

Progressive cystic lesion in a middle-aged patient with tuberous sclerosis complex

A case report

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Abstract

Rationale: Tuberous sclerosis complex (TSC) is an uncommon multiple systems disorder. The main characteristics of the disease in the central nervous system include cortical or subcortical tubers, subependymal nodules, and subependymal giant cell astrocytoma. However, progressive cystic lesions in the cerebral hemispheres have rarely been reported in previous studies of TSC.

Patient concerns: We present the case of a 35-year-old man with TSC who was admitted to our hospital for a sudden attack of serious headache, vomiting, and left hemiplegia. Brain computerized tomography and magnetic resonance imaging (MRI) revealed multiple subependymal calcific nodes and multiple cystic lesions in the right frontal, temporal, and parietal lobes. The solid nodule in the lesion demonstrated contrast enhancement.

Diagnoses: The patient was diagnosed with TSC, but the properties of the cystic lesion in the brain were unclear and a tumor was suspected.

Interventions: Emergency operation was performed immediately. Pathological examination of the lesion revealed a vascular malformation, but no tumor cells.

Outcomes: In the fourth year after the surgery, brain MRI revealed a relapse of the cystic mass and surgery was suggested again. However, the patient refused to undergo surgery again.

Lessons: This case describes an atypical MRI presentation of TSC occurring in middle-age. This condition can cause a life-threatening condition and may recur after surgery. Our finding emphasizes the importance of neuroimaging surveillance in patients older than 25 years old and after lesion resection.

Abbreviations: CNS = central nervous system, CT = computerized tomography, FLAIR = fluid-attenuated inversion recovery, MRI = magnetic resonance imaging, PXT = pleomorphic xanthoastrocytoma, SEGA = subependymal giant cell astrocytoma, SEN = subependymal nodule, T1WI = T1-weighted image, T2WI = T2-weighted image, TSC = tuberous sclerosis complex.

Keywords: progressive cystic lesion, tuberous sclerosis complex, tumor, vascular malformation

1. Introduction

Tuberous sclerosis complex (TSC) is an uncommon autosomal dominant disorder with an incidence of 1/6000 to 1/10,000 live births, and a population prevalence of about 1/20,000.^[1] Diagnosis of TSC is made on the basis of clinical presentation and/or genetic testing results. The clinical manifestations of TSC occur in multiple systems, including the skin, brain, kidney, heart,

lung, tooth, and eye.^[2] The central nervous system (CNS) is reported to be involved in more than 90% of individuals with TSC. CNS involvement in TSC mainly manifests as cortical or subcortical tubers, subependymal nodules (SENs), and subependymal giant cell astrocytoma (SEGA).^[1,2]

The present report describes a 35-year-old man with a progressive huge cystic lesion with the pathological diagnosis of vascular malformation without a tumor fraction finding in the right hemisphere. This type of lesion is rarely reported in patients with TSC.

2. Case report

We present the case of a 35-year-old man with TSC who was admitted to our hospital for a sudden attack of serious headache, vomiting, and left hemiplegia. He presented with an intractable complex partial seizure for 31 years, with 5 to 7 episodes per month during the year before admission. Examination of the patient's skin revealed light yellow papules on the nose and cheeks, a skin-colored plaque on the back, and molluscum-like lesions in the sacrococcygeal region (Fig. 1). A previous brain computerized tomography (CT) scan revealed multiple subependymal calcific nodes. Interventional treatment was performed for renal hamartoma 1 month before the visit.

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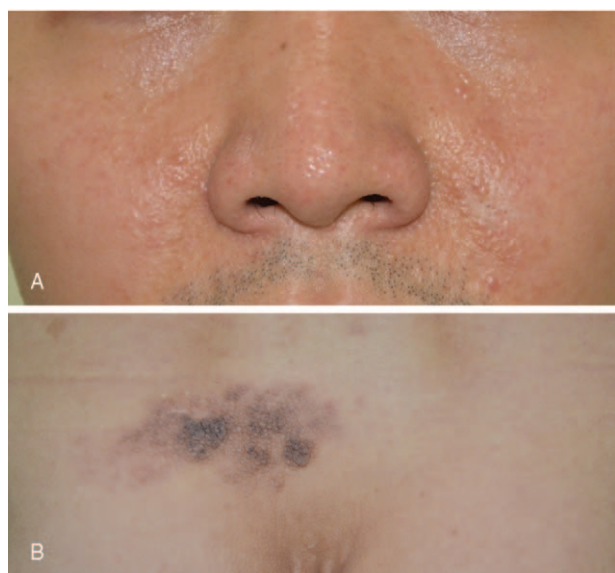


Figure 1. Physical examination revealed light yellow papules on the nose and cheeks (A) and molluscum-like lesions in the sacrococcygeal region (B).

Brain CT and magnetic resonance imaging (MRI) revealed multiple subependymal calcific nodes and multiple cystic lesions in the right frontal, temporal, and parietal lobes. The largest of these lesions was about $5.6 \times 6.0 \text{ cm}^2$ in size. There was a midline structure shift and little hemorrhage. The solid nodule in the lesion demonstrated contrast enhancement (Fig. 2).

Emergency operation was performed immediately, and the cystic lesions were resected. A yellow glue-like substance was found in the cyst. Pathological examination of the solid nodule in the mass revealed a vascular malformation, and no tumor cells were found. Tissue from the nodule did not react with antibodies against CD34 or S100 (Fig. 3). The patient left the hospital with numbness in the upper left limb.

Two weeks after the operation, the patient was admitted to the hospital again and underwent surgery for a sudden left pneumothorax. Thereafter, the patient had an uneventful recovery without any neurological deficits for 3 years after neurosurgery, during which outpatient follow-ups were performed. He took antiepilepsy drugs and presented with subtle seizures manifesting as flushes lasting for several seconds. The patient's seizure frequency decreased to once every 2 to 3 months. However, in the fourth year of follow-up, his seizure frequency gradually increased to 1 to 2 times per month, and brain MRI revealed relapse of the cystic mass. Surgery was suggested again at this time (Fig. 4). However, the patient refused to undergo surgery again.

2.1. Standard protocol, approval, and consent

This case report was approved by the Ethical Committee of West China Hospital, Sichuan University. Written informed consent to publish this case was obtained from the patient.

3. Discussion

Tuberous sclerosis complex is a lifelong disorder involving multiple systems. Typical brain lesions in patients with TSC

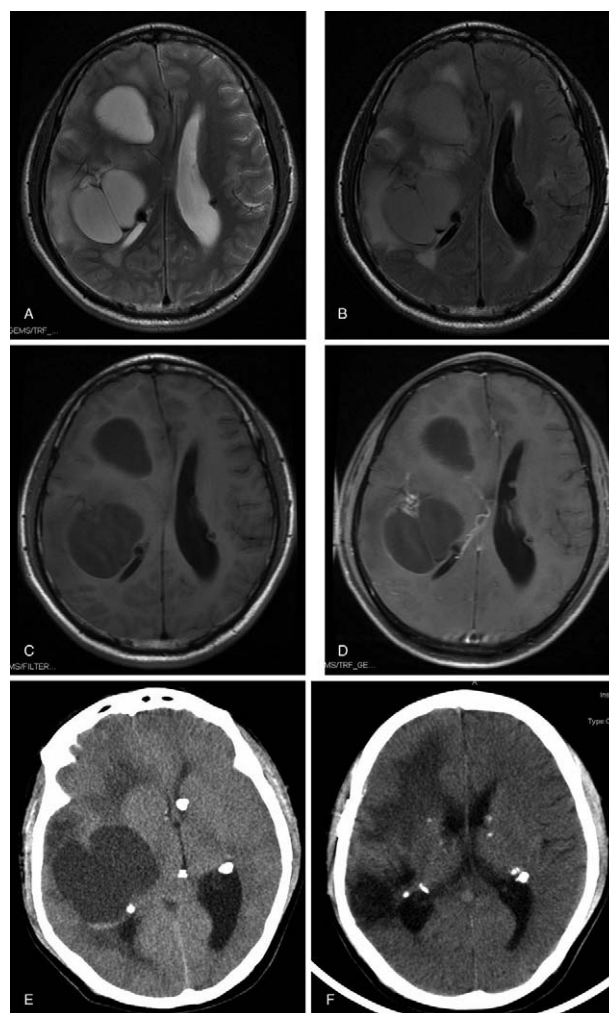


Figure 2. Brain CT and MRI revealed multiple subependymal calcific nodes and multiple cystic lesions in the right frontal and temporal lobes, as well as a midline structure shift. The cystic parts of the lesions were hyperintense on T2WI (A) and FLAIR (B), and hypointense on T1WI (C). The solid nodule in the lesion demonstrated contrast enhancement (D). Brain CT before (E) and after surgery (F). CT=computed tomography, FLAIR=fluid-attenuated inversion recovery, MRI=magnetic resonance imaging, T1WI=T1-weighted image, T2WI=T2-weighted image.

include cortical or subcortical tubers, SENs, and SEGA. In this case, the patient had atypical MRI manifestations. Specifically, MRI revealed a huge cystic mass that was hypointense on T1-weighted images (T1WI) and hyperintense on T2-weighted (T2WI) and fluid-attenuated inversion recovery (FLAIR) images. The lesion included an enhancing nodule. Such findings have rarely been reported in previous studies of TSC. Although cyst-like lesions in the cortex and white matter have been reported in several previous studies of TSC, they have often been small cystic lesions with similar intensity to cerebrospinal fluid on MRI and hypointensity on FLAIR images.^[3,4] Therefore, the cystic mass in this patient was different from previously reported cortical or subcortical tubers.

It is unfortunate that the presence of a tumor was not verified by pathological examination, even though the MRI evaluation revealed a lesion mimicking a tumor. A vascular

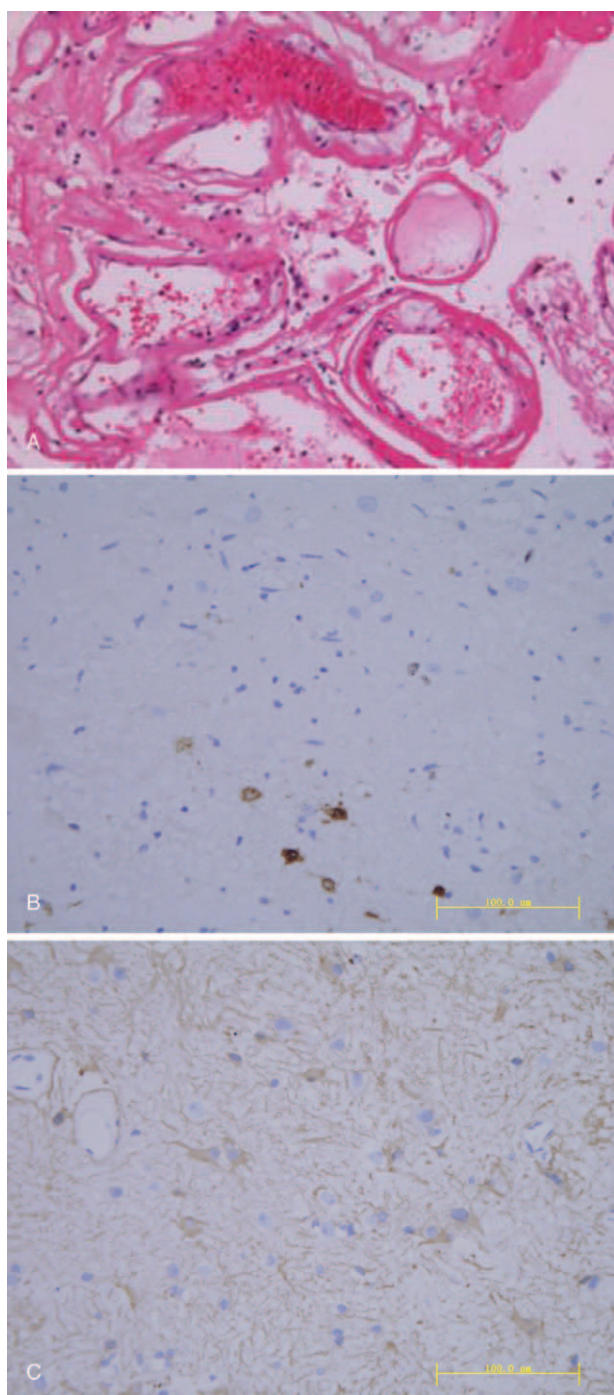


Figure 3. Pathological examination revealed a vascular malformation (A). Staining for NeuN (B) and glial fibrillary acidic protein (C) revealed no tumor cells.

malformation, diffusing neurons, and gliosis were observed upon microscopic examination. However, biomarkers of glioma, ganglioma, and pleomorphic xanthoastrocytoma (PXT) were absent. Previous reports indicate that SEGA is the most common CNS tumor in individuals with TSC, and is an important cause of TSC-related morbidity and mortality.^[5,6] SEGA often occurs in intraventricular locations and presents as a solid lesion.^[6] This is inconsistent with the MRI presentation of our patient. However,

there are several other reports of SEGA with cystic and extraventricular growth.^[7-9] Furthermore, similar cystic masses have been reported in 2 other cases of TSC. These lesions were shown to be cases of PXT and fibrillary astrocytoma.^[10,11] Therefore, the presence of a tumor should be taken into consideration in this case, given the progressive nature of the lesions in the MRI evaluation, although it is difficult to estimate whether the cystic mass in this case was a SEGA with atypical MRI presentation, a rare tumor associated with TSC, or a non-neoplastic lesion. Our findings imply that in patients with atypical brain MRI characteristics other than cortical or subcortical tubers, SENs or SEGA, further differential diagnosis should be considered.

Based on the consensus in the field, brain MRI is often recommended for patients with TSC once every 1 to 3 years until the age of 25 years, as new SEGAs rarely develop after the age of 25 years.^[2,6] Nevertheless, in this case, the patient was admitted to our hospital for a sudden attack of hemiplegia and high intracranial pressure at the age of 35 years, even though no suspicious tumor-like lesions were found in neuroimaging examinations before the age of 25 years. Therefore, in patients with TSC, even in individuals older than 25 years, there is still a risk of the new development of brain lesions that are likely to cause disability and death. Brain MRI should thus be performed periodically to monitor intracranial lesions, especially when there is an increase in the frequency of seizures.

4. Conclusions

Here we present the case of a patient with a rare MRI presentation of TSC occurring in middle-age. The observed lesion may have caused a life-threatening condition and recurred after surgery. Although the properties of the huge cystic mass were unclear, our findings emphasize the importance of neuroimaging surveillance in patients older than 25 years and after lesion resection.

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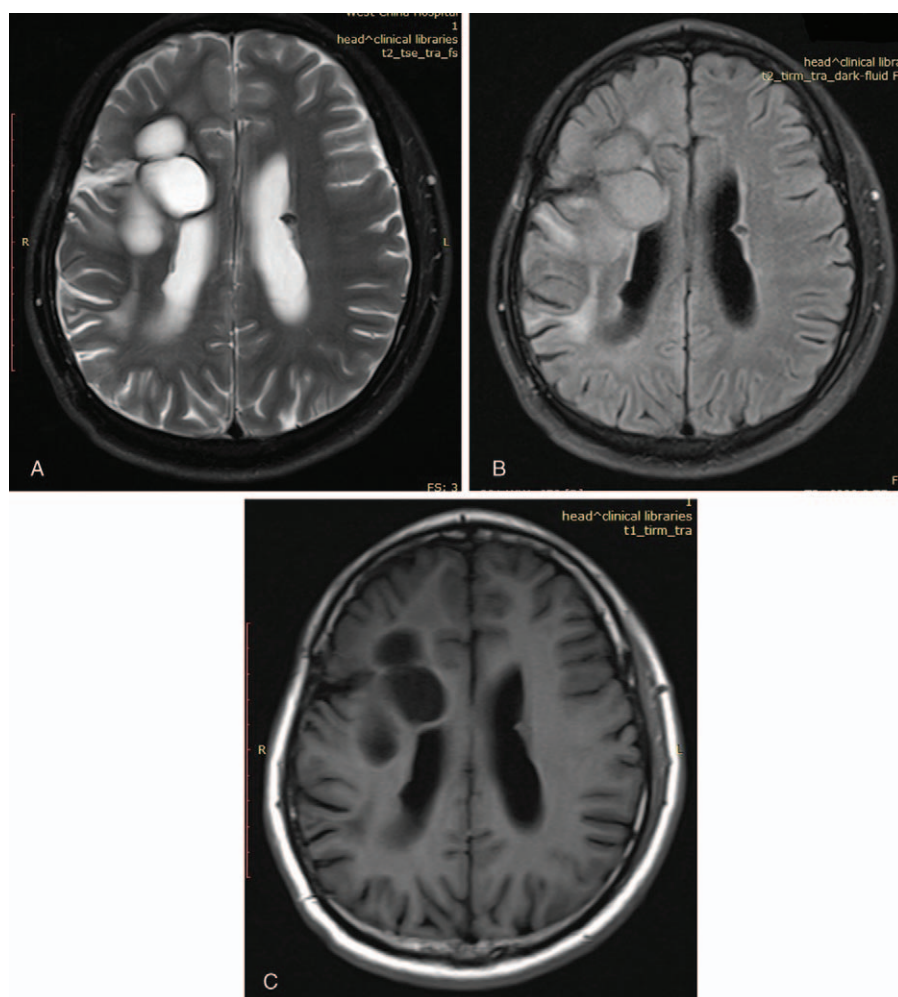


Figure 4. Brain MRI revealed the relapse of the cystic lesion in the right frontal and temporal lobes in the fourth year after surgery. The cystic parts of the lesions were hyper-intense on T2WI (A) and FLAIR (B) and hypo-intense on T1WI (C). FLAIR = fluid-attenuated inversion recovery, MRI = magnetic resonance imaging, T1WI = T1-weighted image, T2WI = T2-weighted image.

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