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*Case Report*

# FIRST SEIZURE IN A 16-YEAR-OLD GIRL ASSOCIATED WITH TUBEROUS SCLEROSIS COMPLEX: A CASE REPORT

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**ABSTRACT**

**Introduction:** Tuberous sclerosis complex (TSC) is a rare autosomal dominant disorder causing benign tumors in multiple organs. It affects 1 in 6,000 births globally, with a prevalence of 1 in 20,000. However, data in Indonesia remain limited. TSC is marked by seizures, developmental delays, and distinct skin lesions.
**Case Report:** A 16-year-old girl experienced her first seizure. She had no prior TSC diagnosis. Clinical examination revealed generalized tonic clonic seizure, cognitive impairment, and distinctive skin features, including hypomelanotic macules, angiofibromas, a shagreen patch, and non-renal hamartomas. A non-contrast head CT scan confirmed multiple punctate calcifications in the periventricular regions of both lateral ventricles, consistent with TSC. Diagnosis was delayed until her first seizure.
**Discussion:** Diagnosing TSC is challenging. Seizures are often the first noticeable sign. Cognitive delays highlight the need for early screening in children with learning difficulties, particularly when TSC symptoms are present. Limited awareness among healthcare providers and the public contributes to delayed diagnosis. Mutations in TSC1/TSC2 genes disrupt the mTOR pathway, leading to abnormal cell growth and hamartoma formation, increasing seizure risk. Raising awareness is crucial for early detection and timely intervention.
**Conclusion:** TSC often goes undiagnosed until adolescence due to limited awareness and missed early signs. Seizures are a key warning sign requiring evaluation, making TSC a crucial consideration in new-onset seizures, particularly with characteristic skin or brain findings. Early detection and comprehensive care are essential for preventing complications and improving quality of life.
**Keywords:** tuberous sclerosis complex; seizures; epilepsy; TSC1; TSC2

## INTRODUCTION

Tuberous Sclerosis Complex (TSC) is a rare autosomal dominant genetic disorder that leads to the growth of benign tumors in various organs, including the brain, kidneys, liver, skin, heart, and lungs. The global incidence is estimated at 1 in 6,000 live births, with a prevalence of 1 in 20,000 people. In Indonesia, epidemiological data on TSC remain scarce, highlighting the need for more comprehensive studies to understand its national impact.

TSC is caused by mutations in the *TSC1* or *TSC2* genes, which encode the tumor suppressor proteins

hamartin and tuberin. These proteins form a complex that inhibits the mammalian target of rapamycin (mTOR), a key regulator of cell growth and proliferation. When this pathway becomes dysregulated due to gene mutations, it results in abnormal cell growth and tumor formation across multiple organ systems.

Case reports from Indonesia illustrate the diverse clinical spectrum of TSC. In one case, two siblings exhibited distinct manifestations—one with renal angiomyolipomas, hepatic lipomas, and brain lesions, and the other with subependymal giant cell astrocytoma and renal involvement. Another report described a 17-year-old girl with a de novo *TSC2* mutation, whose symptoms were dominated by neuropsychiatric features. These cases emphasize the importance of early diagnosis and multidisciplinary care.

This report discusses a 16-year-old girl who presented with her first seizure and was later diagnosed with TSC. Despite early signs such as cognitive impairment, generalized tonic-clonic seizures, and classic skin findings (hypomelanotic macules, angiofibromas, shagreen patches), the diagnosis had been previously overlooked—likely due to limited awareness. A non-contrast head CT revealed characteristic periventricular calcifications, confirming the diagnosis. Improved education and early recognition are critical for timely intervention and better outcomes in TSC patients.

## CASE REPORT

A 16-year-old female was brought to the hospital by her parents with the chief complaint of sudden-onset seizures, which occurred for the first time on February 10, 2025. The patient experienced five seizure episodes at home, each lasting approximately three minutes, followed by two additional episodes in the emergency department, each lasting about 30 seconds. The seizures were characterized by generalized tonic-clonic movements involving both upper and lower limbs, accompanied by upward deviation of the eyes. The patient was conscious prior to the seizures but became unresponsive between episodes and experienced postictal confusion before eventually

regaining full consciousness. Her parents denied any preceding history of fever, trauma, headache, or nausea and vomiting.

The patient has never attended formal education, as she would become agitated and aggressive when her parents attempted to enroll her in kindergarten. To date, she remains illiterate and is unable to read or write. Additionally, she has shown no ability to engage in social interaction with peers or others in her surroundings.

On physical examination, the patient was found to have good nutritional status and vital signs within normal limits. General examination revealed hypomelanotic macules on the frontal region of the head, as well as facial angiofibromas and subcutaneous hamartomas. A shagreen patch was observed on the chest. On the back, hamartomas were noted, and on the lower extremities, hypomelanotic macules were present on both the right and left crura. Neurological examination did not reveal any significant abnormalities.

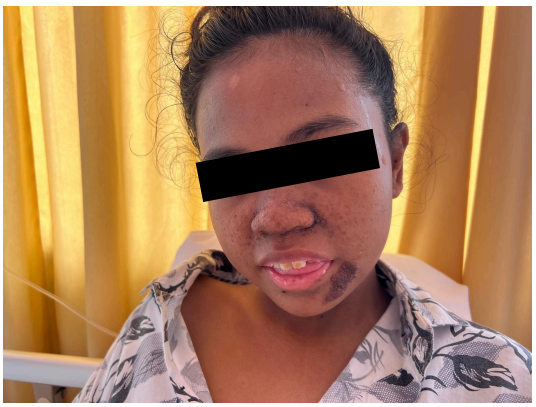

Figure 1. Hypomelanotic macules on the frontal region of the head, facial angiofibromas, and subcutaneous hamartomas.

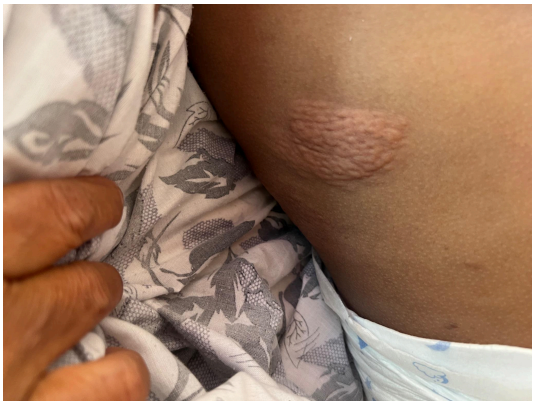

Figure 2. A shagreen patch on the chest

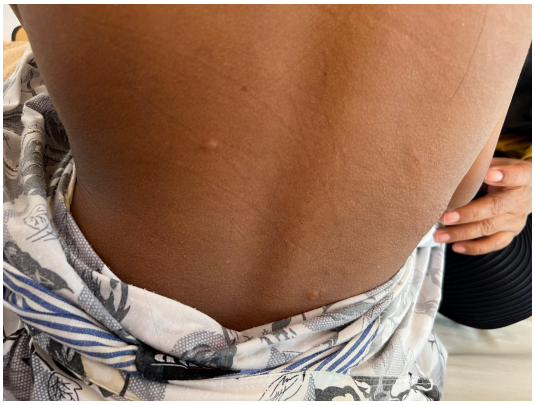

Figure 3. Hamartomas on the back

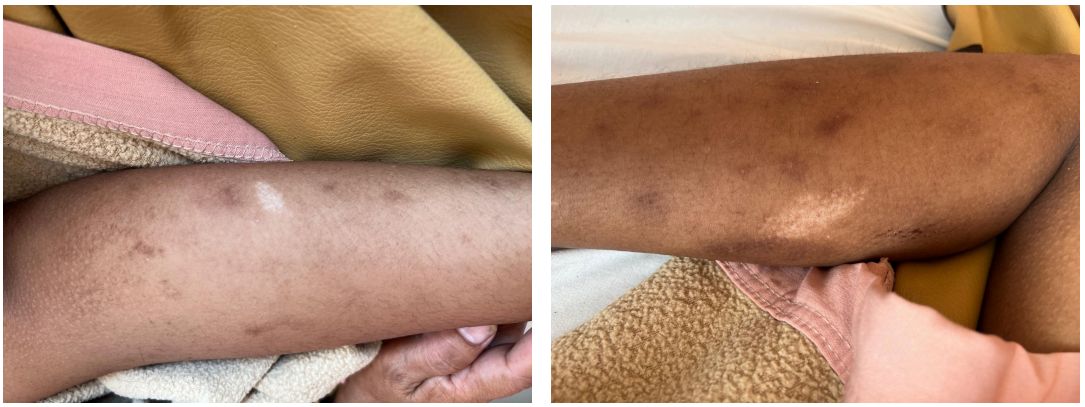

Figure 4. Hypomelanotic macules on both right and left crura

Laboratory findings on the first day of hospitalization showed leukocytosis, with a white blood cell count of 20.57 × $10^3$/µL, suspected to be a reactive response to the seizure episodes. The patient also presented with microcytic hypochromic anemia, with a hemoglobin (HGB) level of 10.2 g/dL and a mean corpuscular volume (MCV) of 59.2 fL. This anemia is strongly suspected to be secondary to chronic disease or possibly iron deficiency.

A non-contrast head CT scan revealed multiple punctate calcifications in the periventricular regions of both lateral ventricles, raising suspicion for Tuberous Sclerosis Complex (TSC). Further evaluation with a contrast-enhanced MRI of the brain was recommended. However, due to equipment limitations at our facility, the patient was referred to a tertiary care

hospital for the MRI examination.

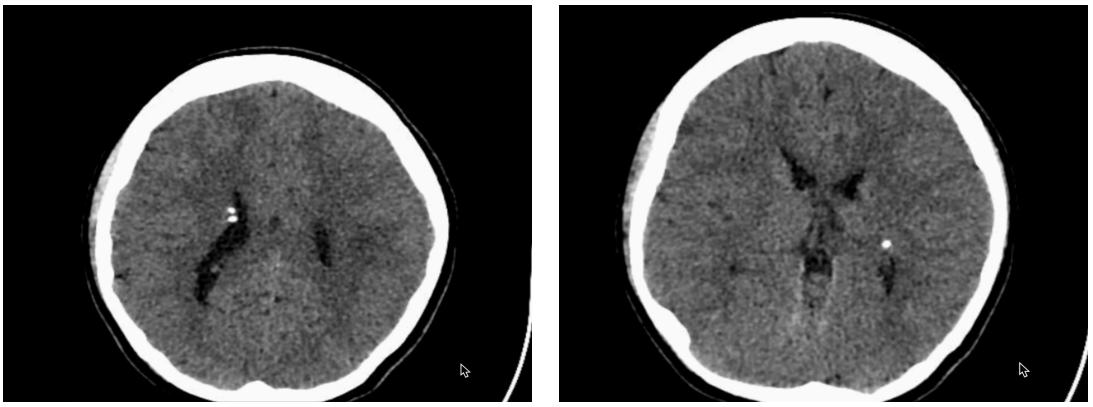

Figure 5. Non-contrast head ct scan showing multiple punctate calcifications in the periventricular regions of both lateral ventricles, raising suspicion for Tuberous Sclerosis Complex (TSC)

Based on the clinical history, physical findings, and supporting investigations, a definitive diagnosis of Tuberous Sclerosis Complex was established according to the 2012 International TSC Consensus Criteria. In this case, the TSC is presumed to result from a de novo mutation, as there is no family history of similar conditions.

## DISCUSSION

*Definition*

Tuberous Sclerosis Complex (TSC) is a rare autosomal dominant genetic disorder characterized by benign tumor growths (hamartomas) in multiple organs, particularly the brain, skin, kidneys, heart, lungs, and eyes. It results from mutations in the TSC1 (chromosome 9q34) or TSC2 (chromosome 16p13) genes, which regulate cell growth via the mTOR pathway. Dysfunction in this pathway leads to uncontrolled cell proliferation, organ dysfunction, and a wide clinical spectrum ranging from mild skin lesions to severe neurological and psychiatric complications. Approximately 70% of cases arise from de novo mutations, while 30% are inherited.

*Epidemiology*

TSC prevalence ranges globally from 3.8–8.8 per 100,000 individuals, with incidence rates around 0.28–0.56 per 100,000/year. Variability reflects diagnostic practices and awareness. Data from Germany, France, and Taiwan show a consistent link between TSC and epilepsy, highlighting its healthcare burden. In Indonesia, national data remains scarce, indicating a need

for further epidemiological research.

*Pathophysiology*

Mutations in TSC1/TSC2 impair the hamartin–tuberin complex, resulting in hyperactivation of mTORC1, a key regulator of protein synthesis, cellular metabolism, and autophagy. This leads to abnormal cell growth, tumor formation, reduced autophagy, and metabolic imbalance, particularly glycogen accumulation, which contributes to tumorigenesis.

*Clinical Manifestations*

Tuberous Sclerosis Complex can affect multiple organs. On the skin, it may cause light-colored patches, facial fibrous nodules, thickened skin on the lower back, fibrous growths around the nails, and small white spots on the body. In the brain, there may be abnormal tissue, growths near the brain cavities, and tumors that can block fluid flow. Seizures often begin in infancy and may be accompanied by developmental delays and behavioral difficulties. In the kidneys, benign tumors made of fat, muscle, and blood vessels, as well as cysts, may appear and can cause pain, bleeding, or impaired kidney function. In the heart, muscle tumors can be found even before birth or in early infancy, sometimes disrupting heart rhythm or blood flow, although they usually shrink over time. In the lungs, some adult women develop cyst-like damage that leads to shortness of breath. In the eyes, benign growths may be found in the retina but rarely affect vision. Developmental disorders, difficulties in social interaction, attention problems, anxiety, mood changes, and sleep disturbances are also common and can significantly impact quality of life.

*Diagnosis*

The diagnosis of Tuberous Sclerosis Complex is based on clinical evaluation supported by imaging and genetic testing. Doctors look for specific skin findings, brain abnormalities, kidney or heart tumors, and eye lesions that are characteristic of the condition. Brain imaging using MRI or CT scans can reveal structural changes such as cortical growths or tumors near the brain's ventricles. Kidney imaging with ultrasound, CT, or MRI may detect fatty tumors or cysts. Genetic testing can confirm mutations in the

TSC1 or TSC2 genes, which are responsible for the disorder, although not all patients show identifiable mutations. A confirmed diagnosis typically requires either two major features or one major plus two or more minor features based on established clinical criteria.

*Management*

TSC requires lifelong, multidisciplinary care. Routine MRI brain and abdomen, EEG, cardiac echocardiography, and ophthalmologic exams are critical. Vigabatrin is first-line for infantile spasms; mTOR inhibitors (e.g., everolimus) are used for SEGA and renal AML. Neuropsychiatric screening via the TAND Checklist is recommended annually to guide early intervention.

## CONCLUSION

Tuberous sclerosis complex (TSC) presents substantial diagnostic challenges, particularly in settings with limited recognition of its early neurological and dermatological manifestations. This case demonstrates how longstanding neurocognitive impairment and unrecognized cutaneous stigmata may lead to delayed diagnosis, with seizures ultimately becoming the first clinical event that prompts medical evaluation. Given that neurological involvement—manifesting as epilepsy, cognitive deficits, and characteristic structural brain abnormalities—is central to disease morbidity, early detection is critical.

A deeper understanding of the effects of *TSC1* and *TSC2* mutations on mTOR pathway dysregulation further underscores the need for prompt neurological assessment and timely initiation of appropriate management strategies to prevent progression of cortical and subependymal lesions. Enhancing clinician awareness of the neurocutaneous presentation of TSC, incorporating routine neurological screening in at-risk individuals, and ensuring coordinated multidisciplinary care are essential steps to reducing diagnostic delay and improving long-term neurological outcomes.

In summary, early recognition of neurological manifestations and comprehensive, neurologically focused management are

fundamental to optimizing prognosis and quality of life in individuals with TSC.

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