tomography angiography.

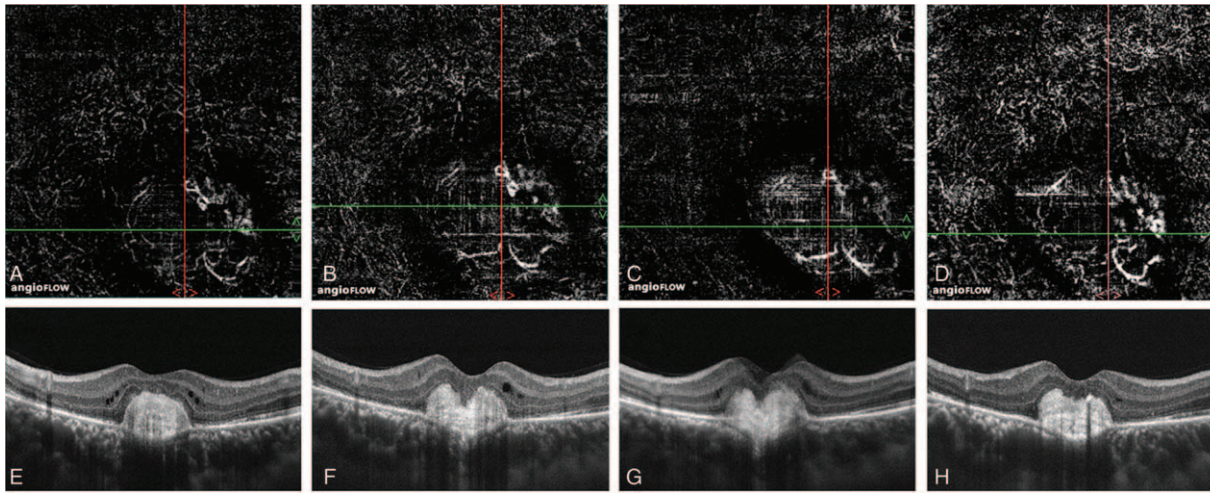

FIGURE 4. Follow-up of optical coherence tomography angiography (OCTA) of the patient from Figure 3. (A) and (E) At a week after the first injection, part of vessels disappeared especially periphery ones. Intraretinal cystic edema reduced apparently on the correlated B-scan. (B) and (F) CNV lesion remained almost stable after two injections (once every two weeks). (C) and (G). Two weeks after the third injection (six weeks after the first treatment), no distinct deterioration or improvement was found compared to last images. (D) and (H) After 4 injections (eight weeks after the first treatment), the lesion remained stable with the formation of scar and no obvious edema or persistent hemorrhage was seen on OCT-B scan. CNV = choroidal neovascularisation, OCTA = optical coherence tomography angiography.

REFERENCES

1. Stuart A, Ford JA, Duckworth S, et al. Anti-VEGF therapies in the treatment of choroidal neovascularisation secondary to non-age-related macular degeneration: a systematic review. *BMJ Open.* 2015;5:e007746doi: 10.1136/bmjopen-2015-007746.
2. Sickenberg M, Schmidt-Erfurth U, Miller JW, et al. A preliminary study of photodynamic therapy using verteporfin for choroidal neovascularization in pathologic myopia, ocular histoplasmosis syndrome, angioid streaks, and idiopathic causes. *Arch Ophthalmol.* 2000;117:327–336.
3. Chang LK, Spaide RF, Brue C, et al. Bevacizumab treatment for subfoveal choroidal neovascularization from causes other than age-related macular degeneration. *Arch Ophthalmol.* 2008;126:941–945.
4. Chan WM, Lai TY, Liu DT, et al. Intravitreal Bevacizumab (Avastin) for choroidal neovascularization secondary to central serous chorioretinopathy, secondary to punctate inner choroidopathy, or of idiopathic origin. *Am J Ophthalmol.* 2007;143:977–983.
5. Cohen SY, Laroche A, Leguen Y, et al. Etiology of choroidal neovascularization in young patients. *Ophthalmology.* 1996;103:1241–1244.
6. de Carlo TE, Bonini Filho MA, Chin AT, et al. Spectral-domain optical coherence tomography angiography of choroidal neovascularization. *Ophthalmology.* 2015;122:1228–1238.
7. Kuehlewein L, Sadda SR, Sarraf D. OCT angiography and sequential quantitative analysis of type 2 neovascularization after ranibizumab therapy. *Eye (Lond).* 2015;29:932–935.
8. Jia YL, Tan O, Tokayer J, et al. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. *Opt Express.* 2012;20:4710–4725.
9. Jia YL, Bailey ST, Wilson DJ, et al. Quantitative optical coherence tomography angiography of choroidal neovascularization in age-related macular degeneration. *Ophthalmology.* 2014;121:1435–1444.
10. Spaide RF, Klancnik JM Jr, Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. *JAMA Ophthalmol.* 2015;133:45–50.
11. Mastropasqua R, Di Antonio L, Di Staso S, et al. Optical coherence tomography angiography in retinal vascular diseases and choroidal neovascularization. *J Ophthalmol.* 2015;2015:343515.
12. Kuehlewein L, Bansal M, Lenis TL, et al. Optical coherence tomography angiography of type 1 neovascularization in age-related macular degeneration. *Am J Ophthalmol.* 2015;160:739–748.
13. Bellou S, Pentheroudakis G, Murphy C, et al. Anti-angiogenesis in cancer therapy: hercules and hydra. *Cancer Lett.* 2013;338:219–228.
14. Carpineto P, Mastropasqua R, Marchini G, et al. Reproducibility and repeatability of foveal avascular zone measurements in healthy subjects by optical coherencetomography angiography. *Br J Ophthalmol.* 2015doi:10.1136/bjophthalmol-2015-307330.
15. Coscas G, Lupidi M, Coscas F, et al. Optical coherence tomography angiography during follow-up: qualitative and quantitative analysis of mixed type I and II choroidal neovascularization after vascular endothelial growth factor trap therapy. *Ophthalmic Res.* 2015;54:57–63.
16. Gao SS, Liu G, Huang D, et al. Optimization of the split-spectrum amplitude-decorrelation angiography algorithm on a spectral optical coherence tomography system. *Opt Lett.* 2015;40:2305–2308.