Macular Telangiectasia Type 1: Capillary Density and Microvascular Abnormalities Assessed by Optical Coherence Tomography Angiography

ALEXANDRE MATET, ALEJANDRA DARUICH, ALI DIRANI, AUDE AMBRESIN, AND FRANCINE BEHAR-COHEN

• PURPOSE: To describe microvascular abnormalities and capillary density in macular telangiectasia type 1 (MT1) using optical coherence tomography angiography (OCTA), and correlate them with fluorescein angiography (FA).

• DESIGN: Observational case series.

• METHODS: Seven patients with MT1 and 12 age-matched controls were included. Focal microvascular dilations were identified on 3 × 3 mm OCTA and early-frame FA images. OCTA images were processed to determine the global capillary density after subtraction of larger vessels and cystoid edema cavities. Local capillary densities were calculated inside 100-μm circles around telangiectasias, projected over superficial (SCP) and deep capillary plexuses (DCP). They were compared to a random sample of 100-μm circles generated in each OCTA image. FA images were processed to measure mean perifoveal intercapillary areas (PIA), inversely reflecting capillary density.

• RESULTS: In MT1 eyes, fewer telangiectasias were identified with OCTA than with FA ($P = .016$), exclusively localized in the DCP ($P = .016$). Rarefaction of both capillary plexus and abnormal microvascular morphology were better identified by OCTA than by FA. The global capillary density on OCTA was significantly lower in MT1 eyes than in fellow and control eyes, respectively: SCP, 0.347 vs 0.513 ($P = .004$) and 0.560 ($P = .0005$); DCP, 0.357 vs 0.682 ($P = .016$) and 0.672 ($P = .0005$). Capillary density was significantly reduced around telangiectasias in both SCP ($P = .021$) and DCP ($P = .042$). Capillary density of the SCP correlated inversely with the mean PIA on FA ($r = -0.94$, $P = .017$). LogMAR visual acuity was inversely correlated with SCP ($r = -0.88$, $P = .012$) and DCP capillary densities ($r = -0.79$, $P = .048$).

• CONCLUSIONS: OCTA confirmed that global and focal capillary depletion is associated with MT1. (Am J Ophthalmol 2016;167:18–30. © 2016 Elsevier Inc. All rights reserved.)

MACULAR TELANGIECTASIA TYPE 1 (MT TYPE 1) IS a congenital or developmental vascular disorder affecting mostly male subjects and consisting of focal, exudative dilations of perifoveal retinal capillaries.[1] It is usually unilateral, may extend beyond the macula, and therefore may be part of the larger spectrum of Coats disease.[2] Historically, the condition has been termed "miliary aneurysms" by Leber,[3] "idiopathic juxtafoveal telangiectasis" (group 1A-1B) by Gass and Blodi,[1] "Type 1 aneurysmal telangiectasia" by Yannuzzi and associates,[4] and finally MT type 1 in the recent classification by the MacTel Study Group.[5]

In contrast with type 2 idiopathic macular telangiectasia or "MacTel2," in which telangiectasias develop along with pathognomonic degenerative alterations of the retinal architecture linked to Müller cell depletion,[6,7] MT type 1 is primarily a vascular disease, complicated by macular edema originating from the exudative telangiectasias.[4] Fluorescein angiography (FA) allows the visualization of telangiectasias, but its ability to image the fine perifoveal capillaries at high resolution and to discriminate between the superficial and deep capillary plexuses is limited. Moreover, these lesions and the surrounding perifoveal capillaries are visible exclusively during the early frames of the sequence, since details are progressively submerged by dye diffusion from telangiectasias.

Optical coherence tomography angiography (OCTA) is a recent noninvasive imaging technology based on the detection of flows that provides a representation of the microvascular morphology. Absence of dye diffusion and higher resolution help to overcome limitations of FA to image the perifoveal capillary network.[8,9] Moreover, the segmentation of volumes acquired by OCTA produces a separate visualization of the superficial and the deep retinal capillary plexuses. To date, several groups have employed OCTA to describe normal features of the

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From the Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital. Fondation Asile des Aveugles, Lausanne, Switzerland (A.M., A.Daruich, A.Dirani, A.A., F.B.-C.); and Inserm, U1138, Team 17, From Physiopathology of Ocular Diseases to Clinical Development, Université Paris Descartes Sorbonne Paris Cité, Centre de Recherche des Cordeliers, Paris, France (F.B.-C.).

Inquiries to Francine Behar-Cohen, Hôpital Ophtalmique Jules-Gonin, Avenue de France 15, CP 133, 1000 Lausanne 7, Switzerland; e-mail: francine.behar@gmail.com

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macular microvasculature[10–14] and to describe fine alterations involving both plexuses in several vascular disorders, such as retinal vein occlusion,[15–17] diabetic retinopathy,[18–20] and MT type 2.[21,22] Furthermore, the recent adjunction of quantitative tools has expanded the ability of OCTA to investigate highly detailed abnormalities of the retinal microvasculature, such as vessel density or non-flow areas.[9,23]

Imaging MT type 1 eyes with OCTA, we have described the vascular abnormalities ("telangiectasias") and their vascular microenvironment. We used a quantitative analysis of OCTA images to compare the macular capillary density of MT type 1 eyes with fellow eyes and with healthy control eyes. We then correlated OCTA findings with FA imaging.

METHODS

• **SUBJECTS:** This observational case series adhered to the tenets of the Declaration of Helsinki and Swiss federal regulations and was approved by the local Ethics Committee of the Swiss Department of Health (CER-VD no. 19/15). The study was conducted from June 1 to October 1, 2015, at Jules-Gonin Eye Hospital, Lausanne, Switzerland.

Medical records, optical coherence tomography (OCT), OCTA, FA, and indocyanine green angiography (ICGA) images from 7 consecutive subjects presenting with MT type 1 were retrospectively analyzed. The diagnosis of MT type 1 was based on the presence of unilateral, exudative telangiectasia affecting the macular area, without any clinical sign or history suggestive of vascular occlusion, posterior segment inflammation, or other causes of secondary macular telangiectasia. Exclusion criteria were age <18 years and spherical equivalent <−2 diopter (D) or >+2 D.

Twelve eyes from 12 healthy subjects imaged by OCTA were selected from the local OCTA database based on age and sex to serve as a control group.

• **IMAGE ACQUISITION AND SEGMENTATION:** The instrument used for en face OCT and OCTA images, Angiovue RTx 100, is based on the AngioVue Imaging System (Optovue, Inc, Fremont, California, USA) to obtain amplitude decorrelation angiography images. This instrument has an A-scan rate of 70 000 scans per second, using a light source centered on 840 nm and a bandwidth of 50 nm. Each OCTA volume contains 304 × 304 A-scans with 2 consecutive B-scans captured at each fixed position before proceeding to the next sampling location. Split-spectrum amplitude-decorrelation angiography (SSADA) was used to extract the OCT angiography information. Each OCTA volume is acquired in 3 seconds and 2 orthogonal OCTA volumes were acquired in order to perform motion correction to minimize motion artifacts arising from microsaccades and fixation changes. Angiography information displayed is the average of the decorrelation values when viewed perpendicularly through the thickness being evaluated.

In order to obtain comparable 3 × 3-mm OCTA scans between subjects, volumes were automatically segmented by the software provided by the manufacturer to provide images of the superficial plexus (3 μm below the inner limiting membrane to 16 μm below the outer border of the inner plexiform layer) and deep plexus (16–69 μm below the outer border of the inner plexiform layer). We controlled the correct segmentation for each patient before reporting the data.

The central macular thickness was measured on the Angiovue RTx 100 OCT in the central subfield of an Early Treatment Diabetic Retinopathy Study (ETDRS) grid centered on the fovea.

FA and ICGA were performed on Spectralis (Heidelberg Engineering, Heidelberg, Germany). Early frames (≤50 seconds after dye injection) were acquired with a 30-degree lens to visualize the macular microvasculature. Image quality was optimized using the "sharpen" tool of the Heidelberg Eye Explorer software (Version 1.9.10.0; Heidelberg Engineering). Angiograms were rotated and cropped to match the 3 × 3-mm OCTA scans centered on the fovea, using ImageJ (Version 1.50c4, Wayne Rasband; National Institutes of Health, Bethesda, Maryland, USA).

• **IDENTIFICATION OF MICROVASCULAR ABNORMALITIES:** OCTA images from normal and MT type 1 subjects and FA and ICGA images from MT type 1 eyes were presented randomly to 3 masked independent observers (A.A., A.Da., F.B.C.) during separate sessions for each imaging modality. Lesions identified as microvascular abnormalities were labeled by each observer, and those labeled by 2 observers or more were retained. The interobserver reliability was assessed using a 2-way, mixed-model intraclass correlation coefficient based on the number of lesions identified per OCTA, FA, or ICGA image. Numbers of lesions in the deep and superficial capillary plexuses on OCTA were compared using a Wilcoxon signed-rank paired test.

• **QUANTITATIVE DETERMINATION OF CAPILLARY VESSEL DENSITY ON OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY:** The vascular densities of the capillary network in the superficial and deep plexuses were assessed by a custom semi-automated, intensity-based algorithm on Matlab (Mathworks, Natick, Massachusetts, USA).

First, original grayscale OCTA images were processed to detect pixels corresponding to vascular flow. In each image (Figure 1, Top and Bottom left), a region of interest (ROI) inside the foveal avascular zone that did not include dark areas corresponding to intraretinal cystoid cavities was manually outlined to define the background intensity of the intervascular retinal tissue. Using the threshold intensity $I_{threshold} = Mean\ (ROI\ pixels) + 2 \times$