Characteristics Upon Presentation of Patients with Type 2 Macular Telangiectasia in Puerto Rico

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Objective: To describe the systemic disease associations and clinical features upon initial presentation of a cohort of patients with type 2 macular telangiectasia who live in Puerto Rico.

Methods: A retrospective review of patients with macular telangiectasia was performed in 4 private retina practices in Puerto Rico. The demographic and clinical characteristics were recorded.

Results: Twenty-one patients who were diagnosed with macular telangiectasia were included in the analysis. The median age of presentation was 62 years; 86% were female, and all patients were Hispanics. The median visual acuity at presentation was 20/50. A prior medical diagnosis of type II diabetes mellitus was found in 15 (71.4%) patients, essential hypertension in 12 (57.1%), and dyslipidemia in 9 (42.9%). All patients had bilateral disease. The most common ocular findings were the presence of right-angle vessels in 32 (76.2%) eyes and angiographic hyperfluorescence temporal to the fovea, found in 22 (52.4%) of the affected eyes. One eye had evidence of choroidal neovascularization.

Conclusion: Our cohort showed a higher prevalence of type 2 diabetes in patients with type 2 macular telangiectasia than in other cohorts. It also supports the findings of other studies showing that macular telangiectasia patients are more likely to have type 2 diabetes and hyperlipidemia. However, the increased prevalence of diabetes and hyperlipidemia may be due to selection bias, and further studies are needed to assess the significance of these findings.

Key words: Macular telangiectasia, Retina, Puerto Rico

Macular telangiectasia is a rare macular disease, initially termed idiopathic juxtafoveal retinal telangiectasia, characterized by abnormal vascular dilation of the capillaries in the juxtafoveal area of the macula (1). Since 2006 the classification of macular telangiectasia has been simplified by Yannuzzi et al. into three distinct groups, each with a presumed independent etiology, based on bio-microscopical, fluorescing angiography (FA), and optical coherence tomography (OCT) findings (1). Macular telangiectasia has been categorized into three types: Type 1 is usually characterized by a unilateral presentation and is predominant in males; Type 2 usually presents bilaterally in middle-aged people; and Type 3, which is the rarest presentation, usually presents with a vaso-occlusive etiology (1).

The pathophysiology of macular telangiectasia is still a subject of debate. Initially, Gass et al. proposed an etiology that entailed vascular insufficiency, which led to hypoperfusion, subsequent retinal tissue injury, and atrophy (2). However, recent developments by Powner et al. have shown that the areas affected by macular telangiectasia have an abnormally dilated vasculature in the deep plexus and depletion of Muller cells (3,4). These contributions, and imaging studies, such as OCT and laser ophthalmoscopy, suggest that macular telangiectasia's vascular changes are the secondary features of a neurodegenerative process (4–6). Although precisely what triggers the process of neurodegeneration remains unclear, the loss of Muller cells is thought to play an essential role in the pathologic process (7–9).

The prevalence of macular telangiectasia is estimated to be in the order of 0.12% (5,10). Furthermore, the improved ability to diagnose macular telangiectasia using digital imaging

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techniques such as FA and OCT suggests that prior studies may have underestimated this condition's prevalence. Symptoms typically start in the fifth to the sixth decade (5,11). Associated systemic conditions usually include hypertension, diabetes, and heart disease (1,12). Although several studies are underway in search of possible treatments for macular telangiectasia, there is currently no proven therapy (9,12).

To our knowledge, no prior studies have analyzed the clinical characteristics and systemic disease associations of patients living in Puerto Rico with a diagnosis of macular telangiectasia. With this study, we seek to improve our understanding of the clinical spectrum, severity, and demographics of this disease in our Puerto Rican population.

Materials and Methods

This retrospective study was approved by the Institutional Review Board at the University of Puerto Rico, complied with the Health Insurance Portability and Accountability Act of 1996, and followed the tenets of the Declaration of Helsinki. A requirement for patient informed consent was waived, as the study was considered of minimal risk due to the de-identified data collection and retrospective nature. We reviewed the charts from the four private retina practices. Charts from May 1, 2012, to November 31, 2019, with an International Classification of Diseases (ICD) diagnostic code for retinal telangiectasia (ICD-10-H35.071, ICD-10-H35.072, and ICD-10-H35.073) were selected for review. After carefully reviewing clinical records and imaging studies, all patients meeting diagnostic criteria for macular telangiectasias type 2 (MT2) were included in the study.

Demographic features, including the patients' age and sex, and clinical data including systemic disease history, best-corrected visual acuity (BCVA), and examination findings were recorded. When available, imaging studies were reviewed, including color fundus photography, fundus autofluorescence, FA and indocyanine green angiography, and spectral-domain OCT were reviewed by a single masked retina specialist to improve ascertainment. Descriptive statistical analysis was performed using the Google Sheets® software program.

Results

A total of 21 Hispanic patients were identified with a diagnosis of MT2, 18 (86%) females and 3 (14%) males. The median age of diagnosis was 62 years (range 49-75). Systemic findings included prior medical diagnosis of type II diabetes mellitus in 71.4% (n=15) of patients, arterial hypertension was present in 57.1% (n=12) of patients, dyslipidemia in 42.9% (n=9), hypothyroid in 19% (n=4), arthritis in 14.2% (n=3), neuropathy in 14.2% (n=3), and osteoporosis in 9.5% (n=2) (See Table 1). Other prior diagnoses identified were coronary artery disease, asthma, emphysema, and Sjogren's syndrome. There was only one patient recorded as a daily smoker. At presentation, the median BCVA was 20/50. All eyes had a visual acuity of 20/200 or better; 78.6% of eyes had 20/50 or better; 40.5% of eyes had 20/30 or better. No eyes had 20/20 visual acuity. Three patients (14.3%) had a history of bilateral cataract surgery, and one had unilateral surgery.

Table 1. Demographic Characteristics and Systemic Diseases of Patients with Type 2 Macular Telangiectasia

Number of patients (n)	**21**
Median age (y)	62
Gender (%)	
Female	86
Male	14
Race (%)	
Hispanic	100
History of Systemic Disease (%)	
Type 2 Diabetes Mellitus	71
Arterial Hypertension	57
Dyslipidemia	43

The most common findings were the presence of right-angle vessels in 32 eyes (76.2%), telangiectatic vessels in 28 eyes (66.7%), yellow crystalline deposits in 26 eyes (61.9%), and angiographic hyperfluorescence temporal to the fovea in 22 eyes (52.4). Other findings included an epiretinal membrane in 12 eyes (28.6%), pigment hyperplasia in 10 eyes (23.8%), macular cysts in 3 eyes (7.1%), and retinal transparency was found in 2 eyes (4.8%) (See Table 2). One patient had a choroidal neovascular membrane, which was unilateral.

Table 2. Retinal Findings in Patients with Type 2 Macular Telangiectasia

Ocular characteristics		
Feature	**Eyes affected**	**Bilateral**
Right Angle Vessels	32/42 (76.2%)	14/21 (66.7%)
Telangiectatic Vessels	28/42 (66.7%)	14/21 (66.7%)
Yellow Deposits (Crystals)	26/42 (61.9%)	11/21 (52.4%)
Temporal Hyperfluorescence	22/42 (52.4%)	11/21 (52.4%)
Fluorescein Leakage	15/42 (35.7%)	7/21 (33.3%)
Epiretinal Membrane	12/42 (28.6%)	4/21 (19.1%)
Pigment Hyperplasia	10/42 (23.8%)	3/21 (14.3%)
Macular Cysts	3/42 (7.1%)	1/21 (4.8%)
Retinal Transparency	2/42 (4.8%)	1/21 (4.8%)

Discussion

We retrospectively evaluated the demographic features of MT2 in patients of four private retina practices in Puerto Rico. As in other Caucasian cohorts, the median age at diagnosis in our study was in the sixth decade of life (2,13,14). Our cohort was predominantly female, and all patients had bilateral disease, which concurs with features of MT2 as described by Gass and Blodi (2,13). All eyes had visual acuity better than 20/200; 78.6% of eyes had a visual acuity of 20/50 or better, and 40.5% of eyes had a visual acuity of 20/30, suggesting that patients had already begun to experience visual acuity loss, as would be

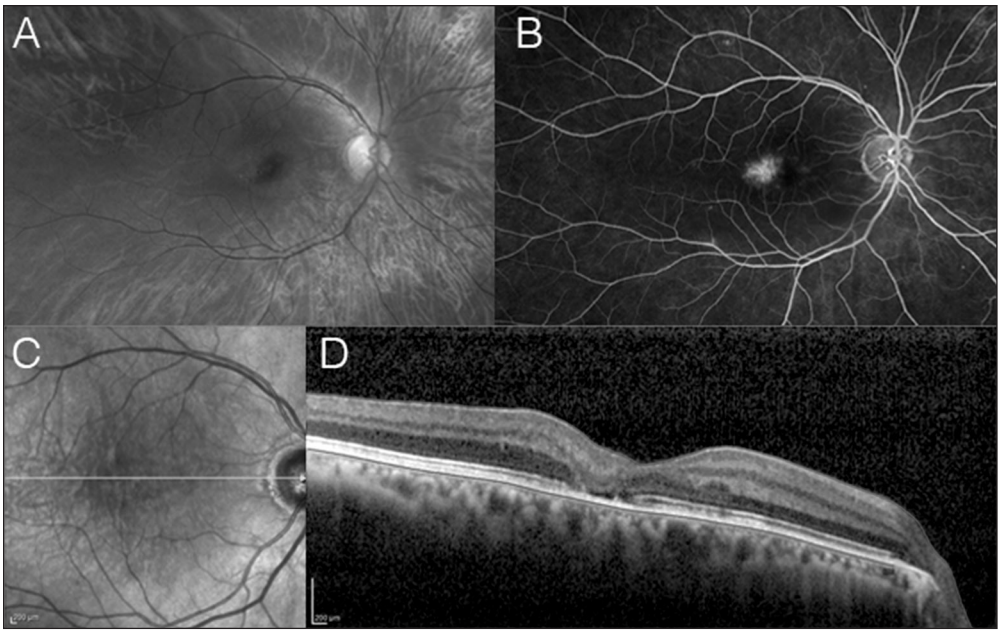

Figure 1. Right eye fundus images of a patient with Type 2 macular telangiectasia. Color fundus photograph (A) showing telangiectatic vessels and crystalline deposits temporal to the fovea. The late phase of a fluorescein angiogram (B) showing hyperfluorescence temporal to the fovea. A spectral domain optical coherence tomography photograph (C) and cross-section (D) revealing the corresponding atrophic changes in the outer neurosensory retina.

expected (14,15). Other cross-sectional multicenter studies report similar visual acuity findings indicating that severe vision loss in patients with MT2 is overall rare (16).

In our cohort, type 2 diabetes was prevalent in 71.4% of patients, which is higher than the expected prevalence of 32.6% for Puerto Ricans in the 65 - 74 age group, and also higher than other cohorts of patients with MT2 (17,18). Although we can observe a possible association between type 2 diabetes mellitus and MT2 consistent with extensive studies in other western population cohorts (13), we must be careful to jump to conclusions due to the clinics in our study having a selection bias towards diabetic patients who have a higher frequency of visual loss and disease. Our cohort also supports other investigators' findings suggesting that patients with MT2 are more likely to have type 2 diabetes and hyperlipidemia even when differences in age and sex are accounted for amongst cohorts (19). In contrast, the proportion of patients with hypertension in our cohort was lower than expected when compared to other studies (13).

The most common clinical findings in our study included right angle vessels, telangiectatic vessels, yellow deposits, and temporal hyperfluorescence. These findings are comparable to those of other studies on different cohorts (1,5). MT2 was described as perifoveal telangiectasia by Gass-Blodi's classification (2); in accordance to their description, clinical findings were limited to the perifoveal area (1,2). Some of the key features of MT2, such as cystoid changes subsequent retinal atrophy may be analyzed, quantified, and monitored with OCT (1). Yannuzzi et al. propose that the presence and progression of these cysts may be due to a neurodegenerative process in which Muller cells are distorted and consequently lead to retinal atrophy (1).

Although choroidal neovascularization is not a hallmark feature of MT2, it remains a potential complication for these patients (20). The retinal pigment epithelium (RPE) anomalies, which are present in these patients may pave the way for the development of sub-clinical sub-RPE extension of neovascular membranes (20). In our cohort one patient had evidence of choroidal neovascular membranes at presentation. The neovascular membrane was comprised of a combination of subretinal and sub-RPE components, which would categorize it as a composite of Type 1 and Type 2 CNVM. The presence of this patient further supports Yannuzzi et al.'s observation of the presence of such membranes in patients with MT2 (20).

Epiretinal membranes have been known to be idiopathic or secondary to a present ocular pathology; in the case of MT2, it has been demonstrated they can occur concomitantly (21). Epiretinal membranes were seen in 28.7% of eyes. The formation of these membranes is speculated to be a manifestation of Muller cell dysfunction and atrophy, secondary to the loss of macular pigment (5). The loss of Muller cells and their capacity to regulate endothelial and metabolic functions of adjacent cells cause rupture of the blood-retina barrier potentially causing edema and an epiretinal membrane (12,21).

The use of multimodal imaging is of utmost importance when evaluating patients suspected or confirmed as having MT2 (12). Color fundus photography allows us to evaluate the presence of subtle lesions that can be missed by biomicroscopy or OCT (12,22). While OCT angiography may help identify perfusion anomalies and perifoveal capillary dilations, traditional FA may show the typical perifoveal leakage, which may help clinicians establish a diagnosis (12,23).

As with all retrospective studies, our data must be interpreted with caution. As not all patients were evaluated with all the different imaging modalities available, ascertainment bias may have been introduced. However, we sought to improve our ascertainment by having all imaging studies, when available,

reviewed by a single masked retina specialist. Our study was also limited by the small sample size; however, we included all the charts at 4 private retina practices. Other limitations included variability among different imaging platforms used by the various ophthalmology clinics. Referral bias may have been introduced as less severe cases of MT2 may have remained not referred by primary ophthalmologists. Similarly, selection bias may be present as many patients may have been diagnosed with MT2 incidentally, as they were being screened or evaluated for the presence of diabetic retinopathy at the respective retina practices.

Resumen

Objetivo: Describir las asociaciones de enfermedades sistémicas y características clínicas en la presentación inicial de una cohorte de pacientes con telangiectasia macular tipo 2 que viven en Puerto Rico. Métodos: Revisión retrospectiva de pacientes con telangiectasia macular tipo 2 en cuatro prácticas de retina privadas en Puerto Rico. Se analizaron las características demográficas y clínicas. Resultados: Veintiún pacientes con diagnóstico de telangiectasia macular tipo 2 fueron incluidos en el análisis. La edad mediana en la presentación fue 62 años; 86% eran mujeres y todos los pacientes eran hispanos. La agudeza visual mediana en la presentación fue 20/50. Un diagnóstico previo de diabetes mellitus tipo II fue encontrado en 15 (71.4%) de los pacientes, hipertensión esencial en 12(57.1%) y dislipidemia en 9 (42.9%). Los hallazgos oculares más comunes fueron vasos en ángulo recto en 32 (76.2%) ojos, e hiperfluorescencia temporal en 22 (52.4%) ojos. Solo un ojo se encontró que tenía neovascularización coroidea. Conclusiones: La prevalencia de diabetes tipo 2 es más alta en nuestra cohorte cuando comparamos otras cohortes de telangiectasia macular tipo 2. Nuestra cohorte también confirma los hallazgos de otros estudios que encuentran que los pacientes con telangiectasia macular tipo dos son más probables en tener diabetes tipo dos e hiperlipidemia. Sin embargo, la prevalencia de diabetes e hiperlipidemia elevada puede ser debido a sesgo de selección. Se requieren estudios adicionales para evaluar nuestros resultados.

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