e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(3); 878-885

Original Research Article

Swept Source Based Optical Coherence Tomography Angiography (SS-OCTA) Features in Patients with Idiopathic Macular Telangiectasia Type 2 (Mactel-2) in an Indian Population

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Received: 25-12-2023 / Revised: 23-01-2024 / Accepted: 26-02-2024
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Conflict of interest: Nil

Abstract:

Purpose: To quantitavely evaluate the vascular density in perifoveal and foveal region as well as Subfoveal choroidal thickness (SFCT) of Idiopathic Macular Telangiectasia type-2 (MacTel 2) patients through Swept Source Optical Coherence Tomography (SS-OCT) and Optical Coherence angiography (SS-OCTA).

Materials and Methods: It was a prospective observational study in which MacTel 2 patients were compared with age matched normal controls. Group 1 included a total of 26 eyes of 13 MacTel Type 2 patients. Group 2 included 26 eyes of 13 ages and sex matched normal controls. All patients underwent a comprehensive ophthalmologic examination. All patients and controls underwent a Swept Source Optical Coherence Angiography (SS-OCTA). Data collected included vascular density (VD) in foveal and perifoveal quadrants, Subfoveal Choroidal thickness (SFCT) as well as morphological features on OCT.

Results: Mean Best corrected Visual acuity (BCVA) in logMAR of Mactel 2 patients and control group were 0.57±0.37 and 0.15±0.15 (p =<0.001). The most common findings on OCT Angiography images were decrease in vascular density in superficial vascular plexus. The retinal foveal vascular density was significantly lower in patients in MacTel-2 than the control group (20.68±6.73 vs 24.89±3.87, p=0.008). Besides vascular density was also lower in all four perifoveal quadrants. The mean SFCT was 307.46 microns and 275.15 µm in patients with MacTel-2 and control group respectively. Though SFCT was lower in Mactel patients, the difference was not statistically significant (p=0.177)

Conclusions: Reduced Vascular density in foveal and parafoveal areas is an important OCTA imaging biomarker in patients with Mactel Type 2. Subfoveal Choroidal thickness does not appear to be significantly reduced in Mactel type 2 eyes compared to the control group.

Keywords: Optical Coherence Tomography Angiography, Idiopathic Macular Telangiectasia, Swept Source Optical Coherence Tomography.

Introduction

Idiopathic macular telangiectasia type-2 (MacTel 2) is a bilateral retinovascular disease that affects both males and females generally in fifth to seventh decades of life.[1,2] It refers to macular capillary ectasia without any specific cause though Muller cell dysfunction appears to be the primary pathology. [3] The MacTel project which is ongoing research collaboration, initiated in 2015, to study this disease has thrown more light on the understanding of the disease process. [4]

The disease is characterized by changes in macular capillary network and neural atrophy,[5] which are the hallmark of this disease. Though it is a bilateral disease, the dis- ease severity is asymmetrical. Early clinical manifestation of the disease includes loss of retinal transparency temporal to the fovea, superficial retinal crystalline deposits, right angled venules, and presence of intraretinal cystoid spaces in the fovea. [1] In later stages, there is pigment plaque formation due to migration of RPE cells. In some cases, choroidal neovascular membrane formation is noted in later stages. [6]

Fluorescein angiography is considered by many to be the gold standard in diagnosis of MacTel-2. The classic appearance of bilateral dye leakage from telangiectatic vessels temporal to the fovea is pathognomonic of early stage of MacTel-2. But since Spectral domain OCT (SD-OCT) is a non-invasive procedure and provides some useful visualization of retinal changes, it has now become the Investigation of choice in diagnosis and follow up of MacTel-2 patients. [3] Swept Source OCT (SS

OCT) is the latest advancement over SD OCT. It employs a greater wavelength of 1050 nm which provides greater depth of penetration, better view of choroid and vivid images even in presence of media opacities. Characteristic findings of the disease on OCT include Macular thinning, Hyporeflective cavitations in the inner and outer retinal layers, atrophic changes in the outer retinal layer, [7,8] and breaks in the ellipsoid zone. Progression of the disease is characterised by shrinkage of the outer retinal layers and reduction in the central foveal thickness. [9,10,11]

OCT angiography (OCTA) is a new non-invasive imaging modality which allows visualization of both superficial and deep capillary plexus and also helps in assessing FAZ (Foveal Avascular Zone). Besides it provides enface visualization of the superficial and deep capillary layers, as well as the choroidal vasculature. Hence, of late it is being used commonly to study vascular characteristics of MacTel 2. Data obtained from the algorithm have been analysed for different metrices such as vessel density of the superficial and deep retinal vascular plexus, circularity index as well as size of FAZ. Toto et al [12] have described an interesting OCTA based grading system for this disease which is based on either temporal, nasal or circumferential location of MacTel.

Materials and Methods

Our study was a prospective observational study. Approval was obtained from the Institutional ethics committee of VIMS (Vivekananda Institute of Medical Sciences, Kolkata, India), where the study was conducted and performed in compliance with the ethical standards set out in the declaration of Helsinki. Written Informed consent was obtained from all patients before their enrolment. All MacTel 2 Patients presenting in Eye Outpatient Department between August 2021 to August 2023 were enrolled in the study. Patients were diagnosed as MacTel 2 based on their characteristic clinical features and confirmation was done with the help of OCT findings.

Inclusion criteria: Patients diagnosed with MacTel Type 2

Exclusion criteria:

1. History of ocular trauma
2. Refractive error of > 4D
3. Eyes with preexisting retinal disorders
4. Eyes with other ocular problems such as glaucoma, uveitis, optic neuropathy etc
5. Eyes with History of previous vitrectomy surgery
6. Eyes with Image quality< 60

All patients and controls underwent a comprehensive ophthalmologic examination, including measurements of best corrected visual acuity (BCVA,) slit lamp examination of anterior segment, IOP measurement by Non-contact Tonometer and dilated fundus examination.

Image Acquisition: All these patients then underwent Swept Source OCT (SSOCT) of the macula along with swept source-based OCT Angiography (SSOCTA) imaging. All the images were taken by experienced technicians. SS-OCTA was performed using Topcon DRI OCT Triton (Topcon Inc., Japan). It has a 1050nm wavelength light source, and a scanning speed of 100,000 A-scans/sec. It provides uniform scanning sensitivity allowing superior visualization of the vitreous and choroid in the same scan.

Active Eye tracking incorporated in the machine during capture of OCTA images ensures OCTA images are free of motion artifacts. The inbuilt IMAGENET® 6 software enables dynamic viewing of the SSOCT and SS-OCTA data, providing fundus images simultaneously. The software then automatically segments the OCTA scans into superficial capillary plexus (SCP), Deep capillary Plexus (DCP), Outer retina and choriocapillaries. (Figure 1)

To evaluate the superficial retinal plexus, we used the default settings of the machine. The boundary segmentation lines for superficial capillary plexus as per the default settings extend from 2.5 microns beneath the ILM (inner limiting membrane) to 15.6 microns beneath the interface of IPL/INL (Inner Plexiform layer / Inner Nuclear layer). In this way we were able to include all the vessels of this plexus. The default setting for deep capillary plexus extends from 15.6 microns beneath the IPL/INL to 70.2 microns beneath the IPL/INL interface.

The Subfoveal choroidal thickness (SFCT) was automatically measured by radial OCT scans (12 x 12mm). It provided detailed choroidal thickness measurement and choroidal thickness maps in Subfoveal location (central 1 mm). In images where the automated measurements were not accurate, a manual measurement was performed. The default settings of the machine to measure SFCT extends from Bruchs' membrane to Choroid sclera interface.

Image Analysis: All the images were then assessed and analyzed by an experienced clinician. Only images with signal strength> 60 were selected for analysis. The software automatically calculates the vascular density in the fovea and all the four parafoveal quadrants, namely- superior, inferior, temporal and nasal. In recent times, multiple authors have proposed OCTA grading of MacTel 2. Chen et al have proposed classification based on various factors such as location of telangiectatic vessels, FAZ status, presence of neovascularization etc. We have used classification system proposed by Toto et al because of its simplicity and ease of use. They

have graded OCTA images according to the lateral extension of vascular anomalies, using the foveal centre as the main landmark. Vascular anomalies were evaluated in term of vessel calliper (regular or irregular such as telangiectatic vascular abnormalities and/or microaneurysm), vessels coarse irregularities (regular or irregular such as distorted or right angled) and vessel density (normal or rarified).

OCTA Grading Characteristics (Toto et al)

1. Vascular anomalies in the deep and/or superficial plexus temporal to the fovea.
2. Vascular anomalies in the deep and/or superficial plexus temporal and nasal tothe fovea.
3. Markedly diffuse circumferential vascular anomalies in the deep and superficial plexus.
4. Neovascularization in the outer retina with any OCTA signs of grade 1 to 3

Statistical Analysis: The statistical software SPSS (version 22, IBM Corp, USA) has been used for statistical analysis. Snellen's vision data was converted to logarithm of Minimum Angle of Resolution (logMAR) vision for statistical analysis. Categorical variables are expressed as number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test or Fisher's Exact Test as and when appropriate. Continuous variables are expressed as Mean, Median and Standard Deviation and compared across the groups using unpaired t-test. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant. Spearman rank correlation coefficient has been used for correlation analysis.

Results

13 patients (26 eyes) with previous diagnosis of MacTel-2 and 13 patients (26 eyes) of normal age and sex matched controls were enrolled at the Retina services of Ophthalmology clinic of VIMS, Kolkata. The mean age +/- standard deviation (SD) was 63.54 ± 6.96 years in patients with MacTel type-2 and 65.85 ±7.78 years in the control group (p=0.156). In the MacTel-2 group 14(53.85%) patients were male and 12(46.15%) were female whereas in the control group 10(38.46%) were male and 16 (61.54%) were female (p= 0.296). There were no statistically significant differences between the two groups as regards to age and sex. In our study the mean BCVA in logMAR in MacTel-2 patients and controls were 0.57±0.37 and 0.15±0.15 respectively which was statistically significant (p =<0.001). (Table 1) Optical coherence tomography angiography provided detailed images of the retinal microcirculation in all patients with MacTel-2. The retinal foveal vascular density was significantly lower in patients with MacTel-2 than that of the control group (20.68±6.73 in Mactel 2 and 24.89±3.87 in controls. (p=0.008). Parafoveal vascular density of superficial capillary plexus was also significantly decreased between the two groups. We had separately analyzed vascular density (VD) in four parafoveal quadrants namely superior, inferior, temporal and nasal. In our study we found parafoveal VD to be decreased in all four quadrants in Mactel 2 patients. (Table -2).

As discussed earlier we had graded patients in Mactel 2 group as per the classification suggested by Toto et al. [12] In MacTel-2 eyes, 4 (15.38%) of 26 eyes showed a grade-1 OCTA; 9 (34.62%) eyes had grade-2 OCTA, 8 (30.77%) eyes had a grade-3 OCTA whereas 5 (19.23%) eyes had grade 4 OCTA. (Table 3) The other common findings on OCTA images which we observed frequently were telangiectatic vessels, right angled vennules, vascular invasion in RPE (Retinal pigment Epithelium) and FAZ irregularity. (Figure 2) In patients with Grade 4 OCTA, sub retinal neovascularization was seen as branching capillary network in the avascular slab of OCTA images and hence were classified as grade-4 OCTA.(Figure 3) Higher grades of Mactel 2 implied more advanced disease and more area of macular involvement. In our study we found that there was a positive correlation between Mactel 2 grade and BCVA in logMAR. (R= 0.112, P= 0.586). (Table-4) This correlation was analysed using spearmen, rank correlation coefficient. This implies that visual acuity decreased with advancing stages of Mactel 2.

In 7 Mactel 2 eyes and 3 control eyes we had to manually measure the choroidal thickness. In our study the mean choroidal thickness was 307.46±94.33µm in patients with MacTel-2 and 275±74.65 µm in control group. Choroidal thickness was found to be increased in MacTel-2 patient in respect of control group though the difference was not statistically significant. (p=0.177) (Table 5).

Table1: Baseline Demographics and visual acuity

		Group			
		MACTEL 2	**Control**	**p Value**	**Significance**
Age (years)	Mean ± SD	63.54 ± 6.96	65.85 ± 7.78	0.156	Not Significant
Male Gender	Numbers/total	14/26	10/26	0.296	Not Significant
	& %	53.85%	38.46%		
BCVA(logMAR)	Mean ± SD	0.57 ± 0.37	0.15 ± 0.15	<0.001	Significant

Table 2: Foveal and parafoveal Vascular Density

	Group		
	MACTEL 2	Control	
	Mean± SD	Mean± SD	p Value
Foveal Vascular Density	20.68 ± 6.73	24.89±3.87	0.008
Parafoveal Vascular Density			
Superior	46.72±4.76	49.07±2.27	0.027
Inferior	46.10±4.47	48.72±3.38	0.021
Nasal	46.21±2.75	47.92±2.45	0.022
Temporal	46.40±4.81	49.15±2.89	0.016

Table 3: Grading of MacTel 2 patients based on OCT-A findings

OCTA Grading	No. of Mactel 2 patients(n)	Total (%)
1	4	15.38
2	9	34.62
3	8	30.77
4	5	19.23
Total	26	100

Table 4: Correlation between BCVA (logmar) and OCTA gradings of Mactel 2 patients

Spearman's rho	OCTA GRADING and BCVA (logMAR)	**Correlation Coefficient (R)**	-0.082
		p Value	0.691

Table 5: Distribution of MacTel 2 patients and control in respect to choroidal thickness

	Group				p Value	Significance
	MACTEL 2		Control			
	Mean	Std. Deviation	Mean	Std. Deviation		
Subfoveal Choroidal Thickness (microns)	307.46	94.33	275.15	74.65	0.177	Not Significant

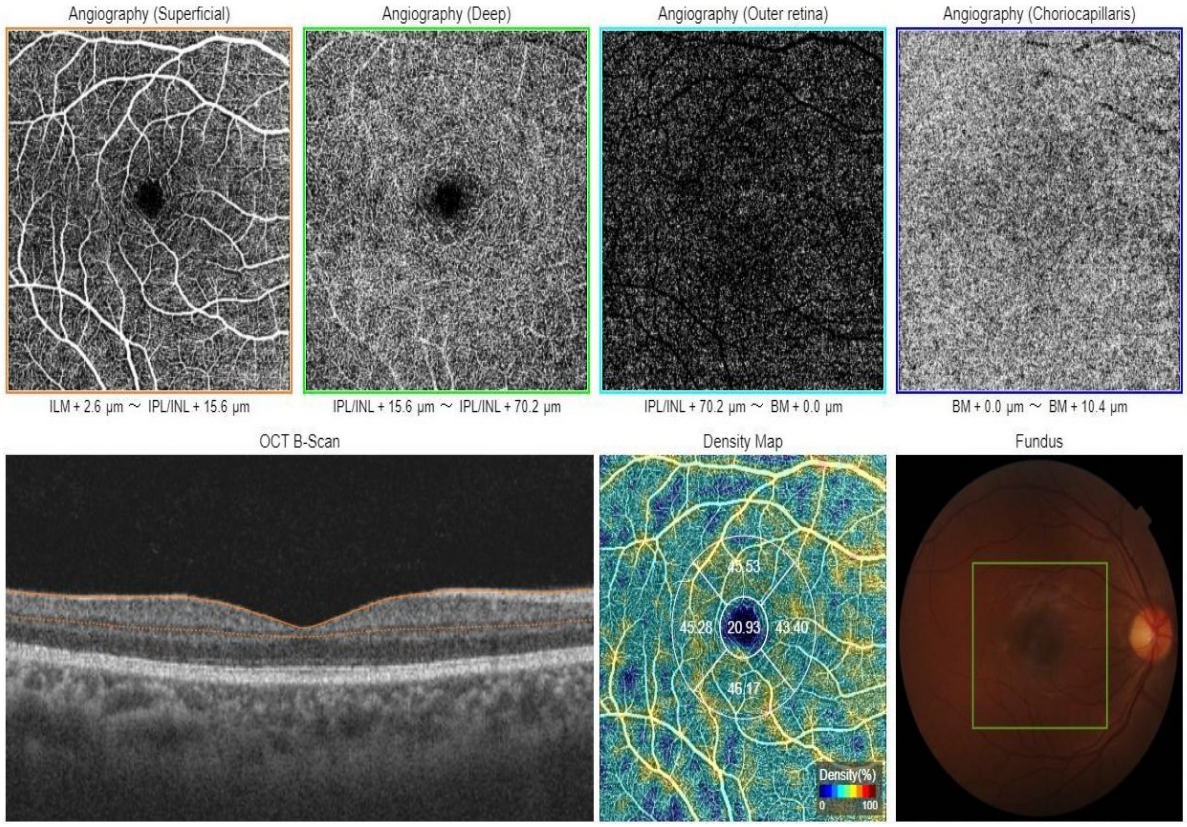

Figure 1: OCTA of Normal (control) patient

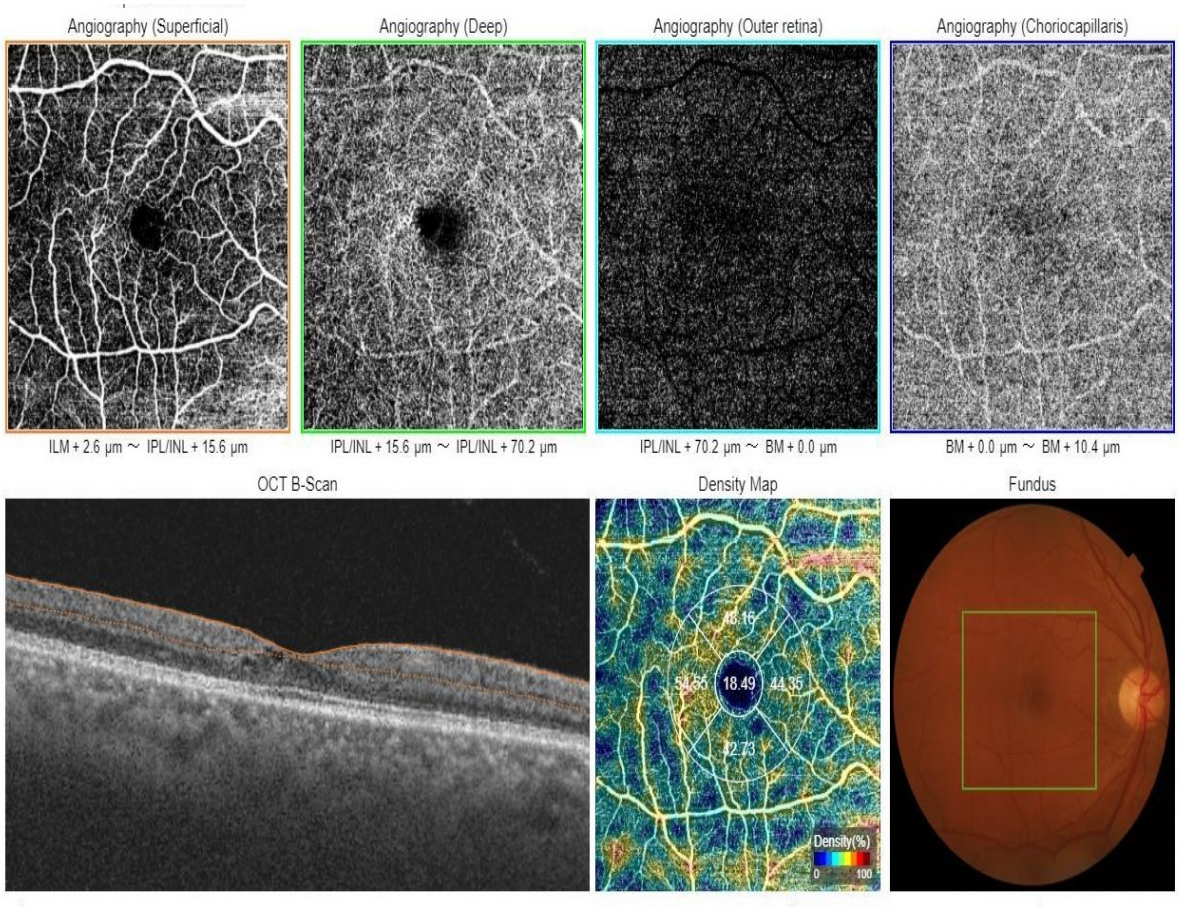

Figure 2: OCTA of MacTel 2 patient

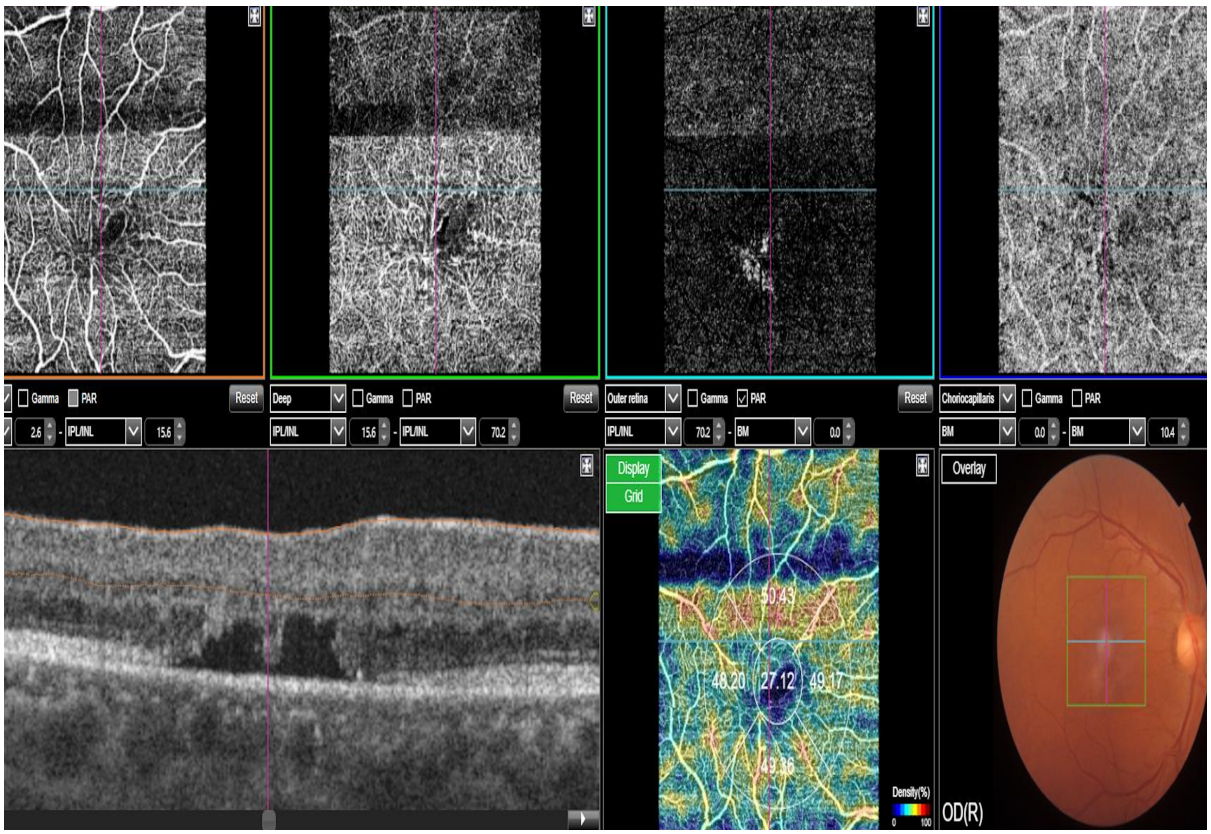

Figure 3: OCTA of Mactel 2 patients with neovascularisation (Grade 4)

Discussion

MacTel-2 is a neurodegenerative disease which has non-specific symptoms until in advanced stages when it shows sub retinal neovascularisation. OCT Angiography is a new imaging technique that helps in visualization of choroidal and retinal circulation. It can also visualize and analyse separately the two main retinal vascular plexuses that cannot be distinguished by conventional imaging techniques such as FFA. [13- 15]

Our study is unique in the sense that we have used a swept source OCT based machine unlike other machines which are spectral domain OCT. As a result of higher wavelength used(1050nm) in SSOCT, it is easier to identify choroid sclera interface and choroidal thickness than conventional machines. Different machines have different techniques to study OCT signals of moving blood cells. Topcon uses an innovative OCTA algorithm called OCTARA (OCTA Ratio Analysis) which aims to provide improved detection sensitivity of low blood flow and reduced motion artifacts without compromising axial resolution.[16] It is also useful to analyze correlation between capillary proliferation in the outer retina and ellipsoid zone loss. [17] Though it is imperative to note here that the OCTA machine used in this study did not have the requisite technology to calculate vascular density in deep capillary plexus.

In our study 61-70 years age group is the most affected group (53.85%) . We observed mainly bilateral involvement with MacTel-2 which is not like Chharbel Issa et al. [18] study where they showed one eye was apparently healthy and other one is affected with MacTel-2.

Our study found that there was a reduction in vessel density compared to that of age matched normal controls, which was significant for both the foveal and parafoveal capillary plexuses. Our findings were consistent with that of Toto et al [12] who also found decrease in vascular density in both foveal and perifoveal superficial capillary plexus. Since they had also studied deep capillary plexus they observed more prominent ectasia of the deep vessels compared to that of the superficial vessels which was in accordance with other authors investigating vessel density by OCTA. [4,19] These results were also in accordance with those of Ziemer et al. [20] Who found a loss of capillary density in the superficial plexus and enlargement of vessels and larger intervascular spaces in the deep plexus.

On the other hand Berna Dogan et al [21] found no significant differences between Mactel 2 patients and controls in superficial capillary plexus though they found parafoveal vascular density in deep plexus to be significantly lower in Mactel 2 eyes. In contrast Spaide et al. [4] have found a loss of functional vessels, particularly in the deep plexus. Ersoz et al [22] did not find any difference in FAZ area, perimeter and vessel density between eyes MacTel 2 and healthy eyes.

Runkle et al [23] found that changes in OCTA scans had more predilections to temporal perifoveal area. Besides vessel density they also measured EZ- RPE (ellipsoid zone to retinal pigment epithelium) thickness and found it to be lower in Mactel 2 than healthy eyes.

In this study Subfoveal choroidal thickness of MacTel-2 patients is increased compared to age matched control group though it was not statistically significant (p=0.177). Though various studies have studied choroidal thickness in MacTel-2 patients, the results have been identical. Chhablani et al. [24] did not observe any significant difference in the choroidal thickness as compared to sex and age matched controls. On the contrary Nunes et al. [25] found choroid to be thicker in Mactel 2 eyes than normal eyes and even suggested that thick choroid may be an early manifestation of MacTel-2 eyes. They hypothesized it to be due to compensatory choroidal changes caused by muller cell dysfunction or may be due to increase in the outward production of the vascular endothelial growth factor by RPE. Kumar et al. [26] showed the co-occurrence of MacTel-2 with pachychoroid group of disorders. So, the thickened choroid may be an early manifestation of MacTel-2 and it may be a valuable diagnostic clue to identify these MacTel-2 patients.

Our study had several limitations. Our sample size was small. Hence we were not able to perform any significant comparison between stages since there were not enough patients in each group. Some of the limitations were related to image acquisition by Triton machine. It can numerically analyze vascular density only in SCP and not in DCP. For this reason we were not able to get data regarding vascular density in DCP. The other limitations were lack of Blinding protocol and selection of contralateral eyes of the same patient and controls for comparison.

Conclusion

In summary, OCTA provided detailed information about macular microvasculature in both MacTel 2 and healthy eyes. Reduced Vascular density in foveal and parafoveal areas is an important OCTA imaging biomarker in patients with Mactel Type 2. Choroidal thickness does not appear to be significantly reduced in Mactel type 2 eyes compared to the control group. Further larger studies are required to study vascular density and choroidal thickness in Mactel 2 patients.

Acknowledgements: Mr Sanjay Kejriwal, Director, Shradha Healthcare

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