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Tuberous sclerosis complex with pancreatic angiomyolipoma in a young woman with long-standing epilepsy: A case report from Papua New Guinea

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Case Report

Keywords: Tuberous sclerosis complex, Pancreatic angiomyolipoma, Cortical tubers, Cortical dysplasia, Subependymal nodules, Epilepsy, Papua New Guinea

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Case Report

Tuberous sclerosis complex with pancreatic angiomyolipoma in a young woman with long-standing epilepsy: A case report from Papua New Guinea

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Highlights

- Definite tuberous sclerosis complex (TSC) diagnosed in a 23-year-old woman with childhood-onset epilepsy.
- Neuroimaging revealed calcified subependymal nodules, cortical tubers, and left parieto-temporo-occipital cortical dysplasia.
- Dermatological evaluation confirmed 3–4 facial angiofibromas and >6 shagreen patches on the lower extremity.
- Contrast-enhanced abdominal CT characterized a fat-containing pancreatic angiomyolipoma (-12 to -34 HU) with normal kidneys, liver, and spleen.
- Multidisciplinary care and mTOR inhibitor (everolimus) planning are vital in resource-limited settings.

Abstract

Tuberous sclerosis complex (TSC) is an autosomal dominant multisystem hamartomatous disorder driven by hyperactivation of the mechanistic target of rapamycin (mTOR) signaling pathway, whose recognition may be delayed in resource-limited settings. TSC is caused by a mutation that affects 2 genes: TSC1 (Tuberous Sclerosis Complex, located on chromosome 9) or the TSC2 gene (located on chromosome 16). We report a 23-year-old woman with childhood-onset epilepsy, mild intellectual disability, and educational difficulties—despite being enrolled as a Grade 12 student who presented, accompanied by her guardians with recurrent focal seizures, transient mutism, expressive aphasia, short-term memory impairment, severe headache, and visual disturbance. Specialist dermatological assessment confirmed 3–4 facial angiofibromas and more than six shagreen patches on

the lower extremity, alongside hypomelanotic macules noted at initial evaluation. Brain magnetic resonance imaging (MRI) and computed tomography (CT) demonstrated bilateral calcified subependymal nodules, non-enhancing cortical–subcortical tubers, and left parieto-temporo-occipital cortical dysplasia. Ophthalmological examination revealed reduced right visual acuity, right peripapillary exudative and pigmentary changes, and a left hemianopic visual-field defect, with no retinal hamartomas present. Abdominal ultrasound identified an echogenic pancreatic lesion that was characterized on contrast-enhanced CT as a fat-containing pancreatic angiomyolipoma (AML), exhibiting a hypodense rim with attenuation values of -35 to -52 Hounsfield units (HU), while the kidneys, liver, and spleen appeared unremarkable. Follow-up imaging showed gastric antral wall thickening without elevation of gastric or pancreatic enzymes. Inflammatory markers showed a persistently elevated erythrocyte sedimentation rate, whereas Treponema pallidum hemagglutination, hepatitis C serology, antinuclear antibody, and extractable nuclear antigen panels were unremarkable. Following discontinuation of sodium valproate and titration of levetiracetam seizure control was achieved, although mild irritability emerged without aggressive behavior. Treatment with the mTOR inhibitor everolimus has been planned alongside ongoing multidisciplinary follow-up. This case underscores the value of coordinated multisystem evaluation in adults with long-standing epilepsy and expands the recognized extrarenal visceral spectrum of TSC.

Keywords: Tuberous sclerosis complex; Pancreatic angiomyolipoma; Cortical tubers; Cortical dysplasia; Subependymal nodules; Epilepsy; Papua New Guinea

1. Introduction

Tuberous sclerosis complex (TSC) is an autosomal dominant multisystem disorder caused by loss-of-function mutations in either the TSC1 or TSC2 tumor suppressor genes, leading to constitutive activation of the mechanistic target of rapamycin (mTOR) signaling pathway and the development of benign hamartomatous lesions across the brain, skin, kidneys, heart, lungs, eyes, and other organs [1,2]. Central nervous system (CNS) involvement carries substantial morbidity, as epilepsy frequently coexists with neurodevelopmental, cognitive, and behavioral manifestations [1,8]. Characteristic neuropathological hallmarks include cortical tubers, subependymal nodules (SENs), and subependymal giant cell astrocytomas (SEGAs), with cortical tubers and associated focal cortical dysplasia serving as primary epileptogenic substrates [1,9].

In the present case, brain magnetic resonance imaging (MRI) demonstrated distinct left parieto-temporo-occipital cortical dysplasia accompanied by serpentine diffusion alterations on apparent diffusion coefficient (ADC) mapping. Ictal or postictal dysfunction may manifest not solely

through motor phenomena, but also via transient or persistent impairments in expressive language, awareness, memory, and behavior. Furthermore, because ocular lesions such as retinal astrocytic hamartomas or achromic patches may occur [1], emergent visual symptoms warrant concurrent ophthalmological and neurological evaluation. Cutaneous manifestations, specifically facial angiofibromas, hypomelanotic macules, and shagreen patches frequently serve as the earliest and most accessible clinical indicators of the disorder [1].

Angiomyolipomas (AMLs) represent the most prevalent visceral manifestation of TSC and predominantly affect the kidneys, where they constitute a major diagnostic criterion [1,2]. Conversely, extrarenal AMLs, including those arising within the pancreas, are exceptionally rare and are classified as non-renal hamartomas under the minor diagnostic criteria [1,3]. Herein, we report the case of a 23-year-old woman with childhood-onset epilepsy in whom multimodal neuroimaging revealed calcified subependymal nodules, cortical tubers, and left parieto-temporo-occipital cortical dysplasia, establishing definite TSC as the underlying etiology of her longstanding seizure disorder. To the authors' knowledge, this represents the first documented case of TSC complicated by a pancreatic AML in Papua New Guinea (PNG).

2. Case presentation

2.1. Patient information

A 23-year-old woman with epilepsy since early childhood presented to our outpatient clinic for neurological reassessment and a second opinion, consistently accompanied by her guardians. She was an adult living with mild intellectual disability and longstanding educational struggles, although she remained enrolled as a Grade 12 student. Over the preceding three months, she had experienced approximately two to three focal seizures per month despite reported adherence to prescribed antiseizure therapy. TSC had been suspected clinically during childhood, but prior electroencephalography records, molecular genetic testing, and detailed family history were unavailable at presentation.

2.2. Clinical presentation

Prior to reassessment, the patient developed recurrent severe headaches accompanied by fever, vomiting, dizziness, and blurred vision, followed by a focal seizure characterized by side-to-side neck movements and subsequent transient mutism. Although speech partially recovered,

expressive aphasia and short-term memory impairment persisted. Neurological examination demonstrated preserved consciousness, intact auditory comprehension, full motor strength, normal sensation, coordination, deep tendon reflexes, and gait; expressive language dysfunction remained the predominant focal deficit. Throughout clinical evaluations, she remained calm and cooperative under the close support of her guardians, exhibiting no aggressive behavior.

2.3. Ophthalmological findings

The patient reported a three-week history of progressive visual blurring, predominantly affecting the right eye. Comprehensive ophthalmological assessment revealed best-corrected visual acuity of 6/12 in the right eye (improving with pinhole and refraction) and 6/6 in the left eye. Pupillary light reflexes, color vision, extraocular motility, anterior segments, and intraocular pressures were unremarkable. Fundoscopy and optical coherence tomography (OCT) revealed right peripapillary exudative changes and localized pigmentary atrophy (Fig. 1), with no retinal astrocytic hamartomas or retinal achromic patches identified. Confrontation visual-field testing documented a left homonymous hemianopic defect despite predominantly right-sided subjective blurring.

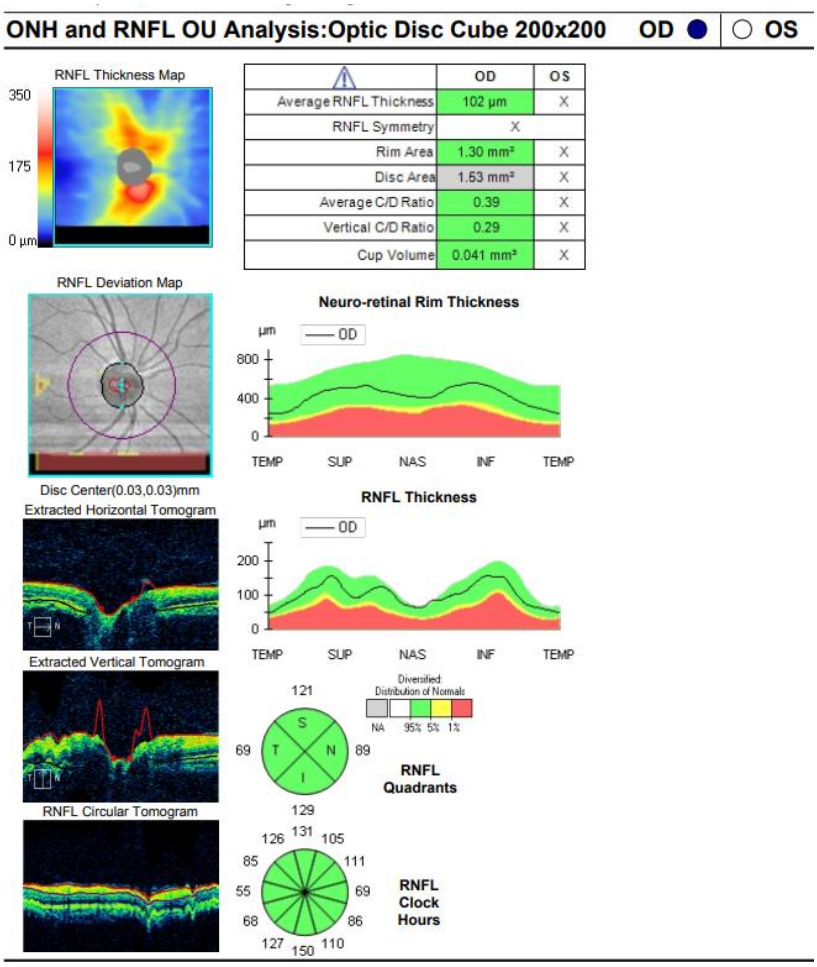


Fig. 1. Optic nerve head (ONH) and retinal nerve fibre layer (RNFL) analysis acquired via spectral-domain optical coherence tomography (Optic Disc Cube 200×200 protocol), demonstrating right peripapillary alterations without retinal astrocytic hamartomas.

2.4. Cutaneous findings

Specialist dermatological evaluation confirmed 3–4 discrete reddish-brown papular facial angiofibromas distributed across the malar and nasal regions, as well as more than six hyperpigmented, leathery plaques characteristic of shagreen patches over the lower extremity (Fig. 2). Additionally, multiple hypomelanotic macules (≥3 lesions measuring at least 5 mm in diameter) had been documented during her initial physical examination.

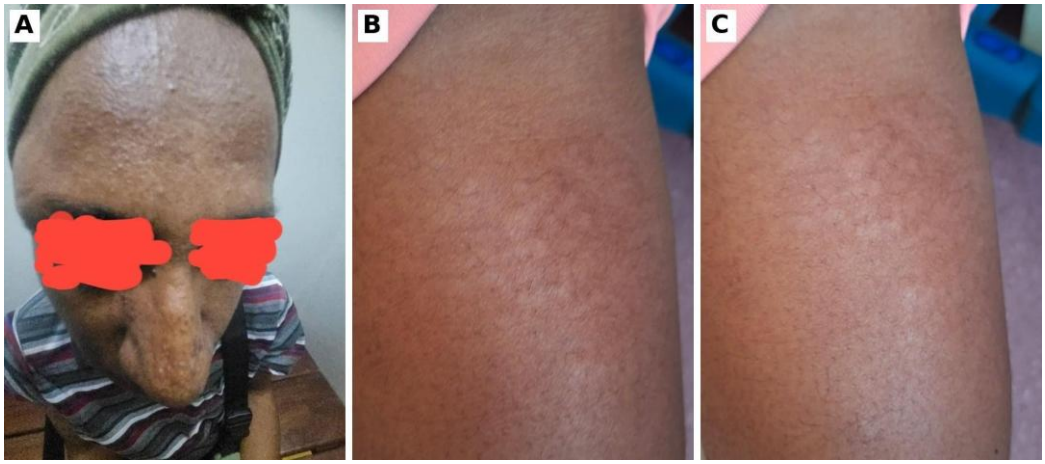


Fig. 2. Cutaneous manifestations of TSC confirmed by specialist dermatological examination. (A) Facial angiofibromas (3–4 discrete papules across the central face; eyes masked for patient anonymity). (B, C) Multiple (>6) shagreen patches exhibiting characteristic peau d'orange texture over the lower extremity.

3. Diagnostic assessment

3.1. Laboratory investigations

Complete blood count, renal function tests, liver enzymes, and serum electrolytes were within normal limits. The erythrocyte sedimentation rate (ESR) was persistently elevated at 50 mm/h initially and 45 mm/h on repeat testing (reference range: 0–29 mm/h). Treponema pallidum hemagglutination (TPHA) and hepatitis C virus serologies were negative. Antinuclear antibody (ANA) and extractable nuclear antigen (ENA) profiles obtained at follow-up were negative, arguing against an underlying systemic vasculitis or connective tissue disorder. Serum amylase, lipase, and gastric biomarkers showed no elevation.

3.2. Magnetic resonance imaging of the brain

Multiplanar, multisequence contrast-enhanced MRI of the brain demonstrated multiple bilateral subependymal nodules along the lateral ventricular walls exhibiting susceptibility-induced signal dropout consistent with calcification, alongside multiple non-enhancing cortical and subcortical tubers with characteristic T2-weighted and fluid-attenuated inversion recovery (FLAIR) hyperintensity and T1-weighted hypointensity (Fig. 3). Furthermore, distinct cortical dysplasia involving the left parieto-temporo-occipital region was identified, characterized by cortical thickening, blurring of the gray–white matter junction, and serpentine diffusion alterations on

ADC mapping. No abnormal parenchymal or leptomeningeal contrast enhancement or subependymal giant cell astrocytoma was present.

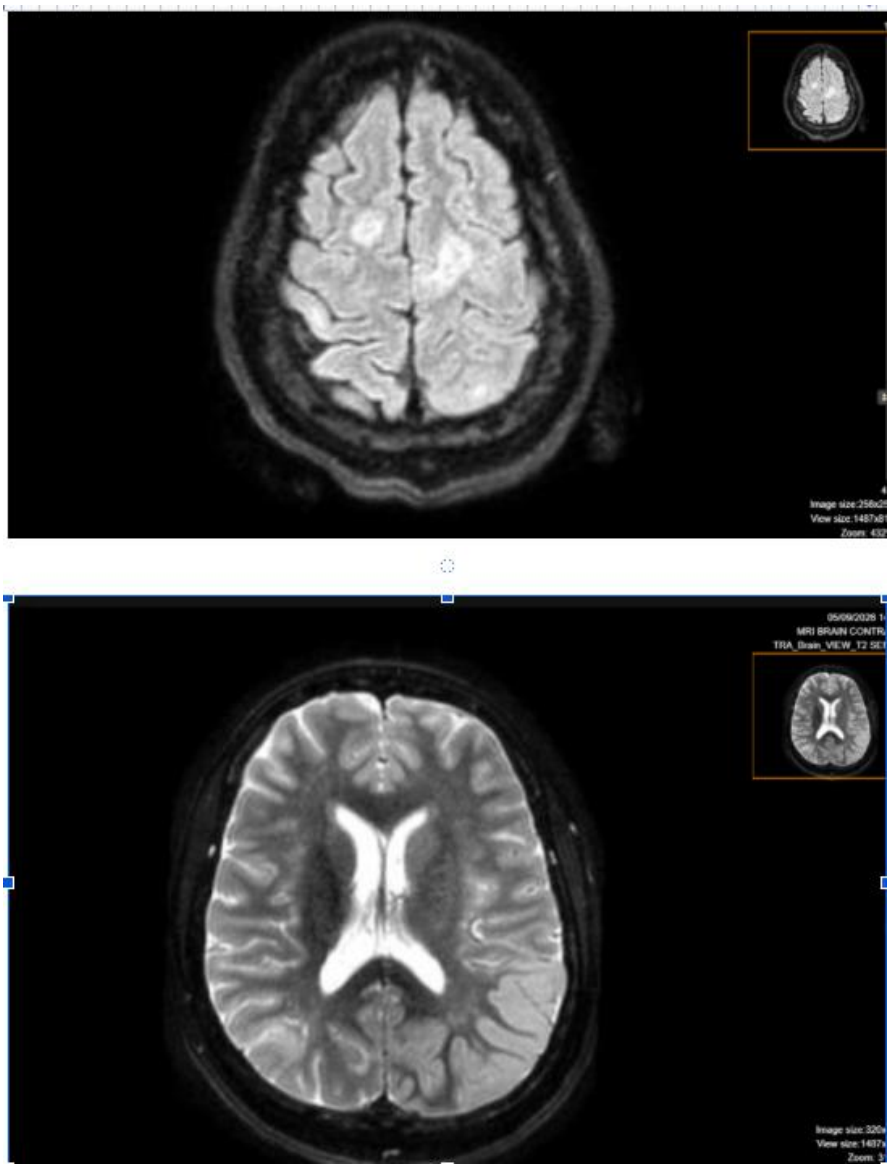


Fig. 3. Axial FLAIR and T2-weighted MRI of the brain demonstrating deep frontal and subcortical hyperintense tubers, radial white matter migration lines, left parieto-temporo-occipital cortical dysplasia with gray–white matter blurring, and bilateral calcified subependymal nodules.

3.3. Computed tomography of the brain

Non-contrast CT of the brain confirmed multiple discrete, hyperdense calcified subependymal nodules lining the walls of the lateral ventricles bilaterally, together with punctate cortical–subcortical parenchymal calcifications corresponding to calcified cortical tubers (Fig. 4). No ventriculomegaly, obstructive hydrocephalus, or acute intracranial hemorrhage was observed.

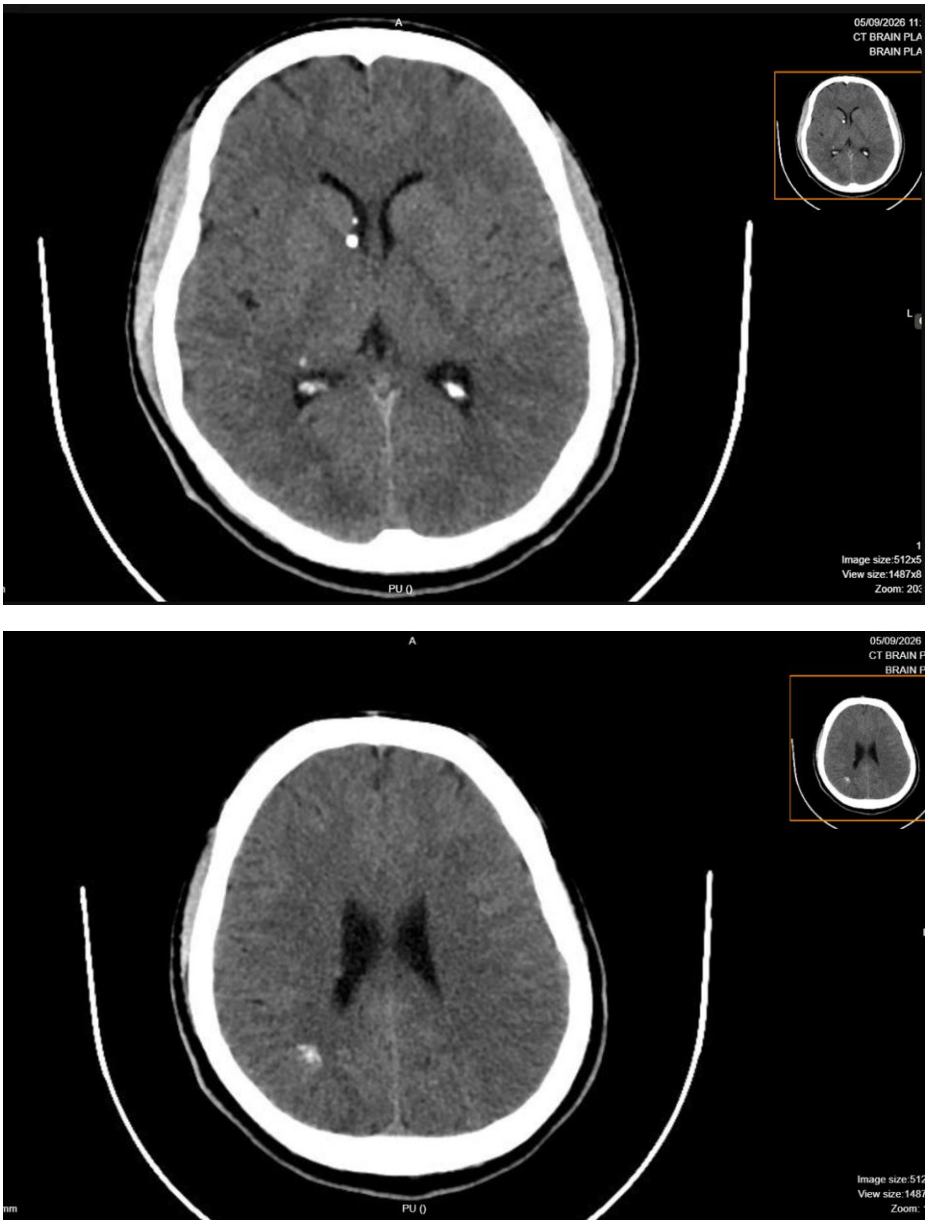


Fig. 4. Axial non-contrast CT of the brain demonstrating multiple hyperdense periventricular calcified subependymal nodules along the lateral ventricles and focal cortical–subcortical parenchymal calcifications.

3.4. Abdominal imaging

Grey-scale abdominal ultrasonography identified a well-circumscribed, homogeneously hyperechoic focal lesion within the pancreas measuring, suggestive of an echogenic fat-containing lesion apeearing angiomyolipoma (Fig. 5). Subsequent multiphasic contrast-enhanced CT of the abdomen and pelvis confirmed a well-defined, fat-containing pancreatic subtly enhancing lesion measuring approximately 2.2 × 1.8 cm, characterized by a distinct peripheral hypodense lipid-attenuating rim with quantitative attenuation values ranging from -12 to -34 Hounsfield units (HU),

consistent with a pancreatic angiomyolipoma (Fig. 6). Both kidneys, the liver, and the spleen demonstrated normal parenchymal attenuation and morphology, with no renal angiomyolipomas, cysts, or hepatic lesions detected. Given the rare pancreatic location and absence of histopathological sampling, the lesion was established as a radiological diagnosis pending specialist surgical review. Follow-up abdominal imaging additionally demonstrated focal thickening of the gastric antral wall, although serum gastric and pancreatic enzyme levels remained entirely normal.

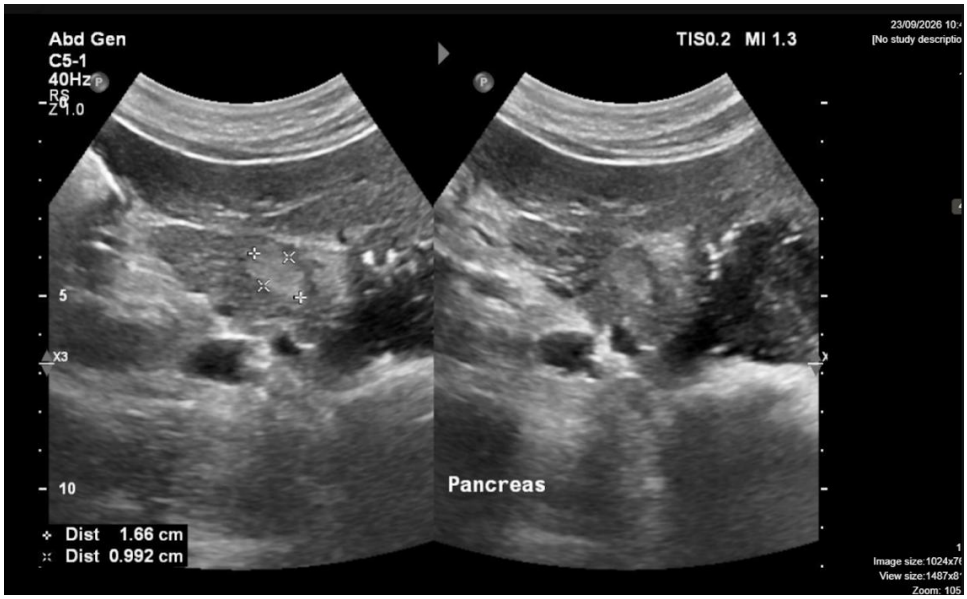


Fig. 5. Grey-scale abdominal ultrasound demonstrating a well-circumscribed, hyperechoic focal lesion within the pancreatic parenchyma.

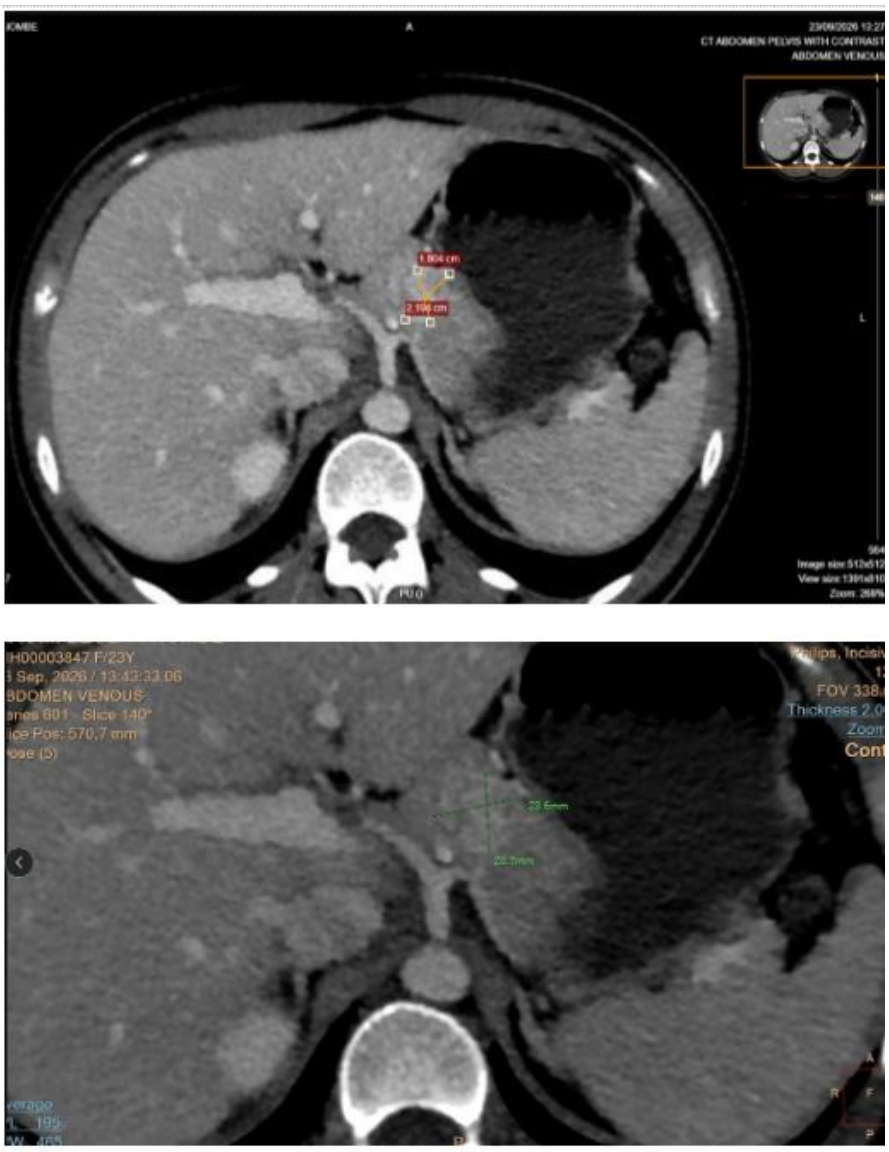


Fig. 6. Contrast-enhanced axial CT of the abdomen demonstrating a well-defined, fat-containing pancreatic lesion (measuring 2.2 × 1.8 cm) with a hypodense lipid-attenuating rim (-12 to -34 HU) consistent with a pancreatic angiomyolipoma, alongside normal hepatic, splenic, and renal parenchyma.

4. Therapeutic intervention

4.1. Antiseizure therapy

Prior to neurological reassessment, the patient was maintained on an antiseizure regimen containing extended-release sodium valproate alongside levetiracetam. Following comprehensive clinical and neuroimaging review, sodium valproate was discontinued.

4.2. Multidisciplinary management

Following a multidisciplinary team case conference, a coordinated management plan was established integrating neurology, ophthalmology, dermatology, clinical psychology, hepatobiliary surgery, interventional radiology, and TSC surveillance services. Psychological support and caregiver counseling were initiated to address her cognitive challenges and mild mood fluctuations. Ongoing ophthalmological surveillance was arranged to monitor the left homonymous hemianopic defect and right peripapillary changes. Surgical and interventional radiology consultations were obtained regarding surveillance versus potential tissue sampling of the pancreatic AML, and upper gastrointestinal endoscopy was advised to evaluate the gastric antral wall thickening prior to initiating systemic mTOR inhibitor therapy with everolimus. Transthoracic echocardiography and high-resolution chest CT demonstrated no cardiac rhabdomyomas or pulmonary lymphangioleiomyomatosis (LAM).

5. Follow-up and outcomes

Following optimization of levetiracetam monotherapy, the patient achieved complete cessation of focal seizures, with no further clinical ictal events reported by the patient or her guardians at short-term review. Her guardians noted mild emergent irritability without aggressive behavior, which was managed effectively through cognitive-behavioral counseling and caregiver support strategies. Serial ophthalmological assessments confirmed stable visual acuity and unchanged fundoscopic findings. Dermatological diagnoses of 3–4 facial angiofibromas and >6 lower-extremity shagreen patches were formally verified (Fig. 2). Follow-up abdominal imaging revealed persistent gastric antral wall thickening with normal gastric and pancreatic enzyme levels. The patient remained clinically stable with her guardians actively supporting her daily care and Grade 12 schooling, although she missed her subsequent scheduled outpatient surveillance appointment.

6. Discussion

According to the 2021 International Tuberous Sclerosis Complex Consensus Group diagnostic criteria [1], our patient fulfills the requirements for a definite clinical diagnosis of TSC by exhibiting five major features—hypomelanotic macules (≥3, ≥5 mm), facial angiofibromas (3–4 lesions), shagreen patches (>6 lesions on the lower

extremity), multiple cortical tubers, and bilateral calcified subependymal nodules—in addition to one minor feature represented by a non-renal hamartoma (pancreatic angiomyolipoma) (Supplementary Table S1) [1]. Although identification of a pathogenic TSC1 or TSC2 variant is independently sufficient for diagnosis [1], molecular genetic testing was unavailable, reflecting a common diagnostic barrier in low-resource healthcare environments. Establishing a definitive diagnosis in adulthood despite clinical suspicion during childhood highlights how limited access to specialized neuroimaging and multidisciplinary subspecialty services can delay recognition in Papua New Guinea and similar regions.

Neurological and neuropsychiatric manifestations including drug-resistant epilepsy, intellectual disability, and TSC-associated neuropsychiatric disorders (TAND) are driven by early developmental structural brain abnormalities [1,8,9]. Epilepsy affects 80%–90% of individuals with TSC and frequently presents in infancy or early childhood [9]. In our patient, multimodal neuroimaging demonstrated calcified subependymal nodules, cortical–subcortical tubers, and prominent left parieto-temporo-occipital cortical dysplasia, providing a clear epileptogenic substrate for her recurrent focal seizures. Her postictal transient mutism and persistent expressive aphasia, occurring alongside intact comprehension and motor function, reflect selective dysfunction of dominant hemispheric language networks, while her mild intellectual disability and academic struggles requiring continuous guardian support even as a Grade 12 student exemplify the lifelong cognitive burden of TAND [1,8]. Furthermore, the mild irritability observed following levetiracetam dose escalation aligns with recognized behavioral adverse effects of antiseizure medications in adults with epilepsy, which must be carefully distinguished from baseline neuropsychiatric symptoms [7,8].

Cutaneous and ophthalmological examinations revealed both classic and atypical features. While the presence of 3–4 facial angiofibromas represents a hallmark cutaneous sign of TSC [1,5], the distribution of more than six shagreen patches over the lower extremity is atypical compared with the classic lumbosacral predilection [1]. From an ophthalmological standpoint, retinal astrocytic

hamartomas and retinal achromic patches were absent in our patient [1]. Instead, she exhibited right peripapillary exudative and pigmentary changes alongside a left homonymous hemianopic visual-field defect, the latter correlating anatomically with her left parieto-temporo-occipital cortical dysplasia affecting the retrochiasmal optic radiations and necessitating formal perimetric mapping.

Visceral involvement in TSC most commonly manifests as renal angiomyolipomas, which constitute a major diagnostic criterion due to their high prevalence and risk of spontaneous retroperitoneal hemorrhage [1,2]. By contrast, extrarenal AMLs particularly primary pancreatic AMLs are exceedingly rare and are categorized under non-renal hamartomas as a minor diagnostic criterion [1,3]. On cross-sectional imaging, the detection of macroscopic intralesional fat (-10 to -100 HU on non-contrast or contrast-enhanced CT) is diagnostic of an AML, whereas lipid-poor variants may mimic pancreatic neuroendocrine tumors or solid pseudopapillary neoplasms and require biopsy [3]. In our patient, contrast-enhanced abdominal CT demonstrated a well-defined pancreatic mass containing a distinct peripheral fat-attenuating rim (-12 to -34 HU), allowing confident radiological characterization as a pancreatic AML while confirming completely normal kidneys, liver, and spleen. Additionally, the incidental finding of gastric antral wall thickening may reflect gastrointestinal hamartomatous polyps or mucosal hyperplasia associated with TSC [6], warranting endoscopic evaluation.

Targeted systemic therapy with mTOR inhibitors directly addresses the underlying molecular pathophysiology of TSC [1,2,4]. Landmark randomized controlled trials, including EXIST-2 and EXIST-3, demonstrated that oral everolimus significantly reduces angiomyolipoma volume, improves cutaneous angiofibromas, and decreases seizure frequency in treatment-resistant TSC-associated epilepsy [2,4]. Because our patient achieved complete seizure remission following optimization of levetiracetam monotherapy, the planned introduction of everolimus is primarily aimed at controlling her pancreatic AML and cutaneous manifestations [2,4]. However, given her baseline gastric antral wall thickening, endoscopic assessment and close clinical surveillance for mTOR inhibitor-induced stomatitis and gastrointestinal mucosal toxicity are essential prior to and during therapy [2,4,6].

7. Conclusion

We report a 23-year-old woman with childhood-onset epilepsy, mild intellectual disability, and academic struggles who received a definitive diagnosis of tuberous sclerosis complex in adulthood following multimodal neuroimaging and specialist dermatological evaluation. Her clinical phenotype encompassed five major diagnostic features 3–4 facial angiofibromas, >6 lower-extremity shagreen patches, hypomelanotic macules, cortical tubers with left parieto-temporo-occipital cortical dysplasia, and bilateral calcified subependymal nodules alongside a rare fat-containing pancreatic angiomyolipoma (-35 to -52 HU) as a minor feature, with normal kidneys, liver, and spleen and no retinal hamartomas. This two-decade diagnostic delay underscores the necessity of maintaining a high index of suspicion for TSC among children and adults presenting with unexplained epilepsy and characteristic skin lesions in resource-limited settings such as Papua New Guinea, where early neuroimaging and coordinated multidisciplinary care can substantially improve long-term neurological and systemic outcomes.

8. Limitations

Histopathological biopsy of the pancreatic angiomyolipoma and endoscopic biopsy of the focal gastric antral wall thickening were not performed; consequently, these visceral findings rely on characteristic radiological appearances. Nevertheless, this does not alter the definitive clinical diagnosis of TSC, which is robustly established by five major diagnostic criteria [1]. Additionally, molecular genetic testing for TSC1/TSC2 mutations was unavailable locally, and the patient missed her subsequent outpatient follow-up visit, precluding longer-term evaluation of her planned everolimus therapy.

Key learning points

- TSC is a multisystem neurocutaneous disorder; adults with long-standing epilepsy, cognitive challenges, and subtle cutaneous signs warrant comprehensive multisystem evaluation.
- Careful dermatological inspection for facial angiofibromas (≥3) and atypical extralumbar shagreen patches provides high-yield bedside diagnostic clues when genetic testing is unavailable.

- Left parieto-temporo-occipital cortical dysplasia in TSC can simultaneously serve as an epileptogenic focus, cause expressive language dysfunction, and produce retrochiasmal homonymous visual-field defects.
- While renal AMLs represent a major diagnostic criterion, rare fat-containing pancreatic AMLs (-35 to -52 HU on CT) qualify as non-renal hamartomas (minor criterion) and can occur with completely normal kidneys.
- Baseline gastric antral wall thickening in TSC warrants endoscopic evaluation before initiating systemic mTOR inhibitor therapy with everolimus.

Ethics approval and consent to participate

Ethical clearance for this study and publication of the clinical case was granted by the Pacific International Hospital (PIH) Institutional Research Ethics Committee (Institutional Review Board), Port Moresby, Papua New Guinea (approval documentation attached).

Patient consent

Written informed consent for publication of this case report and all accompanying clinical and radiological images was obtained from the patient and her legal guardians. All personal identifiers have been removed or masked to ensure patient anonymity.

Funding

This research received no specific funding.

Declaration of competing interests

The authors declare that they have no competing financial interests or conflicts of interest.

Data availability

The clinical and neuroimaging data analyzed in this case report are available from the corresponding author and the Pacific International Hospital medical imaging archive upon reasonable request.

CRediT authorship contribution statement

Messay Gebrekidan Woldecherkos: Conceptualization, Image review, Image analysis, Data curation, Supervision, Writing – original draft.
Aamir Siddiqui: Conceptualization, Investigation (clinical management), Writing – review & editing.
Bina Basnet Thapa: Image review, Data curation, Writing – original draft.
Alfonso Blanch: Image review, Image analysis, Data curation, Writing – original draft.

Syed Waqar Ahmed: Investigation, Writing – review & editing.
Muhammad Imran: Investigation (ophthalmology assessment), Writing – review & editing.
Kyaw Khine: Investigation, Writing – original draft, Writing – review & editing.
Michael Shawel Lemma: Conceptualization, Investigation, Writing – review & editing.
Temesgen D. Nurye: Investigation (clinical management), Writing – review & editing.

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Supplementary material

Supplementary Table S1. Updated 2021 International TSC Consensus Group clinical diagnostic criteria (Northrup et al. [1]) and clinical/radiological features documented in this patient.

Major diagnostic features

#	Major Feature (2021 Consensus Criteria) [1]	Status in Present Patient
1	Hypomelanotic macules (≥3, at least 5 mm diameter)	**Present (noted at initial examination)**
2	Angiofibromas (≥3) or fibrous cephalic plaque	**Present (3–4 facial angiofibromas confirmed by dermatologist)**
3	Ungual fibromas (≥2)	Absent
4	Shagreen patch	**Present (>6 shagreen patches on lower extremity confirmed by dermatologist)**
5	Multiple retinal hamartomas	Absent (no retinal hamartomas on fundoscopy/OCT)
6	Multiple cortical tubers and/or radial migration lines	**Present (multiple tubers, radial migration lines, and left parieto-temporo-occipital cortical dysplasia)**
7	Subependymal nodules (SENs)	**Present (bilateral, calcified)**
8	Subependymal giant cell astrocytoma (SEGA)	Absent
9	Cardiac rhabdomyoma	Absent (normal echocardiography)
10	Lymphangioleiomyomatosis (LAM)†	Absent (normal chest CT)
11	Angiomyolipomas (≥2)† [typically renal]	Absent in kidneys (renal parenchyma normal on CT)

† Note: A combination of the two major clinical features (lymphangioleiomyomatosis and angiomyolipomas) without other features does not meet criteria for a definite diagnosis [1].

Minor diagnostic features

#	Minor Feature (2021 Consensus Criteria) [1]	Status in Present Patient
1	"Confetti" skin lesions	Absent
2	Dental enamel pits (≥3)	Absent

3	Intraoral fibromas (≥2)	Absent
4	Retinal achromic patch	Absent
5	Multiple renal cysts	Absent (normal kidneys on CT)
6	Non-renal hamartomas	**Present (fat-containing pancreatic angiomyolipoma, -12 to -34 HU on CT)**
7	Sclerotic bone lesions	Absent

Diagnostic Rule (Northrup et al., 2021 [1]): Definite TSC is established by the presence of two major features, or one major feature plus at least two minor features, or identification of a pathogenic TSC1 or TSC2 variant. Possible TSC is defined by either one major feature or at least two minor features. The present patient fulfills 5 major features and 1 minor feature, establishing Definite TSC.

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Institutional Review Board (IRB)
Exempt Research Determination Letter

IRB Reference Number:	IRB-26001B
Submission Date:	10/07/2026
Principal Investigator:	MESAY WOLDECHERKOS
Department:	Radiology & Imaging
Study Title:	Tuberous Sclerosis Complex Unmasked After Decades of Undiagnosed Childhood-Onset Epilepsy: A Case Report with Pancreatic Angiomyolipoma from Papua New Guinea

Determination

Date: Thursday, 8 October 2026

Dear Dr. WOLDECHERKOS,

The **Pacific International Hospital** Institutional Review Board (IRB) has reviewed the submission requesting an ethical and regulatory determination for the above-referenced project.

Based on the documentation provided, it has been determined that this proposed project qualifies for **Exempt Review** under the Hospital IRB Policy and applicable ethical and regulatory standards.

Exemption Category Retrospective Case Study

Basis for Determination

After review of the submitted protocol and supporting documentation, the IRB determined that:

☐ The research involves no more than minimal risk to participants.

☐ Adequate provisions exist to protect confidentiality and privacy.

☒ The research falls within an approved exemption category.

☐ No additional IRB review is required unless significant changes are made to the study.

Conditions of Approval

This exemption determination is granted subject to the following conditions:

1. The study shall be conducted exactly as described in the submitted protocol.
2. Any modification to study objectives, methods, participant population, data collection procedures, consent process, or research personnel must be submitted to the IRB for review prior to implementation.
3. The Principal Investigator is responsible for maintaining participant confidentiality and data security throughout the study.
4. Any unanticipated problems involving risks to participants shall be reported to the IRB within -- days.
5. The IRB reserves the right to suspend or withdraw this exemption determination if new information indicates increased risk to participants.

Exemption Validity

☒ This exemption remains effective unless protocol modifications require further review.

OR

☐ This exemption is valid until:

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Institutional Review Board (IRB)
Exempt Research Determination Letter

Final Determination

IRB Status: **EXEMPT**

The Principal Investigator may proceed with the research activities described in the approved submission upon receipt of this letter.

IRB Review Information

IRB Reference No.	IRB-26001B
Date Reviewed:	08/10/2026
Review Type:	Exempt
Reviewer Name:	
Reviewer Position:	

Approval

(Signature with date)
Name:
IRB Chairperson/Designee

Aamir Siddiqui
DR. AAMIR SIDDIQUI
MEDICAL DIRECTOR
PACIFIC INTERNATIONAL HOSPITAL

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Disclaimer

This determination applies only to the protocol and documents reviewed by the IRB. Any protocol amendments, changes to study personnel, modifications to recruitment methods, or changes affecting participant risk must be submitted to the IRB for reassessment before implementation.