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Case Report

An atypical presentation of retinal astrocytic hamartoma with co-occurring SEGA in a tuberous sclerosis patient ☆,☆☆

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ABSTRACT

Tuberous sclerosis complex (TSC) is a genetic disorder that causes noncancerous growths and tumors in various body systems. This case report discusses an unusual eye condition called retinal astrocytic hamartoma (RAH) in a TSC patient, along with a brain tumor called subependymal giant cell astrocytoma (SEGA). These conditions, linked to TSC gene mutations, can be atypical in size and cause complications like vitreous hemorrhage. Surgical treatment is generally effective. Recognizing similarities between SEGA and RAH can help with early detection and comprehensive care for TSC patients.

Introduction

Tuberous sclerosis complex (TSC) is a relatively rare genetic disorder, affecting approximately 1 in 6000 individuals, and it is inherited with an autosomal dominant pattern. TSC is characterized by the formation of hamartomas in various organs, including the brain, kidney, lungs, skin, and heart [1,2]. These hamartomas result from mutations in 2 genes, TSC1 and TSC2, which play a role in controlling cell growth [3].

While TSC primarily affects organs like the brain and kidneys, it can also manifest in the eyes [4]. Retinal astrocytic hamartoma (RAH) is a distinctive ocular symptom of TSC, appearing as a yellow-gray lump within the retina's nerve fiber layer. RAH may exhibit characteristics like calcification and slightly dilated retinal arteries [5,6].

Earlier studies utilized time-domain optical coherence tomography (OCT) to examine RAH features, but this imaging technique's limited resolution posed challenges in accurately visualizing certain aspects, such as the precise depth of the

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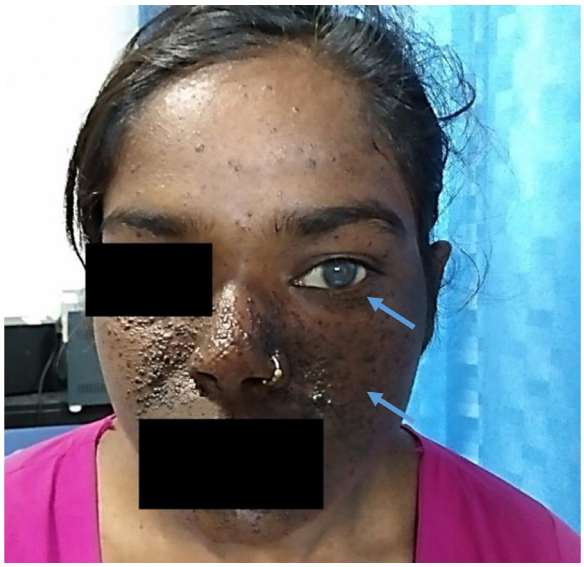

Fig. 1 – Young female patient with adenoma sebaceum and leukocoria in the left eye (blue arrows).

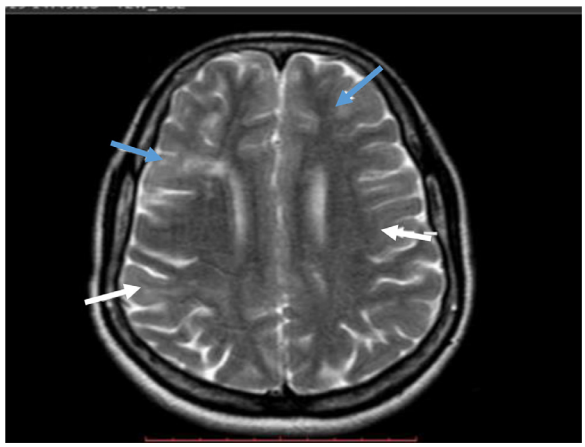

Fig. 2 – MRI Brain shows flame-shaped cortical tubers (blue arrows) in bilateral frontal lobes (solid arrows) and bilateral parietal lobes (white arrows) on hyperintense on T2W image.

tumor within the retinal nerve fiber layer [7–9]. This report presents a rare case of a giant RAH, shedding light on an unusual pathological manifestation of TSC, which can offer valuable insights for physicians encountering similar cases.

Case presentation

We present a case of an 18-year-old female, with a history of seizure disorder since the age of 13, who presented to the Radiology Department, seeking further evaluation for her condition. Her most recent seizure episode occurred 1 month back. Upon examination, the patient exhibited distinctive clinical features including maculopapular hyperpigmented skin lesions distributed in the characteristic malar pattern, consistent with adenoma sebaceum. Additionally, a left corneal opacity, indicative of leukocoria, was observed as shown in Figure 1. Notably, the patient's past medical history included ocular surgery. Following comprehensive informed consent, a series of diagnostic tests were initiated to elucidate the extent of her condition.

Subsequent investigations unveiled a complex presentation indicative of TSC. Neuroimaging through an MRI brain revealed the presence of diffusely distributed cortical tubers, abnormal growths in the brain, and areas of increased brightness on T2-weighted images (white matter hyperintensities), indicative of abnormal tissue as shown in Figure 2.

The MRI findings also include white matter T2/FLAIR hyperintensities, bilateral asymmetric subependymal calcified nodules, and a lesion morphologically consistent with a subependymal giant cell astrocytoma adjacent to the left foramen of Monroe. A substantial solitary ocular lesion, that measured 1.3 cm anteroposteriorly, 1.1 cm transversely, and 1.2 cm craniocaudally, exhibits isointensity on T1, hypo-intensity on T2, and isointensity to slight hypointensity on FLAIR relative to the surrounding tissue. Peripheral blooming foci are evident on T2 with moderate contrast enhancement on T1 contrast-enhanced images. The ocular lesion lacks diffusion restriction as shown in Figure 3.

Further insights were gleaned from ocular B-mode sonography, which unveiled a heteroechoic mass lesion resembling a mulberry, emerging from the temporal quadrant of the left globe. Measuring approximately 1.2 cm anteroposteriorly and 1.1 cm transversely, this lesion exhibited flat calcified plaques at its base, directed towards the retina. Accompanying this anomaly were basal focal retinal detachment and diffuse subacute to chronic vitreous hemorrhage. Remarkably, the lesion spared the optic nerve head and displayed marked internal vascularity on color Doppler imaging as shown in Figure 4.

After a thorough assessment confirming the presence of a RAH, the patient was promptly referred to the Department of Ophthalmology for specialized management. Initially treated with photodynamic therapy, the patient unfortunately experienced a loss to follow-up. Subsequently, the patient reappeared with significant vision loss in the left eye due to a serous retinal detachment, which was addressed through a series of intravitreal bevacizumab sessions. While some improvement in the serous retinal detachment was noted, the underlying astrocytic hamartoma persisted. Regrettably, the patient's left eye vision could not be restored, resulting in permanent visual impairment.

Discussion

TSC is a genetic condition marked by a range of abnormal tissue growths and benign tumors, which encompass congenital-hypopigmented skin patches facial angiofibromas, brain astrocytomas near ventricles or beneath brain lining, heart muscle tumors (cardiac rhabdomyoma), kidney angiomyolipoma, and noncancerous growths (RAHs). About 40% of instances are inherited within families using an

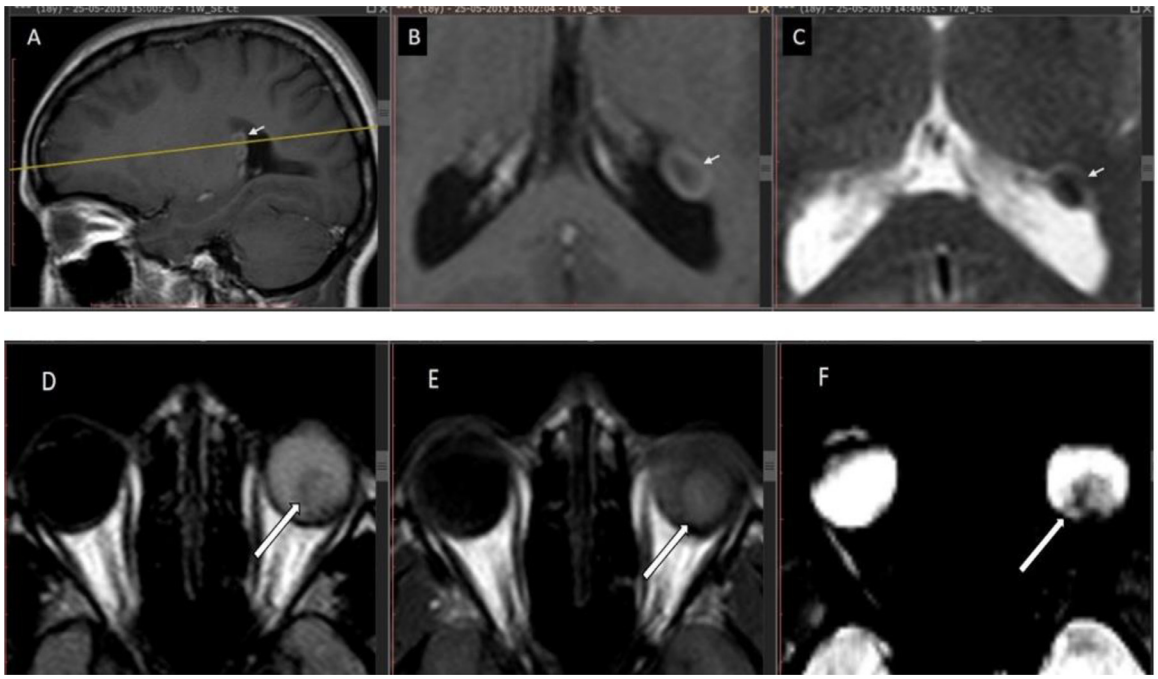

Fig. 3 – Contrast-enhanced MRI Brain shows round to oval enhancing mass lesion (white arrows) arising from the antrum of the left lateral ventricle (A and B), in close proximity to the foramen of Monroe appearing peripherally hyperintense with central hypointensity on T2W image (C) and shows round to oval enhancing mass lesion (white arrows) arising from juxta-papillary location of left globe, iso to hypointense on FLAIR (D), mildly hyperintense compared to surrounding media on T1W image (E) and blooming foci on T2 (F).

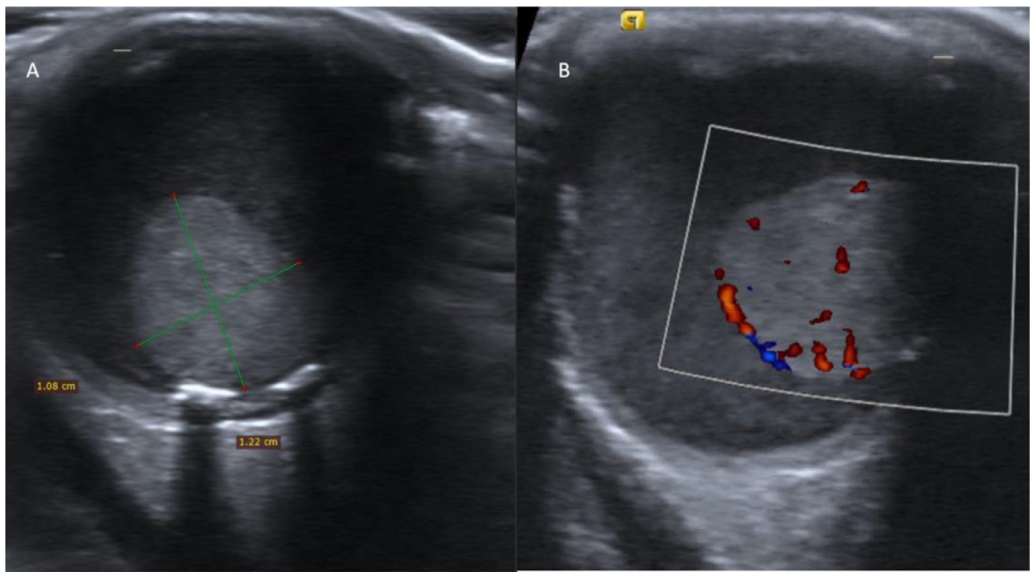

Fig. 4 – Ocular B mode ultrasound shows a heterogeneously hyperechoic multinodular mass lesion with foci of calcification (A) and internal vascularity (B).

autosomal dominant pattern, whereas about 60% of cases are not hereditary and develop spontaneously. Despite having a genetic foundation, the illness is likely to have molecular recessive characteristics. The genetic makeup of about half of all TSC cases is linked to chromosome 9q34, and the other half is linked to chromosome 16p13.23. Clinical signs are present in both sorts of patients in a similar way. Even though the Vogt triad—facial angiofibromas, intellectual impairment, and uncontrollable epilepsy—has been used to diagnose TSC. Ocular involvement in TSC can take many different forms, including iris hypopigmented patches, noncancerous growths (RAHs), and areas where the retinal pigment epithelium is missing

pigment [10–13]. In our case 18-year-old female with a history of seizures was diagnosed with TSC after presenting with distinctive clinical features and neuroimaging findings, including a RAH.

Approximately 50% of TSC patients develop RAHs, with half of them affecting both eyes [14]. RAHs can present as small, noncalcified sessile growths within the retinal nerve fiber layer (RNFL), nodular lesions with a yellow-white appearance, which may be calcified, or a combination of both, as shown in Figure 1A. These lesions typically have a diameter ranging from 0.5 to 5.0 mm, with larger occurrences being infrequent. The first histological illustration of RAH was credited to Van der Hoeve, revealing a fibrous structure with glial cells inside the RNFL, along with areas exhibiting dystrophic calcification. The glial cells come in various forms, including Müller cells, large gemistocytic astrocytes, and polymorphic astrocytes. It's been proposed that RAHs in TSC originate from undifferentiated glioneurocytes during the retina's embryonic development.

The most common type of brain tumor in TSC, occurring in 5%-10% of patients, is subependymal giant cell astrocytoma (SEGA) [15]. These tumors comprise a variety of abnormal glial cells, which can be polygonal, epithelioid, gemistocytic, or spindle-shaped, characterized by pleomorphism, thick eosinophilic cytoplasm, nuclear inclusions, and nuclei shifted towards the cell's border. They often embed themselves into a highly vascular support system and organize into patterns resembling sheets, clusters, or pseudo-rosettes. Notably, these tumors can contain numerous calcified areas [16]. It's essential to recognize that SEGA associated with TSC can occasionally exhibit aggressive behavior, leading to sudden increases in intracranial pressure, vision impairment, and even fatalities. In contrast, those occurring in the brain, similar to their counterparts in the retina, typically remain asymptomatic and are diagnosed through radiographic assessment.

The prognosis is generally favorable when surgically removing or alleviating SEGA. Similarly, RAH often remain stable without significant growth. Notably, very young children, often under the age of 5, are more likely to exhibit noticeable aggressive behavior in both brain and retinal cases. These findings, coupled with the pathological and histological similarities between SEGAs and RAHs resembling mulberries, underscore the importance of screening individuals with type III TSC and the necessity for collaborative efforts between neurosurgeons and ophthalmologists [17–20].

This case underscores the importance of interdisciplinary collaboration between radiology and ophthalmology in diagnosing and managing TSC patients, especially when complex ocular and intracranial manifestations coexist. The challenges faced in treating a rare and aggressive RAH in this young patient highlight the need for improved understanding and treatment strategies for such complex cases, ultimately enhancing patient care in the field.

Conclusion

In conclusion, TSC is a rare genetic disorder characterized by a wide range of tissue growth abnormalities and benign tumors, including ocular manifestations like RAHs. This case, which demonstrates the co-occurrence of SEGA and RAH, highlights the heterogeneity of TSC presentations, emphasizing the need for comprehensive screening and interdisciplinary collaboration in diagnosis and management. While the Vogt triad aids in diagnosis, not all patients exhibit all 3 signs, and the clinical presentation of ocular involvement can vary. Radiographic assessments play a crucial role in identifying intracranial and retinal manifestations. A favorable prognosis is often achievable with appropriate interventions, and ongoing research into the genetic basis of these manifestations is vital for improving diagnosis, treatment, and patient outcomes in TSC.

Ethical approval

This report was deemed exempt from formal ethical approval by the authors' institutions.

Author contributions

Sayantan Patra: identification and workup of case, illustrations, and critical review; Soumya Suvra Patra: literature review, data analysis, manuscript draft, and review; Both authors declare that they have approved this article for submission.

Patient consent

Signed consent for a case report was obtained from the patient's legally authorized representative (LAR). The IRB approval was taken from VMMC & Safdarjung Hospital Ethics Committee.

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