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editor@sciencepub.net
nbmeditor@gmail.com

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Optical Coherence Tomography Angiography in Patients with Behcet Uveitis

Ahmed Eisa Abu Zaid, MSc, Amin E. Nawar, MD, FRCS (Glasg), Mohammad El Bradey, MD, Magdy Moussa, MD

Department of Ophthalmology, Faculty of Medicine, Tanta University, Egypt.
E-mail: ahmeabuzaid@gmail.com

Abstract: Purpose: to assess optical coherence tomography angiography (OCT-A) changes in patients with Behcet uveitis (BU). **Method:** This is a prospective, cross-sectional non-interventional study that was carried out on 30 eyes of 18 Behçet uveitis patients compared to 20 eyes of 10 normal subjects matched for age, sex and refraction. Swept source optical coherence tomography (SS OCT) was performed for all cases. OCT-A was also performed to assess areas of capillary non perfusion and to measure the foveal avascular zone (FAZ) in both superficial and deep capillary plexuses (SCP and DCP). **Results:** The BCVA was markedly reduced in patients with BU (,) p value <0.001. Macular edema, peripheral retinal vascular leakage and optic disc hyperfluorescence were the main angiographic findings in BU patients. Epiretinal membrane was the most common presentation in SS OCT followed by cystoid macular edema. Furthermore, FAZ was significantly enlarged in BU patients in both SCP and DCP (,) p value 0.005. BCVA was positively correlated with both SCP and DCP (,) p value 0.033. **Conclusions:** OCT-A is a new imaging modality that can assess foveal ischemia by measuring FAZ in SCP and DCP in BU patients.
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Keywords: Behcet uveitis, Optical coherence tomography angiography, Foveal avascular zone, superficial capillary plexus, Deep capillary plexus.

1. Introduction

Behcet disease (BD) occurs all over the world with tendency to present along the old 'Silk Road' with highest prevalence in Turkey (approximately 80–370 cases per 100,000), Japan and Iran, and lower prevalence in North American and northern European population.[1] BD occurs more frequently in the third decade of life with predilection towards male gender.[2] Recurrent oral ulcers are the most frequent clinical presentation (97-100%), followed by genital ulcers (62-100%), other clinical manifestations are present in variable percentages like erythema nodosum, papulopustular lesions, arthritis, uveitis, thrombophlebitis, gastrointestinal and central nervous system involvement.[1] Ocular manifestations occurs in 40% to 70% of BD patients[3]

Anterior segment affection in the form of iridocyclitis with or without hypopyon, keratitis, episcleritis, scleritis can occur in BD. In addition, posterior segment complications may be present like retinal vasculitis,[4,5] occlusive or non-occlusive periphlebitis, retinal neovessels, optic neuritis, retinal infiltrates and optic disc edema. Furthermore, vitritis, vitreous hemorrhage, traction on the retina may occur with subsequent. reduction of visual acuity.[6]

Optical coherence tomography angiography (OCTA) is a new non-invasive imaging technique. It can provide 3D high-resolution images of different retinal and choroidal vasculature.[7,8] It is superior in visualization of perifoveal microvasculature to fluorescein angiography in inflammatory and non inflammatory retinal and choroidal vascular diseases.[9,10] Recently, a swept-source wide field (SS-WF) OCT angiography (OCTA) device has allowed assessment of capillary perfusion in the posterior pole and mid-periphery.[11]

The aim of our study was to characterize and analyze perifoveal microvascular changes in eyes with Behçet Uveitis using SS-OCTA.

2. Materials and methods

Study design:

This is a prospective, cross-sectional non-interventional study that was carried out on 30 eyes of 18 Behçets uveitis patients presented to Ophthalmology outpatient clinic in Tanta University Hospitals. Results were compared to 20 eyes of 10 normal age/sex/refraction-matched subjects not suffering from any other ocular or systemic disease between January 2019 and January 2020.

Participants:

Diagnosis of BD followed the criteria of ISGBD. All patients presented with clinically active uveitis involving the posterior segment in the form of vitritis in association with retinal vascular sheathing, retinal vascular leakage on FA, retinal infiltrates, optic disc edema, or anterior uveitis.[12] Exclusion criteria included cases with advanced Behçet with ocular complications such as dense cataract, severe vitritis and posterior synechia interfering with pupillary dilatation, patients with media opacity preventing good quality of images, any physical and or mental handicap preventing ability to sit still during the examination, any other retinopathy or vitreoretinal disorders as diabetic retinopathy. Furthermore, patients with previous intraocular surgical interventions as vitrectomy, cataract extraction and laser photocoagulation, high refractive error as high myopia (<6.0 diopters) or hypermetropia (>+6.0 diopters), patients with any contraindication of fundus fluorescein angiography (FFA) such as renal disease, pregnancy or allergy were excluded of our study.

Thorough ophthalmic evaluation was performed for all patients including BCVA using logMAR units for statistical analysis, applanation tonometry to measure the intraocular pressure (IOP), anterior segment examination using slit lamp, posterior segment examination by indirect ophthalmoscopy and slit lamp biomicroscopy.

Colour fundus photography, fundus fluorescein angiography by Heidelberg fluorescein angiography device (Spectralis, Heidelberg, Germany) were performed for all patients at the time of presentation, in addition, *Optical Coherence Tomography (OCT) & Optical Coherence Tomography Angiography (OCTA)* using a swept source OCT device (Topcon DRI OCT Triton Swept source OCT, Topcon, Japan) were done for all cases.

As regarding imaging protocol by swept source OCT (SS OCT) for each patient, radial scan mode was used that comprised 12 radial lines (9 mm or 12 mm in length; 1024 A-scans x 12) centered onto the fovea.

Considering SS OCT-A imaging, the standard acquisition protocol for SS-OCTA images consisted of a 6 x 6 mm^2 area centered onto the fovea. In cases when higher resolution images were needed, 4.5 x 4.5 mm^2 or 3 x 3 mm^2 acquisition areas were used instead. The interface produced by the SS-OCTA software displayed b-scan OCT image with flow overlay. The b-scan showed the automatic segmentation slabs deployed by the software to delineate the superficial capillary plexus (SCP), deep capillary plexus (DCP), outer avascular retina, and choriocapillares and provided a red color code for the retinal vascular plexuses and purple color code for the choriocapillaris.

In OCT-A images, areas of Capillary hypo/non-perfusion appeared as irregular grayish areas with hypointensity. For quantitative analysis FAZ was measured manually in both the SCP and DCP in square millimeters.

Statistical Analysis

All data collected in the study were entered into an electronic database via Microsoft Excel 2013 (Microsoft Corp., Redmond, WA). Statistical analysis was performed using Statistical package for the Social Science (SPSS) Statistics Version 16 (IBM, Armonk, New York, USA). Continuous variables were reported as Mean ± Standard Deviation (SD). Chi-square and Fisher-exact tests were used for comparing categorical variables and Wilcoxon signed rank test for numerical variables.

3. Results

Demographic data of all patients and control group were illustrated in table (1). The BCVA was markedly reduced on patients with BD with p value <0.001 as illustrated in table (2). Macular edema, peripheral retinal vascular leakage and optic disc hyperfluorescence were the main angiographic findings in BD patients as illustrated in table (3). As regarding structural macular changes detected by SS OCT, epiretinal membrane was the most common presentation followed by cystoid macular edema, ~~and~~ foveal atrophy and finally subretinal fluid, this is summarized in table (4). FAZ area was enlarged in BD patients in both SCP and DCP compared with control group with statistical significance with p value 0.005 as illustrated in tables 5,6. The BCVA was positively correlated with both SCP and DCP with statistical significance only with SCP with p value 0.033 as shown in table 7 and figure 1. Areas of capillary hypo/non perfusion by OCT-A was detected in 24 eyes of BU compared to 13 eyes detected by fundus fluorescein angiography.

Table 1: Age (years) & Sex:

		Groups				T-Test	
		Patients		Control		t	P-value
Age (year)	Range	22 - 48		27 - 35		0.790	0.434
	Mean ± SD	32.900 ± 7.378		31.000 ± 2.749			
Male		14	78%	6	60%	1.600	0.206
Female		4	22%	4	40%		
Total		18	100%	10	100%		

Table 2: BCVA (LogMAR)

BCVA (LogMAR)	Groups		T-Test	
	Patients	Control	t	P-value
Range	0 - 1	0 - 0.2	6.950	<0.001*
Mean ±SD	0.780 ± 0.303	0.100 ± 0.082		

Table 3 FFA Changes

	Yes		No	
	N	%	N	%
Macular edema	17	56.67	13	43.33
Retinal vascular leakage Periphery	16	53.33	14	46.67
Optic disc hyperfluorescence	15	50.00	15	50.00
Peripheral ischemia	11	36.67	19	63.33
Posterior pole ischemia	13	43.33	17	56.67
Retinal or optic disc neovascularizations	4	13.33	26	86.67

Table 4: Structural assessment by SS-OCT

	Yes		No	
	N	%	N	%
Subretinal fluid	5	16.67	25	83.33
Epiretinal membrane	17	56.67	13	43.33
Foveal atrophy	11	36.67	19	63.33
Cystoid macular edema	16	53.00	14	47.00

Table 5 FAZ in SCP by OCTA

FAZ area in the SCP (mm^2)	Groups		T-Test	
	Patients	Control	t	P-value
Range	0.195 - 1.292	0.251 - 0.325	2.953	0.005*
Mean ±SD	0.537 ± 0.257	0.295 ± 0.024		

Table 6 FAZ in DCP by OCTA

FAZ area in the DCP (mm^2)	Groups		T-Test	
	Patients	Control	t	P-value
Range	0.331 - 4.740	0.354 - 0.501	2.982	0.005*
Mean ±SD	0.742 ± 0.315	0.440 ± 0.053		

Table 7 Relation between BCVA (LogMAR) and Foveal Atrophy and Epiretinal Membrane

		BCVA (LogMAR)			T-Test	
		N	Mean	± SD	t	P-value
Foveal atrophy	Yes	11	0.955	± 0.121	2.632	0.014*
	No	19	0.679	± 0.333		
Epiretinal membrane	Yes	17	0.941	± 0.133	4.160	<0.001*
	No	13	0.569	± 0.338		

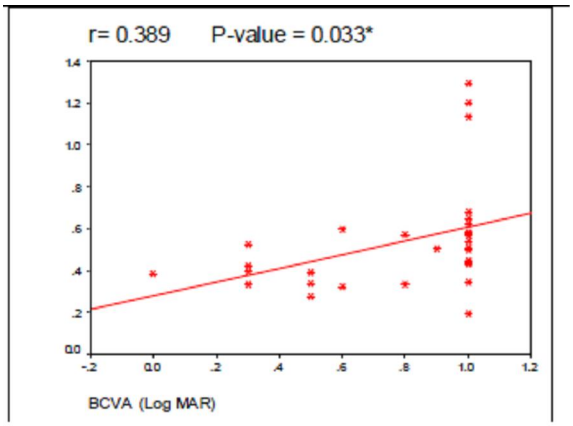

Figure (1): Correlation between the BCVA and FAZ area in SCP showing positive correlation with p value 0.033.

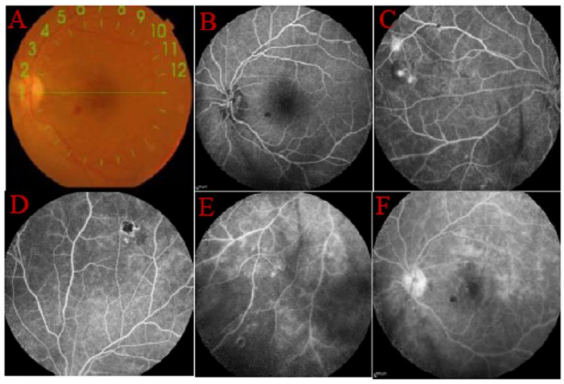

Figure (2): (A) Color fundus photo showing blunted foveal reflex, attenuated vessels and parafoveal hemorrhage.

(B-F) FFA (early and late phases) showing multiple vitreous floaters, late disc edema (hot disc), diffuse macular edema. There are large areas of capillary non-perfusion at the retinal midperiphery with late staining of large retinal veins.

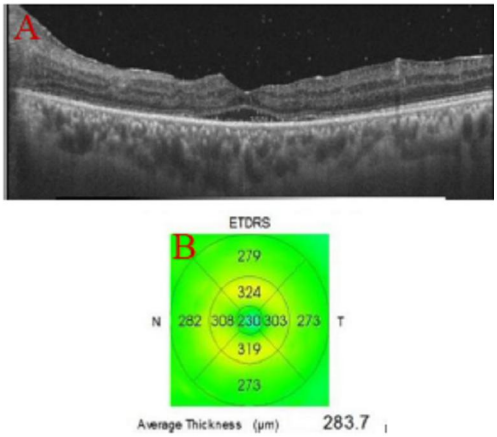

Figure (3): (A) SS-OCT horizontal line scan passing through the fovea showing diffuse macular edema with shallow neurosensory macular detachment and totally adherent epiretinal membrane ERM. (B) Macular map analysis shows increased macular thickness with central thickness of 230 µm.

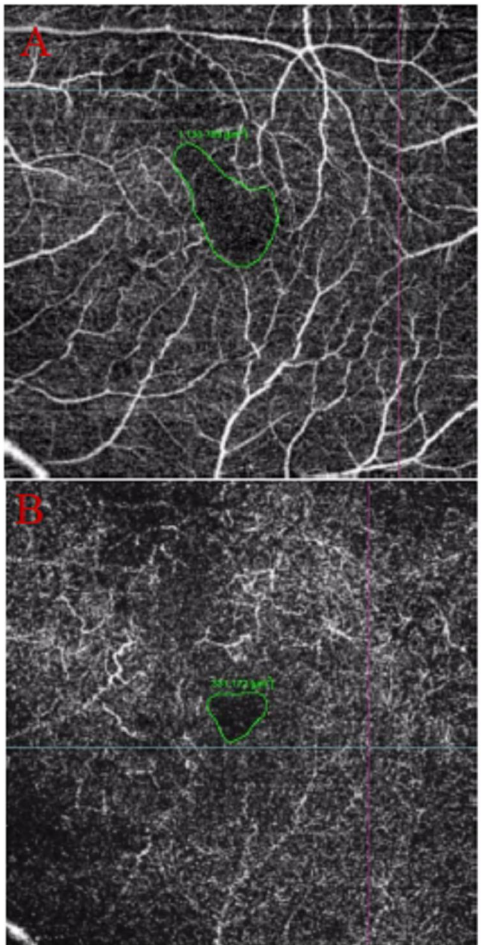

Figure (4): OCT-A (6x6 mm2 scan) showing (A) FAZ area =1.133 mm2 in SCP & (B) FAZ area = 0.331 mm2 in DCP. There are parafoveal hypo/nonperfusion (ischemia involving 2 quadrants) of SCP and DCP.

4. Discussion

Behcet disease is one of the most important causes of loss of vision resulting in bilateral non-granulomatous posterior or panuveitis.[13] Fundus fluorescein angiography (FFA) and OCT are the main tools for diagnosis and follow up of cases of Behcet uveitis (BU).[14] This prospective study evaluated perifoveal microvascular changes in eyes with BU using SS-OCTA and detected the presence of hypo/non-perfusion areas with enlargement of FAZ areas of both SCP and DCP.

In the present study, Behcet uveitis (BU) was mainly detected in males with a mean age of 32 years. This is coincident with F.M. Türkcü, et al [15] and M. KHAIRALLAH, et al [16] who detected more male predominance with a mean age of 33 years and 31 years respectively.

In our cohort, the BCVA (LogMAR) for BU patients was markedly reduced as compared to control group (P<0.001). Moreover, the study observed that the main OCT findings in BU patients were cystoid macular edema (CME) and epiretinal membrane (ERM). Similarly, S. Emre, et al[17] and R. Agrawal, et al[18] reported the presence of CME & ERM in most patients as the main OCT finding in BU affecting visual prognosis.

This study reported areas of capillary hypo/non-perfusion in both SCP and DCP as the most common OCTA finding with enlarged FAZ in SCP and DCP compared to control group. These results were statistically significant (P=0.005). These OCTA findings appear to be consistent with S. Emre, et al[17] and T. Somkijrungroj, et al[19] who documented more ischemia in the DCP, this was explained that the DCP is not directly connected to arterioles.[20]

Regarding our study, the BCVA was significantly correlated with FAZ ~~area~~ in SCP, this is similar to F.M. Türkcü, et al[15] M. KHAIRALLAH, et al[16] and E. Coskun, et al [21] who reported a positive correlation between FAZ & BCVA denoting that macular ischemia is the main factor affecting visual prognosis in BU.

Furthermore, M. Waizel, et al [22] reported that FAZ ~~areas~~ of SCP and DCP were significantly enlarged in comparison to the control group but in contrast to our study, the correlation between the FAZ area of SCP or DCP and the BCVA was not statistically significant.

OCT-A detected capillary hypo/non perfusion in 24 eyes compared to 13 eyes of posterior pole ischemia detected by FFA confirming the superiority of OCT-A over FFA in detecting macular ischemia, however, FFA proved to be superior to OCTA in detecting optic disc hyperfluorescence, vasculitis as peripheral leakage that can't be detected by OCTA, rendering it indispensable tool for BU management.[16]

Our study has several limitations, first, the sample size is relatively small. Second, quantitative analysis of FAZ ~~area~~ was performed manually. Third, the correlation between disease duration and FAZ areas was not performed. In addition, patients were evaluated at different points of time irrespective the management of BU, so further studies are needed to correlate these findings with the treatment received. A final limitation that scanning of the macular area with OCT-A was restricted to an area of 6 x 6 mm^2 and additional 9 x 9 mm^2 imaging would be needed to identify peripheral lesions.

Conclusion:

Foveal ischemia detected by enlarged FAZ areas in SCP and DCP detected by OCT-A contributes in visual deterioration in BU patients.

None of the authors has any financial interest to disclose.

No conflicts of interest.

Declarations

Ethics Approval and Participants' Consents

The Ethical Committee of the Faculty of Medicine, Tanta University, Egypt approved the research. Written consent was obtained from all participants.

Consent for Publication

Not available

Data Availability

The datasets used during the current study are available from the corresponding author on a reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contribution

AME performed ophthalmic clinical and ophthalmological evaluation of all patients, MM performed data collection for all patients and statistical analysis, ME shared in performing ophthalmic investigations like fundus fluoresceine angiography, OCT-A for all patients, AEN performed shared in performing ophthalmic investigations like fluoresceine angiography and OCT-A and follow up of all patients, all authors contributed in writing, editing approval and revision of the manuscript.

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