Quantitative Evaluation of Parafoveal Microvasculature Changes in Eyes with Exudative Circumscribed Choroidal Haemangioma : An Optical Coherence Tomography Angiography Study

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Research article

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Abstract

Background: To quantitative evaluation of parafoveal microvasculature changes in eyes with exudative circumscribed choroidal haemangioma (CCH) compared with age- and gender-controlled healthy eyes.

Methods: This was a cross-sectional, case-control study. 82 eyes of eighty-two subjects including 41 eyes of forty-one subjects in the exudative CCH group and 41 eyes of forty-one subjects in the age- and gender-controlled healthy eye group were enrolled in this study. Optical coherence tomography angiography (OCTA) was performed in each subject, and the capillary density (CD) of superficial plexus, deep capillary plexus, and the choriocapillaris as well as the area of foveal avascular zone (FAZ) were noted and analyzed between two groups.

Results: The CD of the superficial plexus (44.51 ± 3.58 % vs 47.93 ± 2.94%) and deep plexus (47.75 ± 5.60% vs 52.66 ± 5.04%) of retina as well as the vessel density of choriocapillaris (54.42 ± 6.36% vs 61.83 ± 3.65%) significantly decreased in eyes with exudative CCH compared with age- and gender-controlled healthy eyes (all $P < 0.001$). Although we found that the FAZ areas in the exudative CCH group was larger than that of the healthy eye control group (0.30 ± 0.11mm^2 vs 0.27 ± 0.87mm^2), however, no statistical significance was found between two groups ($P = 0.164$).

Conclusions: OCTA is a rapid, non-invasive, high-resolution procedure with which could monitor the parafoveal microvasculature changes in eyes with exudative CCH. We found that not only the CD of the superficial plexus and deep plexus but also the CD of choriocapillaris significantly decreased in eyes with exudative CCH compared with age- and gender-controlled healthy eye group.

Trial registration: This study was registered on the https://www.clinicaltrials.gov (trial registration number: NCT04449900)

Background

Circumscribed choroidal haemangioma (CCH) is an uncommon, potentially congenital benign vascular hamartomas which typically manifests as an elevated reddish-orange mass located posteriorly to the equator, mostly in the macular and peripapillary region[1–4]. CCH is often asymptomatic tumor commonly go undiagnosed until symptoms develop due to subretinal fluid (SRF) and macular edema[1, 5, 6]. Despite its benign nature, cystoid macular edema (CME) or SRF due to the exudations from the exudative CCH can cause visual impairment[7]. If untreated, long-term poor visual acuity of 20/200 or worse was noted in almost 50% of symptomatic cases[1], suggesting early diagnosis and treatment of exudative CCH are very important.

Diagnosis is often suspected clinically, and multimodal imaging is considered to be useful for the differential diagnosis of CCH from other malignant tumors such as melanoma[8–10]. On fluorescein angiography (FA), exudative CCH appears varying degrees of hyperfluorescence in all phases[1]. Besides, it shows early rapid filling with extreme hyperfluorescence in early phase and a “washout” phenomenon

in late phase on indocyanine green angiography (ICGA)[11–13]. Enhanced depth imaging (EDI) optical coherence tomography (OCT) of exudative CCH shows a smooth dome-shaped elevation of the choroid with expansion of medium- and large- sized choroidal vessels which often company with SRF or intra-retinal edema[3, 14, 15]. Optical coherence tomography angiography (OCTA) is a rapid, non-invasive, new imaging technology which could provide the capillary density (CD) of superficial and deep capillary plexus as well as the CD of choriocapillaris of the superficial, the latter two of which could not be seen on conventional FA or ICGA[16, 17]. However, little knowledge is known about the parafoveal microvasculature changes in eyes with exudative CCH on OCTA. Interestingly, Sioufi and colleagues[14] reported that eyes with previous or current CME and/or SRF had reduced CD of deep plexus compared with the contralateral “normal” eyes in a retrospective chart review of 14 patients with CCH. However, some ophthalmologists considered the contralateral “normal” eyes of patients with CCH are not absolutely healthy[5, 18]. For example, Kim et al revealed that elevated choroidal thickness and increased risk of central serous chorioretinopathy in the fellow eyes of patients with CCH[5]. Therefore, it is necessary to quantitative evaluation of parafoveal microvasculature changes in eyes with exudative CCH compared with healthy eyes without any disease. To the best of our knowledge, this is the first cross-sectional, case-control study to use OCTA to quantitative evaluation of parafoveal microvasculature changes in Eyes with exudative CCH compared with age- and gender-controlled healthy eyes.

Methods

This was a cross-sectional, case-control study and was approved by the Institutional Review Board (IRB) of Sun Yat-sen University and all procedures were conducted in accordance with the tenets of the Declaration of Helsinki. This study also adhered to CONSORT guidelines and the written informed consent was obtained from all the enrolled subjects after explanation of the nature and possible consequences of this study. This study was registered on the https://www.clinicaltrials.gov (trial registration number: NCT04449900).

Subjects

82 eyes of eighty-two subjects including 41 eyes of forty-one patients with exudative CCH and 41 eyes of forty-one age- and gender-controlled healthy volunteers (healthy eye control group) who visited Zhongshan Ophthalmic Center of Sun Yat-sen University between March 1st, 2017 and May 30th, 2020 were enrolled in this study. For patients with exudative CCH, the inclusion criteria were treatment naïve patients with exudative CCH which caused subfoveal retinal detachment and/or intraretinal fluid, and the exclusion criteria were with any other ocular diseases or any severe uncontrolled systemic diseases, such as uncontrolled hypertension, coronary heart disease, liver failure, and kidney failure. For the healthy eye control group, only one eye (randomized by computer) of a subject was included, and the both eyes of the subject should have no ocular diseases and the best-corrected visual acuity (BCVA) should be 20/20 or better. Besides, all the subjects with high diopter > − 6D, long eye axis > 26.0 mm, or the quality of the acquired OCTA images below 7/10 would be excluded from this study.

General examinations

Subjects' detailed demographics at baseline including age, gender, and medical history were noted. All the enrolled subjects underwent a complete ocular examination, including BCVA measurement, slitlamp examination, intraocular pressure, fundus photography, FA, ICGA, EDI-OCT (Spectralis HRA + OCT; Heidelberg Engineering, Germany), and OCTA (RTVue XR Avanti; Optovue Inc., Fremont, CA, USA). Central foveal thickness (CFT) was determined by averaging vertical and horizontal CFT values measured manually from the inner retinal surface to the retinal pigmented epithelium (RPE) line as we previously described[19]. Patients with exudative CCH underwent contrast-enhanced MRI of both the orbits and the brain as well as B-scan ultrasonography to make sure the diagnosis and to determine the largest basal diameter and thickness of the tumors. Other features including the presence of CME or SRF on EDI-OCT and the distance of tumor from the nearest border to the optic nerve as well as foveola were also noted.

OCTA image acquisition protocol

3 × 3 mm scanning pattern of OCTA centered on the fovea was performed for each subject. The OCTA self-software (version 2017.1.0.155) could automatically segment the en face OCT into four layers including superficial, deep, outer retina, and choroidal capillary in order to determine the CD of superficial and deep capillary plexus as well as the choriocapillaris. The protocol and principal algorithm of OCTA have been previously described[16, 20]. All the images were reviewed, individually, by two experts (KL and CH) to confirm the quality of the images and accuracy of the segmentation.

Image analysis

The acquired images were analyzed using the OCTA self-software (AngioVue® software, version 2017.1.0.155). For parafoveal vessel density, the software automatically calculated the density (%) of blood vessels of both superficial plexus and deep plexus in a 300 μm-wide ring surrounding the foveal avascular zone (FAZ). Specifically, new version of AngioVue® software provides the vessel density of choroidal capillary (Bruch's membrane [BRM] – 10 μm to BRM + 30 μm). However, new version of software is no longer possible to measure the FAZ areas of superficial and deep retinal layers separately. Therefore, the FAZ area was measured using the image of the retinal slab from the internal limiting membrane (ILM) to the outer plexiform layer (OPL) plus 10 μm by AngioVue software (version 2017.1.0.155).

Statistical analysis

All data were expressed as the means ± standard deviation. Data was analyzed using SPSS 19.0 software (IBM Corporation, Armonk, NY). Decimal BCVA were transferred to the logarithm of minimal angle of resolution (logMAR) value for analysis. Comparisons between groups were made using the Chi-square test for categorical variables and the independent-sample *t*-test for continuous variables. Correlations between continuous variables were analyzed using Pearson's correlation analysis, and noncontinuous variables were used Spearman's correlation analysis. A *P* value less than 0.05 was considered statistically significant.

Results

Baseline characteristics of enrolled subjects

A total of 82 eyes of eighty-two subjects (41 eyes in the exudative CCH group and 41 eyes in the age- and gender-controlled healthy eye control group) were enrolled in this study. The baseline demographic and clinical characteristics of all enrolled subjects were shown in Table 1. There were 22 females (53.7%) and 19 males (46.3%) in the exudative CCH group, and 21 females (51.2%) and 20 males (48.8%) in the healthy eye control group. The mean age of the patients with exudative CCH was 37.85 ± 13.80 (range, 16–66 years), and the mean age of subjects in healthy eye control group was 38.07 ± 12.38 (range, 18–67). No statistical significance was seen neither for the gender nor for the mean age between the CCH group and the healthy eye control group (P = 0.852 for gender and P = 0.940 for mean age).

Table 1
The baseline characteristics of the enrolled subjects.

Outcomes	Patients with CCH (n = 41)	Healthy control subjects (n = 41)	*P* value
Gender			
Female, n (%)	22 (53.7%)	21 (51.2%)	0.852*
Male, n (%)	19 (46.3%)	20 (48.8%)	0.852*
Age, mean ± SD (median, range), years	37.85 ± 13.80 (35.0, 16–66)	38.07 ± 12.38 (36.0, 18–67)	0.940†
BCVA, mean ± SD (logMAR)	0.87 ± 0.43	-0.07 ± 0.12	**0.001**†
Baseline CFT, mean ± SD, μm	408.56 ± 181.94	243.15 ± 21.06	**0.001**†
Baseline diameter of the tumor, mm	8.92 ± 2.20 (range 5.7–14.7)	N/A	N/A
Baseline thickness of the tumor, mm	3.37 ± 1.04 (range 1.8–6.2)	N/A	N/A
Tumor Distance to optic disk, mean ± SD (median, range), mm	2.11 ± 1.62 (1.78, 0–6.10)	N/A	N/A
Tumor Distance to foveola, mean ± SD (median, range), mm	2.11 + 1.44 (1.98, 0–4.98)	N/A	N/A
Macular features at baseline			
Active CME only, n (%)	7 (17.07%)	N/A	N/A
Active SRF only, n (%)	24 (58.54%)	N/A	N/A
Active SRF and CME, n (%)	10 (24.39%)	N/A	N/A
*Pearson χ^2 test, † Independent-sample t-test,			
CCH, circumscribed choroidal haemangioma; BCVA, best-corrected visual acuity; logMAR, logarithm of the minimal angle of resolution; CFT, central foveal thickness; SD, standard deviation; CME, cystoid macular edema; SRF, subfoveal subretinal fluid			

The mean CFT in exudative CCH group was 408.56 ± 181.94 μm, which has statistical significance compared with the mean CFT (243.15 ± 21.06 μm) in the healthy eye control group ($P < 0.001$). 7 eyes had active CME (17.07%), 24 eyes had active SRF (58.54%), and 10 eyes had both active CME and SRF (24.39%) in the exudative CCH group. Besides, the mean distance of tumor from the nearest border to the optic nerve was 2.11 ± 1.62 mm (range, 0–6.10 mm) and the mean distance of tumor from the nearest border to the foveola was 2.11 + 1.44 mm (range, 0–4.98 mm).

Capillary density of retinal superficial plexus and deep plexus

The parafoveal microvasculature features on OCTA in eyes with exudative CCH and in healthy eye control group were shown in Table 2. The mean parafoveal CD of superficial plexus was 44.51 ± 3.58% in the exudative CCH group, which was lower than that of healthy eye control group (47.93 ± 2.94%) with statistical significance ($P < 0.001$). Similar results were found for the mean parafoveal CD of deep plexus. The parafoveal CD of deep plexus was significantly decreased in the exudative CCH group (47.75 ± 5.60%) compared with that of healthy eye control group (52.66 ± 5.04) ($P < 0.001$).

Table 2
Parafoveal microvasculature features on OCTA in eyes of different groups

	Eyes with CCH (n = 41)	Eyes in healthy subjects (n = 41)	*P* value
BCVA, mean ± SD (median, range), LogMAR	0.87 ± 0.43 (0.80, 0.30–2.00)	-0.07 ± 0.12 (0, -0.3–0)	**0.001***
CFT, mean (median, range), mm	408.56 ± 181.94 (356, 134–952)	243.15 ± 21.06 (243, 209–287)	**0.001***
Foveal avascular zone area, mean ± SD (median, range), mm^2	0.30 ± 0.11 (0.31, 0.13–0.68)	0.27 ± 0.87 (0.28, 0.11–0.46)	0.164
Capillary density of retina, mean ± SD (median, range), %			
Superficial plexus	44.51 ± 3.58 (44.20, 40.20–54.40)	47.93 ± 2.94 (48.54, 40.10–53.80)	**0.001***
Deep plexus	47.75 ± 5.60 (49.20, 28.70–56.70)	52.66 ± 5.04 (53.14, 40.30–59.80)	**0.001***
Capillary density of choriocapillaris, mean ± SD (median, range), %	54.42 ± 6.36 (55.00, 38.10–71.10)	61.83 ± 3.65 (62.20, 52.10–68.50)	**0.001***

All *P* values were compared with normal eyes using independent-sample *t*-test.

*Statistically significant result.

OCTA, optical coherence tomography angiography; CCH, circumscribed choroidal haemangioma; BCVA, best-corrected visual acuity; logMAR, logarithm of the minimal angle of resolution; CFT, central foveal thickness

Capillary density of choriocapillaris

New version of AngioVue® software (version 2017.1.0.155) provides the CD of choroidal capillary, therefore, we compared the CD of choriocapillaris between two groups and found that the parafoveal CD of choroidal capillary was significantly decreased in the exudative CCH group (54.42 ± 6.36%) compared with that of healthy eye control group (61.83 ± 3.65) ($P < 0.001$).

Foveal avascular zone area

FAZ areas in two groups were shown in Table 2. The mean FAZ area was larger in the exudative CCH group (0.30 ± 0.11 mm^2) compared with that of healthy eye control group (0.27 ± 0.87 mm^2). However, there was no statistical significance between the exudative CCH group and the healthy eye control group (P = 0.164). Representative images of two groups were shown in Fig. 1.

Correlation between OCTA variables and BCVA at baseline

To further know whether the decreased CD of retinal superficial plexus, deep plexus, and choriocapillaris as we as the FAZ area had correlation with baseline BCVA, we performed the Pearson's correlation analysis, however, we found that baseline BCVA was not correlated with any of the parameters including CD of retinal superficial plexus (r = − 0.025, P = 0.876), CD of deep plexus (r = − 0.026, P = 0.871), CD of choriocapillaris (r = − 0.096, P = 0.550), or FAZ area (r = − 0.146, P = 0.365).

Discussion

In this cross-sectional, case-control study with 82 eyes of eight-two subjects, we quantitatively assessed and compared the parameters of parafoveal microvasculature in eyes with treatment-naïve exudative CCH (n = 41) with those of age- and gender-controlled healthy eyes (n = 41) using OCTA. To the best our knowledge, this is the first cross-sectional, case-control study revealing the parafoveal microvasculature changes in eyes with exudative CCH compared with age- and gender-controlled healthy eyes. We found that not only the vessel density of the superficial vascular complex and deep vascular complex of retina but also the vessel density of choriocapillaris significantly decreased in eyes with exudative CCH compared with healthy eyes (P < 0.001). Although we found that the FAZ area in the exudative CCH group was larger than that of the healthy eye control group, however, no statistical significance was found between two groups (P = 0.164).

OCTA is a non-invasive procedure with depth resolved imaging technique which allows the visualization and quantitation of the CD of superficial and deep retinal capillary plexus as well as choriocapillaris[21, 22]. Although FA and ICGA remain invaluable in the diagnosis of many retinal and choroidal diseases, however, both FA and ICGA are invasive procedures need the injection of dye, which are time-consuming, and also carry the risk of complications, such as severe allergic reactions or even death. Compared with FA and ICGA, OCTA has many advantages: Firstly, it is a non-invasive procedure without the need of injection of dye, which could avoid the risk of related complications. Besides, OCTA is less time-consuming but could provide a great quantity of information such as CD of superficial and deep retinal capillary plexus, choriocapillaris which is not possible on FA or ICGA. Therefore, OCTA has become widely used clinically to diagnose a variety of ophthalmological diseases, such as age-related macular degeneration, diabetic retinopathy, artery and vein occlusions, and glaucoma[23].

Up to date, there are still only a few publications on retinal parafoveal microvasculature of choroidal tumors on OCTA. Valverde and colleagues reported in a retrospective comparative analysis that eyes with choroidal nevus showed no statistical significance on the CFT, superficial and deep FAZ, and CD of both superficial plexus and deep plexus compared with the contralateral eyes[24]. In contrast, Valverde et al[24] found that eyes with melanoma showed significant increase on CFT, enlarged superficial and deep FAZ, as well as the reduction in CD of superficial and deep plexus. Therefore, they suggested that OCTA could be a useful modality for the differential diagnosis between choroidal nevus and melanoma. Further, Li and her colleagues demonstrated that significant enlargement of deep FAZ and significant reduction in CD of superficial and deep plexus in the eyes with treatment-naive choroidal melanoma compared with fellow eyes, besides, they demonstrated that the parafoveal microvascular changes had an inverse correlation with the presence of SRF and the increasing tumor size[25]. Interestingly, Sioufi and colleagues[14], for the first time, reported that eyes with previous or current CME and/or SRF had reduced CD of deep plexus in a retrospective chart review of 14 patients with CCH (9 patients had previous or current CME and/or SRF and 5 patients had no CME and/or SRF). In this retrospective chart review study, Sioufi reported that the CD of superficial plexus as well as the FAZ area of superficial and plexus had no statistical significance compared with the contralateral “normal” eyes among the 9 patients with CCH who had previous or current CME and/or SRF[14]. However, some ophthalmologists considered that the contralateral “normal” eyes of patients with CCH are not absolutely normal[5, 18]. For example, Kim et al revealed that elevated choroidal thickness and increased risk of central serous chorioretinopathy in the fellow eyes of patients with CCH[5]. Therefore, it is necessary to quantitative evaluation of parafoveal microvasculature changes in eyes with exudative CCH compared with healthy normal eyes. In our cross-sectional, case-control study with 82 eyes of eight-two subjects, we revealed that the CD of superficial plexus and deep plexus as well as choriocapillaris significantly decreased in eyes with exudative CCH compared with age- and gender-controlled healthy eyes (Table 2). To further know whether the decreased CD of retinal superficial plexus, deep plexus, and choriocapillaris as we as the FAZ area had correlation with baseline BCVA, the Pearson’s correlation analysis revealed that baseline BCVA was not correlated with any of the parameters including CD of retinal superficial plexus, deep plexus, choriocapillaris, or the FAZ area.

Specifically, our study for the first time revealed that the CD of choriocapillaris decreased in eyes with exudative CCH. As we know, retinal oxygen consumption is much higher in the macula[26–29]. The reduction in blood flow from choriocapillaris secondary to exudative CCH would lead to metabolic stress and ischemia, which would stimulate factors to promote tumor vascularization such as VEGF-A[30, 31]. As we know, VEGF-A may affect the permeability of blood vessels and cause macular edema or aggravate preexisting macular edema. Therefore, we speculated that CD of choriocapillaris might be used as an indicator of the effectiveness of treatments for exudative CCH. Further exploration of this hypothesis could reveal the correlation of parafoveal microvasculature changes and exudative CCH.

Limitations of this study included relatively small number of enrolled subjects. Besides, only exudative CCH which caused CME and/or SRF were included. We believed that future study including eyes with CCH without CME or SRF would provide more information about parafoveal microvasculature changes for

various kinds of CCH. However, even with these limits, our age- and gender-controlled study provided some valuable information for the parafoveal microvasculature changes in eyes with exudative CCH compared with healthy eyes.

Conclusion

In conclusion, OCTA is a rapid, non-invasive, high-resolution procedure with which could monitor the parafoveal microvasculature changes in eyes with exudative CCH. Our study revealed that not only the vessel density of the superficial vascular complex and deep vascular complex of retina but also the vessel density of choriocapillaris significantly decreased in eyes with exudative CCH compared with age- and gender-controlled healthy eyes.

Abbreviations

CCH
circumscribed choroidal haemangioma; SRFsubretinal fluid; CME:cystoid macular edema; FA:fluorescein angiography; ICGA:indocyanine green angiography; EDI:enhanced depth imaging; OCT:optical coherence tomography; OCTA:optical coherence tomography angiography; CD:capillary density; IRB:Institutional Review Board; BCVA:best-corrected visual acuity; CFT:central foveal thickness; FAZ:foveal avascular zone; BRM:Bruch's membrane; ILM:internal limiting membrane; OPL:outer plexiform layer; logMAR:logarithm of minimal angle of resolution.

Declarations

Ethics approval and consent to participate

This study was approved by Institutional Review Board of Sun Yat-sen University and the study was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consents from the guardians were obtained after explanation of the nature and possible consequences of the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

KL and CH conducted the study, contributed to the data analysis, and drafted the paper. YZ, FX, XZ, LC, YG, and LL made contributions to acquisition of data and drafting. CJ contributed to the design of the study, analysis for the data, and was responsible for revising the paper. All authors have read and approved the manuscript.

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References

1. Shields CL, Honavar SG, Shields JA, Cater J, Demirci H. Circumscribed choroidal hemangioma: clinical manifestations and factors predictive of visual outcome in 200 consecutive cases. Ophthalmology. 2001;108(12):2237–48.
2. Zhang Y, Liu W, Fang Y, Qian J, Xu G, Wang W, Li L, Shen Y, Gao Q. Photodynamic therapy for symptomatic circumscribed macular choroidal hemangioma in Chinese patients. Am J Ophthalmol. 2010;150(5):710–5.e711.
3. Sen M, Honavar SG. Circumscribed choroidal hemangioma: An overview of clinical manifestation, diagnosis and management. Indian J Ophthalmol. 2019;67(12):1965–73.
4. Balasubramaniam SC, Pellegrini M, Staurenghi G, Pulido JS. INFRARED IMAGING OF CIRCUMSCRIBED CHOROIDAL HEMANGIOMAS. Retina (Philadelphia Pa). 2017;37(6):1134–9.
5. Kim RS, Jain RR, Brown DM, Bretana ME, Kegley EN, Singer MA, Aragon AV, Schefler AC. Elevated Choroidal Thickness and Central Serous Chorioretinopathy in the Fellow Eyes of Patients with Circumscribed Choroidal Hemangioma. Ocular oncology pathology. 2018;4(6):375–80.
6. Karimi S, Nourinia R, Mashayekhi A. Circumscribed Choroidal Hemangioma. Journal of ophthalmic vision research. 2015;10(3):320–8.
7. Lee JH, Lee CS, Lee SC. EFFICACY OF DOUBLE DOSE PHOTODYNAMIC THERAPY FOR CIRCUMSCRIBED CHOROIDAL HEMANGIOMA. Retina (Philadelphia Pa). 2019;39(2):392–7.

8. Chawla R, Tripathy K, Sharma A, Vohra R. Swept source optical coherence tomography-angiography of choroid in choroidal hemangioma before and after laser photocoagulation. Indian J Ophthalmol. 2017;65(8):751–4.
9. Gan NY, Zimmer C, Lam WC. Multi-Spectral Imaging of Circumscribed Choroidal Hemangioma Introduction. Opthalmic Surg Lasers Imaging Retin. 2017;48(7):572–5.
10. Flores-Moreno I, Caminal JM, Arias-Barquet L, Rubio-Caso MJ, Catala-Mora J, Vidal-Martí M, Muñoz-Blanco A, Filloy A, Ruiz-Moreno JM, Duker JS, et al. En face mode of swept-source optical coherence tomography in circumscribed choroidal haemangioma. Br J Ophthalmol. 2016;100(3):360–4.
11. Arevalo JF, Shields CL, Shields JA, Hykin PG, De Potter P. Circumscribed choroidal hemangioma: characteristic features with indocyanine green videoangiography. Ophthalmology. 2000;107(2):344–50.
12. Shields CL, Shields JA, De Potter P. Patterns of indocyanine green videoangiography of choroidal tumours. Br J Ophthalmol. 1995;79(3):237–45.
13. Verbeek AM, Koutentakis P, Deutman AF. Circumscribed choroidal hemangioma diagnosed by ultrasonography. A retrospective analysis of 40 cases. International ophthalmology. 1995;19(3):185–9.
14. Sioufi K, Say EAT, Ferenczy SC, Shields CL. PARAFOVEAL MICROVASCULAR FEATURES ON OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN EYES WITH CIRCUMSCRIBED CHOROIDAL HEMANGIOMA. Retina (Philadelphia Pa). 2018;38(6):1091–9.
15. Rojanaporn D, Kaliki S, Ferenczy SR, Shields CL. Enhanced depth imaging optical coherence tomography of circumscribed choroidal hemangioma in 10 consecutive cases. Middle East African journal of ophthalmology. 2015;22(2):192–7.
16. Mao J, Lin J, Zhu L, Liu C, Yu X, Zhang C, Chen Y, Zhang Y, Shen L. **Quantitative Assessment of Retinal Capillary Vessel Density and Foveal Avascular Zone Area in Central Serous Chorioretinopathy Using OCTA**. *Ophthalmologica Journal international d'ophtalmologie International journal of ophthalmology Zeitschrift fur Augenheilkunde* 2020:1–9.
17. Spaide RF, Klancnik JM Jr, Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. JAMA ophthalmology. 2015;133(1):45–50.
18. Sobol EK, Francis JH, Abramson DH, Freund KB, Spaide RF, Barbazetto I. SUBFOVEAL CHOROIDAL THICKNESS AND VASCULAR ARCHITECTURE IN FELLOW EYES OF PATIENTS WITH CIRCUMSCRIBED CHOROIDAL HEMANGIOMA. Retina (Philadelphia Pa). 2020;40(4):758–64.
19. Lai K, Li Y, Zhou L, Zhong X, Huang C, Xu F, Lu L, Ge J, Jin C. Comparison of the effects of photodynamic therapy, intravitreal ranibizumab and combination for polypoidal choroidal vasculopathy under 1 + PRN regimen. BMC Ophthalmol. 2018;18(1):144.
20. Jia Y, Tan O, Tokayer J, Potsaid B, Wang Y, Liu JJ, Kraus MF, Subhash H, Fujimoto JG, Hornegger J, et al. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. Optics express. 2012;20(4):4710–25.

21. Sorour OA, Sabrosa AS, Yasin Alibhai A, Arya M, Ishibazawa A, Witkin AJ, Baumal CR, Duker JS, Waheed NK. Optical coherence tomography angiography analysis of macular vessel density before and after anti-VEGF therapy in eyes with diabetic retinopathy. International ophthalmology. 2019;39(10):2361–71.
22. Or C, Sabrosa AS, Sorour O, Arya M, Waheed N. Use of OCTA, FA, and Ultra-Widefield Imaging in Quantifying Retinal Ischemia: A Review. Asia-Pacific journal of ophthalmology (Philadelphia Pa). 2018;7(1):46–51.
23. de Carlo TE, Romano A, Waheed NK, Duker JS. A review of optical coherence tomography angiography (OCTA). International journal of retina vitreous. 2015;1:5.
24. Valverde-Megías A, Say EA, Ferenczy SR, Shields CL. DIFFERENTIAL MACULAR FEATURES ON OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN EYES WITH CHOROIDAL NEVUS AND MELANOMA. Retina (Philadelphia Pa). 2017;37(4):731–40.
25. Li Y, Say EA, Ferenczy S, Agni M, Shields CL. ALTERED PARAFOVEAL MICROVASCULATURE IN TREATMENT-NAIVE CHOROIDAL MELANOMA EYES DETECTED BY OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY. Retina (Philadelphia Pa). 2017;37(1):32–40.
26. Provis JM, Penfold PL, Cornish EE, Sandercoe TM, Madigan MC. Anatomy and development of the macula: specialisation and the vulnerability to macular degeneration. Clinical experimental optometry. 2005;88(5):269–81.
27. Curcio CA. Photoreceptor topography in ageing and age-related maculopathy. Eye. 2001;15(Pt 3):376–83.
28. Mustafi D, Engel AH, Palczewski K. Structure of cone photoreceptors. Prog Retin Eye Res. 2009;28(4):289–302.
29. Kur J, Newman EA, Chan-Ling T. Cellular and physiological mechanisms underlying blood flow regulation in the retina and choroid in health and disease. Prog Retin Eye Res. 2012;31(5):377–406.
30. Missotten GS, Notting IC, Schlingemann RO, Zijlmans HJ, Lau C, Eilers PH, Keunen JE, Jager MJ. Vascular endothelial growth factor a in eyes with uveal melanoma. Archives of ophthalmology (Chicago Ill: 1960). 2006;124(10):1428–34.
31. Strozyk EA, Desch A, Poeppelmann B, Magnolo N, Wegener J, Huck V, Schneider SW. Melanoma-derived IL-1 converts vascular endothelium to a proinflammatory and procoagulatory phenotype via NFκB activation. Exp Dermatol. 2014;23(9):670–6.
32. Legends.

Figures

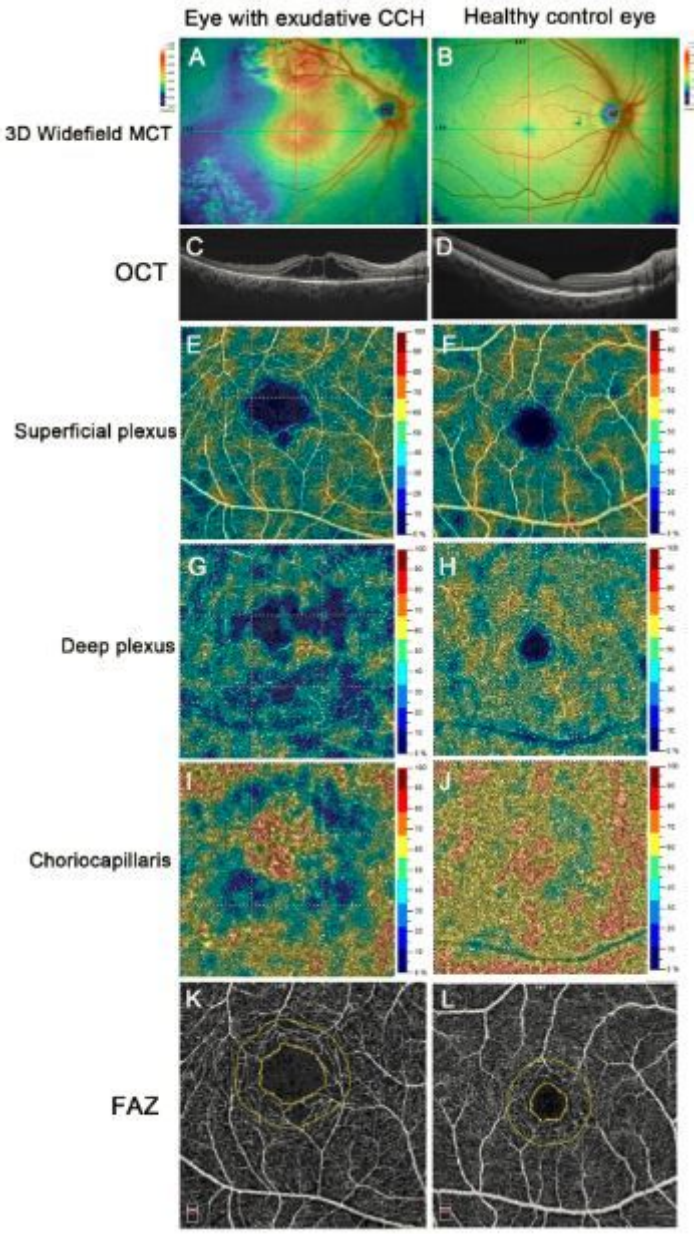

Figure 1

Representive images of an eye with exudative circumscribed choroidal haemangioma (CCH) and a healthy control eye on optical coherence tomography angiography (OCTA). The images on left column were the OCTA images of the right eye in a patient with exudative CCH and the images on the right column were the OCTA images of the healthy right eye in an age- and gender-controlled healthy volunteer. (A) The 12 × 9 mm 3D Widefield MCT scan provided an overview of the retinal thickness, which obviously showed the CCH with its edge superior to the foveola together with increased central foveal thickness (CFT). (B) showed the normal retinal thickness in the healthy eye. (C) showed cystoid macular edema (CME) on OCT in the eye with exudative CCH. (D) showed the normal CFT in the healthy eye. (E-J) showed that the capillary density (CD) of superficial plexus (E-F), deep plexus (G-H), and the CD of choriocapillaris (I-J) significantly reduced in the eye with exudative CCH compared with the healthy control eye, respectively. (K) showed the area of foveal avascular zone (FAZ) was smaller than that of the healthy eye

(L), however, no statistical significance was found between the exudative CCH group and the healthy eye control group (P = 0.164).

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