CASE REPORT

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Retinal Astrocytoma in a 6-year-old Girl with Tuberous Sclerosis Complex

Selda ÇELİK DÜLGER[a], Mehmet Yasin TEKE[b], Alper DİLLİ[c]

[a]Ulucanlar Eye Research Hospital, Ankara, TURKEY
[b]Ulucanlar Eye Research Hospital, Department of Ophthalmology, Ankara, TURKEY
[c]Dışkapı Training and Research Hospital, Department of Radiology, Ankara, TURKEY

ABSTRACT Tuberous sclerosis complex (TSC) is neurocutaneous genetic disorder with hamartomas in various organ systems. Retinal astrocytoma that is one of the major diagnostic criteria of tuberous sclerosis, tends to be multiple and bilateral in patients with TSC. Retinal astrocytoma that is occurred in almost half of the patients with TSC, may start to appear in the first years of life. We report multiple and bilateral retinal astrocytomas in a 6-year-old girl with TSC that was diagnosed with genetic testing in a pediatric clinic five years ago. The patient was under vigabatrin treatment and follow-up by neurology department of pediatrics for epileptic seizures. Fundus examination of both eyes showed six astrocytic hamartomas on the retina and optical coherence tomography (OCT) demonstrated dome-shaped, elevated lesions arising from inner retinal layers with shadowing in the rest of the retinal layers.

Keywords: Retinal astrocytoma; retinal neoplasms; tuberous sclerosis complex; optical coherence tomography

Tuberous sclerosis complex (TSC) is a multisystemic neurocutaneous genetic condition with an incidence of almost 1 in 6000 to 10000 live births.[1] It is autosomal dominant inheritance and approximately two-thirds of the cases occur with spontaneous mutation. The clinical presentation caused by dysfunction of hamartin and tuberin proteins that are products of TSC1 and TSC2 genes is quite variable. The disease is characterized by hamartomas affecting multiple organs, including skin, brain, heart, kidney, lungs and eye.[2]

The ophthalmologic manifestations of TSC are retinal astrocytoma and retinal achromic patch that are among the clinical diagnostic criteria of TSC. Retinal astrocytoma associated with TSC is a benign retinal tumor arising from retinal nerve fiber layer and tends to be multiple in each eye.[3] It is a benign yellow-white, well-circumscribed, elevated retinal tumor that occurs in association with tuberous sclerosis or, less commonly, neurofibromatosis, or in isolation.[4] It may appear as translucent lesions overlying the retinal blood vessels and may have lumpy appearance like ‘ white mulberry’. Approximately 53% of TSC patients may develop retinal astrocytoma.[5]

In this study, we present this report because of six retinal astrocytomas in both eyes of a very young patient.

CASE REPORT

A 6-year-old-female presented to our clinic with blurred vision in both eyes. At seven months of age, seizures developed and she was diagnosed with epilepsy. She has been using vigabatrin for seizures at a dose of 500 mg twice a day since the time of diagnosis. The diagnosis of tuberous sclerosis complex had been made with genetic testing in a pediatric clinic five years ago. The biological parents had been also investigated in terms of the condition and found to be unaffected. The possible other system involve-

Correspondence: Selda ÇELİK DÜLGER
Ulucanlar Eye Research Hospital, Ankara, TURKEY
E-mail: drsldclk@gmail.com

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ment associated with tuberous sclerosis have being evaluated periodically. Cardiac, pulmonary and renal evaluations were unremarkable. At clinical examination, facial angiofibromas were observed over her face. Her magnetic resonance imaging (MRI) of the brain revealed multiple cortical tubers in both hemispheres and subependymal giant cell astrocytoma (SEGA) in the inferomedial of caudate nucleus in the right cerebral hemisphere (Figure 1). Millimetric nodules were observed in the periventricular subependymal area.

At her ophthalmological examination, the best-corrected visual acuity (BCVA) was 20/25 in both eyes. Intraocular pressures were in the normal limits and the anterior segment examination of both eyes including lids, conjunctiva, cornea, anterior chamber and iris were unremarkable. Fundus examination revealed three side-by-side yellowish-white, rounded retinal lesions abutting the superior edge of the optic nerve in right eye. In the same eye, two lesions with the same features were also observed in the superonasal of these three lesions and inferotemporal of the fovea. In the left eye, a lesion about 4 disc diameter in size was observed on the superior temporal artery. All lesions were protruding into the vitreous cavity and has non-calcified appearance (Figure 2). The retinal lesions were observed more prominent at fundus photograph using red-free light (Figure 3). Optical coherence tomography imaging demonstrated dome-shaped, elevated lesions arising from inner retinal layers with shadowing in the rest of the retinal layers (Figure 4).

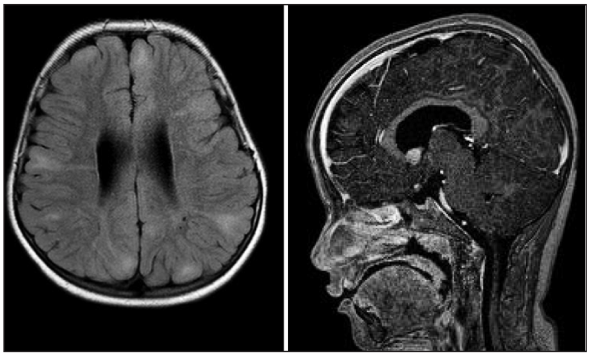

FIGURE 1: A) Axial magnetic resonance imaging (MRI) of the brain **B)** demonstrating multiple tubers in both hemispheres. Sagittal MRI demonstrating subependymal giant cell astrocytoma at typically intraventricular location.

DISCUSSION

TSC can be diagnosed by the presence of clinical criteria and by genetic testing. Two major or 1 major and 2 minor clinical features are necessary to diagnose. The new, updated diagnostic clinical criteria now include 11 major features and six minor features.[6] Making identification the mutation in TSC1 and TSC2 genes is independent diagnostic criterion regardless of the clinical findings. However, 10% to 25% of the patients have no mutations identification by conventional genetic testing. Therefore, negative results of genetic testing should not exclude TSC.[6]

Retinal astrocytoma is significant ocular manifestation of the tuberous sclerosis complex and it usually manifests morphologically as flat-translucent type and large- nodular type.[7] In individuals who have no other clinical evidence of tuberous sclerosis, retinal astrocytomas are often unilateral and unifocal.

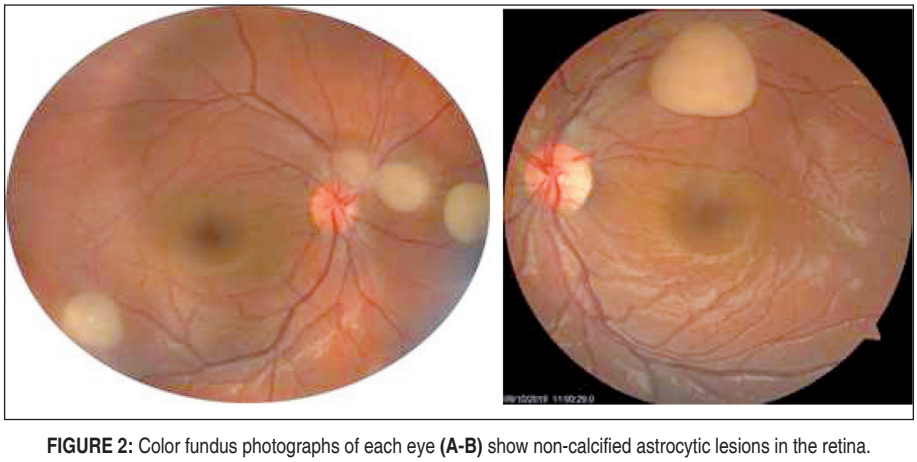

FIGURE 2: Color fundus photographs of each eye **(A-B)** show non-calcified astrocytic lesions in the retina.

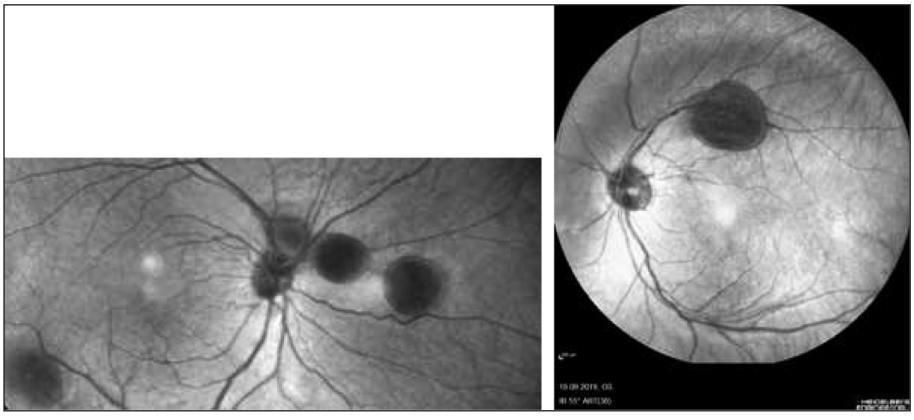

FIGURE 3: Fundus photographs of the same lesions using red-free light. The lesions are more prominent. **(A-B)**

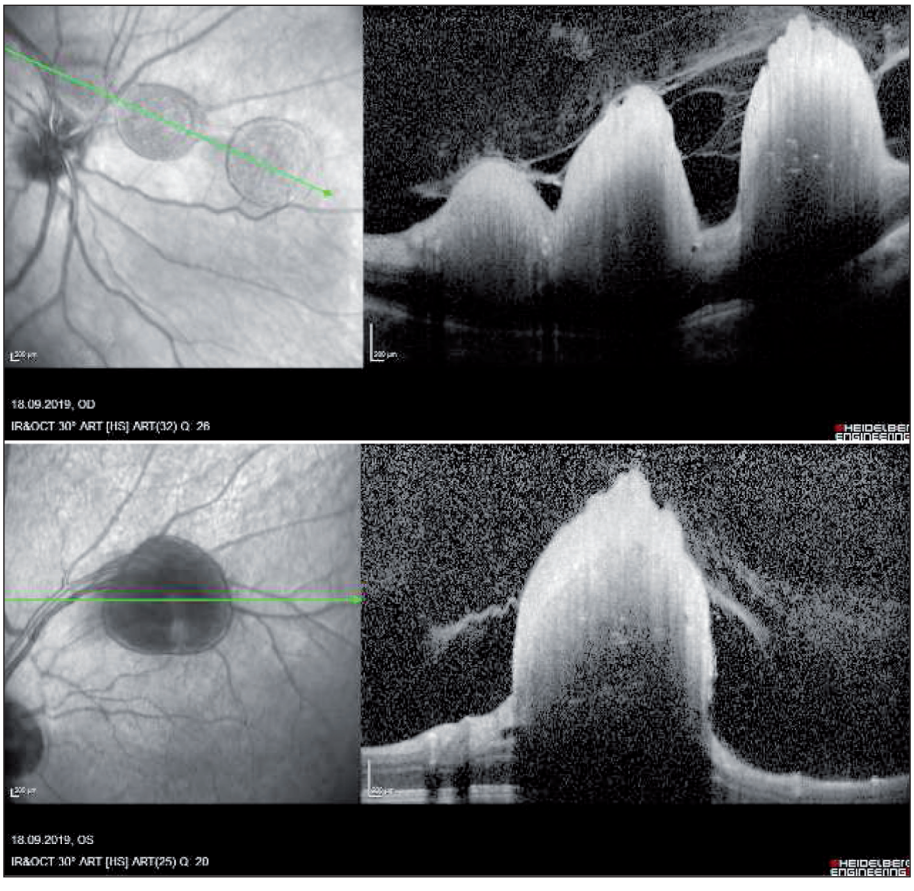

FIGURE 4: Optical coherence tomography shows **A)** three side-by-side retinal astrocytomas at the nasal edge of the optic disc. The elevated lesions with full-thickness retinal involvement and shadowing effect are observed. **B)** Dome-shaped hyperreflective lesion is observed overlying the retinal blood vessels in the left eye. Note the prominent vitreous condensation overlying the lesions.

This tumor can behave more aggressively, occurring progressive enlargement, exudation, vitreous hemorrhage and retinal detachment, sometimes resulting in loss of the eye. Retinal astrocytomas associated with TSC have relatively static behavior, but there have been several reports about showing aggressive progression in the literature.[8] That can inadvertently lead the clinician to the diagnosis of retinoblastoma.[8] Retinal astrocytoma has similar histopathologic features to the tubers in brain seen in TSC patients.[6]

Erol et al. performed a study of 20 children with 5.9 mean age ranged from 2 to 17 years. Retinal astrocytoma was detected in 25% of the patients. It was emphasized that low prevalence found in the study was related to the low mean age.[9] In a study with a higher mean age, the prevalence was found to be 44%.[10] Retinal astrocytoma in TSC is less common in early ages, but it can emerge in time. Our case was interesting in terms of having five retinal astrocytomas in the right eye and one in the left eye at an early age. Retinal astrocytoma detected at an early age can be a significant diagnostic marker, especially in cases with no other findings of TSC.[6] Early TSC diagnosis can allow possible disease-modifying treatment and close monitoring for sequelae of TSC. In conclusion, in patients with tuberous sclerosis, retinal astrocytoma may become apparent from the first decade of life and frequently is multiple and bilateral.

Informed Consent

Written informed consent was obtained from the parents for publication of this case report and accompanying images.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Mehmet Yasin Teke;* ***Design:*** *Selda Çelik Dülger, Alper Dilli;* ***Control/Supervision:*** *Mehmet Yasin Teke;* ***Data Collection and/or Processing:*** *Selda Çelik Dülger;* ***Analysis and/or Interpretation:*** *Selda Çelik Dülger, Alper Dilli;* ***Literature Review:*** *Selda Çelik Dülger;* ***Writing the Article:*** *Selda Çelik Dülger;* ***Critical Review:*** *Mehmet Yasin Teke;* ***References and Fundings:*** *Alper Dilli, Selda Çelik Dülger;* ***Materials:*** *Selda Çelik Dülger, Mehmet Yasin Teke.*

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