Original Article

Understanding the structural changes following photodynamic and transpupillary thermotherapy for choroidal hemangioma using optical coherence tomography and optical coherence tomography angiography

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Purpose: To study optical coherence tomography (OCT) and optical coherence tomography angiography (OCT-A) features of circumscribed choroidal hemangioma (CCH) following treatment with photodynamic therapy (PDT) and transpupillary thermotherapy (TTT). **Methods:** A retrospective chart review of consecutive patients treated for CCH over 2 years (May 2016–April 2018). The investigations, in addition to comprehensive eye examination, included color fundus photography, B-scan ultrasonography, OCT, and OCT-A. **Results:** The study included 16 eyes of 16 patients (9 males and 7 females). The mean age at presentation was 43.5 ± 9 years (range 33–62 years). Macula (*n* = 6) and superior arcade (*n* = 5) were the common tumor locations. Twelve eyes received multiple treatment sessions: TTT (seven eyes; mean 2.4 sessions) and PDT (five eyes; mean 2 sessions). Four eyes were observed because vision was not threatened. Pretreatment OCT features were Bruch's membrane atrophy (15 eyes), retinal pigment epithelial atrophy (13 eyes), outer retinal abnormalities (12 eyes), and macular subretinal fluid (12 eyes). Pretreatment OCT-A features were complete loss of choriocapillaris (16 eyes), irregularly arranged fine arborizing vessels (11 eyes), and more than 50% signal void hyporeflective areas (12 eyes). Posttreatment OCT-A showed persistence of choriocapillaris loss, flat scar with fibrosis and thinning of choroid in all eyes treated with TTT, and persistence of deeper choroidal vessels and no loss of choriocapillaris in eyes treated with PDT. **Conclusion:** OCT and OCT-A help understand the structural outcome following PDT and TTT in circumscribed choroidal hemangioma.

Key words: Circumscribed choroidal hemangioma, optical coherence tomography, optical coherence tomography angiography, photodynamic therapy, transpupillary thermotherapy

Choroidal hemangioma is a rare, benign vascular tumor presenting as a solitary, well-defined, circumscribed lesion or a diffuse variant, which is usually associated with Sturge–Weber syndrome.[1,2] A circumscribed choroidal hemangioma (CCH) usually presents as a solitary, orange-colored elevated lesion with or without surrounding exudative retinal detachment. It is most commonly seen posterior to the equator and typically around the optic disc or involving the macula. In most instances, it is diagnosed clinically by its characteristic location and typical appearance though, it may be misdiagnosed with either amelanotic choroidal melanoma or choroidal metastasis. Ultrasonography (USG) with its characteristic features such as acoustic solidity, high surface reflectivity, and internal reflectivity confirms the diagnosis. A majority of the tumors at the posterior pole are asymptomatic, but may cause reduction of vision when associated with exudative retinal detachment, subretinal fluid (SRF), and cystoid macular edema (CME). Treatment for choroidal hemangioma is one of the laser therapies – focal laser photocoagulation, transpupillary thermotherapy (TTT), photodynamic therapy (PDT) with or without anti-vascular endothelial growth factor (VEGF) injection, and plaque brachytherapy. These treatments help in shrinkage of the tumor with formation of scar and resolution of fluid from the macular area.[3]

In enhance depth imaging optical coherence tomography (EDI-OCT), choroidal hemagioma appears as sloping choroidal mass with expansion of medium- and large-sized choroidal vessels without compression of choriocapillaris, SRF with speckles, and photoreceptor layer abnormalities.[4] PDT using verteporfin with or without anti-VEGF injection is the most common mode of treatment for CCH close to the optic disc and macula because this form of treatment prevents collateral damage to the surrounding normal areas when compared with focal laser or TTT.[5] The optical coherence tomography angiography (OCT-A) helps in understanding the vascular flow patterns in hemangioma and the structural alterations in the choriocapillaris layer.[6] There is very limited information regarding structural changes occurring at the retinal and

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choroidal layers following PDT or TTT for CCH. In this study, we describe the OCT and OCT-A features of CCH before and after treatment with PDT and TTT.

Methods

A retrospective consecutive case series of patients diagnosed with CCH at a tertiary eye institute from May 2016 to April 2018 were included in this study. All patients received a comprehensive eye examination including the presenting and best-corrected visual acuity, intraocular pressure, slit-lamp examination, and indirect ophthalmoscopy. The diagnosis of CCH was confirmed using multimodal imaging such as A-scan and B-scan USG, fundus fluorescein angiography (FFA), indocyanine green angiography (ICG-A), spectral-domain OCT, and OCT-A. The tumors were classified using the Collaborative Ocular Melanoma Study (COMS) criteria.[7] Spectral-domain OCT (DRI-OCT Triton Swept-source; Topcon, Tokyo, Japan) recorded the location of SRF in relation to the tumor, outer retinal layer abnormalities, and macula status. OCT-A (DRI-OCT Triton Swept-source; Topcon) 12 × 12 mm scan over the tumor area was used to study the superficial retinal, deep retinal, and choriocapillaris layers. A validated semi-automated segmentation algorithm was applied to identify relevant retinal layers, and manual corrections were performed as necessary to ensure accurate segmentation. In particular, we evaluated en face angiograms of the choriocapillaris slab, which was defined by a layer starting at the outer boundary of the Bruch's membrane and ending at approximately 20 μm beneath the Bruch's membrane.

The following baseline features were recorded in all the patients: age, sex, location of tumor, and presenting and best-corrected Snellen's visual acuity converted to logMar for

statistical analysis. Tumor dimensions including base diameter and height of lesion were measured using A- and B-scan USG with a 10-MHz transducer (Sonomed B 3000; Sonomed Technology Inc., Lake Success, New York, NY, USA). A 5-line horizontal and vertical raster OCT scan was performed over the tumor to study its configuration, shadowing, optical reflectivity, Bruch's membrane thickness/atrophy, retinal pigment epithelium (RPE) thickness/atrophy, outer retinal abnormalities, presence of SRF, intraretinal fluid, macular schisis/SRF, and CME. OCT-A using a 12 × 12 mm scan centered over the tumor and the choriocapillary layer documented the arrangement of choroidal vessels, signal void areas, presence of club-shaped choroidal vessels, and hypereflective border at the margin of tumor on OCT-A. FFA and ICG-A were performed in all patients prior to treatment.

All the patients were treated by either multiple sessions of PDT with/without anti-VEGF injection or TTT depending on the tumor location and presence of macular SRF. PDT was the treatment of choice though TTT was offered when the patients could not afford the former treatment. The PDT parameters were as follows: molecule – vertrporfin 6 mg/m^2 body surface (Visudyne; Norvatis Ophthalmics, Hettlingen, Switzerland); wavelength – 689 nm; light dose – 50 J/cm^2; exposure time – 83 s per spot; and instrument – Coherent Lumenis Opal PDT laser (Lumenis Inc., Santa Clara, CA, USA). Depending on the response to PDT estimated by the resolution of SRF at macula and reduction in tumor thickness, multiple sessions of PDT were administered. In one patient, there was inadequate response to PDT, and hence intravitreal anti-VEGF (ranibizumab, 0.5 mg/0.05 mL) was injected a week prior to the schedule day of PDT. The TTT parameters were as follows: instrument –810 nm diode laser (Iris Medical OcuLight SLx; Iridex Corporation, Mountain View, CA, USA);

Table 1: Patient demographic details

Patient	Age	Sex	Location	Pre-op VA	Post-op VA*	Tumor basal diameter pre and post	Tumour thickness pre and post	Treatment	Treatment response	Follow up (months)
1	39	F	Superior	20/40, N36	20/25, N6	10 (5)	4 (2)	TTT (2)	flat scar	10
2	62	F	Inferior	20/100, N18	NA	7.8	3.8	NO		-
3	38	M	Inferior	20/30, N10	20/30, N8	7 (5)	3 (2)	TTT (2)	flat but no fibrosis	6
4	41	F	Temporal	20/20, N6	NA	10	3	NO		-
5	57	F	Superior	20/25, N6	NA	3	1.2	NO		-
6	42	M	Macula	20/500, N36	20/600, N36	10 (5.7)	5 (1.3)	TTT (3)	flat scar with fibrosis	24
7	30	M	Nasal, Mac SRF	20/200, N24	20/125, N24	8 (8)	4 (3.5)	TTT (2)	incomplete scar	4
8	57	M	Superior	20/20, N6	NA	5	2.8	NO		-
9	46	M	Macula	20/200, N24	20/100, N24	NA	NA	PDT (2)+ ACCENTRIX	incomplete scar	15
10	43	F	Superior, Mac SRF	20/50, N36	20/25, N6	8.8 (7)	4 (2)	TTT (3)	flat	4
11	37	F	Macula	20/600, N36	20/125, N18	9 (2)	3 (1.6)	TTT (2)	flat scar with fibrosis	4
12	41	M	Macula	20/40, N18	20/200, N36	10 (10)	4 (4)	PDT (2)	incomplete scar	6
13	45	M	Macula	20/320, N24	20/125, N12	6 (2)	2.5(NA)	TTT (3)	flat scar with fibrosis	6
14	54	M	Macula	20/30, N6	20/50, N24	5.6 (3.4)	3	PDT (2)	persistent srf	5
15	34	M	superior	20/25, N6	20/20, N6	7 (4)	2	PDT (1)	flat	11
16	31	F	Temporal	20/25, N6	20/20, N6	6 (4.5)	2	PDT (2)	flat	4

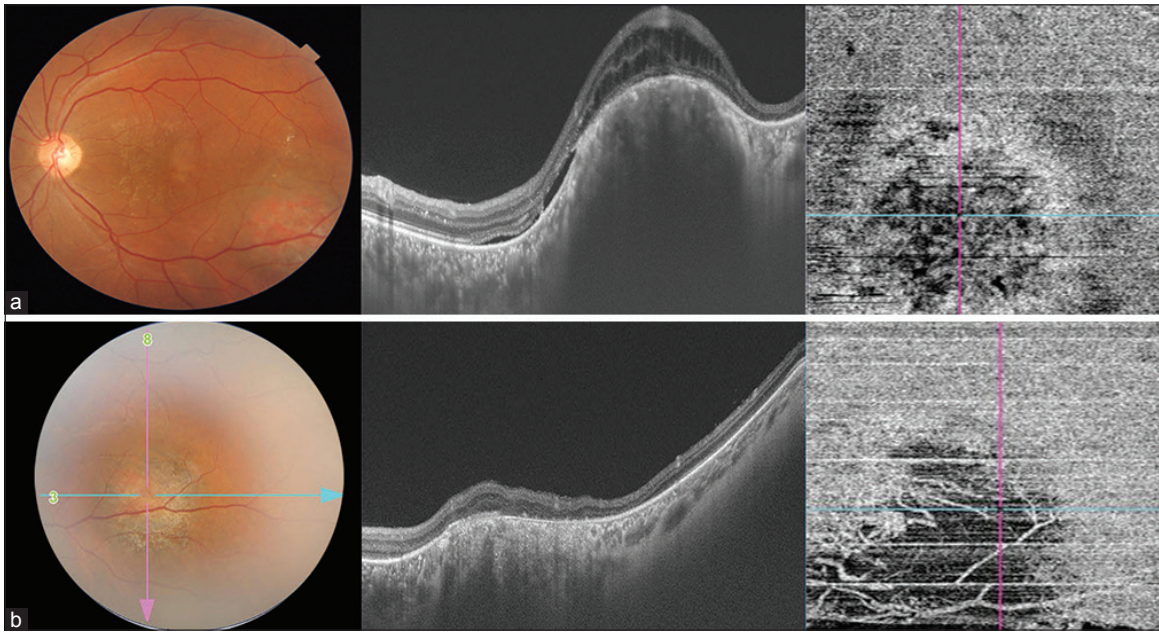*Post op vision of 12 treated eyes are available

Figure 1: (a) Fundus photograph – circumscribed orange-colored elevated lesion seen. OCT – dome-shaped choroidal hemangioma with presence of subretinal and intraretinal fluids over the tumor. OCT A in the choriocapillary layer – hyporeflective areas suggestive of loss of choriocapillaris with irregularly arranged vessels. (b) Fundus photograph post TTT – reduction in tumor size with RPE atrophy. OCT – decrease in tumor height and SRF and atrophy of outer retinal layers. OCT A showed complete loss of choriocapillaris extending beyond the margin of tumor and absence of deeper choroidal vasculature
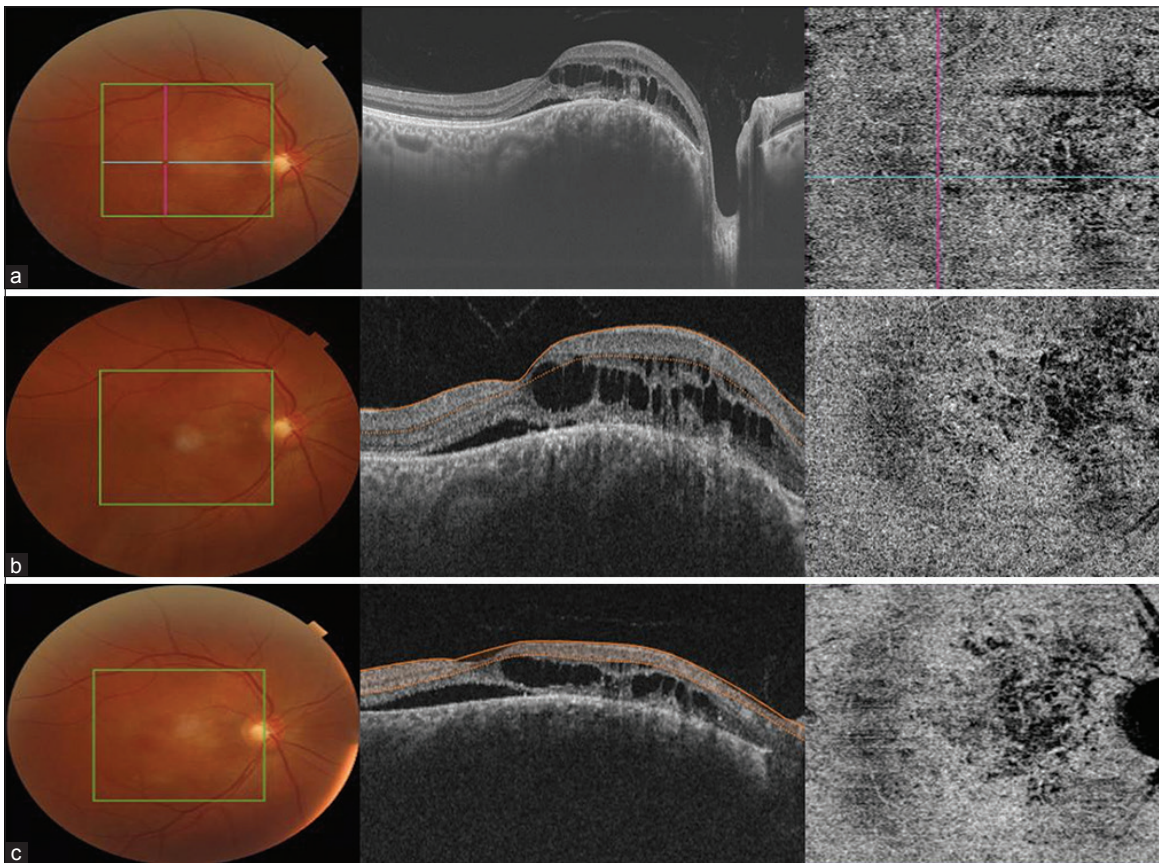
Figure 2: (a) Fundus photograph – orange-colored lesion nasal to macula involving fovea. OCT showed elevated mound of tumor with presence of subretinal and intraretinal fluids. OCT A showed hyporeflective areas suggestive of loss of choriocapillaris. (b) Post first PDT session – OCT showed persistence of SRF fluid with few schitic areas. OCT A showed loss of choriocapillaris with presence of deeper choroidal vasculature. (c) Post second PDT session – OCT showed decrease in tumor size as well as SRF and intraretinal fluids. OCT A showed fewer areas of loss of choriocapillaris and deeper choroidal vasculature

Table 2: OCT and OCTA characteristic features of choroidal hemangioma

Pt	OCT configuration	Shadowing	Optical reflectivity	Bruch mem thick/atrophy	RPE thick/atrophy	IS-OS defect	ELM defect	SRF with deposits	IRF	Outer plexiform deformities	Macular SRF	CME	OCTA-choriocapillary loss	Irregular arranged vessels	Signal void	Club shaped choroidal vessels	Hyperreflective border
1	dome	yes	low	yes	yes	yes	yes	yes	no	no	yes	no	yes	yes	yes <25%	no	yes
2	dome	yes	high	yes	yes	no	no	yes	yes	no	yes	no	yes	yes	yes >50%	yes	no
3	dome	partial	low	yes	yes	no	no	yes	yes	yes	yes	no	yes	yes	yes >50%	no	yes
4	dome	yes	high	yes	no	no	no	no	no	no	no	no	yes	no	yes <25%	no	no
5	plateau	partial	low	yes	no	no	no	no	no	no	yes	no	yes	no	yes <25%	no	no
6	dome	partial	low	yes	yes	yes	yes	yes	yes	yes	yes	no	yes	yes	yes >50%	yes	no
7	dome	yes	low	yes	yes	no	yes	no	yes	yes	no	no	yes	no	yes >50%	no	no
8	plateau	partial	low	no	no	no	no	no	no	no	no	no	yes	no	yes <25%	no	no
9	plateau	partial	low	yes	yes	yes	yes	yes	yes	yes	yes	no	yes	yes	yes >50%	yes	no
10	dome	yes	low	yes	yes	yes	yes	yes	no	no	yes	no	yes	yes	yes >50%	no	no
11	dome	yes	high	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	yes >50%	yes	yes
12	dome	yes	low	yes	yes	yes	yes	yes	no	yes	yes	no	yes	yes	yes >50%	no	yes
13	dome	yes	high	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes >50%	yes	no
14	dome	yes	high	yes	yes	yes	yes	yes	no	yes	yes	no	yes	yes	yes >50%	no	no
15	plateau	partial	low	yes	yes	yes	no	yes	no	no	no	no	yes	yes	yes >50%	no	no
16	dome	yes	high	yes	yes	yes	no	yes	no	no	no	no	yes	yes	yes >50%	no	no

power – 300–400 mw; and exposure duration – 2–5 min. TTT was repeated till complete regression of the tumor.

Complete regression of tumor was defined as a decrease in the height of the lesion with or without scarring/fibrosis and absence of SRF; partial regression was defined as residual lesion with persistent SRF. At the last follow-up, we recorded best-corrected visual acuity and the tumor features on the color fundus photography, B-scan USG, OCT, and OCT-A such as presence/absence of SRF, subretinal deposits, outer retinal layer atrophy, choriocapillaris loss, and signal void areas. Any local complications such as tumor recurrence, persistent or recurrent SRF, and foveal atrophy were noted at the last follow-up.

Statistical analysis

Qualitative variables were described in percentages, and quantitative variables were described by their mean and standard deviation. A P value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS (IBM, SPSS statistics, Version 16; SPSS Inc., Chicago, IL, USA) software.

Results

A total of 16 patients (9 males and 7 females) diagnosed to have CCH were included in the study. The mean age at presentation was 44 + 9 years (median 41.5 years; range 30–62 years). The common tumor locations were at macula (six eyes) and superior quadrant (five eyes). The other baseline characteristics are shown in Table 1. The most common tumor configuration (12 eyes) in our series was smooth, dome-shaped involving macula and superior quadrant. The other configurations were plateau-like (4 eyes) and tumor shadowing (10 eyes). Macular SRF was seen in 12 of 16 eyes. These patients were symptomatic and hence were treated with TTT (n = 7 eyes) or PDT (n = 4 eyes) and PDT with anti-VEGF injection (1 eye). The remaining four patients were asymptomatic and observed for any alteration in visual acuity or increase in tumor size. The mean follow-up was 8 + 6 months (median 6 months; range 4–24 months).

Pretreatment OCT features (16 eyes) were the following: low optical reflectivity (9/16 eyes), Bruch's membrane thickness/atrophy (15/16 eyes), RPE thickening (13/16 eyes), outer retinal abnormalities (12/16 eyes), presence of SRF (12/16 eyes), intraretinal fluid (7/16 eyes), macular SRF (12/16 eyes), and CME (2/16 eyes). Pretreatment OCT-A features (16 eyes) were the following: loss of choriocapillaris (16/16 eyes), hyporeflective lesions with over 50% signal void areas (12/16 eyes), and irregularly arranged vessels (11/16 eyes) [Table 2].

The average TTT sessions were 2.4 and the average PDT sessions were 2. Post treatment, we could obtain artifacts-free OCT and OCT-A quality photographs only in seven patients (seven eyes) [Table 3]. OCT showed characteristic tumor regression features such as complete atrophy of outer retinal layers (7/7 eyes), resolution of SRF above the tumor (TTT 3/3 eyes and PDT 2/4 eyes), resolution of SRF in the macular area (TTT 3/3 eyes and PDT 3/4 eyes), and presence of subretinal deposits (5/7 eyes). OCT-A showed tumor regression features such as complete loss of choriocapillaris (3/7 eyes), partial signal void areas (7/7 eyes), and presence of deeper choroidal vessels (5/7 eyes). SRF was persistent above the tumor (2/5 eyes) and over the foveal area (1/5 eyes) following repeat PDT sessions. In view of persistence of SRF, an intravitreal

Table 3: OCT and OCTA features post treatment in eyes with good images (*n*=7)

Patient	Treatment	SRF above the tumor	Macular SRF	Outer retinal layer atrophy	Total retinal atrophy	Persistent SRF	Subretinal deposits	OCTA Complete loss of choriocapillaries	Partial signal void	presence of deep choroidal vessels
1	TTT (2)	no	no	yes	no	no	yes	yes	yes	no
2	TTT (3)	no	no	yes	yes	no	no	yes	yes	no
3	PDT (2)+ ACCENTRIX	yes	no	yes	no	no	yes	no	yes	yes
4	TTT (2)	no	no	yes	no	no	yes	yes	yes	no
5	PDT (2)	no	no	yes	no	no	yes	no	yes	yes
6	PDT (2)	yes	yes	yes	no	yes	no	no	yes	no
7	PDT (2)	no	no	yes	no	no	yes	no	yes	no

ranibizumab (0.3 mg in 0.05 mL) was injected followed by PDT after 1 week. This resulted in reduction in SRF and height of tumor after 6 weeks. The mean tumor thickness on the USG was 3.08 mm (1.2–5.0 mm) and reduced to a mean of 2.3 mm (1.3–4.0 mm) following treatment. We also observed alteration in the Bruch's membrane, RPE, and outer retinal layers in 11 eyes (70%) patients.

Of seven TTT treated eyes, there was flat scar with complete regression of tumor in six eyes; of five PDT-treated eyes, two eyes showed flat scar, two eyes had partial regression of tumor, and one eye had persistent SRF at macula. The best-corrected visual acuity following treatment improved by 2 or more lines in two TTT-treated eyes and was stable in the remaining five eyes. The vision was stable in three PDT-treated eyes and decreased by 2 more lines in two PDT-treated eyes. Local complications such as persistence of SRF was evident in three eyes, total retinal atrophy in one eye, but in none of the treated eyes there was tumor reactivation at the last follow-up. None of the patients reported any adverse events related to PDT or TTT.

Representative case images of choroidal hemangioma treated with TTT [Fig. 1] and PDT [Fig. 2] showing OCT and OCT-A features depicting structural changes in the outer retinal and choroidal layer are shown.

Discussion

Choriodal hemangioma is usually a clinical diagnosis and is based on the presentation and tumor characteristics. The ancillary tests such as USG, FFA, ICG-A, and OCT may be needed to differentiate it from other diseases.[8-10] Each of these tests provides exclusive and unique information. USG provides the anatomical characteristics of the tumor, FFA and ICG-A provide the retinal vascular features of the tumor, and the OCT provides the deeper retinal and choriocapillaris features. It can also be a useful tool to assess the response to treatment such as the volume reduction and SRF resolution. The tumor thickness measurements in USG and OCT are not interchangeable. It is reported that the tumor thickness measured by ED-OCT is 27% less than that measured by USG.[11] In one-third of the eyes, alterations in Bruch's membrane, RPE, and outer retinal layers are reported in ED-OCT[4] though we observed these alterations in nearly three-quarter of eyes in our series of patients. This might be attributed to either late presentation of the patient or

long-term sequelae in the tumors such as loss of choriocapillaris and deeper choroidal vessels causing atrophy of RPE and Bruch's membrane, and loss of photoreceptors. Similar findings and irregularly arranged vessels in the superficial and deep choroidal layers with signal void areas have been reported previously.[12,13]

The treatment of choroidal hemangiomas is either by TTT or PDT. TTT utilizes 810-nm diode laser with a large spot (2–3 mm), adequate power (300–1200 mW), and long exposure time (2–14 minutes); this increases temperature and causes irreversible cytotoxic effect, sclerosis of vascular channels, and partial or complete tumor regression.[14] Gündüz reported a 42% complete and 53% partial regression of tumor following TTT and at least three-quarters of patients in their reported series improved by 2 or more Snellen lines.[14] These authors also reported the possibility of CME (11.5%), preretinal fibrosis (5%), focal iris atrophy (11.5%), and retinal vascular occlusion (2.5%). PDT causes site-specific regression of tumor without causing damage to the overlying retina and the retinal vasculature. Lack of blood supply leads to apoptosis and necrosis-induced damage of the choroidal vasculature contributing significantly to tumor cell destruction.[15] Invariably, a week after PDT these vessels recanalize, and thus, there is less destruction of the choroidal layers with intact outer retinal layers.[16]

In the treatment of CCH, an anatomical success is defined as the reduction in the macular thickness and resolution of SRF; this is measured by OCT. Functional success is defined as the restoration of foveal anatomy with intact outer retinal layers; this is measured by OCT-A. In our patients, OCT-A showed complete loss of choriocapillaris and absence of deeper choroidal vessels in all TTT-treated eyes (*n* = 7). In the PDT-treated eyes the tumor size reduced without fibrosis; in addition, there was no loss of choriocapillaris and persistence of deeper choroidal vessels. In view of the tumor reduction without damaging the choroidal vessels, PDT should be the treatment of choice in CCH, particularly the ones involving macula and papillomacular bundle. Improvement or stabilization of visual acuity after PDT for CCH reportedly ranges from 73% to 100%.[17] In our series, improvement of vision was recorded in the TTT-treated than the PDT-treated eyes. This is attributed to the fact that the extramacular lesions were preferentially treated with TTT. In a majority of patients, more than one PDT treatment was needed because the treatment goal was also resolution of the tumor, in addition to

the resolution of the subretinal and intraretinal fluids.[18] Partial regression despite two PDT treatment sessions in two of five patients in this series could be attributed to macular location of tumor with basal diameter more than 6 mm and height close to 3 mm. A possible combination of intravitreal anti VEGF with PDT could help in faster resolution of SRF.[19] In general, PDT is more expensive than TTT because the former also involves the photosensitizing dye and the combination of anti-VEGF makes it less affordable. Subthreshold OCT-A-guided TTT could be an alternative to PDT where the OCT-A-guided information on the vascular flow is effectively used to titrate the TTT of CCH.

The limitations of our article include retrospective nature of the study, lesser number of patients, variable follow-up, and lack of standardized treatment protocol for PDT. The strength of our study lies in imaging the choroidal hemangioma on OCT-A following TTT or PDT treatment to study the effect on the outer retinal layers and choroidal vessels.

Conclusion

OCT and OCT-A help in better understanding of the vascular flow patterns in choroidal hemangioma. In addition, the OCT-A imaging can serve as a guide to retreatment following TTT or PDT. PDT leads to lesser tissue damage, but longer implications of these changes are not yet known.

Conflicts of interest

There are no conflicts of interest.

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