Original Article

Is Type 2 Macular Telangiectasia a Bilateral and Symmetrical Disease Entity?

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Abstract

Purpose: To study the inter-eye asymmetry in cases diagnosed with type 2 macular telangiectasia (MacTel).

Methods: Herein, type 2 MacTel cases were staged as per Gass and Blodi classification with multiple imaging techniques. Based on disease stage symmetry, two groups identified. Group 1: Symmetrical stage and Group 2: Asymmetrical stage MacTel disease. Prevalence, demography, and clinical features of MacTel cases showing inter-eye asymmetry were analyzed.

Results: Two hundred and eighty eyes of 140 patients diagnosed clinically with type 2 MacTel (84-Group 1 and 56-Group 2) were evaluated. Eighty-nine (64%) were female, and the median age of the entire cohort was 62.5 years (inter-quartile range: 57.0–68.75). MacTel disease with asymmetric stage was seen in 56 (40%) of the 140 patients. At presentation, a two-stage difference was noted in 46% (n = 26) of the patients with asymmetrical MacTel disease. A 10% conversion from symmetrical to asymmetrical disease stage was noted at the final visit. Of the 280 eyes evaluated for type 2 MacTel disease, 12 (4%) eyes showed no findings suggestive of MacTel on clinical examination and fluorescein angiography, optical coherence tomography (OCT), and OCT angiography when available and were labeled as unilateral type 2 MacTel disease.

Conclusions: Type 2 MacTel can show inter-eye disease stage asymmetry. Unilateral type 2 MacTel disease is a distinct stage in MacTel which would need further evaluation and consideration while staging.

Keywords: Disease stage, Macular telangiectasia, Retinal imaging, Symmetry, Type 2 macular telangiectasia

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Introduction

Gass and Blodi described type 2 macular telangiectasia (MacTel) as a macular perifoveal disease entity usually of both eyes affecting the deep capillary network and associated with inner and outer retinal structural changes.[1] The disease affects individuals between 5th and 7th decades of life and causes slowly progressive central vision loss due to foveal atrophy and/or neovascular membrane proliferation. Gass and Blodi defined the different clinical features of type 2 MacTel and divided them into five different stages starting with the presence of occult telangiectatic vessels identified as diffuse late-phase temporal perifoveal hyperfluorescence on fluorescein angiography (FA) in stage 1, loss of retinal transparency without clinically evident telangiectatic vessels in stage 2, prominent right-angle retinal venules in stage 3, retinal pigment hyperplasia in stage 4, and ending with the development of subretinal neovascular membrane (SRNVM) in stage 5.[1] A number of imaging techniques such as FA, optical coherence tomography (OCT), fundus autofluorescence (FAF), confocal blue reflectance (CBR), and recently OCT angiography (OCTA) have been found capable of diagnosing both early and advanced stages of type 2 MacTel.[2-7]

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The exact underlying mechanism of the disease remains unclear. The initial description of the disease by Gass and Oyakawa suggested an underlying vascular etiology.[8] However, the current understanding suggests that type 2 MacTel is an acquired, bilateral neurodegenerative disease with associated reduction of macular pigments lutein and zeaxanthin and secondary reactive vascular changes.[9-11] To this, a contrary study published recently by Chandran *et al*. presented the microvascular changes on OCTA to occur before the visible structural changes on OCT in fellow eyes of patients with asymmetric MacTel.[12] Although type 2 MacTel is considered as a familiar bilateral disease, there are very few papers in the literature which detail the asymmetric pattern of this disease entity.[12,13] These studies primarily described the OCT and OCTA features in the fellow eyes of cases diagnosed with type 2 MacTel on clinical examination and retinal imaging. However, the major drawback in both these papers was that they did not use FA to detect stage 1 disease as defined by Gass and Blodi.[1] They relied on the noninvasive imaging tests such as OCT and OCTA to describe the clinical features in asymmetrical MacTel. Furthermore, there is a lack of literature on the asymmetrical distribution in disease stage between both eyes at presentation in patients with type 2 MacTel. Information regarding the prevalence of asymmetrical distribution at presentation, the level of disease stage asymmetry, and its changes over follow-up is limited in literature.

With this background, we planned to study the prevalence, demographic, and clinical features of type 2 MacTel cases showing inter-eye disease stage asymmetry at presentation and at the last follow-up visit. We also intended to evaluate cases of apparent unilateral type 2 MacTel disease in this study.

Methods

This was a single-center retrospective review of clinical records and retinal imaging features of cases diagnosed with type 2 MacTel between January 2013 and June 2021. The study complied with the tenets of the Declaration of Helsinki and was approved by the local Institutional Review Board/ Ethics Committee (C-2021-03-003). Because the study was a retrospective analysis, waiver for informed consent was obtained.

Type 2 MacTel was diagnosed based on clinical features as described by Gass and Blodi[1] and was confirmed with CBR and OCT images in all cases. The presence of dilated right-angled vessels on clinical examination was identified as stage 3 disease as per Gass and Blodi classification. FA was performed in a limited number of patients either to confirm the suspected diagnosis of type 2 MacTel or to identify macular neovascularization secondary to type 2 MacTel. OCTA images were evaluated when available. Only patients having imaging scans of both eyes were included in the study.

Multicolour® imaging was performed using the confocal scanning laser ophthalmoscope technology on the Spectralis device (Heidelberg Engineering, Heidelberg, Germany). On the multicolor image, the diagnosis of type 2 MacTel was made based on the description provided in our previous publication on Multicolour® imaging in type 2 MacTel.[14] The confocal blue and green reflectance channels were used to identify the nonproliferative signs of type 2 MacTel such as perifoveal graying and loss of retinal transparency, superficial retinal crystals, dilated right-angled vessels, and retinal pigment epithelial hyperplasia/plaques. A confocal infrared reflectance channel was used to identify the presence and extent of SRNVM.

Macular volumetric OCT assessments consisting of 512 A-scans per line with 30° scanning area and 25-line horizontal raster volume scans centered at the fovea performed with the spectral domain Spectralis (Heidelberg Engineering, Heidelberg, Germany) device were evaluated. OCT scans having a quality score ≥20 were used for analysis and interpreting of the findings. The presence of the following features of type 2 MacTel was looked for as described in the previous publication from the same group: [15] (1) irregularity of the foveal contour, (2) internal limiting membrane drape sign, (3) hyperreflectivity of the middle retinal layers, i.e., between the inner plexiform to the outer plexiform layers, (4) identification of retinal crystals as superficial hyperreflective retinal dots, (5) hyporeflective inner and outer retinal cavities, (6) outward bending of inner retinal layers, (7) hyperreflective retinal pigment clumps (RPC) with underlying shadowing, and (8) SRNVM.

FA was also performed on the Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany) device. Characteristic findings noted on FA were the identification of the telangiectatic capillaries predominantly temporal to the fovea in the early phase and a diffuse hyperfluorescence in the late phase.[16] OCTA images were analyzed where available to look for the features in type 2 MacTel.[17,18] All OCTA scans with signal strength index ≥60, with proper segmentation and with no artifacts were evaluated for the study.

All the images were analyzed by two independent observers (H.N. and N.R.) for the accurate disease staging. Cases showing disagreement between the two observers were solved after consulting with the senior experienced ophthalmologist (R.V.) in the study. After achieving a common consensus and based on the clinical, multicolor, FA, OCT, and OCTA (RTVue-XR Avanti; Optovue, Fremont, CA, USA) findings, eyes were classified into one of the five different stages as proposed by Gass and Blodi.[1] In this study, a fellow eye of a patient with type 2 MacTel disease that did not show vascular or structural changes after verification with available retinal imaging modalities such as FA and OCT and OCTA when available was labeled as unilateral type 2 MacTel [Table 1].

Patients with other as well as concomitant macular pathologies were excluded from the study. Patients with poor-quality images in either eye were excluded from the study.

Table 1: Classification and staging of type 2 macular telangiectasia

Stages	Clinical features
Unilateral disease	Absence of clinical and retinal imaging findings on FA and OCT and on OCTA when available with fellow eye showing confirmed findings of type 2 MacTel
Stage 1	Presence of diffuse hyperfluorescence on late-phase angiography in the study eye in the absence of clinical features of type 2 MacTel
Stage 2	Presence of increased perifoveal greying and loss of retinal transparency
Stage 3	Presence of dilated right-angled venules
Stage 4	Presence of intraretinal pigment clumping
Stage 5	Presence of SRNVM

MacTel: Macular telangiectasia, FA: Fluorescein angiography, OCT: Optical coherence tomography, OCTA: OCT angiography, SRNVM: Subretinal neovascular membrane

On the basis of the disease stage in both eyes, cases were classified into two groups: Group 1 – Eyes with similar disease stage in both eyes, labeled as symmetrical MacTel group, and Group 2 – Eyes with different disease stages between both eyes, labeled as asymmetrical MacTel group. Early type 2 MacTel disease was defined as eyes showing findings between stages 1 and 2 while advanced type 2 MacTel disease was defined as eyes showing findings between stages 3 and 5.

The clinical details of each patient were collected retrospectively by review of records, including age, gender, laterality, visual acuity, and systemic disease, if any, and total follow-up duration. For assessing the changes in the disease stage at the last follow-up visit, only eyes with a minimum follow-up duration ≥6 months were analyzed. At the last follow-up visit, best-corrected visual acuity and disease stage were documented. The analysis was planned with the intention to study the disease stage symmetry at presentation and its conversion from asymmetrical to symmetrical disease or vice-versa at the final follow-up visit.

Statistical analysis

All data were analyzed using GraphPad Prism version 9.3.0 (463) for Windows, GraphPad Software, San Diego, California USA, www.graphpad.com. The Shapiro–Wilk normality test was used to test the normality of the data sets. Snellen's vision data were converted to logMAR vision for statistical analysis. Categorical variables such as gender, presence of diabetes mellitus, and disease stages were described as numbers and percentages. Quantitative continuous variables such as age and logMAR visual acuity were described in median value with inter-quartile range (IQR). Quantitative variables between the two groups were analyzed using the Mann–Whitney *U* test for nonparametric data. Fisher's exact test was used to compare the categorical data between the two groups. Cohen's kappa statistic was applied to calculate interobserver agreement between the two observers. Interpretation of kappa statistic (κ) was done as suggested by Viera and Garrett.[19] $P < 0.05$ was considered statistically significant.

Results

In total, 280 eyes of 140 patients diagnosed with type 2 MacTel disease were included in the study. There were 89 (64%) females, and the median age of study participants was 62.5 years (IQR: 57.0–68.75). A history of diabetes mellitus was noted in 75% ($n = 105$) of the patients.

Of a total of 140 study patients, 84 (60%) patients showed symmetrical stage type 2 MacTel (Group 1), and 56 (40%) patients showed asymmetrical stage type 2 MacTel (Group 2) in both eyes at presentation. The level of agreement between the 2 observers was strong with a Cohen's Kappa statistic $\kappa = 0.89$. More than 50% of cases in both symmetrical and asymmetrical type 2 MacTel groups belonged to stage 2 at presentation. Furthermore, the disease severity (i.e., early versus advanced) between the two groups was not statistically significant ($P = 0.22$). Further subgroup analysis of the asymmetrical group showed 10 patients with early disease stage and 8 patients with advanced disease stage in both eyes, respectively. The median logMAR visual acuity in the early disease stage group was 0.153 with an IQR from 0.000 to 0.375 which was significantly better compared to the visual acuity in the advanced disease stage group (median = 0.54; IQR: 0.21–0.735) ($P = 0.003$). Similarly, subgroup analysis of the symmetrical group showed 50 patients with early disease stage and 34 patients with advanced disease stage in both eyes, respectively. The median logMAR visual acuity in the early disease stage group (median = 0.3; IQR: 0.125–0.48) was significantly better compared to the visual acuity in the advanced disease stage group (median = 0.48; IQR: 0.3–0.6) ($P < 0.001$). The asymmetrical group type 2 MacTel showed a statistically significant better visual acuity compared to the symmetrical group type 2 MacTel in the early disease stages ($P = 0.047$) but not so in the advanced disease stages ($P = 0.707$). Visual acuity at presentation in the asymmetrical type 2 MacTel group (logMAR vision = 0.18) was significantly better compared to the visual acuity in the symmetrical group (logMAR vision = 0.44) ($P = 0.043$). The level of difference in the stages between the two eyes is mentioned in Table 2. Approximately one-half of the patients showed a two-level difference in the stage between the two eyes, and <5% of the patients showed a four- or a five-level difference between the two eyes in our study.

In this study, we noted 15 eyes which did not show features of type 2 MacTel on clinical examination. The analysis of all sections of the volumetric horizontal OCT scans of these eyes was without any signs of type 2 MacTel. There were 3 eyes in the study which lacked the features of type 2 MacTel on clinical examination and OCT but showed the classical perifoveal diffuse hyperfluorescence on late-phase FA. These eyes were labeled as stage 1 type 2 MacTel as per Gass and Blodi classification.[1] In the remaining 12 eyes, FA did not show any signs of type 2 MacTel in the late phase. In addition, OCTA images which were available for 3 eyes did not show any features of type 2 MacTel. In the remaining 9 eyes, OCTA

images were not available for comment. The fellow eyes of these cases showed some stage of type 2 MacTel. These eyes were labeled as unilateral type 2 MacTel. Comparisons between the demographic, clinical, and disease stages between the two groups are mentioned in Table 3.

Of the 280 eyes evaluated for different stages of type 2 MacTel in this study, we identified 12 (4%) eyes with unilateral type 2 MacTel wherein the confirmed features of MacTel were noted only in the fellow eye of these patients [Table 4]. These eyes did not show any FA and OCT changes in these eyes. In three eyes where OCTA was done, no abnormality related to type 2 MacTel was identified. The median age of presentation for this subgroup of patients was 56.0 years (IQR: 51.25–73.25 years). Eight of the 12 (66%) patients were men, and 50% of cases had a history of diabetes mellitus. There were 3 (25%) eyes with stage 1 disease, 7 (58%) eyes with stage 2 disease, and 1 (8%) eye each of stage 4 and stage 5 disease affecting the fellow eye in this subgroup of cases [Figures 1-3]. Follow-up details were available in 5 of the 12 (42%) patients with unilateral disease. The median follow-up duration of these patients was 44 months (IQR: 6–110.5 months). A two-level disease stage progression was noted at the last visit in one patient while the remaining four patients did not show progression in the disease stage.

Table 2: Difference in disease stages between 2 eyes in type 2 macular telangiectasia (*n*=56)

Level of difference	Number of patients (%)
1-stage difference	15 (27)
2-stage difference	26 (46)
3-stage difference	13 (23)
4-stage difference	1 (2)
5-stage difference	1 (2)

Details of 67 (48%) patients were available at the last follow-up visit. The median time interval between the first and last visit was 35 months with an IQR from 9 to 87 months. There were 36 (54%) patients showing symmetrical disease stage and 31 (46%) patients with asymmetrical disease stage at this visit. Seven of 67 (10%) patients showed a change in the disease symmetry type from symmetrical to asymmetrical disease at the last follow-up visit from the initial visit. The level of change in the disease stage progression at the last follow-up visit from the first visit is mentioned in Table 5. At the last visit, no disease progression in 95 (85%) eyes, 1-stage disease progression in 18 (16%) eyes, 2-stage disease progression in 15 (13%) eyes, and 3-stage disease progression in 6 (5%) eyes was noted.

Long-term follow-up (≥5 years) details were available in 24 (17%) patients. At the final follow-up visit, symmetrical disease stage was noted in 13 (54%) patients while asymmetrical disease stage was noted in 11 (46%) patients in this subgroup of cases. The difference in the disease stage between both eyes in such patients is described in Table 6.

Discussion

This study reports about the prevalence of inter-eye asymmetry and level of difference in the disease stages between two eyes in type 2 MacTel cases. We noted that in patients with disease stage asymmetry, visual acuity was significantly better in the early disease stage group compared to the advanced disease stage group. To the best of our knowledge, this study appears to be the first study to compare the asymmetricity between the two eyes in a large cohort of type 2 MacTel cases.

Bilaterality is characteristic for type 2 MacTel disease while on the other hand, there are a few case series in literature which comment about its unilateral presentation.[12,16,20] Although clinical features are usually rather symmetric, they may be

Table 3: Comparison between symmetrical and asymmetrical macular telangiectasia at presentation

	Symmetrical MacTel	Asymmetrical MacTel	*P*
Number of patients	84	56	
Number of eyes	168	112	
Median age (IQR) (years)	63.0 (58.0-69.0)	61.5 (57.0-68.0)	0.327
Gender, *n* (%)			
Male	29 (35)	22 (39)	0.594
Female	55 (65)	34 (61)	
Number of patients with history of diabetes mellitus, *n* (%)	66 (79)	39 (70)	0.24
Median logMAR visual acuity (IQR)	0.44 (0.18-0.57)	0.18 (0.125-0.48)	0.043
Stages, *n* (%)			
Unilateral type 2 MacTel	0	12 (11)	<0.001
Stage 1	0	3 (3)	0.063
Stage 2	100 (60)	43 (38)	0.006
Stage 3	12 (7)	14 (12)	0.145
Stage 4	32 (19)	22 (20)	>0.999
Stage 5	24 (14)	18 (16)	0.734
Number of eyes showing early disease stages (stage 1-2) *n* (%)	100 (60)	58 (52)	0.22
Number of eyes showing advanced disease stages (stage 3-5), *n* (%)	68 (40)	54 (48)	

MacTel: Macular telangiectasia, IQR: Interquartile range, logMAR: Logarithm of the minimum angle of resolution

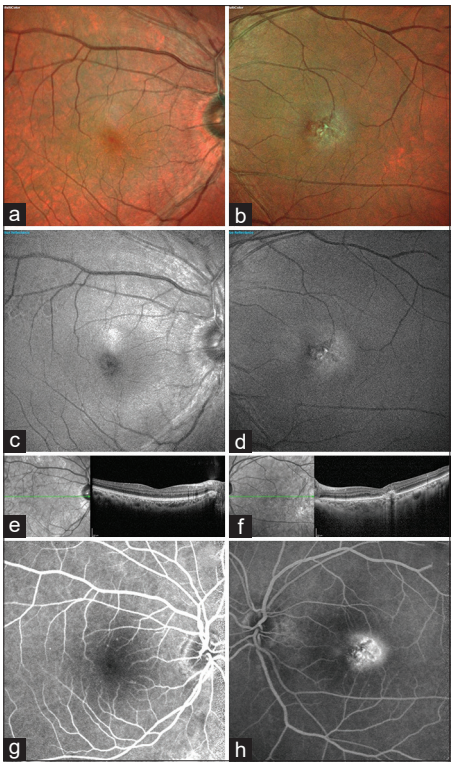

Figure 1: Comparison of clinical and imaging features between two eyes of a patient diagnosed with unilateral type 2 macular telangiectasia (MacTel). A 58-year-old male, diagnosed with diabetes mellitus for the last 18 years presented to the retinal clinic with complaints of blurring and visual distortion in the left eye. His visual acuity in the right and left eye was 6/6, N6 and 6/24, N12, respectively. His anterior segment examination findings were within normal limit. Dilated fundus examination of both eyes revealed clinical features of stage 5 MacTel in the left eye while classical features of MacTel disease were not identified in the right eye, (a and b) Comparison of multicolor images between both eyes shows the presence of perifoveal greying, right-angled vessel dipping and retinal pigment clumps with a probable macular neovascularization in the left eye suggestive of advanced type 2 MacTel disease. The right eye multicolor does not show any clinical features of type 2 MacTel such as perifoveal greying and loss of retinal transparency, (c and d) Confocal blue reflectance images of both eyes show perifoveal temporal hyper reflectance in the left eye but not in the right eye, (e and f) Optical coherence tomography images of both eyes shows the features of type 2 MacTel with macular subretinal neovascularization in the left eye and no signs of early disease in the right eye, (g and h) Late phase fluorescein angiography (FA) image does not show the classical temporal hyperfluorescent leakage in the right eye to confirm early-stage type 2 MacTel disease. Hyperfluorescent dots are noted superior to fovea suggestive of microaneurysms due to early-stage nonproliferative diabetic retinopathy. Left eye late phase FA image shows the diffuse and focal hyperfluorescence to confirm proliferative type 2 MacTel disease

more advanced in one eye than the other.[20] We noted in our study that 40% of patients diagnosed with type 2 MacTel presented with asymmetric disease stage in both eyes. A 2-stage difference between two eyes was more frequently encountered. A large-scale study published by the MacTel study research group described the baseline characteristics of eyes diagnosed with type 2 MacTel.[21] However, the study did not provide

Table 4: Demographics of unilateral type 2 macular telangiectasia cases at presentation

Variable	Value
Number of patients (*n*)	12
Number of eyes (*n*)	12
Male: female	8:4
Median age (years) (IQR)	56.0 (51.25-73.25)
Number of patients with a history of diabetes mellitus, *n* (%)	6 (50)
Number of eyes with follow-up data available, *n* (%)	5 (42)
Median follow-up interval (months) (IQR)	44 (6-110.5)

IQR: Interquartile range

Table 5: Difference in the disease stage between both eyes at first and last follow-up visit

	At presentation (*n*=56), *n* (%)	At last visit (*n*=31), *n* (%)	*P*
1-stage difference	15 (27)	12 (39)	0.336
2-stage difference	26 (46)	8 (26)	0.07
3-stage difference	13 (23)	9 (29)	0.611
4-stage difference	1 (2)	1 (3)	>0.999
5-stage difference	1 (2)	1 (3)	>0.999

Table 6: Difference in the disease stage between both eyes at first and last follow-up visit in patients with ≥5-year follow-up duration (*n*=24)

	Number of patients (%)
Number of differences	13 (54)
1-stage difference	3 (12)
2-stage difference	2 (8)
3-stage difference	5 (21)
4-stage difference	1 (4)
5-stage difference	0

information regarding the asymmetry and the level of asymmetry between the two eyes. We noted that the vision was less affected in the asymmetric type 2 (≥20/30) MacTel group compared to the symmetric MacTel group. In addition, we noted the asymmetry in the disease stage showed better vision in early disease stages than in advanced disease stages. Hence, we can infer that asymmetric disease type associated with early disease stages have better visual acuity. Even at the mean final follow-up interval of 48.3 ± 43.11 months, asymmetry in the disease stage was prevalent in 46% of cases, but the more commonly prevalent of 2-stage difference (46% vs. 26%) between the two eyes had reduced to a one-stage difference (27% vs. 39%).

The clinically visible biomicroscopic features of type 2 MacTel were described as stages 2–5 in the Gass and Blodi classification.[1] The characteristic FA findings include the visibility of late diffuse perifoveal hyperfluorescence in the absence of SRNVM and presence of diffuse and focal intense hyperfluorescence in the presence of SRNVM.[18] There is a

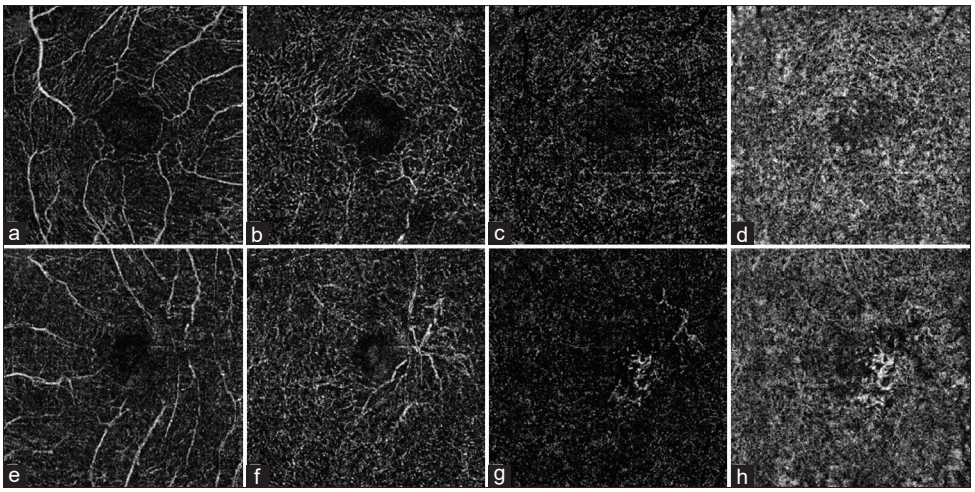

Figure 2: Optical coherence tomography angiography (OCTA) images of the patient described in Figure 1. OCTA 3 mm × 3 mm scans were performed with *RTVue* XR Avanti, (*Optovue* Inc., Fremont, CA, USA) machine for both eyes, (a-d) OCTA images of the right eye does not show any abnormal vascular telangiectatic vessel in the superficial or deep capillary plexus to suggest early-stage type 2 macular telangiectasia, (e-h) OCTA images of the left eye show the abnormal telangiectatic vessels in the temporal perifoveal region with crowding and bunch of vessels suggestive of the development of abnormal macular neovascularization. The neovascular process can be seen to extend into the outer retina and choroidal slab segmentation on the OCTA images

small subset of eyes which do not show any biomicroscopic clinical features of type 2 MacTel. These eyes are usually fellow eyes of confirmed cases of type 2 MacTel.[12,22] In our study, we noted 5% cases (15/280) belonging to this category while the multi-center MacTel study group reported 3% cases belonging to this similar category.[21] A number of imaging modalities like FA, OCT, and most recently OCTA have been used to describe the imaging characteristics of this very early stage type 2 MacTel.[1,6,12,13] Late-stage temporal perifoveal hyperfluorescence on FA was noted by Gass and Blodi in very early stage of type 2 MacTel and labeled this as stage 1 disease in their classification. Alex *et al*. noted temporal retinal thinning and hyperreflective dots in the retina in 28 eyes with very early stages of type 2 MacTel and Chandran *et al*. noted telangiectasias and foveal avascular changes on OCTA in 4 eyes in the absence of structural OCT changes.[12,13] However, in both these studies, FA was not conducted to look for the temporal perifoveal hyperfluorescence as seen in stage 1 disease. In this study, of the 15 eyes with no features of type 2 MacTel on clinical biomicroscopic examination and no abnormal OCT findings, 3 eyes showed late-phase temporal hyperfluorescence of FA and hence, they were labeled as stage 1 disease. The remaining 12 eyes showed no abnormal findings on FA and OCT and on OCTA when available. Such a category of eyes which did not show clinical or imaging features related to type 2 MacTel were labeled as unilateral type 2 MacTel cases in our study. A similar disease severity staging system ranging from category 0 to 4 was described by Wong *et al*. based on clinical findings on color fundus photography and imaging findings on FAF, FA, OCT, and microperimetry.[3] In our study, we lacked FAF and OCTA images in all 12 cases of unilateral type 2 MacTel disease, preventing us from classifying them as stage 0 disease. However, it is clinically important to diagnose these groups of cases to avoid a wrong diagnosis as most clinicians would diagnose type 2 MacTel only in the presence of bilateral disease.

We observed some differences between patients with unilateral type 2 MacTel and patients with a higher disease stage, i.e., eyes ≥stage 1. There were significantly more males affected with unilateral disease than patients affected with a higher stage ($P = 0.03$). Although patients with unilateral disease were younger (median age = 56.0 years) and less frequently associated with diabetes mellitus ($n = 6$, 50%), these findings were not statistically significant ($P > 0.05$). In our study, also we identified one such patient who showed clinical biomicroscopic features of type 2 MacTel (stage 2) after a follow-up duration of 44 months. Furthermore, it is important to longitudinally follow-up, these preclinical cases to see if they would develop clinical features of type 2 MacTel in future.

The strengths of the current study are the large cohort of cases from a single center, imaged on the same FA, OCT, and OCTA devices during the entire length of the study, thereby providing consistency in the imaging findings across the different disease stages. This paper also provides information regarding the longitudinal data of patients with type 2 MacTel and also looks at details regarding the conversion to the clinical stage of MacTel at the final follow-up visit from the preclinical stage. There are a few drawbacks associated with this study. The major drawback is its retrospective study design, a diverse cohort of patients with type 2 MacTel disease at follow-up visits, and inconsistent use of FAF and OCTA in all cases. We did not perform more advanced retinal imaging such adaptive optics which might have shown very early changes of MacTel in unilateral eyes.[23,24]

Finally, despite being commonly thought of as a bilateral symmetrical disease, type 2 MacTel can exhibit inter-eye disease stage asymmetry as well as disease asymmetry (unilateral

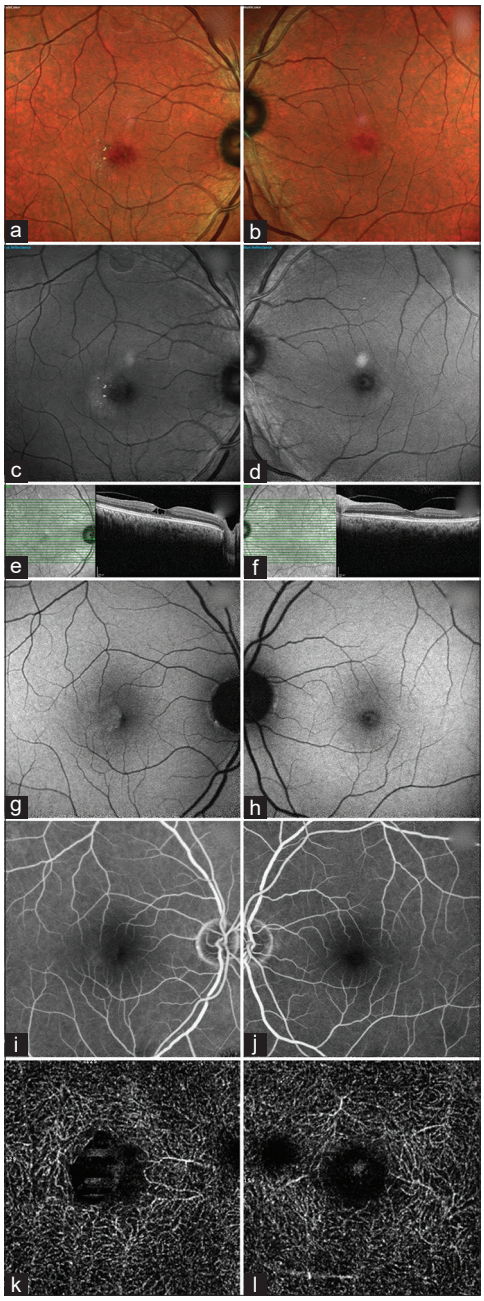

Figure 3: Another case of unilateral type 2 macular telangiectasia (MacTel) comparing the clinical and imaging findings between both eyes. A 52-year-old male, with no systemic history of diabetes mellitus presented for a routine eye examination to the retinal clinic. He had no eye complaints. His visual acuity in the right and left eye was 6/9, N6 and 6/6, N6, respectively. His anterior segment examination findings were normal. Dilated fundus examination of both eyes revealed clinical features of stage 2 MacTel such as temporal perifoveal greying and loss of retinal transparency in the right eye along with the presence of yellow superficial retinal crystals. Left eye examination showed no features of type 2 MacTel disease, (a-l) Comparison of multimodal imaging features between two eyes using multicolor fundus photographs, confocal blue reflectance images, optical coherence tomography (OCT), fundus autofluorescence, late phase fluorescein angiography, and OCT angiography images showed absence of any finding of type 2 MacTel disease in the left eye. Right eye findings were confirmatory of stage 2 MacTel

presentation). Unilateral type 2 MacTel disease is a separate stage that would necessitate further investigation and could be considered when staging type 2 MacTel disease.

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Conflicts of interest
There are no conflicts of interest.

References

1. Gass JD, Blodi BA. Idiopathic juxtafoveolar retinal telangiectasis. Update of classification and follow-up study. Ophthalmology 1993;100:1536-46.
2. Kim YH, Chung YR, Oh J, Kim SW, Lee CS, Yun C, *et al.* Optical coherence tomographic features of macular telangiectasia type 2: Korean Macular Telangiectasia Type 2 Study-Report No. 1. Sci Rep 2020;10:16594.
3. Wong WT, Forooghian F, Majumdar Z, Bonner RF, Cunningham D, Chew EY. Fundus autofluorescence in type 2 idiopathic macular telangiectasia: Correlation with optical coherence tomography and microperimetry. Am J Ophthalmol 2009;148:573-83.
4. Charbel Issa P, Berendschot TT, Staurenghi G, Holz FG, Scholl HP. Confocal blue reflectance imaging in type 2 idiopathic macular telangiectasia. Invest Ophthalmol Vis Sci 2008;49:1172-7.
5. Megur B, Megur D, Reddy S. Fluorescein angiography of subretinal neovascular membrane in parafoveal telangiectasia type II demonstrating retino-retinal, retino-subretinal anastomosis. Indian J Ophthalmol 2016;64:840-2.
6. Narayanan R, Majji AB, Hussain N, Hussain A, Jalali S, Mathai A, *et al.* Characterization of idiopathic macular telangiectasia type 2 by fundus fluorescein angiography in Indian population. Eur J Ophthalmol 2008;18:587-90.
7. Toto L, Di Antonio L, Mastropasqua R, Mattei PA, Carpineto P, Borrelli E, *et al.* Multimodal imaging of macular telangiectasia type 2: Focus on vascular changes using optical coherence tomography angiography. Invest Ophthalmol Vis Sci 2016;57:OCT268-76.
8. Gass JD, Oyakawa RT. Idiopathic juxtafoveolar retinal telangiectasis. Arch Ophthalmol 1982;100:769-80.
9. Powner MB, Gillies MC, Zhu M, Vevis K, Hunyor AP, Fruttiger M. Loss of Mlalmoletineolar retintelangiectasia type 2: Focus on vascular chan Ophthalmology 2013;120:2344-52.
10. Charbel Issa P, van der Veen RL, Stijfs A, Holz FG, Scholl HP, Berendschot TT. Quantification of reduced macular pigment optical density in the central retina in macular telangiectasia type 2. Exp Eye Res 2009;89:25-31.
11. Zeimer MB, Spital G, Heimes B, Lommatzsch A, Pauleikhoff D. Macular telangiectasia-changes in macular pigment optical density during a 5-year follow-up. Retina 2014;34:920-8.
12. Chandran K, Giridhar A, Gopalakrishnan M, Sivaprasad S. Microvascular changes precede visible neurodegeneration in fellow eyes of patients with asymmetric type 2 macular telangiectasia. Eye (Lond) 2022;36:1623-30.
13. Alex D, Giridhar A, Gopalakrishnan M, Manayath G, Amar S, Raman R, *et al.* Early spectral-domain optical coherence tomography biomarkers to confirm fellow eye changes in asymmetric type-2 macular telangiectasia: A case-control study (India Macular Telangiectasia Report 1). Retina 2021;41:471-9.
14. Venkatesh R, Pereira A, Bavaharan B, Jain K, Aseem A, Sangai S, *et al.* Relevance of multicolor imaging in type 2 macular telangiectasia. J Curr Ophthalmol 2020;32:375-80.
15. Venkatesh R, Reddy NG, Mishra P, Agrawal S, Mutalik D, Yadav NK, *et al.* Spectral domain OCT features in type 2 macular telangiectasia (type 2 MacTel): Its relevance with clinical staging and visual acuity. Int J Retina Vitreous 2022;8:26.
16. Charbel Issa P, Gillies MC, Chew EY, Bird AC, Heeren TF, Peto T, *et al.*

Macular telangiectasia type 2. Prog Retin Eye Res 2013;34:49-77.
17. Saoji K, Pathengay A, Chhablani J, Panchal B, Doshi S, Saldanha M. Response to anti-vascular endothelial growth factor of abnormal retinal vascular net in para foveal telangiectasia group II images on optical coherence tomography-angiography. Indian J Ophthalmol 2019;67:105-8.
18. Venkatesh R, Reddy NG, Mishra P, Pereira A, Mutalik D, Agrawal S, *et al.* The preproliferative stage in type 2 macular telangiectasia (MacTel type 2). Graefes Arch Clin Exp Ophthalmol 2022;260:121-32.
19. Viera AJ, Garrett JM. Understanding interobserver agreement: The kappa statistic. Fam Med 2005;37:360-3.
20. Bru- C, Tseng JJ, Barbazetto I, Lima LH, Yannuzzi LA. Peculiar manifestation of macular telangiectasia type 2. Retin Cases Brief Rep 2011;5:309-12.
21. Clemons TE, Gillies MC, Chew EY, Bird AC, Peto T, Figueroa MJ, *et al.* Baseline characteristics of participants in the natural history study of macular telangiectasia (MacTel) MacTel Project Report No. 2. Ophthalmic Epidemiol 2010;17:66-73.
22. Bruee C, Chang LK, Freund KB, Yannuzzi LA. Peripheral polypoidal choroidal neovascularization, subretinal hemorrhage, and cataract surgery. Retin Cases Brief Rep 2009;3:364-6.
23. Wang Q, Tuten WS, Lujan BJ, Holland J, Bernstein PS, Schwartz SD, *et al.* Adaptive optics microperimetry and OCT images show preserved function and recovery of cone visibility in macular telangiectasia type 2 retinal lesions. Invest Ophthalmol Vis Sci 2015;56:778-86.
24. Jacob J, Krivosic V, Paques M, Tadayoni R, Gaudric A. Cone density loss on adaptive optics in early macular telangiectasia type 2. Retina 2016;36:545-51.