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Case Report

Tuberous sclerosis with recurrent seizure, dermatological lesions, renal cysts, and hypothyroidism in a female patient in Awka, Nigeria

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Abstract

The incidence of tuberous sclerosis seems to be rising in Nigeria. Tuberous sclerosis with cerebral, renal, thyroid, and dermatological manifestations have not been completely identified. This case report documents a rare case of tuberous sclerosis with cerebral and dermatological lesions, renal cysts, and hypothyroid state. A 28-year-old female patient who presented in our clinic with a history of recurrent seizures for 19 years, a shagreen patch on the right lumbar area, scarring alopecia, and puckering facial angiofibroma. No member of her family had a similar illness. Computerized tomography scan showed multiple echoic cysts in the two kidneys. Her thyroid function tests revealed a hypothyroid state. Brain computerized tomography showed subependymal calcified nodules of the lateral ventricles and prominence of the cerebral sulci, more at the vertex. Electroencephalogram findings were normal. She was placed on oral Carbamazepine 400mg BD and has remained seizure-free for two years**.** Tuberous sclerosis with concomitant renal, cerebral, and dermatological lesions and hypothyroidism, though rare, was presented. The patient had tuberous sclerosis with renal cysts, subependymal nodules, and prominence of the cerebral sulci, with recurrent seizures, ash leaf/shagreen patches, scarring scalp alopecia, and a hypothyroid state.

Keywords: Tuberous Sclerosis; Ashleaf Lesion; Shagreen Patches; Facial Angiofibroma; Scarring Alopecia; Seizure; Renal Cysts; Hypothyroidism.

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Introduction

Tuberous sclerosis complex (TSC) is an autosomal dominant disorder classified as a phakomatosis with neurological, cardiovascular, skin, renal, and retinal manifestations.[1] The prevalence of TSC is about one in 6000. [1] The thyroid effects of TSC are rare [2], and TSC is commonly observed in pediatric subjects.[3] Though the disease can manifest at any age. A high index of suspicion is required to make a diagnosis, as the classical triad of the disease occurs in less than one-half of patients.[1] White matter abnormalities, subependymal nodules, and cortical hamartomas are usually demonstrated using neuro-imaging like computerized tomography (CT) and magnetic resonance imaging (MRI).[4] Here, we present a 28-year-old female patient who had recurrent seizures from the age of 9 years and an asymptomatic hypothyroid state, ashleaf lesions, scalp scarring alopecia, facial angiofibroma, and renal cysts.

Case Presentation

The patient was a 28-year-old female who presented 2 years before this report with facial and mid-back rashes, and episodes of recurrent seizure first noticed 19 years ago. She had occasional spells of dizziness, but had no weight loss, no sweating, and no cold intolerance. She had new-onset hypertension but had no eyelid retraction or protrusion. Her menstrual periods had been regular. She did her secondary and tertiary education in record time. No one in her family had a similar illness. She was single and had no history of use of tobacco snuff, cigarette smoking, alcohol, or substance abuse. Her fingers were not spindled. Her pulse rate was 80/min, full volume, regular, and blood pressure 150/106mmHg left arm, sitting. Apex beat was located at the 5th left intercostal space (LICS) in the mid-clavicular line. S1 and S2 heart sounds were heard, and there were no added heart sounds or murmurs. The chest was clear.

There was no neck mass. The thyroid gland was about 10 x 8cm, soft, and its mobility was uninfluenced by swallowing. The abdomen was full and moved with respiration, and there were no areas of tenderness. There was an ashleaf lesion at the right lumbar region that measured 10 x 12cm (Figure 1), facial angiofibroma (Figure 2), and scarring alopecia (Figure 3). The spleen, liver, and kidneys were not enlarged. Electroencephalogram (EEG) revealed normal findings (Table 1). Computerized tomogram of the brain showed evidence of subependymal nodules of the lateral ventricles (Table 2). Thyroid function test revealed elevated serum thyroid-stimulating hormone (TSH) and reduced serum T4 levels (Table 3), indicating a mild hypothyroid state. Renal sonography and renal CT showed multiple echoic cysts in both kidneys (Figures 5,6). Full blood count, fasting blood sugar, and urinalysis were normal (Table 4). Computerized tomography urography was normal.

Table 1: Electroencephalogram features of the patients

Procedure: Referential Montage was used to record the procedure, and the electrodes were placed using the international 1020 system
Background: Composed of posterior dominant symmetrical 11 Hz alpha waves.
Hyperventilation induced no specific changes.
Abnormality: None seen.
Photic stimulation: Induced no specific changes.
Comments: Normal interictertal EEG does not exclude the presence of seizure disorder.

Table 2: Showing Computerized tomogram of brain findings

Scanogram: There is no abnormal calvarial calcification or lucency. There is also no evidence of chronic raised intracranial pressure.
Gross sectional images: There is no focal intra-cerebral mass lesion, hemorrhage or intra/extra axial collection.
There is no shift of the midline brain structures.
There are subependymal calcified nodules of the lateral ventricles. However, there is no evidence of ventricular obstruction (figure 4).
There is prominence of the cerebral sulci, more at the vertex.
The cerebellum and the structures of the brain stem are grossly normal.
The paranasal sinusis, mastoid aircells and basal skull foramina are within normal limits.
The eye globes are grossly normal.
There is no calvarial fracture.
Conclusion: Tuberous sclerosis (Boutneville disease) with mild frontal atrophy.

Table 3: Thyroid function tests

total triiodothyrorine (T3)	4.57mU/L (1.23 – 3.07mU/L)
Free thyroxin (T4)	0.62mU/L (0.82 – 1.63mU/L)
Thyroid stimulating hormone (TSH)	6.5mU/L (0.38 – 4.3mU/L)

Table 4: Investigation results

Urinalysis		**Full blood count**		**Fasting blood sugar**
Appearance	Amber	Hemoglobin	10.6g/dl	93mg/dl
pH	6.5	White cell count	6000cells/ml,	
SG	1.015	Neutrophils	75%,	
Protein	Nil	Lymphocytes	32%,	
Glucose	Nil	Eosinophils	3%.	
Blood	Nil			
Ascorbic acid	Nil			
Nitrite	Nil			
Bilirubin	Nil			
Urobilinogin	Nil			
SG=specific gravity				

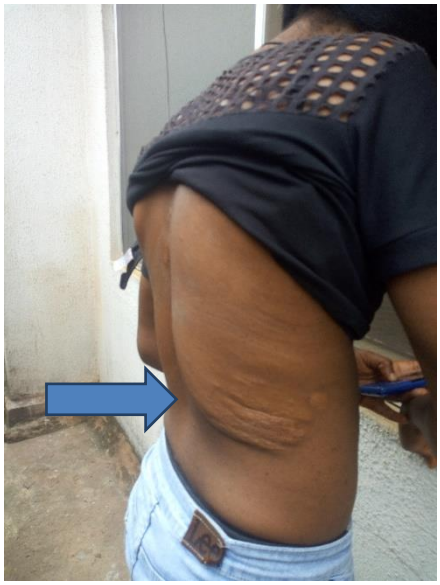

Figure 1: Tuberous sclerosis showing shagreen patch.

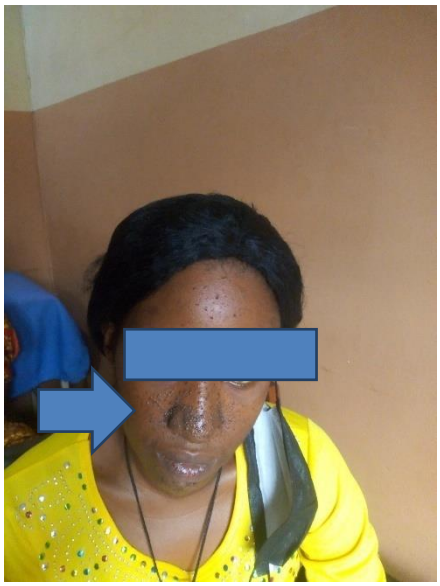

Figure 2: Tuberous sclerosis showing facial angiofibroma

Figure 3: Tuberous sclerosis showing focal scarring alopecia

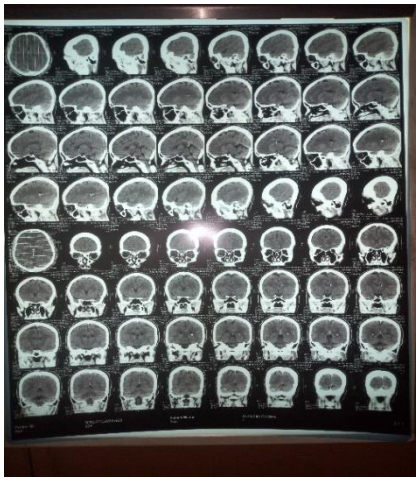

Figure 4a: Computerized tomogram of tuberous sclerosis patient showing subependymal calcified nodules of the lateral ventricles and frontal atrophy

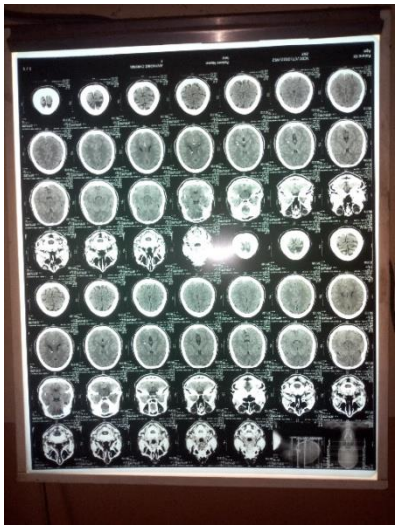

Figure 4b: Computerized tomogram of brain of tuberous sclerosis patient

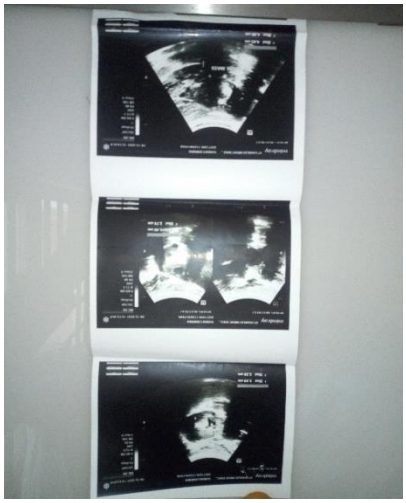

Figure 5: Renal sonography showing multiple cysts

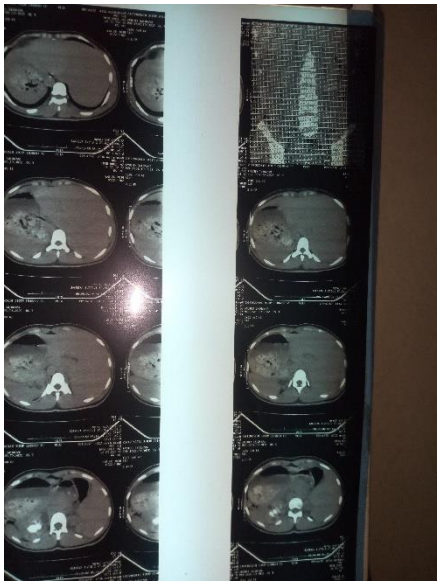

Figure 6: Tuberous sclerosis: computerized tomogram showing multiple echoic cysts in both kidneys

Diagnosis

Based on the history of recurrent seizure of 19 years' duration, facial angiofibroma, ashleaf lesions at the lumbar region, focal scalp scarring alopecia, hypothyroidism, subependymal calcified nodules of the lateral ventricles, and renal cysts, a diagnosis of tuberous sclerosis was made.

The patient was placed on oral Carbamazepine 400mg BD and Amlodipine 10mg nocte. After 2 years of the commencement of these medications, the patient has remained stable without any seizures.

Discussion

Tuberous sclerosis complex is an autosomal dominant disorder classified as major or minor. For definite TSC, there should be two major features or a major feature plus two or more minor features.[5] Our index patient had angiofibromas (Figure 2), shagreen lesions (Figure 1), subependymal nodules (Table 2), three major features, and scarring alopecia (Figure 3). asymptomatic hypothyroidism (Table 3) and multiple renal cysts (Figures 5,6), constituting three minor features of TSC.[5] The diagnosis of TSC in this patient was not made for 17 years, as the patient was managed for recurrent seizures of indeterminate cause for this period. This seizure, perhaps, negatively impacted on her marital status, constituting a stigma impairing marriage.

Our index patient had multiple echoic cysts in both kidneys but was not explored for evidence of angiomyolipoma (AMLs) in the kidney or elsewhere. Evorolimus or any other mammalian target of rapamycin (mTOR) was also not instituted. However, mTORs are recommended for use in AMLs in TSC targeted at reducing the tumor size, as was observed with these drugs in autosomal dominant polycystic kidney disease (ADPKD) following their genesis from chromosome 16. [4, 6,7]

Most TSC cases are detected in the pediatric setting as they present early, many with the classical triad.[5] Although our index patient had the first seizure at 9 years, the diagnosis was masked until the age of 26 years.

Mental retardation is a common feature of TSC. However, this patient did not have mental retardation and had her tertiary education in record time.

Facial angiofibroma in TSC may impose a social stigma and occasionally require some camouflage. Masking the lesion as camouflage was not observed in our patient, as she seemed not perturbed.

Renal cysts in TSC may be ordinary cysts, renal cell carcinoma (RCC), or angiomyolipoma (AMLs).[1] Our patient had renal cysts with unimpaired renal function but with an episode of hematuria. Histological tests were not done. A case report from Nigeria had revealed TSC with acute kidney injury, in contrast to TSC with normal renal function observed in our patient.[8]

The occurrence of hypothyroidism in TSC is rare.[2] Auidell et al observed that in 93 patients with a definite diagnosis of TSC, thyroid abnormalities were found in 20.4% of the patients. They further inferred that thyroid gland lesions might be part of the clinical spectrum of TSC. In their report, it was also noted that thyroid lesions in TSC were usually asymptomatic.[2] We did not notice any clinical features of hypothyroidism but noted elevated serum TSH and mildly depressed serum T4. Whether this was an isolated entity or linked to TSC in our index patient was not evaluated.

Conclusion:

A patient with tuberous sclerosis with concomitant occurrence of renal, cerebral, dermatological lesions, and hypothyroidism, though rare, was presented. The patient has a normal intelligence quotient, has been seizure-free for the past 2 years, has normal renal function, and is not manifesting any clinical symptoms of hypothyroidism.

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