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Choroidal thickness alterations in idiopathic acute retinal vasculitis

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Abstract

Background: To evaluate changes in sub-foveal choroidal thickness in patients with acute idiopathic retinal vasculitis compared with age-matched healthy subjects and unaffected fellow eyes.

Methods: This prospective observational study included 36 eyes of 23 acute idiopathic retinal vasculitis patients (group V) which included a sub-group of 10 eyes of 10 patients with unilateral vasculitis (group UV), and 50 eyes of 25 healthy subjects (group N). The assessment involved demographics, systemic examination, comprehensive ocular examination, fundus photography with/without fundus fluorescein angiography, and spectral domain–optical coherence tomography with enhanced depth imaging.

Results: There was significant difference between the mean sub-foveal choroidal thickness in groups V and N (V: 338.86 ± 28.72 um; N: 296.72 ± 19.45 μm; $p < 0.001$). The eyes of patients with unilateral vasculitis compared with unaffected fellow eyes had no significant difference in best corrected visual acuity (group UV: median = 0.2; range = (0.0–0.3) and group N: median = 0.2; range = (0.0–0.3); $p = 0.35$) but the sub-foveal choroidal thickness was significantly increased in the involved eye (group UV: 333.5 ± 16.68 um; group N: 284.4 ± 15.68 um; $p \leqslant 0.001$). The BCVA was significantly lower in the eyes with anterior chamber inflammation (median = 0.2; range = (0.0–0.3) and; median = 0.1; range (0.0–0.3); $p = 0.002$), but there was no statistically significant difference in sub-foveal choroidal thickness measurement between the two groups of vasculitis patients with and without anterior chamber inflammation (334.3 ± 18.85 um and 336 ± 31.56 um; $p = 0.22$).

Conclusion: The sub-foveal choroidal thickness increases during active inflammation in eyes with idiopathic retinal vasculitis compared with unaffected fellow eyes and healthy control eyes. Thus, measurement of the sub-foveal choroidal thickness on optical coherence tomography with enhanced depth imaging can serve as a non-invasive modality in the diagnosis and monitoring of acute idiopathic retinal vasculitis.

Keywords: choroidal thickness, idiopathic retinal vasculitis, sub-foveal choroidal thickness

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Introduction

Retinal vasculitis is an inflammatory pathology involving retinal vessels which can potentially lead to blindness.[1,2] The typical diagnostic ophthalmoscopic finding is perivascular sheathing which is best demonstrated by vascular staining and dye leakage on fluroscein angiography (FA).[3] Retinal vasculitis can be either primary (idiopathic) or secondary to bacterial, viral, fungal, or parasite infections and retinal vasculitis associated with systemic diseases such as Behcet's disease (BD).[4]

Retinal vasculitis with an infectious etiology and with BD is known to involve the choroid in certain histo-pathological studies demonstrating diffuse infiltration of inflammatory cells into the choroidal layers.[5] The primary site of ocular involvement in vasculitis is the retina but a few studies have also reported choroidal abnormalities as well in

BD in acute stages.[6–9] Published literature on choroidal thickness measurement in retinal vasculitis is mainly available on secondary vasculitis due to infective or BD. In view of absence of studies on evaluation of choroidal involvement in idiopathic retinal vasculitis, we conducted a prospective observational study to measure the sub-foveal choroidal thickness (SFCT) in: (1) patients of idiopathic retinal vasculitis and compared changes in SFCT with (2) age-matched control healthy subjects as well as (3) healthy eyes of unilateral idiopathic retinal vasculitis subjects. Our study aimed to determine whether choroidal thickness is altered in idiopathic retinal vasculitis also, as observed in secondary retinal vasculitis of infective etiology or commoner entity like BD.

Methods

A prospective observational study was conducted in a tertiary eye care institute in North India from June 2017 to May 2018.

The different study groups and their inclusion criteria were as follows: vasculitis group V: patients with acute idiopathic retinal vasculitis with no history of treatment with drugs or laser presenting within 1 month of onset of symptoms; normal group N: eyes of age-matched healthy control subjects and unilateral vasculitis group UV: a sub-group of uniocular involved eyes of retinal vasculitis patient.

The exclusion criteria are as follows: (1) history of treatment with oral steroids for current episode of vasculitis or any other disorder; (2) history of treatment with laser for vasculitis or any other retinal condition; (3) patients with retinal vasculitis because of an identifiable cause (e.g. infection, ischemia, malignancy, or systemic association such as BD); (4) vitreoretinal disorders other than retinal vasculitis currently or in the past; (5) cases with associated choroiditis active or old detected clinically or on fundus fluroscein angiography (FFA); (6) spherical equivalent of refractive error $\geq \pm 6$ D; (7) any media opacity likely to cause attenuation of signal strength in optical coherence tomography (OCT); (8) signal strength 6/10 in OCT; (9) currently on any drugs likely to alter the choroidal thickness; (10) patients with Mantoux reading of $>15 \times 15$ mm.

The diagnosis of retinal vasculitis was made on the ophthalmoscopic criterion of cells in the vitreous associated with clinical evidence of retinal vessels exudation, hemorrhage, retinal edema, and fluorescein angiographic features leakage of dye from retinal vessels with staining of vessel wall.

A detailed systemic and ocular history (onset of symptoms, present, and previous treatments), the demography (age and gender), laterality, systemic co-morbidities were recorded. A detailed history of systemic features in form of oral or genital ulcers, skin lesions, weight loss, chronic cough, and fever was obtained to rule out systemic inflammation/infection.

The clinical examination included assessment of the best corrected visual acuity (BCVA) in Snellen, spherical equivalent of the refractive status of the eye, slit lamp examination of anterior segment for anterior chamber cells/flare, fundus examination using slit lamp with a contact lens or non-contact lens, indirect ophthalmoscopy, digital fundus photography, and FFA were performed. All patients underwent comprehensive blood investigation to rule out infections in the form of complete blood count, syphilis serology, serum calcium/angiotensin-converting enzyme test, chest X-ray, Montoux test, and contrast-enhanced computed tomograph—chest in suspected cases of tuberculosis/sarcoidosis. All eyes underwent OCT with enhanced depth imaging (EDI) to assess the SFCT, using spectral domain OCT (Carl Zeiss Meditec, Inc., 5160 Hacienda Drive, Dublin, CA 94568, USA). The assessment of choroidal thickness was made by a masked observer who was not aware of retinal status of the subjects. The SFCT was measured using the EDI-OCT technique with two perpendicular foveal scans. The fovea was scanned with HD Cross 10-line protocol, with five horizontal and five vertical (eight times averaged) 6-mm B-scans, spaced 0.075 mm apart. Horizontal and vertical line scans centered on the fovea were performed for each eye for SFCT which was described as the distance between the base of the sub-foveal retinal pigment epithelium and the margin of the choroidoscleral junction.[10] All measurements were performed between 08:00 hours and 10:00 hours to avoid diurnal variation in choroidal thickness and were adjusted for axial length. The choroidal thickness measurements, that is, the average of the two scans (vertical and horizontal) was considered as the sub-foveal CT. The various clinical and tomographic features were compared between different groups.

Table 1. Comparison of demographics, clinical features and sub-foveal choroidal thickness in healthy controls (N), patients with acute idiopathic retinal vasculits (V) and uniocular involved eyes of retinal vasculitis (UV) patients compared with contralateral healthy eyes.

Characteristic	Vasculitis group "V" ($n = 36$)	Control group "N" ($n = 50$)	Unilateral vasculitis group "UV" ($n = 10$)	Contralateral eyes group "CUV"($n = 10$)	*p* value
Age	34.61 ± 10.48	32.18 ± 10.30	34.61 ± 10.48	32.18 ± 10.30	0.19
BCVA	Median = 0.2; Range = (0.0–0.3)	Median = 0.2; Range = (0.0–0.3)	Median = 0.2; Range = (0.0–0.3)	Median = 0.2; Range = (0.0–0.3)	0.87
CT	338.86 ± 28.72	296.72 ± 19.45	338.86 ± 28.72	296.72 ± 19.45	<0.001*

BCVA, best corrected visual acuity; CT, choroidal thickness; CUV, contralateral healthy eyes of unilateral vasculitis patients; N, normal healthy age-matched controls; UV, uniocular involved vasculitis patients; V, vasculitis patients.
*Statistically significant.

Statistical analysis

The numerical variables between any two groups were compared using Mann–Whitney *U* Test. Kolmogorov–Smirnov Test was used for testing the normality of data. A generalized estimating equations (GEE) model was used to adjust for inter-eye correlations. *P* value of <0.05 was taken as statistically significant.

Results

This study evaluated 36 eyes of 23 patients in group V (patients with acute idiopathic retinal vasculitis), out of which sub-group of 10 eyes of 10 cases in group UV (uniocular involved eyes of retinal vasculitis patient), and 50 eyes of 25 age-matched normal subjects with no features of vasculitis or any other ocular disease (group N).

The baseline features of the subjects in three groups are summarized in Table 1. The baseline characteristics in all the groups were comparable in terms of the mean age (group V: 34.61 ± 10.48 years; group UV: 34.21 ± 10.48 years; $p = 0.19$; group N: 32.18 ± 10.30; $p = 0.19$), BCVA (group V: median = 0.2; range = (0.0–0.3); group UV: median = 0.2; range (0.0–0.3); $p = 0.87$; group N: median = 0.2; range = (0.0–0.3); $p = 0.87$) and duration of presentation of vasculitis. A representative EDI-OCT image showing the choroid of a healthy subject and that of an eye with acute idiopathic retinal vasculitis, is illustrated in Figure 1(a) and (b). There was significant difference between the mean SFCT in groups V and N (V: 338.86 ± 28.72 um; N: 296.72 ± 19.45 μm; *p* value < 0.001). The eyes of patients with unilateral vasculitis compared with unaffected fellow eyes had no significant difference in BCVA (group UV: median = 0.2; range = (0.0–0.3); group N: median = 0.2; range = (0.0–0.3); $p = 0.35$) but the SFCT was significantly increased in the involved eyes (group UV: 333.5 ± 16.68 um; group N: 284.4 ± 15.68 um; *p* value ≤ 0.001) as shown in Table 1 and as depicted in EDI-OCT image of unilateral vasculitic eye compared with fellow healthy in Figure 2(a) and (b). All eyes with acute idiopathic retinal vasculitis (36 eyes of 23 patients in group V) showed features of active vasculitis on FFA like perivascular hyperfluroscence (focal/diffuse) with capillary non-perfusion areas of varying degree. Patients with neovascularization elsewhere in association with active vasculitis were treated with sectoral/pan retinal photocoagulations and were excluded from study.

Vitreous inflammation was present in all affected patients but group-specific analysis revealed active anterior chamber inflammation in only 10 of affected 36 eyes. BCVA was significantly lower in eyes with anterior chamber inflammation and with no inflammation (median = 0.2; range = (0.0–0.3); and median = 0.1; range = (0.0–0.3); *p* value = 0.002), but there was no statistically significant difference in SFCT measurement between two groups; vasculitis patients with and without anterior chamber inflammation (334.3 ± 18.85 um and 336 ± 31.56 um; $p = 0.22$) as shown in Table 2.

Discussion

In the Indian subcontinent, idiopathic retinal vasculitis is reported by Dogra and colleagues[11] as the second-most common cause of all vasculitis cases, next only to tuberculosis, thus making it an important clinical entity affecting many patients. The primary site of ocular structure involvement

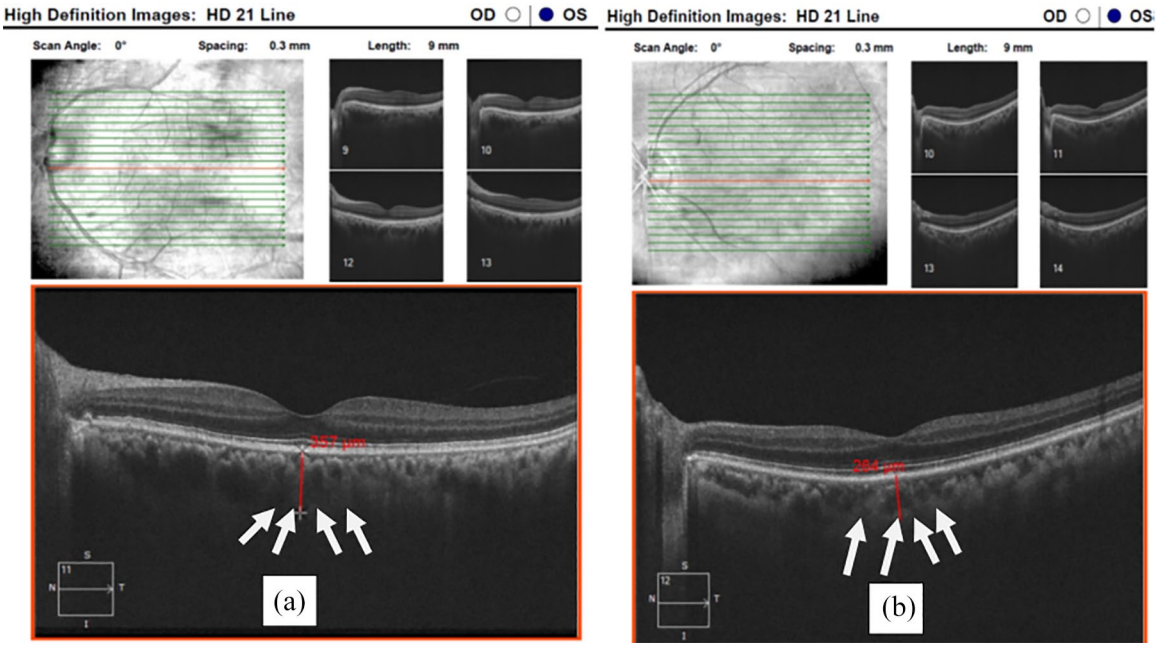

Figure 1. (a) EDI-OCT image of the left eye of a 34-year-old male with acute onset idiopathic retinal vasculitis (vasculitis eye), showing a well-delineated layer of choroid with a clear demarcation of its outer limit (arrows), and a sub-foveal choroidal thickness of 357 µm. (b) EDI-OCT image of the left eye of a 32-year-old healthy male subject (normal eye) depicting normal sub-foveal choroidal thickness of 264 µm (outer limit of choroid labeled with arrows). EDI-OCT, enhanced depth imaging–optical coherence tomography; OD, oculus dexter; OS, oculus sinister.

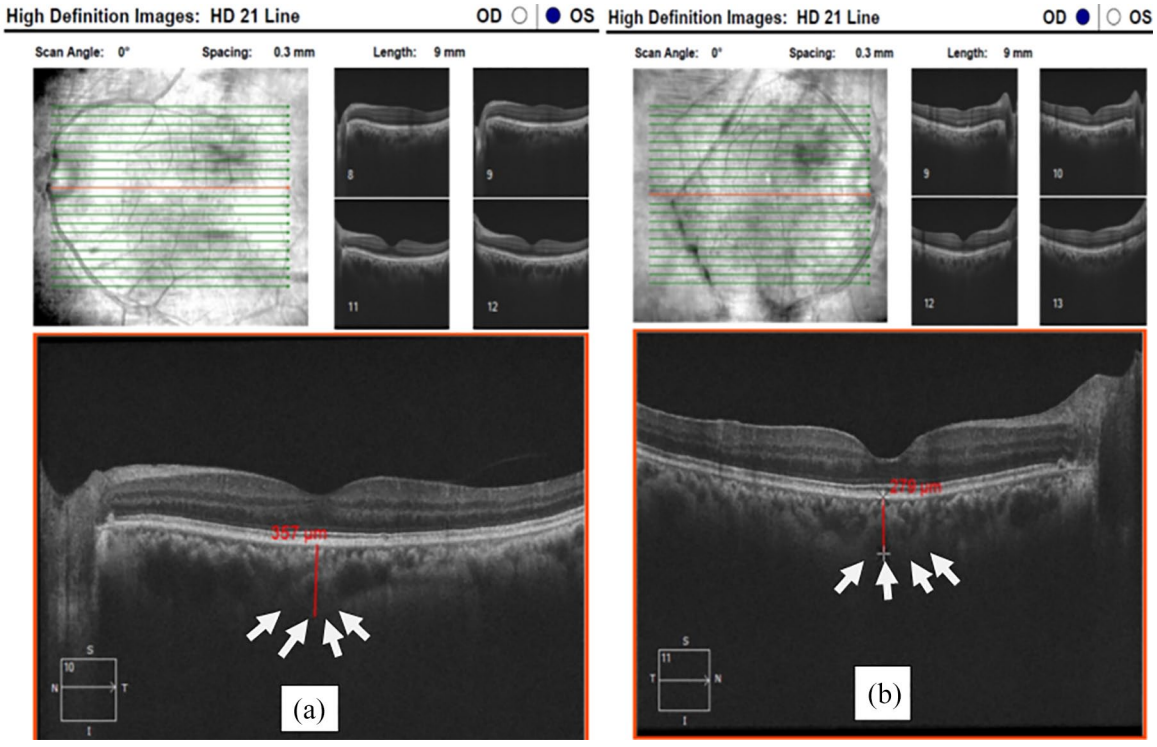

Figure 2. (a) EDI-OCT image of the left eye of a 29-year-old male with acute onset unilateral idiopathic retinal vasculitis (vasculitis eye) showing a well-delineated layer of choroid with a clear demarcation of its outer limit (arrows), and increased sub-foveal choroidal thickness of 356 µm. (b) EDI-OCT image of the right eye of same patient with no features of vasculitis (normal eye) depicting normal sub-foveal choroidal thickness of 279 µm (outer limit of choroid labeled with arrows). EDI-OCT, enhanced depth imaging–optical coherence tomography.

Table 2. Comparison of demographics, clinical features, and sub-foveal choroidal thickness in vasculitis patients (V) with and without anterior chamber inflammation.

	Vasculitis eyes with AC inflammation ($n = 10$)	Vasculitis eyes with no AC inflammation ($n = 26$)	p value
Age	31 ± 8.47	36 ± 10.99	0.20
BCVA	Median = 0.2; range = (0.0–0.3)	Median = 0.1; range = (0.0–0.3)	0.002*
CT	3334.3 ± 18.85 um	336 ± 31.56 um	0.22

AC, anterior chamber; BCVA, best corrected visual acuity; CT, choroidal thickness.
*Statistically significant.

in vasculitis is the retina, but a few studies have also reported choroidal abnormalities in BD in acute stages.[6–9] This study was conducted with an aim to determine whether choroidal thickness is altered in patients with idiopathic retinal vasculitis at presentation. Our findings exhibited that there is significant increase in SFCT in patients with idiopathic retinal vasculitis in acute stages of the disease compared with normal subjects. Our study results also indicated significant increase in the SFCT of the affected eyes in unilateral cases in comparison with healthy eyes. This points to choroidal involvement in diseased eyes of idiopatic retinal vasculitis.

A literature search showed a lack of any published data on SFCT measurement in idiopathic retinal vasculitis; however, studies are available on choroidal thickness in retinal vasculitis associated with systemic disorders such as BD in which concurrent involvement of the choroid is frequently seen.[6,12,13] Our findings are in agreement with those of Onal and colleagues[14] that central SFCT may be used as a non-invasive measure to assess inflammatory activity in early BD. Ishikawa and colleagues[6] also found that SFCT measurement by OCT with EDI is useful for evaluating disease activity in cases of BD, as choroidal thickness was more in acute stages but decreased progressively with treatment. Thus, SFCT can be a non-invasive tool in treatment and monitoring of patients of idiopathic retinal vasculitis also.

The choroid is one of the most vascularized tissues in the human body and is shown to play important roles in the perfusion of outer retinal layers, thermo-regulation of the retina, maintenance of the anatomical position of the retina.[15] It is an important source of oxygen and nutrients to the outer retina and the retinal pigment epithelium. Many published studies have proven that the choroid is influenced by ocular inflammatory conditions such as retinal vasculitis.[6,16,17] It is also suggested that increased vascular permeability in the posterior segment and choroidal effusion is the mechanisms of choroidal thickening during ocular inflammation.[18] Our study exhibited a positive correlation with increased SFCT in both eyes of acute retinal vasculitis patients with bilateral involvement. Similar correlation was also observed in unilaterally affected patients in which the non-involved eyes showed thinner choroids compared with the affected fellow eyes. Leakage from vascular structures can also lead to choroidal thickening in inflammatory conditions which subsequently decreases with appropriate treatment.[19] This increased leakage is a probable source of thickened choroid in idiopathic retinal vasculitis.

The choroidal thickness in females has been shown to be lower but the number of female subjects in our study was low (three subjects with three affected eyes), with no statistical difference between affected and control group.[20] The SFCT has been shown to decrease progressively with age.[21,22] The mean age of all three sub-group subjects in our study was comparable. The presence or absence of inflammation in anterior chamber had no statistically significant effect on choroidal thickness in our study.

The strength of our work compared with previous similar studies is the large number of eyes enrolled in each group and the strict exclusion of subjects with concurrent associated choroiditis. Our study also showed increased choroidal thickness in affected eyes in unilateral cases proving that retinal vascular involvement will significantly alter choroidal thickness in the affected eyes as compared with the normal eyes in the same subject. However, there are certain inherent limitations in

this study. First, the measurement of SFCT may also not be accurate in the eyes that did not show a clear outer limit of the choroid on OCT. Second, SFCT measurement is dependent on a large number of variables, and it is not possible to have a strict control between all groups, especially of all those variables that are likely to intervene with the results and outcomes. Third, the flare meter is an indispensable tool for the quantitative evaluation of inflammation in the anterior chamber where as in this study, we evaluated inflammation in anterior chamber using slit lamp by a single trained observer. Indocyanine angiography (ICG) which is a useful tool for diagnosis of active choroiditis was also employed in selected clinical suspect cases only.

In conclusion, during active inflammation, eyes with idiopathic retinal vasculitis may exhibit increased SFCT compared with unaffected fellow eyes and healthy control eyes. Thus, measurement of SFCT alone on OCT with EDI imaging can serve as a non-invasive modality in diagnosis of acute idiopathic retinal vasculitis patients.

Conflict of interest statement

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Institutional ethics committee approval

The study was performed in accordance with the tenets of the Declaration of Helsinki after obtaining necessary consent from participants. Ethical approval was obtained from institutional ethical committee of Army College of Medical Sciences & Base Hospital vide letter no. 1156/IEC/BHDC/03/2017.

Informed consent

Written consent was obtained from all study participants.

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