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Case Report

Ophthalmology Section

Ocular findings in a Case of Tuberous Sclerosis Complex: A Classic Posterior Segment Presentation

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ABSTRACT

Tuberous Sclerosis Complex (TSC) is a genetic condition caused by autosomal dominant mutations in the tumour suppressor genes TSC1 and TSC2. The most frequent manifestations of this disorder involve benign tumours affecting multiple systems, including neurological, dermatological, renal, cardiac, pulmonary and ocular systems. The classic symptom triad consists of seizures, intellectual disability and cutaneous angiofibromas. Ocular involvement, though often asymptomatic, can reveal characteristic retinal lesions that are valuable for diagnosis and monitoring. A 23-year-old female with a recent diagnosis of TSC was referred to the Department of Ophthalmology for evaluation. She had no visual complaints. Examination revealed characteristic facial angiofibromas and bilateral Retinal Astrocytic Hamartomas (RAH) without any visual impairment. Computed Tomography (CT) imaging also showed bilateral renal angiomyolipomas. Ocular involvement in TSC is common but often asymptomatic. RAH are the most frequent ocular manifestations and are usually stable over time. Recognising these findings can support diagnosis and systemic evaluation, especially in undiagnosed patients. Ocular examination plays an essential role in the multidisciplinary assessment of TSC, aiding in both diagnosis and monitoring. Awareness of these subtle but significant findings is important for early and holistic management.

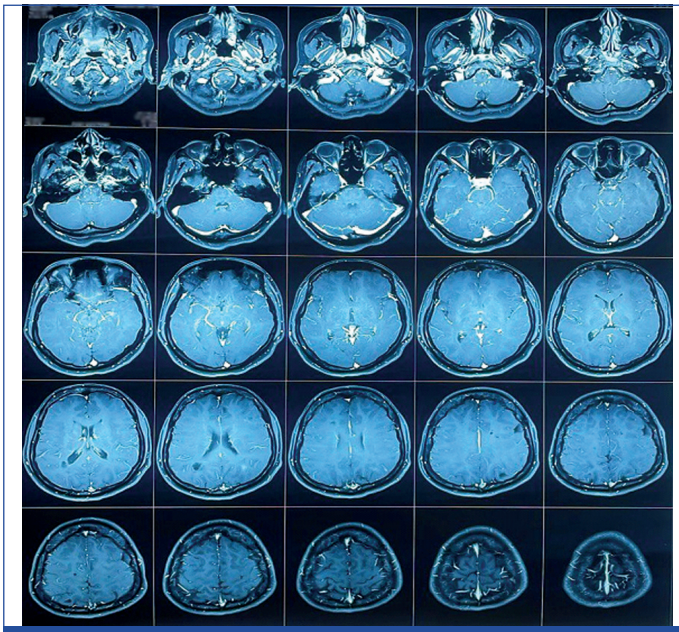
Keywords: Asymptomatic retinal lesions, Autosomal dominant inheritance, Multisystem hamartomas, Neurocutaneous syndrome, Ophthalmic manifestations

CASE REPORT

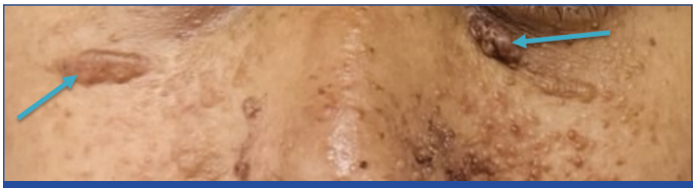
A 23-year-old female was diagnosed with TSC four months ago. Although she had exhibited clinical features of TSC since birth, such as facial angiofibromas over the malar region, she did not seek medical attention as she was not concerned about them. A few months later, she developed abdominal pain and presented to the surgical outpatient department. She was subsequently admitted and scheduled for surgery. As part of the systemic evaluation, she was referred for an ophthalmic examination. There was no history of similar complaints in the family.

Following her admission, she underwent an immediate ophthalmological evaluation at the hospital. She had no visual or ocular complaints, and her medical history was negative for seizures or cognitive deficits. A previous report of Magnetic Resonance Imaging (MRI) was normal, showing no tumors in the brain [Table/Fig-1]. Unaided visual acuity was 6/24 in both eyes, improving to 6/6 with -1.00 DS correction. On external examination, multiple facial angiofibromas (adenoma sebaceum) were noted over the malar region and cheeks [Table/Fig-2], with additional lesions on the neck [Table/Fig-3]. Fundus examination revealed bilateral, elevated, mulberry-shaped white lesions in the superior retina: the right eye had a lesion approximately two and a half optic disc diameters in size, while the left eye had a lesion approximately one optic disc diameter in size, consistent with RAH [Table/Fig-4,5]. The patient was not willing to undergo Optical Coherence Tomography (OCT) or fundus fluorescein angiography.

The patient reported to the surgical department for abdominal pain 3-4 months prior and was diagnosed with a left renal lump. She had also complained of headache and vomiting but did not provide any family history or history of past co-morbidities. There was a family history of behavioural abnormalities in her mother. The diagnosis was made based on the skin abnormality, renal findings, behavioural findings, and imaging [1]. The differential diagnosis included myelinated nerve fibers and choroidal osteoma. CT of the abdomen revealed bilateral renal angiomyolipomas, another common systemic manifestation of TSC [Table/Fig-6]. Later, excision and biopsy were performed for the left kidney.



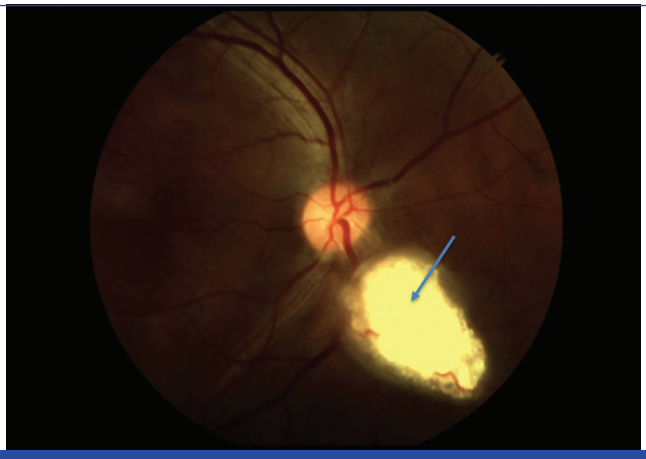
[Table/Fig-1]: Contrast MRI showing no tumour in the brain.



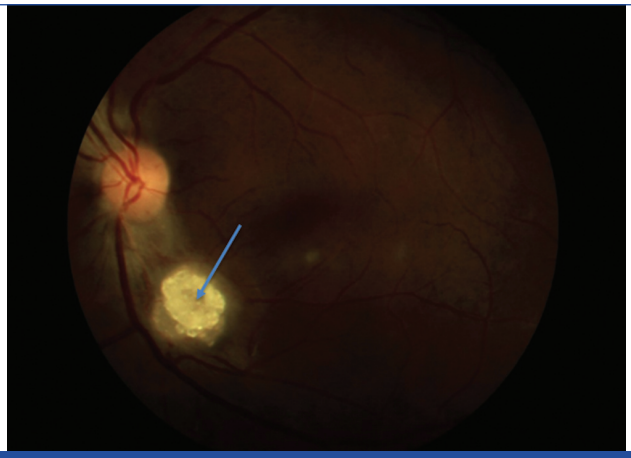
[Table/Fig-2]: Facial angiofibromas over the malar region.

The histopathological report was suggestive of multifocal angiomyolipomas in the left kidney, and tuberous sclerosis-associated

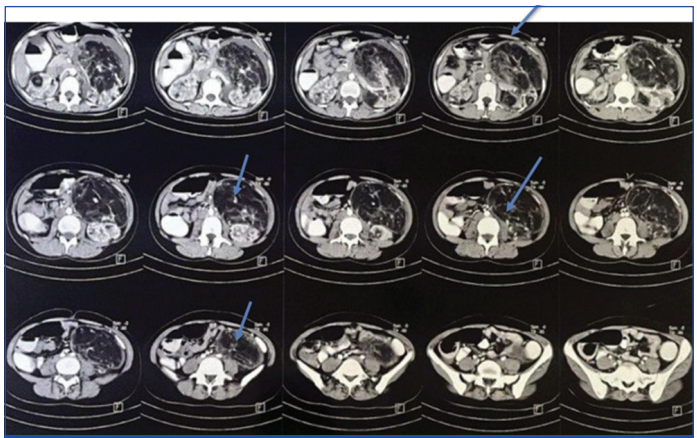
[Table/Fig-3]: Angiofibromas on the neck.



[Table/Fig-4]: Retinal astrocytic hamartoma in the right eye.



[Table/Fig-5]: Retinal astrocytic hamartoma in the left eye.



[Table/Fig-6]: Computed Tomography (CT) abdomen revealed bilateral renal angiomyolipomas, another common systemic manifestation of TSC (multiple well defined hypodense lesion).

angiomyolipomas could be considered. The patient was provided with spectacles based on the ophthalmological evaluation and was counseled for further necessary eye investigations. The surgical team performed a biopsy; however, the patient did not return for follow-up thereafter.

DISCUSSION

The TSC is a multisystem neurocutaneous disorder arising from mutations in either the TSC1 or TSC2 gene. This results in dysregulation of the mTOR pathway and subsequent formation of hamartomatous lesions in various organs, including the brain, skin, kidneys and eyes [2,3]. Though traditionally defined by Vogt's triad—seizures, intellectual impairment and facial angiofibromas—only a minority of affected individuals present with all three features. According to Osborne JP et al., fewer than 30% of patients exhibit the complete triad, highlighting the clinical heterogeneity of TSC [4].

In the present case, a 23-year-old female presented with abdominal complaints and was incidentally diagnosed with TSC during a systemic work-up. She had longstanding dermatological findings in the form of facial angiofibromas but lacked a prior diagnosis due to the absence of neurological symptoms or visual disturbances. This is consistent with data from the TuberOus SClerosis registry to increase disease Awareness (TOSCA) registry, which reported that dermatological manifestations are among the most common and earliest clinical features of TSC, yet are often underrecognised [5].

A noteworthy finding in present case was the presence of bilateral RAHs. These are benign retinal lesions typically seen in 40-50% of TSC patients and are considered a major diagnostic criterion [6,7]. Pelino CJ and Pizzimenti JJ described the classic appearance of RAHs as mulberry-like, white elevated lesions, often peripapillary or in the posterior pole, and bilateral in approximately 50% of cases [8]. In present case, patient exhibited bilateral lesions in the superior retina, measuring approximately 2.5 disc diameters in the right eye and one disc diameter in the left, aligning with published descriptions. Despite the presence of such lesions, the patient remained asymptomatic, which is common in TSC-related retinal hamartomas, as these lesions are generally non progressive and do not typically impair vision [7,9].

The patient refused further investigations such as OCT and fluorescein angiography due to the lack of ocular symptoms. Nevertheless, these imaging modalities are valuable in confirming the diagnosis, assessing lesion depth, and evaluating involvement of adjacent retinal layers, as well as monitoring for complications such as macular oedema or subretinal fluid [10]. In a series by Rowley SA et al., OCT proved crucial in differentiating between calcified and non calcified astrocytomas, which may guide follow-up protocols [11].

In terms of systemic involvement, in present case, patient had bilateral renal angiomyolipomas, confirmed histopathologically post-nephrectomy. Renal angiomyolipomas are among the most frequent visceral findings in adults with TSC and can be asymptomatic or present with flank pain, haematuria, or, in rare cases, retroperitoneal haemorrhage [12]. Kingswood JC et al., in the TOSCA study, emphasised the need for routine imaging to identify such lesions early and reduce morbidity [13]. The patient also reported behavioural issues, and while a detailed neuropsychiatric assessment was not documented, this aligns with the high prevalence of neurobehavioural symptoms (including autism spectrum disorders and attention-deficit hyperactivity disorder) in TSC patients [14].

Interestingly, this patient had no history of seizures or cognitive decline, highlighting the variable expressivity of TSC. Genetic studies suggest that individuals with TSC2 mutations may have more severe systemic involvement than those with TSC1 mutations [15]. However, genetic testing was not performed in this case due to resource limitations and lack of follow-up. From an ophthalmic management standpoint, the patient was provided with spectacles and advised to have regular follow-up. Although retinal hamartomas generally do not require treatment, intervention may be warranted in cases complicated by macular oedema or visual loss. Intravitreal anti-Vascular Endothelial Growth Factor (VEGF) agents like bevacizumab have demonstrated efficacy in reducing retinal oedema and improving visual outcomes in select cases [16,17]. Yüksel N et al., reported

successful resolution of macular oedema in astrocytic hamartomas treated with intravitreal bevacizumab [9]. Other treatment options such as laser photocoagulation and Photodynamic Therapy (PDT) have been employed; however, PDT is generally preferred due to its targeted action and lower complication rate [18].

The delayed diagnosis in this case reflects the broader challenge in TSC management—many patients remain undiagnosed until adulthood due to subtle or overlooked early features. Early identification of cutaneous and ocular signs can play a pivotal role in prompting systemic evaluation and establishing a timely diagnosis. A multidisciplinary approach involving dermatology, ophthalmology, nephrology and genetics is essential for effectively managing these patients [19].

CONCLUSION(S)

This case underscores the importance of a thorough ophthalmic examination in patients with TSC, even in the absence of symptoms. Recognition of classic retinal findings can aid in diagnosis, guide further investigation and support comprehensive patient management like visual acuity and further progression of complication should be monitored in 3 to 6 months.

REFERENCES

[1] Domkundwar S, Babu S. Nutshell of imaging spectrum in tuberous sclerosis complex. MedPulse Int J Radiol. 2021;17(1):13-16.
[2] Crino PB, Nathanson KL, Henske EP. The tuberous sclerosis complex. N Engl J Med. 2006;355(13):1345-56.
[3] Northrup H, Krueger DA. Tuberous sclerosis complex diagnostic criteria update: Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference. Pediatr Neurol. 2013;49(4):243-54.
[4] Osborne JP, Fryer A, Webb D. Epidemiology of tuberous sclerosis. Ann N Y Acad Sci. 1991;615:125-27.
[5] Kingswood JC, d'Augères GB, Belousova E, Ferreira JC, Carter T, Castellana R, et al; TOSCA consortium and TOSCA investigators. TuberOus SClerosis registry to increase disease Awareness (TOSCA) - baseline data on 2093 patients. Orphanet J Rare Dis. 2017;12(1):2.
[6] Shields CL, Shields JA, Eagle RC, Marr BP, De Potter P. Retinal astrocytic hamartoma in 66 consecutive patients with tuberous sclerosis complex. Ophthalmology. 2004;111(4):817-25.
[7] Rowley SA, O'Callaghan FJ, Osborne JP. Ophthalmic manifestations of tuberous sclerosis: A population based study. Br J Ophthalmol. 2001;85(4):420-23.
[8] Pelino CJ, Pizzimenti JJ. Don't berry this clinical finding: Retinal astrocytic hamartomas are the most common ocular finding in tuberous sclerosis complex. Rev Optom. 2018;(7):60-65.
[9] Yüksel N, Ornek K. Intravitreal bevacizumab therapy in a case with macular edema secondary to retinal hamartoma associated with tuberous sclerosis. Cutan Ocul Toxicol. 2011;30(2):149-51.
[10] Rispoli M, Savastano MC, Lambiase A, Bonfiglio V, Minnella AM, Caputo D. Optical coherence tomography findings in retinal astrocytic hamartoma: Diagnostic and follow-up role. Eye (Lond). 2010;24(1):133-35.
[11] Rowley SA, O'Callaghan FJ, Osborne JP. Retinal hamartomas in tuberous sclerosis complex: A clinical review. Eye (Lond). 2001;15(Pt 5):591-97.
[12] Bissler JJ, Kingswood JC. Renal angiomyolipomata. Kidney Int. 2004;66(3):924-34.
[13] Kingswood JC, de Vries PJ, Belousova E, Benedik MP, Carter T, Cottin V, et al. Renal manifestations of tuberous sclerosis complex: Key findings from the TOSCA study. Nephrol Dial Transplant. 2019;34(4):502-13.
[14] de Vries PJ, Whittemore VH, Leclezio L, Byars AW, Dunn D, Ess KC, et al. Tuberous sclerosis associated neuropsychiatric disorders (TAND) and the TAND Checklist. Pediatr Neurol. 2015;52(1):25-35.
[15] Au KS, Williams AT, Roach ES, Batchelor L, Sparagana SP, Delgado MR, et al. Genotype/phenotype correlation in 325 individuals referred for a diagnosis of tuberous sclerosis complex in the United States. Genet Med. 2007;9(2):88-100.
[16] Ornek N, Ornek K, Erdol H. Retinal hamartoma associated with tuberous sclerosis: Treatment and follow-up. Eur J Ophthalmol. 2007;17(4):619-21.
[17] Falconer DS, Papavasileiou E, Patel M, Robson AG, Pavesio CE. Bevacizumab therapy for retinal astrocytic hamartomas in tuberous sclerosis complex: A review. Retin Cases Brief Rep. 2020;14(3):300-05.
[18] Wolfensberger TJ. Retinal astrocytic hamartoma treated by photodynamic therapy. Retina. 2003;23(6):727-29.
[19] Curatolo P, Bombardieri R, Jozwiak S. Tuberous sclerosis. Lancet. 2008;372(9639):657-68.

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