



Peripheral bright streaks in tuberous sclerosis

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ABSTRACT

Purpose: To describe the finding of bright hyperautofluorescent streaks in the peripheral retina in tuberous sclerosis.

Observations: A woman with a pathogenic TSC1 mutation and cutaneous manifestations of tuberous sclerosis underwent fundus examination and was found to have a cluster of thin, yellowish streaks in the inferior peripheral fundus of her left eye. The streaks were hyperautofluorescent in blue light and associated with irregular thickening of the photoreceptor-pigment epithelium complex on optical coherence tomography.

Conclusions and importance: The cluster of outer retinal abnormalities in a sector of the peripheral retina in one eye of a TSC1 patient has features in common with the more centrally located and less numerous lesions called achromatic patches. The resemblance of the streak pattern with the pattern of hypoautofluorescence in X-linked retinopathies suggests that the streaks may represent a clone of cells derived from a single somatic mutation in TSC1. The identification of this lesion type expands the scope of conditions that can be diagnosed by fundus imaging.

Benign stationary hamartomas of the retina are found in half of patients with tuberous sclerosis, a systemic disorder that can produce hamartomas in multiple organs, including the central nervous system, skin, kidney, and eye.¹ Familial cases are autosomal dominant. Prominent and common manifestations include epilepsy, learning difficulties, behavioral problems, and autism. Suspicion of the disease is often evoked by skin lesions, which include adenoma sebaceum (Fig. 1), melanotic macules and patches of nevi. The clinical manifestations are highly variable in type and severity. As in retinoblastoma, one autosomal tumor suppressor gene is mutated from birth and clinical manifestations require a somatic mutation to occur in the other allele.

Tuberous sclerosis can be associated with a variety of ocular anomalies,^{2–4} of which retinal astrocytic hamartomas are ophthalmoscopically most conspicuous. The hamartomas are mostly asymptomatic and harmless, but they make an important contribution to the clinical diagnosis.^{3,5}

Three types of retinal astrocytic hamartomas are described^{1–3}. Type 1 hamartomas are semitransparent, flat, grayish lesions confined to the retinal nerve fiber layer (RNFL) without signs of calcification, type 2 hamartomas are multinodular, calcified lesions of a mulberry-like

appearance, and type 3 contains features of both type 1 and type 2 hamartomas. Type 1 hamartomas may be detectable only by OCT.⁶ Type 1 lesions are not autofluorescent, whereas types 2 and type 3 lesions show dotted hyperfluorescence and a heterogeneous internal structure on optical coherence tomography.⁷ Additionally, patients with tuberous sclerosis can have achromatic patches in the outer retina. They are sharply delineated retinal pigment epithelial defects, ranging in size from 200 µm pin-point lesions to nearly optic disc-size.^{2–4}

1. Case 1

We have observed unusual fundus features in a 53-year old asymptomatic woman who was examined during the course a family work-up. She was found to have a heterozygous c.164dup, p. (Pro56Alafs*14) mutation in TSC1 and mild facial angiofibromatosis (Fig. 1). Best-corrected visual acuity was Snellen 1.0 in both eyes and applanation tonometry 14 mmHg in both eyes. Slit-lamp examination of the anterior segment was unremarkable, and funduscopy with a 90 D lens and conventional 50-degree color fundus photography found no abnormality in the posterior poles. Wide-field fundus photography (Optos Monaco,

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Fig. 1. Facial angiofibromatosis typical of tuberous sclerosis.

Optos Ltd., Edinburgh, UK), however, showed a cluster of thin, bright hyperautofluorescent linear elements in the inferior midperiphery of the fundus (Fig. 2). Three pin-point achromatic patches in the left eye and one in the right eye, which was otherwise normal, were also found to be hyperautofluorescent (Fig. 2). Optical coherence tomography (OCT) scans through the bright streaks showed focal irregularities of overlapping layers of the photoreceptor outer segment/retinal pigment epithelium complex, interspersed with normal-appearing outer layers on adjacent OCT scan lines (Fig. 3 and online supplement). Also noted was a thin wedge-shaped retinal nerve fiber layer defect or nerve fiber displacement gap that extended from the rim of the optic disc in the left eye at 5 o'clock (Fig. 2). Tangent screen visual field examination was unremarkable in both eyes and no other indication of the presence of glaucoma was found.

2. Comment

Bright streaks in a sector of the peripheral retina that autofluoresced in blue light were seen in one eye of a TSC1 tuberous sclerosis patient and they were associated with localized irregularities of the retinal pigment epithelium-photoreceptor complex. The streaks were clearly distinguishable from astrocytic hamartomas in that they were located in the outer retina, not in the inner retina. We suggest that the streaks may be part of the tuberous sclerosis spectrum of fundus abnormalities, possibly a variant of the achromatic patch, a more rounded, localized RPE abnormality that previously has been described in the posterior pole of the eye. Three hypopigmented pin-point lesions of the RPE elsewhere in the same eye and one in the fellow eye were also hyperautofluorescent. We propose that the bright peripheral streaks in the fundus of our patient are elements of tuberous sclerosis, possibly a hitherto unrecognized form of the achromatic patch.

Peripheral streaks have also been reported in other conditions, such as multifocal choroiditis, which is characterized by multiple small chorioretinal spots with variable degrees of inflammation, subretinal neovascularization and subretinal fibrosis. Such streaks are typically curvilinear, located at the level of the retinal pigment epithelium,^{8,9} accompanied by chorioretinal scars, atrophy, hyperpigmentation and peripapillary atrophy¹⁰ and have been reported in presumed ocular histoplasmosis syndrome⁸ and multifocal choroiditis in patients with West Nile virus infection.¹¹

Another condition that should be mentioned is angioid streaks, although they differ in generally being connected to the rim of the optic disc, from where they radiate in a more irregular direction toward the periphery, in contrast to the curvilinear streaks seen in our patient. Additionally, angioid streaks are usually red, although pale streaks can



Fig. 2. Cluster of bright streaks (lower arrow) and a pin-point achromatic patch of the retinal pigment epithelium (upper arrow) on wide-angle color fundus photograph of the left eye (top). A corresponding blue-green autofluorescence fundus photograph showed that both the bright streaks and the achromatic patches were hyperautofluorescent (bottom). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

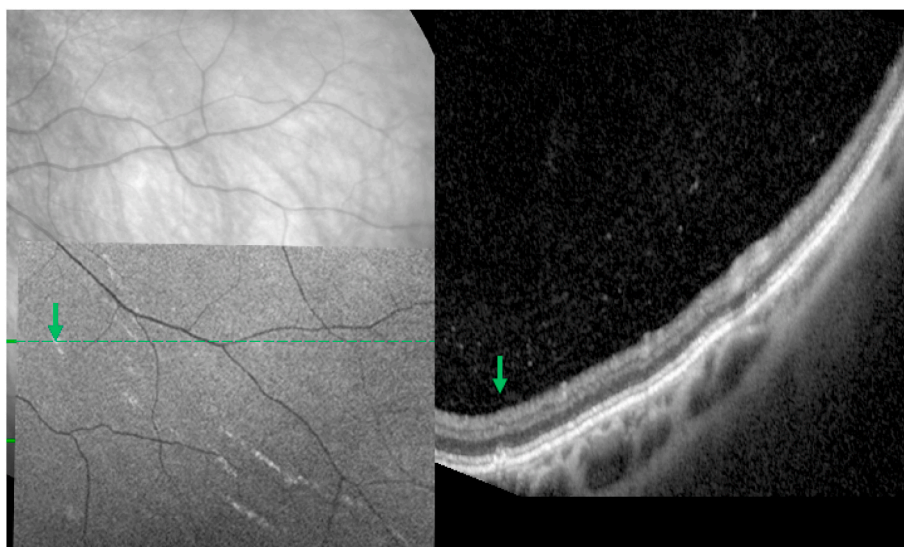


Fig. 3. Optical coherence tomography scan (right) through a hyperautofluorescent streak (left, overlaid on infrared image) in the left eye of a woman with tuberous sclerosis. A localized irregularity of the photoreceptor outer segment/retinal pigment epithelium complex is seen corresponding to the streak. Comparable irregularities were made in several locations, but some parts of the streaks were not associated with any visible OCT abnormalities.

also be seen.

Given that the manifestations of tuberous sclerosis are produced by a second mutation at a locus where one allele is defective from birth, and given that our patient's retinal streaks were confined to a small sector of the fundus in one eye, the entire cluster of streaks may belong to one and the same clone of cells. This hypothesis is supported by the resemblance of the pattern of streaks seen in our patient with the more widespread pattern of hypoautofluorescence seen in carriers of choroideremia, a pattern that is produced by a multiclonal pattern of random gene inactivation in the retinal pigment epithelium (see online supplement).

Our findings from one eye in a single patient are hardly sufficient to definitively establish peripheral bright streaks as a component of the fundus anomalies seen in tuberous sclerosis, but they may encourage other investigators to apply wide-field fundus imaging in tuberous sclerosis patients and thus pave the way for a formal test of the hypothesis by comparison with healthy subjects and patients with other fundus anomalies.

Patient consent

Written consent to publish this case report has been obtained from the patient.

This retrospective study did not require institutional approval.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures relevant to this

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.ajoc.2021.101050>.

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