ejpmr, 2025, 12(6), 594-600

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Cash Study

ISSN 2394-3211

EJPMR

TUBEROUS SCLEROSIS COMPLEX: A CASE REPORT ON CLINICAL AND IMAGING INSIGHTS

Archana*[1], Prakash K. Wari[2], Adarsh GS.[1], Priyanka Bagewadi[1], Varun Wattamwar[1], Preeti V. Kulkarni[1], Venkatrao H. Kulkarni[1]

[1]Soniya Education Trust's College of Pharmacy, Dharwad-580002.
[2]Department of Paediatric, Karnataka Institute of Medical Science and Research Institute, Hubballi-580029.

***Corresponding Author: Archana**

Soniya Education Trust's College of Pharmacy, Dharwad-580002.

Article Received on 25/04/2025 **Article Revised on 15/05/2025** **Article Published on 04/06/2025**

ABSTRACT

Tuberous Sclerosis Complex (TSC) is a rare genetic condition resulting from mutations in the TSC1 or TSC2 genes, leading to abnormal cell growth and the development of benign tumours in various organs. The disorder presents with diverse clinical symptoms, primarily affecting the nervous system, skin, and other tissues. This case report discusses a patient with TSC who exhibited neurological complications, including recurrent seizures, cognitive deficits, and developmental delays, along with distinct dermatological features. The diagnosis was established through clinical assessment and imaging techniques. Treatment involved antiepileptic medications for seizure control and mTOR inhibitors to regulate disease progression. Additionally, supportive therapies were implemented to improve overall well-being. Although advancements in treatment have enhanced disease management, the unpredictable nature of TSC presents ongoing challenges. This case emphasizes the significance of early detection, personalized treatment plans, and a multidisciplinary approach in optimizing patient care

KEYWORDS: Tuberous sclerosis complex, angiofibromas, Hypomelanotic macules, Antiepileptic drugs, mTOR inhibitors, seizure.

INTRODUCTION

Tuberous sclerosis complex (TSC), also referred to as epiloia[1] or Bourneville disease[2], affects approximately 1 in 6,000 to 1 in 14,000 individuals globally[3], impacting both children and adults.[4] It is inherited as an autosomal dominant trait with high penetrance, however only about 20% of cases have a known family history, while the remaining 80% result from de novo mutations in either TSC1 or TSC2.[7] The condition arises due to mutations in either the TSC1 gene on chromosome 9 or the TSC2 gene on chromosome 16.[2] These genes regulate the mTOR pathway, which plays a crucial role in cell growth, energy metabolism, and cortical development. Dysregulation of this pathway contributes to the formation of benign tumours in various organs, including the brain, heart, skin, eyes, kidneys, lungs, and liver.[3]

TSC can be diagnosed based on clinical criteria or genetic testing. A definitive clinical diagnosis requires either 2 major features or 1 major feature along with 2 minor features.[8] TSC is classically identified by Vogt's triad, which consists of facial angiofibromas, intellectual disability, and intractable epilepsy; however, fewer than 40% of affected individuals present with all three features. Neurological symptoms are the most common, with approximately 90% of patients experiencing seizures. Around half of those affected also display cognitive impairments, autism spectrum disorder (ASD), or other behavioural issues. Seizure types vary, including tonic, atonic, and tonic-clonic seizures, with focal seizures and epileptic spasms being the most prevalent. Seizure onset typically occurs before the age of two, with the majority of cases manifesting within the first year of life.[5]

Renal complications are the second most common manifestation of TSC, with angiomyolipomas occurring in 80% of patients and renal cystic disease in around 50%. Pulmonary involvement, specifically lymphangioleiomyomatosis (LAM), is the third most frequent complication, affecting approximately 35% of female TSC patients. The underlying reason for the female predominance in LAM is not well understood. Although children with TSC are generally born with normal kidneys, they often develop cystic disease and angiomyolipomas over time, which can lead to chronic kidney disease (CKD). CKD affects an estimated one million TSC patients worldwide.[6]

The primary goal of epilepsy management in TSC is to control seizures as early as possible following diagnosis,

as prompt intervention may enhance neurodevelopmental outcomes and overall quality of life.[5] Treatment strategies include both pharmacological and non-pharmacological approaches; however, about one-third of patients remain resistant to therapies.[3] While there is no cure for TSC, understanding how the TSC1–TSC2 complex regulates mTOR has led to targeted therapies like mTOR inhibitors. Additionally, because TSC affects multiple organs, lifelong coordinated specialist care is essential to reduce complications and improve quality of life.[9]

Patient Information

A 12-year-old female, was admitted with complaints of fever and abnormal movements.

History of Present Illness

The patient, with a known history of seizure disorder, presented with vomiting. The vomitus contained food particles but was non-foul-smelling and free of blood. This was followed by abnormal movements, including sideward rolling of the eyes, frothing at the mouth, and involuntary passage of urine and stools. She also displayed tonic-clonic movements involving the left upper and lower limbs, lasting for approximately 5–10 minutes. There was no history of fever, head injury, loose stools, abdominal pain, cough, or hurried breathing prior to the episode.

Past Medical and Medication History

The patient experienced her first seizure episode at her 7 months of age, which was treated with iv anticonvulsants, and she was discharged on sodium valproate syrup. At 2 years of age, her valproate dosage was increased, and she was started with brivaracetam (Brevipil), had 5–6 previous hospital admissions for recurrent seizures.

Table 1: Medication History.

Date	Medication	Dosage	Duration	Purpose/Remarks
06/06/2017	Syp Epilex (Sodium Valproate)	5 ml (morning and night)	2 months	Primary antiepileptic therapy.
	Syp Levera (Levetiracetam)	2 ml (morning), 0 ml (afternoon), 3 ml (night)		Adjunct for seizure control.
	Tab Frisium (Clobazam)	5 mg once at night (0-0-1)		Added for anxiolytic and anticonvulsant effects.
06/02/2019	Syp Epilex (Sodium Valproate)	5 ml (morning and night)	6 months	Maintained as the primary anticonvulsant.
	Syp Levera (Levetiracetam)	3 ml (morning and night)		Increased dose to enhance seizure control.
	Tab Frisium (Clobazam)	Discontinued		Suggests stable seizure control without adjunct.
26/04/2022	Syp Epilex (Sodium Valproate)	5 ml (morning and night)	3 months	Maintained dose for seizure control.
	Syp Levera (Levetiracetam)	2 ml (morning and night)		Reduced dose, possibly to manage side effects.
	Tab Frisium (Clobazam)	5 mg once at night (0-0-1)		Reintroduced for breakthrough seizures.
19/07/2022	Syp Epilex (Sodium Valproate)	5 ml (morning and night)	4 months	Continued stable dose.
	Syp Levera (Levetiracetam)	2 ml (morning and night)		No dose changes.
	Tab Frisium (Clobazam)	5 mg once at night (0-0-1)		Adjunctive therapy maintained.
25/11/2022	Syp Epilex (Sodium Valproate)	5 ml (morning and night)	4 months	Continued seizure management with stable dosage.
	Syp Levera (Levetiracetam)	2 ml (morning and night)		Maintained adjunctive therapy.
	Tab Frisium (Clobazam)	5 mg once at night (0-0-1)		Continued for seizure stability.

Family History

There is no family history of seizures, tuberculosis, asthma, or epilepsy.

Birth and Developmental History

Her antenatal period was uneventful, with normal trimesters throughout the pregnancy. She was delivered via lower segment caesarean section (LSCS) with a birth

weight of 2.5 kg, requiring continuous airway breathing (CAB) at birth. There was no history of neonatal ICU admission.

Developmental Milestones

The patient was able to hop and skip but demonstrates immature fine motor skills (~50% development). She uses 2–3 word sentences and maintains key social relationships within her household. However, intellectual disability is present.

Immunization Status

She is partially immunized, having missed the 10-year-old vaccine.

Diet History

The patient's diet history reveals a significant calorie deficit of 65.0%. Additionally, her protein intake (20.6 g) falls short of both the recommended level (28.6 g) and the required intake (40.4 g).

Table 2: Diet History.

Food Item	Calories (kcal)	Protein (g)
1 roti	70	2
1 cup rice	175	4
1 cup vegetable sambar	60	2
1 cup vegetable sabji	50	2
1 apple	59	0.6
1 cup upma	250	6
1 idly	50	2
1 dosa	70	2
Total Intake:	784 kcal	20.6 g
Recommended:	2240 kcal	28.6 g
Required:	2010 kcal	40.4 g
Deficit:	65.0%	19.8g

Diagnosis

EEG Report

- **Impression**
  - Abnormal EEG showing generalized epileptiform discharges.

MRI Report

- **Impression**
  - Multiple enhancing subependymal nodules
  - Multiple cortical and subcortical tubers
  - Linear enhancing white matter lesions
  - Mild dilatation of the lateral ventricles
  - No evidence of intracranial space-occupying lesions

Lab Investigation

The laboratory findings indicate low haemoglobin, low MCHC, and low sodium levels, suggestive of anemia and electrolyte imbalance.

Table 3: Lab Investigations.

Test	Result	Normal Range
Haemoglobin (HB)	9.2 g/dL	12–15.5 g/dL (low)
RBC Count	4.55×10^6/µL	$4.7–6.1 \times 10^6$/µL
PCV/HCT	32.4%	37–47% (low)
Platelets	341×10^3/µL	$150–400 \times 10^3$/µL
MCHC	28.3 g/dL	32–36 g/dL (low)
PDW	9.2%	10–18% (low)
WBC Count	11.1×10^3/µL	$4–11 \times 10^3$/µL (high)
RDW-CV	19.8%	11.6–14.8% (high)
Sodium	132.6 mmol/L	135–145 mmol/L (low)
Chloride	98.5 mmol/L	96–106 mmol/L
Creatinine	0.64 mg/Dl	0.5–1.1 mg/dL

Anthropometric Measurement

The patient is of short stature, with her height below the 3rd percentile and her weight falling within the 10th–50th percentile. Her BMI is within the normal range.

Table 4: Anthropometric Measurements.

Measurement	Current	Expected	Percentile
Weight	30 kg	39.0 kg	10th–50th percentile
Height	132 cm	148 cm	Below 3rd percentile
BMI	17.2 kg/m²	17.7 kg/m²	10th–50th percentile

- **Impression: Normal BMI with Short Stature**

Systemic Examination

During systemic examination, the following observations were made:

- Per Abdomen (P/A): Corresponding quadrants moved equally with respiration; umbilicus was central.
- Cardiovascular System (CVS):
  - Pericardium: Normal
  - Apex beat: Felt at the 5th intercostal space (ICS), medial to the mid-clavicular line
  - Heart sounds: S1 and S2 positive
  - No murmurs detected
- Palpation:
  - Abdomen: Soft
  - No organomegaly detected
- Respiratory System (RS):
  - Bilateral air entry (B/L A/E) was present
  - Bilateral normal vesicular breath sounds (B/L NVBS) were present
  - Bilateral conducted sounds were heard
- Central Nervous System (CNS):
  - CN1: Not assessed (NA)
  - CN2: Bilateral Equal and Reactive to Light (BERL)
  - CN3, 4, 6: Extraocular movements (EOM) intact
  - CN5: Bilateral normal (NA)
  - CN7: Bilateral facial symmetry
  - CN8: Not assessed (NA)
  - CN9, 10: Ultrafine-grained reflex (UFG) intact
  - CN11: Bilateral neck movements Normal
  - CN12: Tongue was central with no fasciculations.

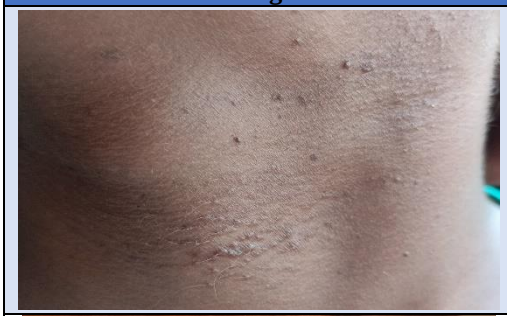
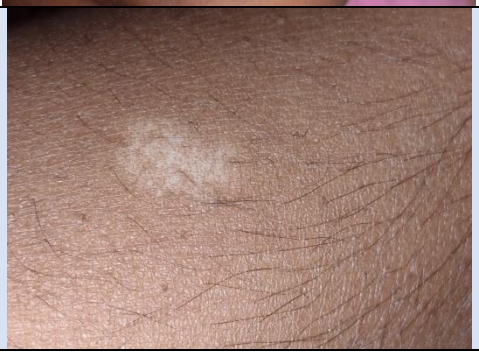
Vital Signs

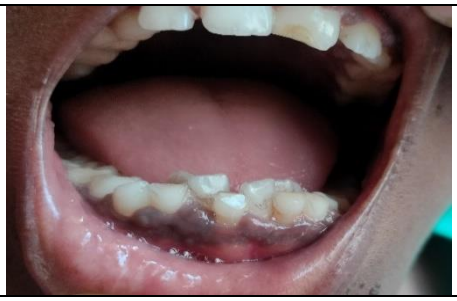
The patient's vital parameters are summarized in the table below:

Table 5: Vital Signs.

Parameter	Value
Heart Rate (HR)	116 beats per minute
Pulse Volume	Good
Respiratory Rate (RR)	32 breaths per minute
SpO2	96%
CRT	<3.8 seconds
Periphery	Warm
Temperature	36.6°C
Blood Pressure (BP)	106/70 mmHg

Table 6: Clinical Observation and Finding.

Image	Clinical observation	Findings
	Shagreen patch	The image shows a thickened, leathery patch of skin with hyperpigmentation, mild scaling, and small papules, characteristic of a shagreen patch seen in tuberous sclerosis complex (TSC). These lesions are located on the neck region of the patient and were first noticed 3-4 years ago as small patches, which have gradually increased in size over time.
	Facial angiofibromas	The image shows multiple small, raised, reddish-brown to skin-colored papules symmetrically distributed over the nose and cheeks, characteristic of facial angiofibromas seen in tuberous sclerosis complex (TSC). These lesions first appeared 3-4 years ago as small papules and have gradually increased in size over time.
	Hypomelanotic macule	The image displays a hypomelanotic macule, a distinct, light-colored patch with an irregular shape, commonly associated with tuberous sclerosis complex (TSC). These hypopigmented spots have been present on the leg and chest since birth, while another lesion developed on the back of the thigh a year ago.

	Gingival fibromas	The image depicts gingival fibromas, which appear as firm, fibrous overgrowths on the gums. These lesions, commonly associated with tuberous sclerosis complex (TSC), can cause gum thickening, an irregular surface, and slight discoloration.

Treatment Plan with Drug Details

The patient is on a comprehensive epilepsy management regimen that includes antiepileptic drugs (AEDs) such as sodium valproate and brivaracetam to control seizures. Sodium valproate enhances GABA activity, making it effective for both acute and long-term seizure management. Brivaracetam, a second-line AED, modulates neurotransmitters and is specifically used for focal seizures. The combination of these AEDs provides synergistic seizure control, reducing seizure frequency and severity.

In addition to AEDs, supportive medications are included to manage associated complications. Gastroprotective agents like ranitidine help reduce gastric acid secretion, preventing irritation and drug-induced gastritis. Antimicrobials such as metronidazole are used to prevent bacterial and protozoal infections, which may arise due to prolonged hospitalization or immunosuppressive effects of certain treatments.

To maintain overall stability, intravenous fluids and electrolyte management are crucial. DNS is administered to ensure proper hydration and electrolyte balance, while hypertonic saline (3% NaCl) helps correct sodium imbalances and prevent hyponatremia, a common issue in patients with prolonged seizures and AED therapy. These interventions collectively aim to optimize seizure control, minimize complications, and support the patient's overall well-being.

Table 7: Treatment Plan with Drug Details.

Drug Name	Dosage &Route	Class	Use	Importance
1\2 DNS	70ml\hr IV	IV fluid therapy	Provides hydration and maintains electrolytic balance	Prevents dehydration and ensures hemodynamic stability during seizures
Inj. Sodium Valproate (Epilex)	3ml IV BD	Antiepileptic drug (AED) \GABA enhancer	Controls seizures by increasing gamma-aminobutyric acid levels, reducing excessive neuronal excitability	Effective in treating generalized and focal epilepsy, as well as infantile spasms
Tab. Brivaracetam (Brevipil)	50 mg, ½ tab BD	Antiepileptic Drug (AED) / SV2A Ligand	Controls focal seizures by modulating neurotransmitter release	Higher affinity for SV2A, better seizure control with fewer psychiatric side effects
Inj. Ranitidine (Rantac)	0.5 cc IV BD	H2 Receptor Antagonist	Reduces gastric acid secretion, preventing irritation	Protects the stomach lining from AED-induced gastritis and reflux
Inj. Metronidazole (Metrogyl)	60 ml IV TID	Prevents bacterial and protozoal infections	Treats or prevents bacterial and protozoal infections	Reduces the risk of aspiration pneumonia due to seizures
3% Normal Saline (NS)	0.6 ml/hr IV	Hypertonic Saline Solution	Corrects sodium levels in hyponatremia	Prevents cerebral edema and maintains sodium balance in prolonged seizures
Syrup Sodium Valproate (Epilex)	7 ml PO BD	Antiepileptic Drug (AED) / GABA Enhancer	Prevents seizures by increasing GABA levels	Dose increased due to breakthrough seizures, essential for long-term seizure management

DISCUSSION

Tuberous sclerosis complex (TSC) is an autosomal dominant disorder caused by mutations in the *TSC1* or *TSC2* genes, leading to abnormal cell growth and the formation of benign tumours in multiple organs. In this case, the patient's neurological symptoms, including recurrent seizures, are attributed to cortical and subependymal tubers visible on MRI. These tubers contribute to epileptogenesis and are a hallmark of TSC. The patient also presented with cutaneous manifestations such as facial angiofibromas, ash-leaf macules, and a shagreen patch, which are characteristic features of TSC and often aid in clinical diagnosis. Additionally, the presence of gingival fibromas highlights oral involvement, which is another common but frequently underrecognized feature of TSC.

The patient was on a long-term antiepileptic regimen consisting of sodium valproate (Epilex), levetiracetam (Levera), and clobazam (Frisium). Sodium valproate, a broad-spectrum antiepileptic drug (AED), was the primary therapy, while levetiracetam was added as adjunct therapy for better seizure control. Clobazam was used intermittently during breakthrough seizures. Despite continuous therapy, the patient experienced breakthrough seizures due to inconsistent medication adherence, which was likely caused by financial constraints. This case highlights the challenges of managing chronic conditions in lower socioeconomic settings, where affordability and access to medication are limiting factors. Upon admission, the patient required intravenous (IV) anticonvulsants and supportive care, including oxygen therapy, to control the seizures. The administration of lorazepam followed by a loading dose of sodium valproate successfully halted the seizure episodes.

The patient's anthropometric assessment revealed short stature and borderline low weight for her age. This could be attributed to chronic illness and the long-term use of antiepileptic drugs. Additionally, the systemic involvement of TSC may have contributed to her poor growth. Socioeconomic factors also played a role, as the patient's diet history revealed a 60% caloric deficit, indicating nutritional insufficiency.

Laboratory investigations revealed mild anaemia, with a haemoglobin level of 9.2 g/dL and low MCHC, suggesting a possible nutritional deficiency. Elevated AST levels indicated mild hepatic involvement, which may have been caused by long-term valproate therapy. The patient also had hyponatremia (Na: 132.6 mmol/L), which could have resulted from chronic medication use or dehydration associated with seizures.

EEG findings revealed generalized epileptiform discharges, consistent with focal or generalized seizures. MRI confirmed the presence of multiple enhancing subependymal nodules, cortical and subcortical tubers, and linear white matter lesions, which are hallmark features of TSC. Additionally, mild dilatation of the lateral ventricles was observed, indicating possible chronic intracranial pressure changes, a common finding in TSC patients with tubers.

The patient's family belongs to a lower socioeconomic class, with her father working as an ironing labourer and her mother as a garment worker. Financial constraints resulted in inconsistent medication adherence, leading to breakthrough seizures and frequent hospitalizations. This case highlights the need for financial assistance programs to support patients with chronic neurological conditions, as consistent medication adherence is crucial for effective seizure management.

CONCLUSION

This case of a twelve-year-old girl with tuberous sclerosis underscores the complexity and multisystem involvement of this genetic disorder. The diagnosis was established based on characteristic clinical features, neuroimaging findings, and systemic manifestations, highlighting the importance of early recognition and thorough evaluation. The case emphasizes that tuberous sclerosis is not limited to a single organ system but requires a multidisciplinary approach involving paediatrics, neurology, nephrology, dermatology, and genetics to ensure optimal management.

Although there is no definitive cure, advances in treatment, such as mTOR inhibitors, have significantly improved disease control and quality of life. Early intervention, regular monitoring, and symptomatic management play a pivotal role in reducing complications such as seizures, cognitive impairment, and renal involvement. Genetic counselling is also crucial for affected families to understand the hereditary nature and future implications of the condition.

This case highlights the importance of awareness among healthcare professionals to facilitate timely diagnosis and appropriate treatment. With ongoing research and better therapeutic options, individuals with tuberous sclerosis can lead fulfilling lives. Strengthening early detection strategies, expanding access to specialized care, and increasing public awareness are essential steps toward improving long-term outcomes for patients with this rare but impactful condition.

ACKNOWLEDGEMENT

We are thankful to the Karnataka Institute of Medical Science and Research Institute, Hubballi, along with the HOD and Chief of the Paediatrics Department, for their support and permission to write this article.

REFERENCE

1. Dzefi-Tettey K, Edzie EK, Gorleku P, Piersson AD, Cudjoe O, Edzie EK. Tuberous sclerosis: a case report and review of the literature. Cureus, Jan. 4, 2021; 13(1).
2. Varghese JJ, Thomas SP, Kallivayalil RA. Tuberous sclerosis: its neurological and neuropsychiatric

aspects and a case report. Kerala Journal of Psychiatry, 2018; 31(1).
3. Curatolo P, Jóźwiak S, Nabbout R. Management of epilepsy associated with tuberous sclerosis complex (TSC): clinical recommendations. European journal of paediatric neurology, Nov. 1, 2012; 16(6): 582-6.
4. Lienda M, Mwila M, Sichula C, Kabengele C, Akombwa M, Zulu C, Banda CH, M'hango H. Diagnosis and Management of Tuberous Sclerosis Complex in a Resource-Limited Setting—A Case Report of a 14-Year-Old Female Zambian Adolescent. Clinical Medicine Insights: Case Reports, Feb. 2025; 18: 11795476251321268.
5. Curatolo P, Nabbout R, Lagae L, Aronica E, Ferreira JC, Feucht M, Hertzberg C, Jansen AC, Jansen F, Kotulska K, Moavero R. Management of epilepsy associated with tuberous sclerosis complex: updated clinical recommendations. European Journal of Paediatric Neurology, Sep. 1, 2018; 22(5): 738-48.
6. Dixon BP, Hulbert JC, Bissler JJ. Tuberous sclerosis complex renal disease. Nephron Experimental Nephrology, Dec. 28, 2011; 118(1): e15-20.
7. Strinidis A, Henske EP. Tuberous sclerosis complex: linking growth and energy signaling pathways with human disease. Oncogene, Nov. 2005; 24(50): 7475-81.
8. Davis PE, Filip-Dhima R, Sideridis G, Peters JM, Au KS, Northrup H, Bebin EM, Wu JY, Krueger D, Sahin M. Presentation and diagnosis of tuberous sclerosis complex in infants. Paediatrics, Dec. 1, 2017; 140(6).
9. Leclezio L, de Vries PJ. Advances in the treatment of tuberous sclerosis complex. Current opinion in psychiatry, Mar. 1, 2015; 28(2): 113-20.