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Retinal Astrocytic Hamartoma Arises in Nerve Fiber Layer and Shows "Moth-Eaten" Optically Empty Spaces on Optical Coherence Tomography

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Purpose: To evaluate the specific spectral-domain (SD) optical coherence tomography (OCT) features of retinal astrocytic hamartoma (RAH) and the relationship of these features with tumor size and location.

Design: Retrospective case series.

Participants: Forty-seven eyes of 42 patients with RAH.

Methods: All patients with clinically confirmed RAH were imaged with fundus photography and SD OCT.

Main Outcome Measures: Precise OCT location of RAH features and the relationship of patient age, visual acuity, tumor size, and tumor location to the presence and size of intralesional optically empty spaces (OESs), appearing as so-called moth-eaten spaces.

Results: Of 42 patients with RAH, 36 (86%) had unilateral disease and 6 (14%) had bilateral disease. Systemic tuberous sclerosis complex was present in 8 patients (19%). The largest tumor (per eye) demonstrated a mean basal diameter of 3.0 mm (median, 2.0 mm) and a mean thickness of 1.9 mm (median, 1.8 mm). The mean tumor proximity to the foveola was 3.0 mm and that to the optic disc was 1.8 mm. Related features included subretinal fluid (n = 9; 19%), cystoid retinal edema (n = 6; 13%), retinal traction (n = 11; 23%), intralesional cavities (n = 28; 60%), and intralesional calcification (n = 29; 62%). On SD OCT, the tumor epicenter was in the nerve fiber layer (n = 47; 100%), with all other retinal layers appearing thinned or compressed. The tumor showed OESs (n = 43; 91%), representing intralesional calcification or cavitation, and each OES showed a mean diameter of 327 μm (median, 200 μm). When comparing the number of OESs per SD OCT cut through the mass, we found no relationship with patient age, tumor diameter and thickness, distance to the foveola or optic disc, tumor calcification, central macular thickness, or logarithm of the minimum angle of resolution (logMAR) visual acuity. However, a correlation of OES number with OES size ($P = 0.01$) and macular tumor location ($P = 0.03$) was found. Further analysis demonstrated OES size correlated with tumor basal diameter ($P < 0.01$), tumor thickness ($P < 0.01$), tumor calcification ($P = 0.01$), and logMAR visual acuity ($P = 0.02$).

Conclusions: Retinal astrocytic hamartomas arose in the nerve fiber layer in every case and demonstrated moth-eaten OES, related to intrinsic calcification or cavitation, in 91% of cases. Macular tumors have a greater number of OESs, whereas larger calcified tumors have larger OES diameter. *Ophthalmology 2016;■:1–8 © 2016 American Academy of Ophthalmology. Published by Elsevier Inc.*

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Retinal astrocytic hamartoma (RAH) is a benign glial tumor generally found as an asymptomatic retinal mass in patients with or without tuberous sclerosis complex (TSC).[1–4] This tumor constitutes one of the major diagnostic criteria for TSC, as established in 1998 by the TSC Consensus Conference.[5] In an analysis of 132 patients enrolled in a tuberous sclerosis program, Aronow et al[4] found 36% had RAH, manifesting as bilateral (43%) and multiple (40%) disease, with average basal diameter of 1.5 mm. They noted that patients with retinal findings were more likely to have concomitant brain subependymal giant cell astrocytoma, cognitive impairment, epilepsy, and renal angiomyolipoma compared with those without retinal lesions.[4]

Typically, RAH is detected with ophthalmoscopy, although fluorescein angiography and optical coherence tomography (OCT) can be useful in the identification of subclinical tumors.[1,6–17] In 2006, Shields et al[6] published the first series on OCT features of RAH using time-domain (TD) technology and found tumor involvement of the inner portion of the retina without identification of a specific layer because of low TD OCT resolution. Additionally, they noted classic clear, so-called moth-eaten areas (or optically empty spaces [OESs]) that were attributed to

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intralesional calcification or cavitation that occasionally were not seen clinically. A subsequent study by Pichi et al[17] using spectral-domain (SD) OCT in 43 patients with TSC revealed more detail on the intrinsic tumor features and led to a proposed classification based on SD OCT findings of tumor size, retinal traction, and intralesional OESs. Optically empty spaces in RAH are visible on both TD OCT and SD OCT and are a relatively common feature of this tumor. In this analysis, we evaluated SD OCT features of RAH for precise tumor localization within the retinal layers and analyzed OESs with regard to number, size, and correlation with tumor features.

Methods

This retrospective, noninterventional case series included 42 patients examined at the Ocular Oncology Service of Wills Eye Hospital, Thomas Jefferson University, Philadelphia, Pennsylvania, between November 2008 and December 2014. Institutional review board approval was obtained at Wills Eye Hospital.

Patient data were extracted retrospectively from medical records and included patient age at diagnosis (months), gender (male or female), race (white, black, Hispanic, or Asian), and systemic associations (neurofibromatosis, tuberous sclerosis). The ocular features included best-corrected logarithm of the minimum angle of resolution (logMAR) or Snellen visual acuity, tumor laterality (unilateral or bilateral), tumor location (quadrant and anteroposterior location), tumor morphologic features (flat, nodule), calcification (absent or present), percentage calcification, intralesional cavity (absent or present), largest tumor basal diameter and thickness (in millimeters by ultrasonography), distance to the foveola and optic disc (in millimeters), and associated ocular findings (subretinal fluid, cystoid edema, retinal traction, epiretinal membrane, vitreous seeds). The anteroposterior location was classified as macula (0−3 mm from the foveola), macula to equator, and equator to ora serrata. No interventions were performed in any of the 42 patients.

Enhanced depth imaging SD OCT was performed using the Heidelberg Spectralis (Heidelberg Engineering, Carlsbad, CA) in all patients who cooperated with office imaging (41/42); the Optovue iVue portable SD OCT (Optovue, Fremont, CA) was used in 1 infant (1/42). The scanning protocol was as follows: All patients underwent macular volume scanning to obtain central macular thickness (CMT) measurements in each eye. In addition, all eyes had 2 central crossline scans through the tumor, with each linear scan bisecting the tumor through its epicenter. If there was more than 1 tumor in an eye, the most posterior tumor was selected for imaging to ensure the highest image quality. The SD OCT features were recorded to include tumor origin by retinal layer, epiretinal membrane, vitreoretinal traction, intrinsic OES, posterior tumor shadowing, vitreous tumor seeding, posterior vitreous detachment, subretinal fluid, cystoid edema, and intraretinal or subretinal exudation. The OESs were studied further for the number and largest size per single horizontal center crossline of tumor. The thickness of individual retinal layers also was noted and recorded as normal, thinned or compressed, thickened, or not visible. The choroidal morphologic features underneath each tumor were judged either as normal, abnormal, or not visible secondary to shadowing.

All data were tabulated using Microsoft Excel 2011 (Microsoft, Redmond, WA), and measures of central tendencies (mean, median, range) were obtained using built-in functions. Statistical analyses for categorical and continuous variables were performed using the paired Student t test and Fisher exact test, respectively. Pearson correlation was performed to assess the number of OESs and relationship to OES size, patient age, logMAR visual acuity, tumor diameter, tumor thickness, distance to the foveola, distance to the optic disc, and CMT. Subgroup analyses between macular (<3 mm from the foveola) versus extramacular (≥3 mm from the foveola) tumors and calcified versus noncalcified tumors were performed to assess the relationship to logMAR visual acuity, CMT, and number and size of OESs. Multivariate analysis was not possible because of the small sample size. A P value less than 0.05 was considered statistically significant for analysis.

Table 1. Patient Demographics

Features	Data
No. of patients	42
Age at OCT (yrs)	
Mean	32
Median	23
Range	1−74
Sex, no. (%)	
Male	27 (64)
Female	15 (36)
Race, no. (%)	
White	41 (98)
Black	1 (2)
Asian	0 (0)
Hispanic	0 (0)
Laterality, no. (%)	
Right eye only	18 (43)
Left eye only	18 (43)
Bilateral	6 (14)
Systemic association, no. (%)	
None	34 (81)
Tuberous sclerosis	8 (19)
Neurofibromatosis	0 (0)

OCT = optical coherence tomography.

Results

There were 47 eyes of 42 patients included in this analysis. Patient demographic data are listed in Table 1. The mean patient age was 32 years (median, 23 years; range, 1−74 years) and most were white (41/42; 98%). There were 8 patients with associated TSC and none with neurofibromatosis.

The clinical features are listed in Table 2. The mean logMAR visual acuity was 0.22 (Snellen equivalent, 20/33), and 1 patient was preverbal with fix-and-follow visual acuity. The mean logMAR visual acuity of eyes with macular tumors was 0.28 (Snellen equivalent, 20/38) compared with 0.18 (Snellen equivalent, 20/30) for those with extramacular tumors, but this did not reach statistical significance (P = 0.261). The tumor was unifocal in 37 eyes and multifocal in 10 eyes. The largest, most posterior tumor per eye was studied. Most tumors (n = 29; 62%) were extramacular, and only 18 were macular (38%). Tumors were flat or sessile in 3 eyes (6%), nodular and noncalcified in 15 eyes (32%), nodular and partially calcified in 15 eyes (32%), and nodular and completely calcified in 14 eyes (30%). The largest mean basal diameter was 3.0 mm and