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Case Report

Giant cyst-like cortical tubers in an adult with tuberous sclerosis presenting as spastic tetraplegia

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ABSTRACT

Introduction and importance: Tuberous sclerosis complex (TSC) is an autosomal dominant disorder caused by inactivating mutations in TSC1 or TSC2 genes, resulting in benign lesions that involve multiple organs including the central nerves system.

Case presentation: A 39-year-old male of known TSC presented with inability to walk for two months. On physical examination, he was consciously oriented and cooperative, but he had spastic tetraparesis in the muscle-motor examination. On brain imaging, cystic lesions of various sizes in the supra and infratentorial regions were observed, consistent with giant cyst-like tubers. However, they could not differentiate from TSC related brain tumors based on the imaging findings. He underwent surgical intervention to resect/evacuate the large cystic lesion, which had the mass effects on the brain stem. The pathologic examinations revealed no malignant changes.

Clinical discussion: Although the cyst-like lesions in the cortex and white matter have been reported in several previous studies of TSC, they usually had a small size and similar intensity to CSF on T2- weighted MRI and low intensity on FLAIR images.

Conclusion: Giant cyst-like cortical tubers are exceedingly rare and atypical findings of tuberous sclerosis complex, which are usually associated with epilepsy and neurological deficits. Though many authors recommend the brain MRI as a screening tool for patients with TSC once every 1–3 years until the age of 25, our report showed that the brain lesions may develop in patients with TSC even after the age of 25. Thus, the MRI should be used periodically in all patients with TSC to timely detect the brain lesions and prevent the patient's disability. Surgical resection is the mainstay of treatment for the symptomatic cystic-like cortical tuber; however, it may recur after resection.

1. Introduction

Tuberous sclerosis complex (TSC) is an autosomal dominant disorder caused by inactivating mutations in TSC1 or TSC2 genes, resulting in benign lesions that involve multiple organs including the central nervous system [1]. Cortical tubers, subependymal giant cell astrocytomas (SGCAs), white matter abnormalities, and subependymal nodules are the hallmark of central nervous system involvement in TSC [2].The less differentiated giant cells, abnormal glial cells, and enlarged neurons forms the focal lesions with loss of normal cortical histology, which are called the tubers of TSC [3].

The most common clinical manifestations of TSC include seizures and mental retardation that closely correlate with the size and number of cortical tubers. However, attention-deficit hyperactive disorder and autism are seen in about one-third of TSC patients [3]. Imaging plays an important role in the presumptive diagnosis of TSC, evaluating the extent of disease, and contributing to the treatment plan [4]. The prognosis TSC is variable, depending on the severity of symptoms. However, mortality can be as high as 40% by age 35 [5].

Herein, the author presents a rare case of tuberous sclerosis with cyst-like cortical tubers presenting as spastic tetraplegia in a 39-year-old male. This work has been reported in line with the SCARE 2020 criteria [6].

2. Case presentation

2.1. Patient information

A 39-year-old male presented to our hospital with inability to walk

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Abbreviations

TSC	Tuberous sclerosis complex
SGCAs	Subependymal Giant Cell Astrocytomas

for two months. On physical examination, he was consciously oriented and cooperative, but he had spastic tetraparesis in the muscle-motor examination. The lower extremity deep tendon reflexes were (+++) with positive Babinski sign and right clonus. The cerebellar function tests, except for the dysdiadochokinesia were intact. No sensory ataxia was noted in his gait. He was a known case of TSC, diagnosed in 2002, and a right temporal lobe cystectomy. He suffered the last TSC related epileptic seizures about 6 years ago. No familial, social, or allergic history was given by the patient.

2.2. Laboratory and radiologic findings

His routine blood exams were within normal limits and he was negative for covid-19. On brain CT images, multiple hypodense lesions in the supra and infratentorial regions, the largest of which was approximately 30 × 31 mm in brain stem with coarse calcifications throughout the cortical and subependymal areas and subtle hydrocephalus were noted [Fig. 1]. On brain MRI exam, the same findings were observed. The lesions were hypointense on T1-weighted images, hyperintense on T2-weighted and FLAIR images with no restricted diffusion and post-contrast enhancement, consistent with tubers having the cystic degeneration [Figs. 2–3]. However, they could not differentiate from TSC related brain tumors based on these imaging findings.

2.3. Therapeutic intervention

After multidisciplinary consultation, the patient was taken up for surgical intervention by the experienced neurosurgery team in the neurosurgery unit to resect/evacuate the largest cystic mass causing the mass effects on the brain stem. The mass was evacuated and sent for pathologic examinations, which later revealed no malignant changes. The operation was terminated without any complication and a drain was maintained in the operation site. The patient was transferred to the ICU for further management. The patient's general condition was good postoperatively. He was conscious, cooperative, and had normal vital signs. On postoperative day 15th, the patient was followed in the inpatient service. His Glasgow coma scale was 14, bilateral upper extremity muscle strength; 3–4/5, and bilateral lower extremity muscle strength; 3/5. He was discharged from the hospital with a monthly follow up recommendation, using a condom catheter for urinary incontinence, and a manual wheelchair, as he was not able to walk independently.

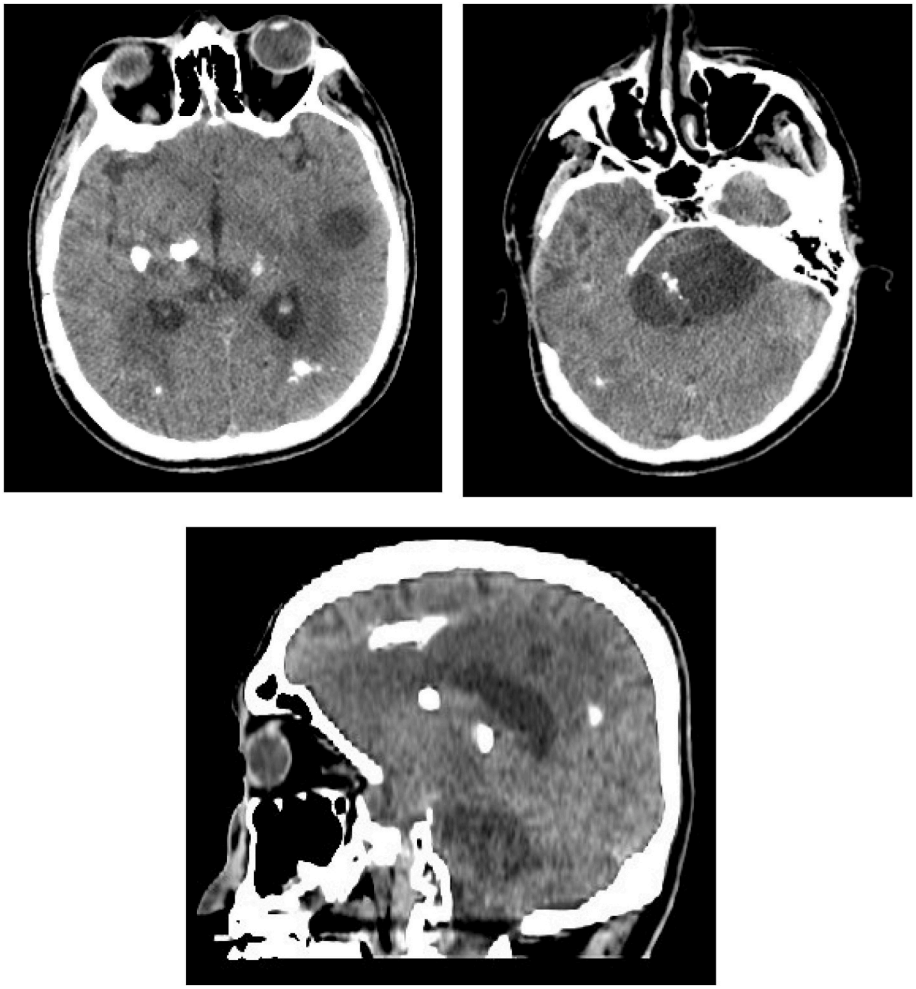

Fig. 1. Non-contrast enhanced brain CT axial and sagittal images, showing multiple hypodense lesions in the supra and infratentorial regions, the largest of which was in the brain stem with coarse calcifications throughout the cortical and subependymal areas.

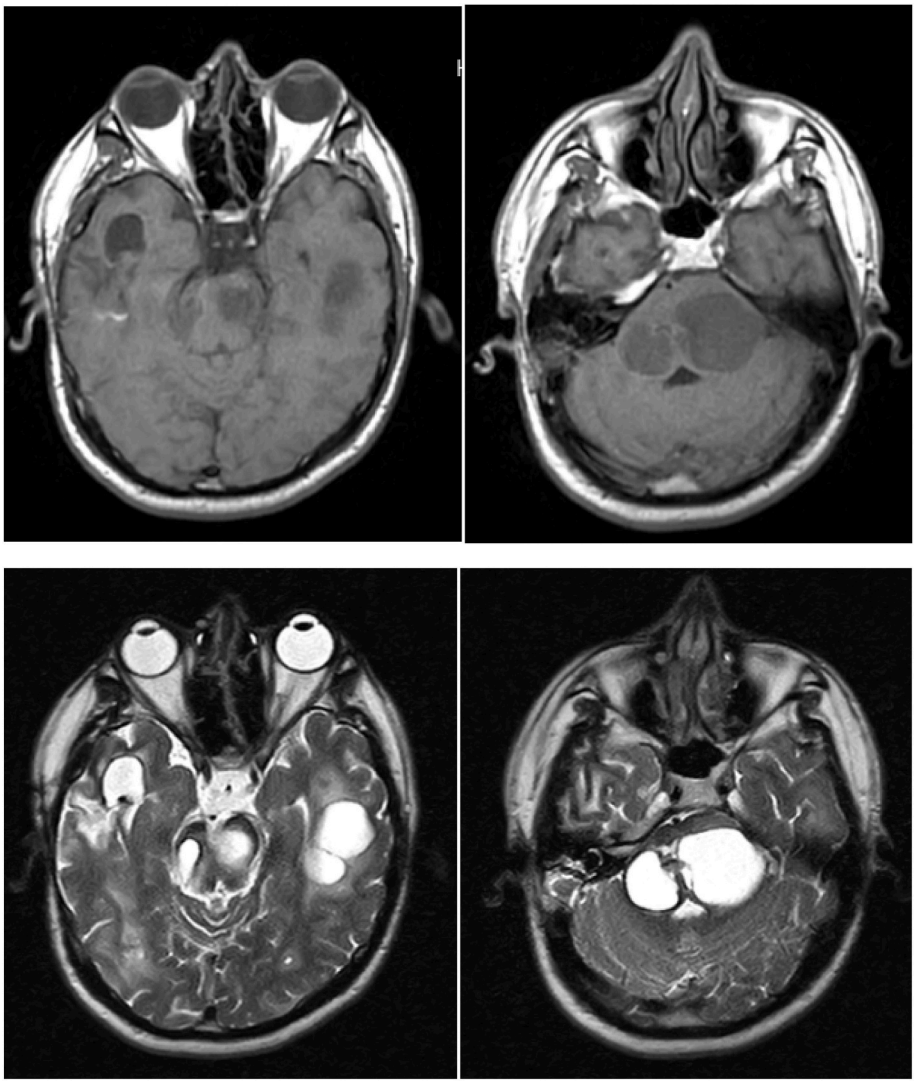

Fig. 2. (a)T1-weighted axial brain MRI images, showing multiple hypointense lesions of various sizes in the supra and infratentorial regions. (b)T2-weighted axial brain MRI images, showing multiple hyperintense lesions of various sizes in the supra and infratentorial regions. (c)T1-weighted post-contrast axial brain MRI images, showing multiple hypointense lesions without contrast enhancement. (d)FLAIR-weighted coronal brain MRI images, showing multiple hyperintense lesions of various sizes in the supra and infratentorial regions.

3. Discussion

Tuberous sclerosis complex was first described in 1835 by Rayer [7]. Bourneville used the term tuberous sclerosis in 1880, to explain the brain pathology of three persons with seizures and learning disabilities [8,9].

It affects both sexes and all ethnicities with a population prevalence of 1/6000 to 1/12,000, and about 2/3 of the cases are sporadic [2].

TSC is a rare hereditary disease resulting in uncontrolled cell growth caused by mutations of the TSC1 or TSC2 genes of the PI3K/AKT/mTOR signaling pathway, which induces overactivation of mammalian target of rapamycin protein (mTOR) [10].

Many organs including the eye, heart, lung, kidney, and skin can be affected by TSC. However, brain involvement is associated with the most significant patient morbidity. The tubers of TSC, are cerebral cortex focal developmental malformations, which are seen in more than 80% of individuals with TSC and believed to form between weeks 8 and 20 of gestation [11].

The most common clinical manifestations of TSC include seizures and mental retardation that closely correlate with the size and number of cortical tubers. However, attention-deficit hyperactive disorder and autism are seen in about one-third of TSC patients [3].

In our case the patient had a history of seizures, but presented to our hospital with the complaint of spastic tetraparesis, which is unusual and atypical for TSC.

Imaging plays an important role in the presumptive diagnosis of TSC, evaluating the extent of disease and contributing to the treatment plan [4].

MRI is more applicable than CT for the detection of cortical tubers. The cortical tubers, usually have high intensity on T2 and low signal intensity on T1-weighted MRI images and only 10% of tubers show post-contrast enhancement. Calcification and central cystic degeneration occasionally may occur [2,12,13].

Although the cyst-like lesions in the cortex and white matter have been reported in several previous studies of TSC, they usually had a small size and similar intensity to CSF on T2 and low intensity on FLAIR images [12,14]. Thus, the cystic masses in our patient was unlike the previously reported cortical or subcortical tubers in TSC. In our case, there were multiple giant cystic lesions in supra and infratentorial regions including the brain stem, which is a rare and atypical imaging

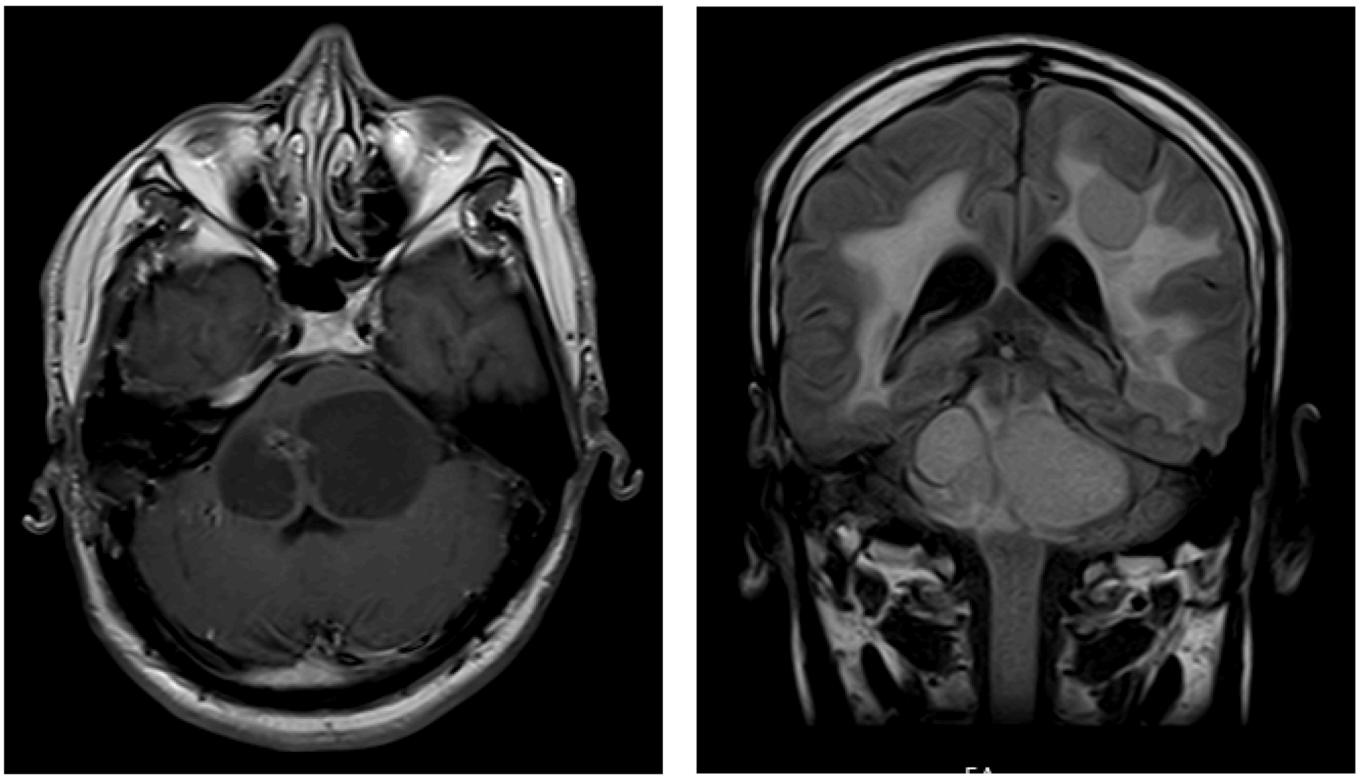

Fig. 2. (*continued*).

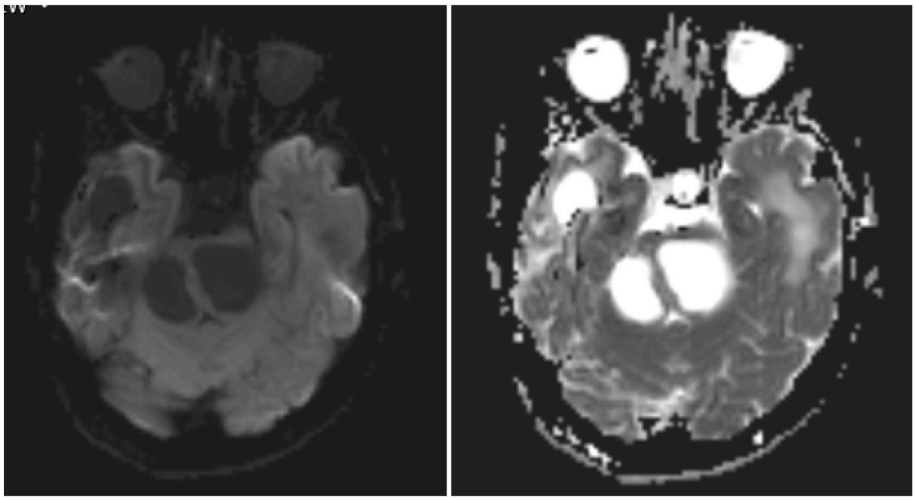

Fig. 3. Diffusion-weighted and ADC brain MRI images, showing multiple lesions of various sizes in the supra and infratentorial regions without restricted diffusion.

finding for TSC.

Martin AG et al. reported a pleomorphic xanthoastrocytoma presented as a large intra-axial cystic lesion with an enhancing mural nodule is in TSC [15]. Besides, SEGA has been reported as the most common CNS tumor in individuals with TSC in many previous reports, but SEGA often appears in intraventricular locations [14]. These are inconsistent with our findings, as the cystic lesions in our case had no enhancing mural nodule and intraventricular location. Moreover, the pathologic analysis of the cystic lesion did not show any malignant cells. Thus, our findings suggest that the tubers in TSC may manifest as supra and infratentorial cystic lesions with atypical features. However, the differential diagnosis should be considered from subependymal nodules, subependymal giant cell astrocytomas, and other brain tumors.

Though Crino et al. recommend annual MRI of the brain until patients are at least 21 years of age and then every 2–3 years [16], many studies recommended it once every 1–3 years until the age of 25, as new subependymal giant cell astrocytomas rarely develop after the age of 25 years [14,17]. These were incompatible with our case. Our patient presented with brain lesions beyond the age of 25 years. Therefore, MRI should be performed periodically in all patients of TSC older than 25 years to timely detect the brain lesion and prevent the patient's disability.

The cyst-like tubers often present with severe epilepsy therefore surgical intervention can be recommended if antiepileptic medication is ineffective. However, multiple tubers and the extension of the epileptogenic tissue outside of tubers may be the challenges for surgery [13,18].

In our case, the patient underwent surgical intervention, aiming to

resect/evacuate the cystic lesion, which caused the mass effects on the brain stem, though the outcome was not more favorable.

This is a rare and surgically proven case; however, lack of the longtime follow-up may be the only limitation for this case report.

4. Conclusion

Giant cyst-like cortical tubers are exceedingly rare and atypical findings of tuberous sclerosis complex, which are usually associated with epilepsy and neurological deficits. Though many authors recommend the brain MRI as a screening tool for patients with TSC once every 1–3 years until the age of 25, our report showed that the brain lesions may develop in patients with TSC even after the age of 25. Thus, the MRI should be used periodically in all patients with TSC to timely detect the brain lesions and prevent the patient's disability. Surgical resection is the mainstay of treatment for the symptomatic cystic-like cortical tuber; however, it may recur after resection.

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Ethical approval

The manuscript has got an ethical review exemption from the Ethical Review Committee (ERC) of our institution, as case reports are exempted from review according to the institutional ethical review committee's policy.

Consent

Written informed consent was obtained from the patient's next of kin for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Registration of research studies

Not applicable

Guarantor

The corresponding author (Habib Ahmad Esmat) is the guarantor for the work and he has the responsibility of access to the data, and controlling the decision to publish.

Author contribution

Not applicable

Declaration of competing interest

The authors declare that they have no conflicts of interest for publication of this case report.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104024.

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