Primary ocular presentation of tuberous sclerosis – A case report

Nancy M Rajasekaran, Saban Horo, Thomas Kuriakose

A 25-year-old man presented with decreased vision in the left eye with hypopigmented elevated subretinal lesion over the optic disk with abnormal vasculature, subretinal and retinal hemorrhages, and fluid in the macula. An area of high spike over the disk with corresponding orbital shadowing was seen on B scan ultrasonography. Fundus fluorescein angiography revealed abnormal vasculature. Systemic examination revealed facial angiofibroma, ashleaf spot, and dental pits with multiple cortical tubers on CT brain. Intravitreal injection of bevacizumab led to visual and tomographic improvement. Abnormal retinal vascularization and exudation in young individuals may be a presenting feature in tuberous sclerosis.

Key words: Aggressive retinal hamartoma, bevacizumab, fundus flurescein angiography, tuberous sclerosis

Tuberous sclerosis is generally a benign neurocutaneous disorder with an autosomal dominant inheritance and it characteristically includes the triad of mental retardation, seizures, and facial angiofibromas.[1] Retinal hamartomas were detected in over 75% of diagnosed cases and is currently listed as the part of the revised major criterion. We report a patient with an aggressive variant of retinal hamartoma (astrocytoma) accompanied with macular edema and neovascularization.

Case Report

A 25-year-old man presented with complaints of decreased vision in the left eye, which he accidently noticed on covering the other eye. There was no history of systemic comorbidities, seizures, or retarded mental development. The best corrected Snellen visual acuity in the right and left eyes were 6/6 and 6/24, respectively. Examination of the anterior segment was normal in both the eyes and so was the vitreous cavity. The optic disk and retinal examination in the right eye were normal. In the left eye, fundus examination demonstrated an elevated lesion in the superior aspect of the optic disk accompanied with marked neovascularization on the surface with retinal hemorrhages and macular edema [Fig. 1a and b]. Systemic examination revealed the presence of adenoma sebaceum, ashleaf spot, dental pits, and subungual fibromas [Fig. 2a-d]. Fundus fluorescein angiography showed tortuous and telangiectatic vessels with slow/no fill in the early phase [Fig. 3a and b], whereas the late phase showed filling up of vessels within the lesion associated with exudation [Fig. 3c and d]. B-scan ultrasonography showed focal calcification, acoustic shadowing behind the lesion [Fig. 4a]. Optical coherence tomography (OCT) over optic disk showed a hyperreflective mass with posterior shadowing [Fig. 4b]. OCT over the macula showed retinal disorganization with fluid-filled spaces and vitreous traction [Fig. 4c]. Computed tomography of the orbit to confirm the extent of the lesion showed multiple cortical tubers [Fig. 5a and b], which had similar attenuation values as compared with the optic disk lesion [Fig. 5c].

Patient was diagnosed to have tuberous sclerosis as he fulfilled the diagnostic criterion and an aggressive variant of a retinal hamartoma was suspected. An intravitreal injection of 1.25 mg bevacizumab (Avastin) was administered and resulted in a three-line visual improvement (approximate early treatment diabetic retinopathy study [ETDRS] letter score of 21) with drastic reduction in macular edema [Fig. 4d].

Discussion

Tuberous sclerosis is a genetic condition that involves various systems of the body and it gets its name from the characteristic cortical tubers that were first described by Désiré-Magloire Bourneville in 1880. It includes a list of major and minor criteria for diagnosis [Table 1].[2]

Among the ophthalmological manifestations, retinal hamartomas constitute the commonest abnormality and are noted in 50–80% of patients. Three basic morphological forms have been described, the commonest being a flat, smooth, salmon-colored lesion located in the superficial retina mostly at the posterior pole. The second form appears as a white, opaque, multinodular lesion resembling a mulberry. The third is a combination of the two comprising a calcific, nodular center surrounded by a smooth, salmon-colored perimeter.[3] Shields *et al*. reported four patients with aggressive retinal astrocytoma with features of retinal neovascularization, serous detachment at macula, and retinal hemorrhages with genetically diagnosed tuberous sclerosis complex.[4]

Various studies have concluded that the tubers found in various organs in this complex have high angiogenic properties with a high surface expression of vascular endothelial growth factors (VEGF) and this could be responsible for the presence

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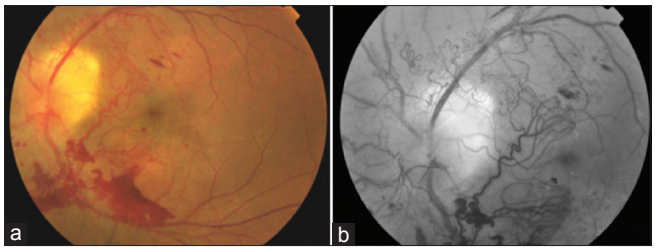

Figure 1: (a) Color and (b) red-free fundus picture of retinal hamartoma with neovascularization, macular edema, and hemorrhages

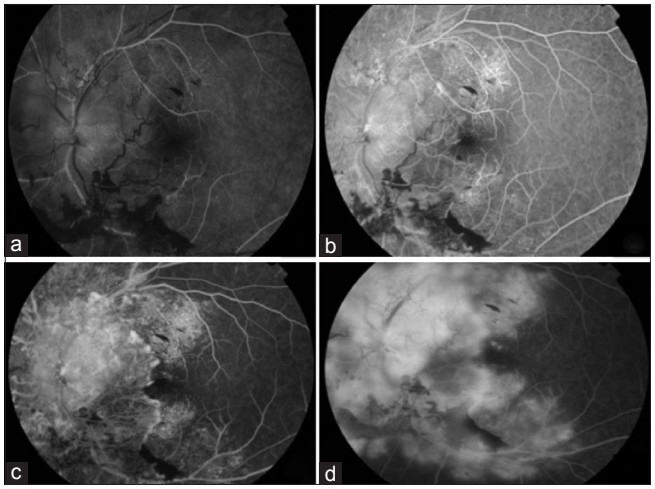

Figure 3: Fundus flurescein angiography showing (a) early phase with slow/no fill, (b) hyperfluorescence with lighting up of new vessels, (c) leakage from new vessels, and (d) hyperfluorescence with leakage and increase in intensity of lesion

of neovascularization simulating a proliferative retinopathy.[5-7] The cause of high angiogenicity only in the aggressive variant is under consideration.[7]

Interventional studies have shown resorption of subretinal fluid after argon laser photocoagulation.[8-10] Pars plana vitrectomy was performed to clear a nonresolving vitreous hemorrhage in a case report.[11] Complete resorption of subretinal fluid and an improvement in visual acuity was observed within 2 weeks after a single treatment with photodynamic therapy in another report.[12] Intravitreal injections of bevacizumab have shown considerable resorption of subretinal fluid, but the duration of treatment and recurrence of edema is questionable.[13] Combined treatment with intravitreal anti-VEGF followed by laser photocoagulation or photodynamic therapy of the retinal tubers may also be considered.[13] Considering the high angiogenicity of the tumor, we have administered one intravitreal injection of bevacizumab, and on follow-up after 2 weeks, the macular edema had decreased with a three-line vision improvement (approximate ETDRS letter score of 21).

Our patient primarily presented with the retinal findings, which could lead us to consider other differential diagnosis such as choroidal osteoma, amelanotic melanoma, choroidal metastasis, capillary hemangioma, or a retinoblastoma. Coincidental findings of cortical tubers on CT scans and subsequent clinical examination led to the diagnosis of tuberous sclerosis in this patient.

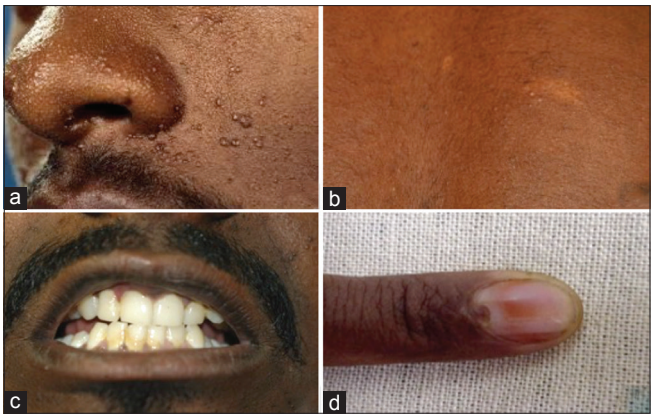

Figure 2: Clinical picture of the 25-year-old male with systemic manifestations of tuberous sclerosis: (a) adenoma sebaceum, (b) ashleaf spot (black arrow), (c) dental pit, and (d) subungual fibroma

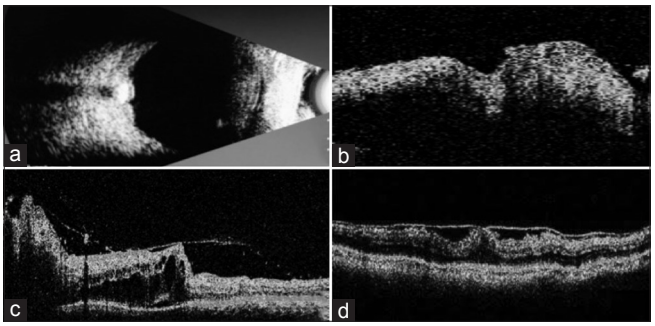

Figure 4: (a) B scan showing focal calcification and acoustic shadowing, (b) OCT over the optic disk showing hyperreflective mass with posterior shadowing, (c) OCT of macula showing retinal disorganization with edema and vitreous traction, and (d) OCT of macula showing decrease in macular edema postinjection of bevacizumab

Table 1: Diagnostic criterion for tuberous sclerosis complex

Major criterion	Minor criterion
Facial angiofibromas	Dental enamel pits
Peri-ungual fibromas	Rectal polyps
Shagreen patch	Bone cysts
Retinal hamartomas	Gingival fibromas
Cortical tubers	Nonrenal hamartomas
Subependymal nodule	Retinal achromic patch
Cardiac rhabdomyoma	Confetti skin lesions
Renal angiomyolipoma	Renal cyst
	Cerebral cortical dysplasia

Conclusion

Retinal hamartomas can have varied clinical presentations and the diagnosis of tuberous sclerosis should be considered in young patients with a unilateral proliferative retinopathy without systemic comorbidities. Aggressive retinal hamartomas can progressively enlarge and result in total exudative retinal detachment and neovascular glaucoma. Intravitreal bevacizumab seems to show improvement, but the duration of therapy and recurrence is not known. However, larger studies

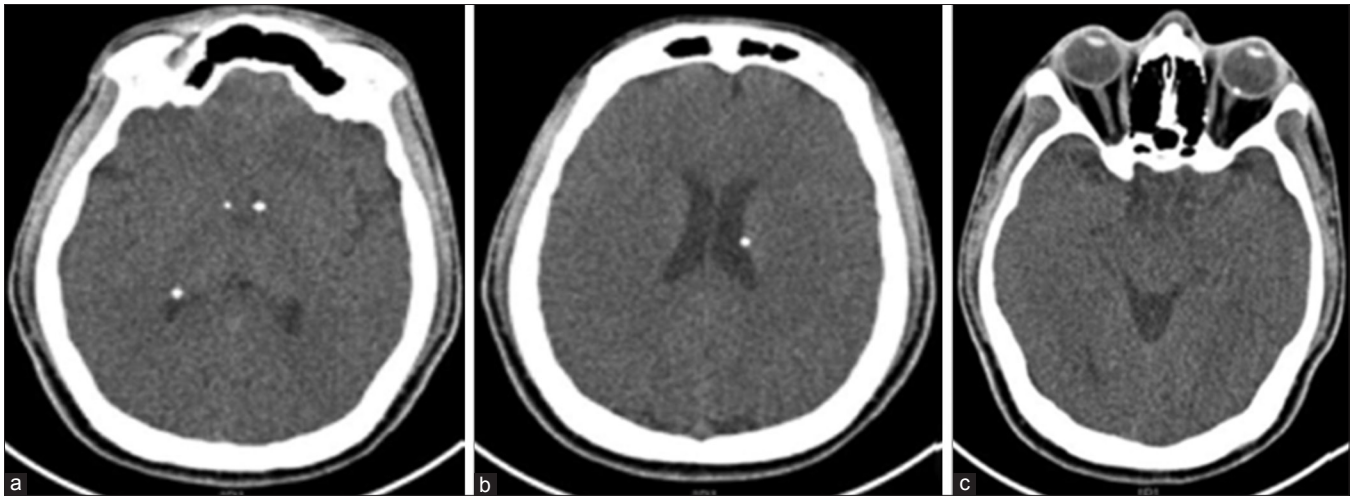

Figure 5: CT scan images (axial views) showing (a and b) cortical tubers and (c) optic disk lesion

with longer follow-up are required to ascertain the long-term outcomes of anti-VEGF therapy in such eyes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Osborne JP, Fryer A, Webb D. Epidemiology of tuberous sclerosis. Ann N Y Acad Sci 1991;615:125-7.
2. Roach ES, Gomez MR, Northrup H. Tuberous sclerosis complex consensus conference: Revised clinical diagnostic criteria. J Child Neurol 1998;13:624-8.
3. Rowley SA, O'Callaghan FJ, Osborne JP. Ophthalmic manifestations of tuberous sclerosis: A population based study. Br J Ophthalmol 2001;85:420-3.
4. Shields JA, Eagle RC Jr, Shields CL, Marr BP. Aggressive retinal astrocytomas in 4 patients with tuberous sclerosis complex. Arch Ophthalmol 2005;123:856-63.
5. Nguyen-Vu PA, Fackler I, Rust A, DeClue JE, Sander CA, Volkenandt M, *et al*. Loss of tuberin, the tuberous-sclerosis-complex-2 gene product is associated with angiogenesis. J Cutan Pathol 2001;28:470-5.
6. Arbiser JL, Brat D, Hunter S, D'Armiento J, Henske EP, Arbiser ZK, *et al*. Tuberous sclerosis-associated lesions of the kidney, brain, and skin are angiogenic neoplasms. J Am Acad Dermatol 2002;46:376-80.
7. Tomida M, Mitamura Y, Katome T, Eguchi H, Naito T, Harada T. Aggressive retinal astrocytoma associated with tuberous sclerosis. Clin Ophthalmol 2012;6:715-20.
8. Mennel S, Meyer CH, Peter S, Schmidt JC, Kroll P. Current treatment modalities for exudative retinal hamartomas secondary to tuberous sclerosis: Review of the literature. Acta Ophthalmol Scand 2007;85:127-132.
9. Bloom SM, Mahl CF. Photocoagulation for serous detachment of the macula secondary to retinal astrocytoma. Retina 1991;11:416-22.
10. Vrabec TR, Augsburger JJ. Exudative retinal detachment due to small noncalcified retinal astrocytic hamartoma. Am J Ophthalmol 2003;36:952-4.
11. Kroll AJ, Ricker DP, Robb RM, Albert DM. Vitreous hemorrhage complicating retinal astrocytic hamartoma. Surv Ophthalmol 1981;26:31-8.
12. Eskelin S, Tommila P, Palosaari T, Kivela T. Photodynamic therapy with verteporfin to induce regression of aggressive retinal astrocytomas. Acta Ophthalmologica 2008;86:794-9.
13. Saito W, Kase S, Ohgami K, Mori S, Ohno S. Intravitreal anti-vascular endothelial growth factor therapy with bevacizumab for tuberous sclerosis with macular oedema. Acta Ophthalmol 2010;88:377-80.