

RETINAL HAMARTOMAS AT DIFFERENT STAGES IN A PATIENT WITH TUBEROUS SCLEROSIS - OCT-SS DESCRIPTION

Paula Dias¹, Anna Linhares¹, and Kenzo Hokazono¹

¹Universidade Federal do Parana

June 27, 2023

RETINAL HAMARTOMAS AT DIFFERENT STAGES IN A PATIENT WITH TUBEROUS SCLEROSIS - OCT-SS DESCRIPTION

Abstract:

A 11-year-old female patient with tuberous sclerosis presented with retinal hamartomas at different stages of evolution in the optical coherence tomography with Sweep Source technology (OCT-SS). The right eye presented with three lesions spectra. Lesion 1, at an earlier stage, maximum thickness (MT) of 336 μm , preserved inner nuclear and inner plexiform layers and disorganization of the ganglion cell layer. Lesion 2, MT of 438 μm and disorganization of the ganglion cell, inner nuclear and inner plexiform layers, but outer plexiform layer apparently preserved. Lesion 3, a hyperreflective dome-shaped proliferation with posterior shadow, MT of 1478 μm , presented “moth-eaten” empty optical spaces, with an apparent complete rupture of the retinal anatomy. In the left eye, the lesion had a MT of 342 μm , preserved the retinal anatomy, located at the level of the retinal nerve fiber layer, and identifiable ganglion cell layer.

Keywords:

Tuberous sclerosis, case report, retinal hamartomas, optical coherence tomography, OCT

Introduction:

Retinal astrocytic hamartoma (RAH) is a benign glial tumor that may be present in patients with Tuberous Sclerosis (TS)¹, a genetic phakomatosis caused by the mutation of the tumor suppressor genes TSC1 or TSC2^{2,3}. To diagnose TS, two major or one major and two minor criteria are necessary, with RAH being a major criteria^{4,5}.

Hamartomas identified through indirect ophthalmoscopy are big enough to change vessels and optic disc anatomy, but RAH not diagnosed in previous fundoscopies may appear in optical coherence tomography (OCT). Using OCT, the prevalence of RAH was identified in 80% of patients with TS⁴. This highlights the clinical relevance of a non-invasive diagnostic method of subclinical lesions and clinical characterization of patients with TS⁴.

The purpose of this report is to describe and characterize retinal hamartomas at different stages of evolution with OCT with Sweep Source technology (OCT-SS) of a patient with TS. It was observed that hamartomas initially compromise the inner retina layers with progression to the outer layers as they grow and calcify. More descriptive studies of OCT aspects are needed to better classify retinal hamartomas, due to their high prevalence in patients with TS.

Case presentation:

A 11-year-old female patient had no findings in both eyes in the slit-lamp biomicroscopic examination. The fundus examination revealed bilateral retinal tumors: six in the right eye (Figure 1A) and five in the left eye (Figure 1B). In the right eye, two lesions were located inferotemporal and two superotemporal, one inferonasal and one superior. The inferotemporal lesion was yellow, elevated, with central calcification and translucent area on the periphery, corresponding to the usual description of transitional hamartomas, also called type III astrocytic hamartomas. The other five lesions were at the arcade level and were yellow/gray-colored, translucent, with imprecise limits, without calcifications and with obscuration of retinal vasculature, corresponding to astrocytic type I hamartomas or flat hamartomas. The left eye presented all tumors at the arcade level: two superotemporal, one inferotemporal, two temporal in the periphery, all corresponding to type I astrocytic hamartomas. There was no retinal detachment, lesions affecting the optic disc or macula in both eyes.

OCT confirmed the diagnosis of TS, revealing dome-shaped hyperreflective masses in both eyes at different stages of evolution. In the right eye, three different spectra of lesions were observed, all of which had a gradual transition to the normal retina. Lesion 1, at an earlier stage, had a maximum thickness of 336 μm , with preserved inner nuclear and inner plexiform layers. Disorganization of the ganglion cell layer was observed (Figure 2A). Lesion 2 had a maximum thickness of 438 μm . A disruption in the normal structure of the retinal layers was observed, with disorganization of the ganglion cell, inner nuclear and inner plexiform layers. Outer plexiform layer was apparently preserved (Figure 2A). Lesion 3, of the transitional type, appeared as a hyperreflective dome-shaped proliferation with posterior shadow, with a maximum thickness of 1478 μm , presenting “moth-eaten” empty optical spaces, with an apparent complete rupture of the retinal anatomy (Figure 2B). In the left eye, Lesion 4 was observed with a maximum thickness of 342 μm , with preservation of the retinal anatomy, located at the level of the retinal nerve fiber layer (RNFL), making it possible to identify the ganglion cell layer, different from lesion 1 (Figure 2C).

The patient was seen 1 year after the OCT examination. The HARs remain stable and the patient maintains a visual acuity of 1.0 in both eyes. She will continue to follow up with her ophthalmologist.

Discussion:

The hamartomas present themselves in a heterogeneous way, being classified in three groups. Type 1 is relatively flat, without calcifications and translucent gray-white. Type 2 is elevated, multinodular, calcified, opaque and “blackberry” shaped. Finally, type 3 characterizes a transitional lesion between those already mentioned. Type 1 injury has been described as the most common form, occurring in up to 70% of cases. Type 2 represents 55% and type 3, 9% of patients⁶. Zhang et al showed the prevalence of type 1 RAH in 94% of cases, type 2 in 7% and type 3 in 19%⁷. These results coincided with the prevalence reported by Kiribuchi et al in Japan⁸, but very different from the prevalence in Western countries, which suggests the importance of ethnicity in RAHs development⁷. These lesions can be found concomitantly. Zhang et al found more than one type of RAH in 17.4% of the TS patients⁷.

Pichi et al proposed a new classification of RAHs based on OCT findings: type I, flat lesion within the RNFL without retinal traction; type II, mildly elevated hyperreflective lesion (height <500 μm) with retinal traction and internal retinal disorganization; type III, elevated retinal mass (height >500 μm) mushroom shaped, with internal retinal calcification with “moth-eaten” appearance; type IV, elevated (height >500 μm) dome-shaped, non-calcified retinal mass with optically empty cavity⁹.

Mutolo et al proposed a new subcategory of hamartomas (Type IIb), in addition to type Iia lesions, described by Pichi et al as type II. Type Iib lesions were characterized by an elevated retinal mass (>500 μm) above the RNFL with or without retinal adhesion or traction on the tumor surface, associated with a heterogeneous intratumoral appearance, which could vary from a full appearance to the presence of tumors to the presence of intralesional little empty spaces or cysts, and to the existence of segmented vascular calcifications; inner retinal layer, outer retinal layer, and full retinal thickness can be involved with or without posterior optical shadowing⁴.

In our report, it was possible to observe 4 different spectra of lesions in the OCT. According to Pichi et

al⁹, lesions can be classified into type I (lesion 4), type II – Iia in Mutolo et al⁴ classification – and type III (lesions 2 and 3, respectively). An injury does not fit this classification (lesion 1). Lesion 1 has type Iia features, but has a maximum thickness <500 µm. Another difficulty for classification was the involvement of the retinal layers. Even though lesion 2 was classified as Iia, it has a different involvement of the retinal layers when compared to lesion 1 – also classified as Iia. The difficulty found in this classification was also reported by Kato et al and Mutolo et al, which reinforces the need for more descriptive studies of OCT aspects^{4,10}.

Zhang et al showed that more than half of type 1 RAHs are located in the temporal retina, often near the end of the arcades⁷. In our report, 66.6% of the lesions in the right eye and 100% of the lesions in the left eye were in the temporal region. However, calcified RAHs – especially type 2 – are more commonly found in the peripapillary region. The observation of greater retinal vascular diameters in the temporal retina, indicating a greater blood supply when compared to the nasal one, may explain the higher incidence of RAHs in this region^{7,11}.

Demonstration of the microstructure of RAHs using OCT is not only useful for detecting small or semi-transparent lesions that are easy to miss on examination, but also facilitates the differentiation of RAH from retinoblastoma, combined retinal hamartoma, and choroidal tumors^{1,6}. Furthermore, some authors have suggested that, over time, translucent tumors may evolve into multinodular lesions that have undergone cystic, hyaline or calcified changes, as if type 2 tumors represent a late stage of the lesions¹², so, OCT may also facilitate the follow-up of lesions^{4,12}.

Conclusion:

This study described 4 different spectra of hamartomas using OCT-SS, which allowed a deeper evaluation of the lesions. Hamartomas initially compromise the inner retina layers with progression to the outer layers as they grow and calcify. OCT is a non-invasive method which assists the diagnosis of subclinical lesions and clinical characterization of patients with TS. More descriptive studies of OCT aspects are needed to better classify retinal hamartomas, due to their high prevalence in patients with TS.

References:

1. Shields CL, Benevides R, Materin MA, Shields JA. Optical coherence tomography of retinal astrocytic hamartoma in 15 cases. *Ophthalmology* 2006;**113** :1553–1557. <https://doi.org/10.1016/j.ophtha.2006.03.032>
2. Krueger DA, Northrup H. Tuberous sclerosis complex surveillance and management: recommendations of the 2012 international tuberous sclerosis complex consensus conference. *Pediatr Neurol* 2013;**49** :255–65.
3. Aziria A, Chapron T, Martin G et al. Tuberous sclerosis: Diagnosis on ocular fundus examination. *J Fr Ophtalmol* 2021;**44** :399-402. <https://doi.org/10.1016/j.jfo.2020.10.010>
4. Mutolo MG, Marciano S, Benassi F et al. Optical coherence tomography and infrared images of astrocytic hamartomas not revealed by funduscopy in tuberous sclerosis complex. *Retina* 2017;**37** :1383–1392.
5. Hodgson N, Kinori M, Goldbaum MH, Robbins SL. Ophthalmic manifestations of tuberous sclerosis: a review: ocular findings in tuberous sclerosis. *Clin Exp Ophthalmol* 2017;**45** :81–6.
6. Rowley SA, O’Callaghan FJ, Osborne JP. Ophthalmic manifestations of tuberous sclerosis: a population based study. *Br J Ophthalmol* 2001;**85** :420–423. <https://doi.org/10.1136/bjo.85.4.420>
7. Zhang C, Xu K, Long Q, Yang Z, Dai R, Du H, Li D, Zhang Z. Clinical features and optical coherence tomography findings of retinal astrocytic hamartomas in Chinese patients with tuberous sclerosis complex. *Graefes Arch Clin Exp Ophthalmol* 2020;**258**(4): 887-892. Doi:10.1007/s00417-019-04476-y
8. Kiribuchi K, Uchida Y, Fukuyama Y, Maruyama H. High incidence of fundus hamartomas and clinical significance of a fundus score in tuberous sclerosis. *Brain and Development* 1986;**8** :509–517.
9. Pichi F, Massaro D, Serafino M et al. Retinal astrocytic hamartoma: optical coherence tomography classification and correlation with tuberous sclerosis complex. *Retina* 2016;**36** :1199–1208.

<https://doi.org/10.1097/IAE.0000000000000829>

10. Kato A, Obana A, Gohto Y, Seto T, Sasano H. Optic coherence tomography appearances of retinal astrocytic hamartoma and systemic features in tuberous sclerosis of Japanese patients. *European Journal of Ophthalmology* 2019;**29**(3): 330-337. Doi:10.1177/1120672118787441
11. Gao L, Wang FH, Chen N, Dong CX, Liu SJ. Non-symmetry in the calibre of retinal blood vessels. *Int J Ophthalmol* 2009;**9** :1537– 1539.
12. Zhang ZQ, Shen C, Long Q et al. Sirolimus for retinal astrocytic hamartoma associated with tuberous sclerosis complex. *Ophthalmology* 2015;**122** :1947–1949.

Legends

Figures 1A and 1B – fundus photography showing six lesions in the right eye (Figure 1A) and five in the left eye (Figure 1B).

Figures 2A, 2B and 2C – OCT showing Lesion 1 (blue arrow), MT of 336 μm , preserved inner nuclear and inner plexiform layers and disorganization of the ganglion cell layer (Figure 2A). Lesion 2 (orange arrow), MT of 438 μm , disruption in the normal structure of the retinal layers with disorganization of the ganglion cell, inner nuclear and inner plexiform layers (Figure 2A). Lesion 3 (yellow arrow), a hyperreflective dome-shaped proliferation with posterior shadow, MT of 1478 μm , presented “moth-eaten” empty optical spaces, with an apparent complete rupture of the retinal anatomy (Figure 2B). Lesion 4 (green arrow), MT of 342 μm , preserved the retinal anatomy, located at the level of the RNFL, making it possible to identify the ganglion cell layer (Figure 2C).

Conflict of interest:

The authors declare that they have no competing interests.

Authors’ contributions:

PBD, ACBL, KH: involved in data collection, literature search, and manuscript preparation. All authors read and approved the final manuscript.

Ethical approval

The article describes a case report. Therefore, no additional permission from our Ethics Committee was required.



