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PHOTO ESSAY

Retinal hamartomas respond to everolimus treatment for tuberous sclerosis: A photo essay

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Key words:

Tuberous sclerosis, retinal hamartomas, everolimus, mammalian target of rapamycin inhibitor, subependymal giant cell astrocytoma

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Abstract

Background: Tuberous sclerosis is characterized by hamartomas in multiple organs including retinal hamartomas. Everolimus is a novel treatment for tuberous sclerosis-related lesions. We present a case where everolimus led to lesion shrinkage, the skin tuberomas, as well as the retinal hamartomas, indicating that its effect can be detected, measured, and monitored with an ocular examination.

Case Report: We describe a 24-year-old female diagnosed with tuberous sclerosis since birth, with multiorgan involvement. The patients had multiorgan involvement, with angiolipomas of the kidney resistant to treatment. She also underwent subependymal giant cell astrocytoma brain tumor resection. The patient was treated with everolimus after recurrent embolization failed to shrink the renal angiolipomas. The tumors responded well to treatment.

Conclusions: Skin lesions disappeared, and fundus photos and repeat retinal optical coherence tomography measurements documented shrinkage of the retinal hamartomas during the 24 months of treatment. We conclude that a simple eye examination can monitor treatment effectiveness.

Background

Tuberous sclerosis is a systemic disorder characterized by hamartomas in multiple organs.[1] Retinal hamartomas are one of its manifestations. Everolimus (mammalian target of rapamycin [mTOR] inhibitor) is a new treatment modality for tuberous sclerosis-related lesions, indicated for the treatment of subependymal giant cell astrocytomas (SEGA) or renal angiomyolipomas.[2] The mutations underlying tuberous sclerosis are TSC1 or TSC2, resulting in activation of mTOR which promotes cell proliferation.[1] Therefore, mTOR inhibition, as everolimus, is the rationale for treating these patients.

Although retinal hamartomas in patients with tuberous sclerosis are usually stable and are not vision threatening, some hamartomas may progress. In the past, laser treatment was presented as a treatment option, with limited success. Treatment with sirolimus was shown to reduce retinal hamartomas in a series of seven patients,[3] and a recent publication also showed retinal astrocytoma regression in response to everolimus.[4]

The aim of this report is to show an easy non-interventional method of monitoring response to treatment, using repeated eye examinations and optical coherence tomography (OCT) measurements of retinal hamartomas.

Case Report

We describe a 24-year-old female diagnosed with tuberous sclerosis since birth, with multiorgan involvement, including rhabdomyoma of the heart, SEGA that was successfully resected, and angiolipomas of the kidney. Ocular history included hyperopic anisometropia amblyopia, operated residual esotropia, and retinal hamartomas [Figure 1].

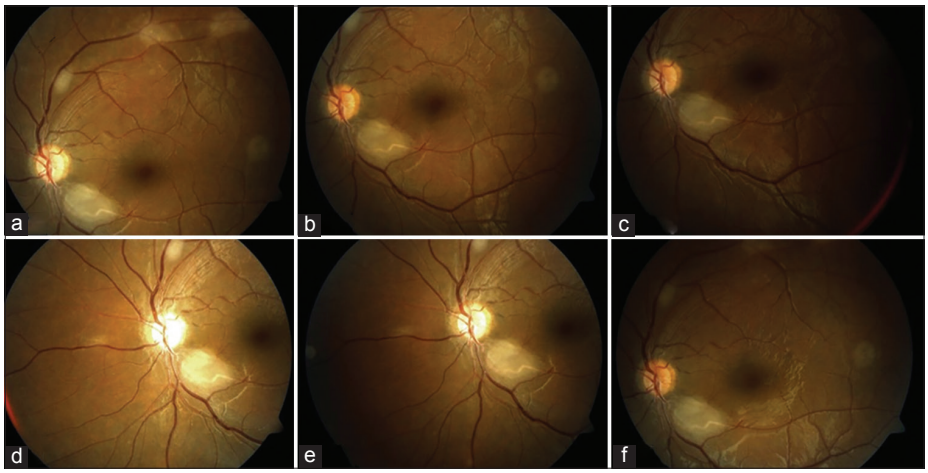

Figure 1: Color fundus photography demonstrating the patient's retinal hamartomas in 2008 before treatment. The patient was unable to undergo optical coherence tomography at that time (a-f)

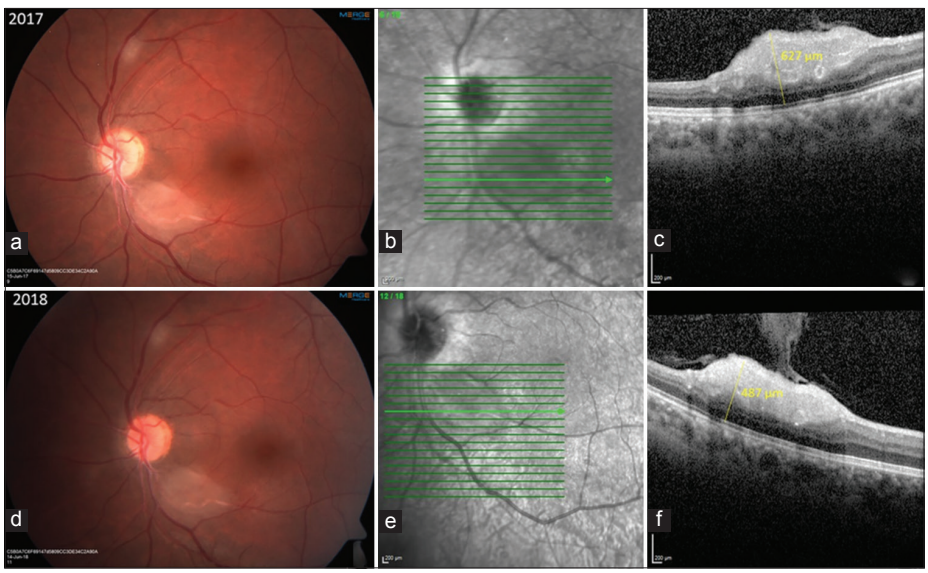

Figure 2: (a-c) Color fundus photography, infrared photography, and optical coherence tomography (OCT) demonstrating two retinal hamartomas in 2017, measurement was done at the point of maximal height, measuring 627 µm. There was a noticeable clinical improvement in lesion size in comparison to 2016 (not shown), before treatment. However, due to young age, limited cooperation, and latent-manifest nystagmus, no OCT could be achieved until 2017. (d-f) The same imaging modalities demonstrating the same retinal hamartomas 1 year later, 2018, undertreatment of everolimus. The measurements were done at the point of lesion's maximal height, perpendicular to the RPE layer. The values of 627 been reduced to 487 microns

Genetic analysis revealed a mutation p.ARG759 c.2275A-T which was absent in both parents. The patient was treated with everolimus after recurrent embolization failed to shrink the renal angiolipomas (lesion size over 3 cm is an indication for treatment). The dosage was started at 2.5 mg and was gradually increased to 12 mg. Repeat ophthalmological examination showed stable visual acuity of 20/30 and 20/40 with normal optic nerve function.

Fundus photos and repeat retinal OCT measurements documented shrinkage of the hamartomas during the 24 months of treatment [Figure 2].

Discussion and Conclusions

Herein, we describe the response to the treatment of retinal hamartomas in a patient diagnosed with tuberous sclerosis, showing multiorgan involvement.

The novelty of our observation is that although treatment was targeted at the renal angiomyolipoma, everolimus also led to a significant shrinkage of face tuberomas and the retinal astrocytic lesions shown clearly on OCT. We hypothesize that there may be a correlation between the regression of these lesions and the regression of lesions in other organs such as brain or kidney.

Furthermore, the visual fundus examination, which is known for detecting retinal hamartomas since 2006, and relatively available measurements using OCT may be valuable tools for monitoring treatment efficacy. We encourage the collaboration of multidisciplinary clinicians to monitor Tuberous sclerosis (TS) patients with internal organs involvement, using fundus eye examination and OCT.

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