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Case Report

Missed for years: tuberous sclerosis complex presenting with status epilepticus and tuberous sclerosis complex associated neuropsychiatric disorders in an adolescent girl

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ABSTRACT

Tuberous sclerosis complex (TSC) is a multisystem neurocutaneous disorder commonly presenting with seizures in early childhood. Delayed diagnosis remains frequent in resource-limited settings. Presentation as status epilepticus during adolescence, particularly with prominent TSC-associated neuropsychiatric disorders (TAND), is uncommon and underreported. A 16-year-old adolescent girl presented with generalized convulsive status epilepticus. She had a history of untreated recurrent seizures since the age of 10 years, along with significant cognitive, behavioural and adaptive functioning impairment. Physical examination revealed multiple characteristic cutaneous stigmata suggestive of TSC. Neuroimaging demonstrated cortical tubers and subependymal nodules and abdominal ultrasonography revealed a renal angiomyolipoma, confirming the diagnosis of TSC. The patient was managed as per standard status epilepticus protocols, resulting in seizure control. Comprehensive evaluation identified significant neuropsychiatric manifestations. Formal screening using the TAND-L checklist revealed multi-domain involvement, including intellectual, behavioural, neuropsychological and psychosocial domains. A multidisciplinary management plan including optimization of antiepileptic therapy, behavioural interventions, low dose risperidone, caregiver counselling and neurodevelopmental follow-up was initiated. This case highlights the consequences of delayed recognition of TSC, where missed neurocutaneous markers resulted in late diagnosis and life-threatening neurological presentation. It underscores the importance of systematic screening for TAND in all individuals with TSC and emphasizes the need for heightened clinical vigilance and multidisciplinary care to improve long-term outcomes.

Keywords: Adolescent, Cutaneous stigmata, Multidisciplinary, Neuropsychiatric disorders, TAND-L checklist

INTRODUCTION

Tuberous sclerosis complex (TSC) is a multisystem genetic disorder with an autosomal dominant mode of inheritance.[1] Spontaneous pathogenic variants account for nearly 65% of cases. The estimated birth incidence is approximately 1 in 6000 live births, with similar prevalence worldwide.[2] TSC is a highly heterogeneous disorder, with clinical manifestations ranging from severe intellectual disability and intractable epilepsy to normal intelligence with minimal neurological involvement. In addition to the brain and skin, multiple organ systems may be affected, including the kidneys, heart, lungs, eyes and bones.[1,2] Molecular genetic studies have identified two causative genes: TSC1 on chromosome 9q34 encoding hamartin and TSC2 on chromosome 16p13 encoding tuberin.[3] The hamartin–tuberin complex regulates the mammalian target of rapamycin (mTOR) pathway, which plays a key role in cell growth and protein synthesis.[3,4] Loss of this regulatory function results in mTOR overactivation and uncontrolled cellular proliferation, leading to the formation of multiple benign hamartomas.[4] Despite well-established diagnostic criteria and recognizable cutaneous markers, delayed diagnosis

of TSC remains common, particularly in resource-limited settings. Late recognition may result in preventable complications, including uncontrolled epilepsy and significant neuropsychiatric morbidity.[5] Presentation during adolescence with status epilepticus, especially in association with TSC-associated neuropsychiatric disorders (TAND), is uncommon and highlights the consequences of missed opportunities for early diagnosis and intervention.

CASE REPORT

A 16-year-old adolescent girl from a lower socioeconomic background was brought to the emergency department with generalized convulsive status epilepticus. She had repeated episodes of generalized tonic–clonic seizures involving all four limbs, each lasting 5-10 minutes, with altered consciousness between episodes.



Figure 1: Multiple facial angiofibroma's (lower arrow) over the malar region and nasal bridge with a fibrous cephalic plaque (upper arrow), characteristic cutaneous manifestation of tuberous sclerosis complex.

Emergency management was initiated immediately as per standard status epilepticus protocol with intravenous antiepileptic medications, antibiotics and fluid resuscitation. Seizure activity was controlled, and the patient regained consciousness within 12 hours. On detailed history, the patient had experienced her first seizure at 10 years of age, for which she was admitted briefly and discharged without continuation of antiepileptic therapy. Subsequently, she had recurrent monthly seizures lasting 4-5 minutes, for which no proper medical evaluation or treatment was sought. Over the preceding one year, seizure frequency increased to multiple episodes per day, yet no hospital admission or investigations were undertaken. The patient had not been enrolled in formal schooling. Although early developmental milestones were reportedly normal, she exhibited significant intellectual and adaptive functioning impairment, requiring assistance with basic self-care activities such as bathing, dressing and brushing. Social interaction was poor and communication was limited. There was no history of consanguinity or family history of neurological or psychiatric illness. Birth history was unremarkable.



Figure 2: Shagreen patch over lumbosacral region.

On clinical examination the patient was of average built with a dull facial expression and poor personal hygiene. Dermatological examination revealed multiple cutaneous stigmata suggestive of a neurocutaneous disorder, including: Multiple small, raised, reddish-brown papules over the malar region and nasal bridge in a butterfly distribution, consistent with facial angiofibromas (Figure 1).



Figure 3: A nodular intraoral fibroma at the tip of tongue (black arrow), consistent with a mucosal hamartomatous lesion in tuberous sclerosis complex.

A firm fibrotic plaque with reddish discoloration was noted over the left forehead, consistent with a fibrous cephalic plaque (Figure 1). There were multiple well-defined hyper and hypopigmented rough plaques with a pebbly texture over the lower back, consistent with a shagreen patch (Figure 2). A nodular fibroma over the tip of the tongue was also present (Figure 3).

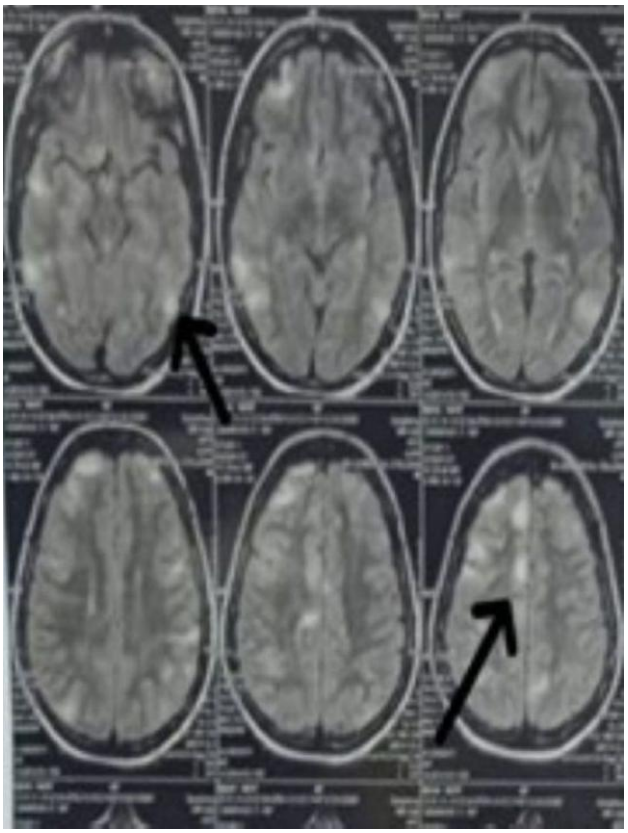


Figure 4: Axial MRI brain image demonstrating multiple cortical tubers and subependymal nodules consistent with tuberous sclerosis complex.

Baseline laboratory investigations including complete blood count, serum electrolytes, renal and liver function tests were within normal limits. Chest radiograph was normal. Magnetic resonance imaging (MRI) of the brain revealed multiple cortical tubers and subependymal nodules, characteristic of TSC (Figure 4). Abdominal ultrasonography showed a left renal nodule suggestive of a renal angiomyolipoma. Ophthalmological evaluation was normal. Echocardiography was normal.

Behaviourally, the patient was mostly quiet with minimal verbal output, poor eye contact and intermittent response to commands. Examination of higher mental functions revealed inappropriate speech and behaviour for age, intermittent shouting, poor attention and memory, impaired comprehension and judgment, and poor insight. Occasional impulsive and aggressive behaviour was noted. These findings were consistent with TSC-associated neuropsychiatric disorders (TAND), so a formal screening for TAND was done by TAND -L checklist which showed involvement of multiple domains including intellectual, behavioural, neuropsychological and psychosocial, with a high cumulative burden, indicating severe TAND.[6] Based on clinical features, neurodevelopmental history and radiological findings, a diagnosis of Tuberous sclerosis complex with TAND was established. The patient was managed with multidisciplinary approach. After stabilization, behavioural therapy and parental counselling were initiated. Speech and occupational therapy were advised. She was started on low dose risperidone. Antiepileptic medication was optimized and neurodevelopment follow up was planned.

DISCUSSION

Tuberous sclerosis complex is a multisystem autosomal genetic disorder characterized by benign hamartomatous lesions affecting multiple organs, most commonly the brain, skin and kidneys.[1]

Table 1: Major and minor diagnostic criteria for tuberous sclerosis complex.

Major criteria's	Minor criteria's
Hypomelanotic macules (>3, >5 mm in diameter)	Confetti skin lesion (>3)
Angiofibroma's (>3) or fibrous cephalic plaque	Ungual fibromas (>2)
	Intraoral fibroma (>2)
	Retinal achromic patch
Dental enamel pits (>3)	Multiple renal cysts
	Nonrenal hamartomas
Shagreen patch	
Multiple retinal hamartomas	
Cortical dysplasia	
Subependymal nodules	
Subependymal giant cell astrocytoma	
Cardiac rhabdomyoma	
Lymphangioleiomyomatosis	
Angiomyolipomas (>2)	

Cutaneous manifestations are seen in up to 96% of patients with TSC, with facial angiofibromas being the most common.[2] Renal involvement, particularly angiomyolipomas, occurs in up to 80% of individuals and may remain asymptomatic for years, as observed in this patient.[2] Seizures occur in approximately 72-85% of individuals with TSC and typically begin within the first three years of life in more than 80% of cases.[7] Presentation in adolescence is uncommon, as observed in our case and initial manifestation as status epilepticus is rare. In the present case, delayed diagnosis despite classical cutaneous markers reflects gaps in awareness and healthcare access. Diagnosis is established using

clinical criteria (Table 1) or genetic testing as outlined by the 2012 International tuberous sclerosis complex consensus conference, which requires the presence of 2 major or 1 major plus 2 minor features for definite diagnosis.[4] TSC-associated neuropsychiatric disorders (TAND) are a major source of morbidity and are frequently under-recognized.[8] "TAND" is an "umbrella" term used for the range of bio-psycho-social difficulties associated with TSC and describes the neuropsychiatric involvement in tuberous sclerosis across 6 "levels" (behavioural, psychiatric, intellectual, academic, neuropsychological and psychosocial).[6-8] Caregivers and their support teams in health, are encouraged to "screen" for TAND at least annually using screening tools such as the TAND-L (Lifetime) or TAND-SQ (self-report quantified) Checklists.[9,10] According to the International consensus recommendations for treatment of TAND, the clinical approach can be summarized in three words Screen, Act, Repeat.[11] Screening in this context refers to a systematic topline check to identify any existing or emerging concerns in the individual with TSC and/or their caregiver system. Appropriate action in form of cognitive, behavioural, occupational or pharmacotherapy must be followed by repeat screening annually.

Although tuberous sclerosis complex is a well-described neurocutaneous disorder, this case is noteworthy for multiple reasons. The patient remained undiagnosed for several years despite the presence of classical cutaneous markers, highlighting missed opportunities for early recognition. Presentation with generalized convulsive status epilepticus during adolescence is uncommon in TSC, where seizures usually begin in early childhood. Furthermore, the case brings attention to the often-under-recognized burden of TSC-associated neuropsychiatric disorders (TAND), with deficits across multiple domains contributing significantly to functional disability. This report emphasizes the need for heightened clinical vigilance, especially in resource-limited settings, where delayed diagnosis can lead to preventable neurological emergencies and long-term morbidity.

CONCLUSION

This case illustrates how delayed recognition of characteristic neurocutaneous markers can lead to late diagnosis of TSC and life-threatening neurological emergencies such as status epilepticus. Early identification, routine screening for TAND and comprehensive multidisciplinary management are essential to improve long-term outcomes in individuals with TSC. And Caregiver education is of utmost important and critical for appropriate health seeking behaviour.

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