Original Article

Cortical Tubers Without Neurological Symptoms: An Uncommon Case of Tuberous Sclerosis Complex

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ABSTRACT

Tuberous Sclerosis Complex (TSC) is a genetic disorder and rare type of neurocutaneous syndrome characterized by development of benign nodules in various organs of the body including the brain, skin, kidneys, and heart. Epilepsy and mental retardation are common neurological manifestations of this disorder in most cases. However, cases with isolated cutaneous findings and preserved neurological function are rare and have not been well reported in the literature. The purpose of this case report is to highlight the phenotypic variation in the TSC phenotype and to stress the need for increased clinical vigilance in atypical cases.

Keywords: Angiofibroma, Cortical tubers, Neurocutaneous syndrome, Shagreen patch, Tuberous sclerosis complex (TSC)

INTRODUCTION

Tuberous Sclerosis Complex (TSC) is a rare genetic neurocutaneous syndrome with autosomal dominant inheritance caused by mutations in the *TSC1* or *TSC2* genes. These genes encode proteins called hamartin and tuberin which play an important role in cellular growth and proliferation through the mTOR (mammalian target of rapamycin) pathway.[1] This disorder is associated with the development of nodules or haematomas in many organs of the body including, the brain, skin, kidneys, heart, and lungs.[2]

The incidence of TSC has been estimated many times and generally falls between 1:6000 and 1:10,000 live births. A comprehensive study in the United Kingdom estimated the incidence at 1:5800 live births,[3] and a more recent study in Germany using the most recent diagnostic criteria estimated the incidence rate to range from 1:6760 to 1:13,520 live births.[4,5]

Neurological manifestations, particularly seizures, developmental delays, and intellectual disabilities, are observed in approximately 80–90% of cases and often dominate the clinical picture.[6,7]

Cutaneous lesions, such as hypomelanotic macules, facial angiofibromas, shagreen patches, and periungual fibromas, are among the earliest and most visible features of TSC.[8] While these dermatological findings are frequently associated with significant neurological symptoms, isolated cutaneous presentations without seizures or cognitive impairments are less commonly reported.[9]Additionally, the absence of seizures in individuals with cortical tubers represents an atypical phenotype of TSC, which can delay diagnosis.[9]

This report discusses the case of a 14-year-old female who presented with progressive skin nodules

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and patches since early childhood. Brain imaging revealed cortical tubers, a hallmark of TSC. However, the patient exhibited no seizures, developmental delays, or cognitive impairments, representing a rare and atypical presentation of this condition. This case highlights the importance of recognizing atypical presentations of TSC to ensure timely diagnosis and management.

CASE REPORT

A 14-year-old female presented to the dermatology clinic with progressive skin nodules on the central region of her face, mostly around the nose which later spread to other parts of the face. They were mostly dark in colour, non-pruritic and non-pustular. Her facial skin lesions first appeared at the age of 5 years and were fewer at this stage, but over the years, they had become more widespread. In addition, her mother observed on her trunk, a different group of skin patches, sparsely distributed. Both upper and lower limbs were relatively spared.

Patient was a product of spontaneous vertex delivery in a hospital. She did not suffer any perinatal injuries such as birth asphyxia or neonatal jaundice. Her developmental milestones were timely attained. There was no history of childhood or teenage onset seizures. She is an average student academically and has not repeated a class. She did not experience seizures, developmental delays, or any cognitive impairment. There is no history of a similar illness in the family.

Physical examination revealed multiple facial angiofibromas, mostly over the malar regions (Figure 1). Hypomelanotic macules on the trunk and each measuring 0.5–3 cm in diameter, along with a single shagreen patch on the left lateral back (Figure 2). There was also a lesion (periungual fibroma) on the medial aspect of her right toenail (Figure 3). Her neurological and the rest of the systemic examinations were normal.

Magnetic resonance imaging (MRI) of her brain revealed multiple cortical and subcortical tubers, consistent with the diagnosis of Tuberous Sclerosis Complex (TSC). There was imaging evidence of subependymal giant cell astrocytoma (SEGA) or hydrocephalus. Abdominal ultrasonography was normal. Echocardiography imaging was also unremarkable, ruling out cardiac rhabdomyomas. Genetic testing was not done due to its unavailability The patient was later referred to the dermatologist for ongoing surveillance of the skin lesions. However, the need for neurological follow-up was emphasised to the patient's mother, considering the imaging evidence of cortical and subcortical tubers, for the potential development of SEGA or seizure disorder. The patient and her family received counselling regarding the nature of the disorder, inheritance patterns, and the risk of transmission to future offspring.

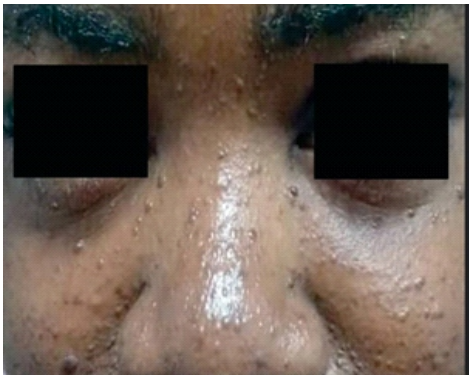

Figure 1. Facial angiofibroma

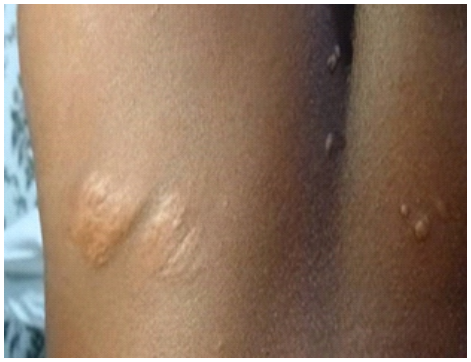

Figure 2. Shagreen patch

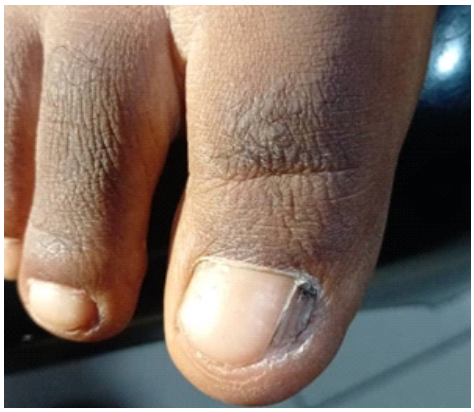

Figure 3 Periungual fibroma

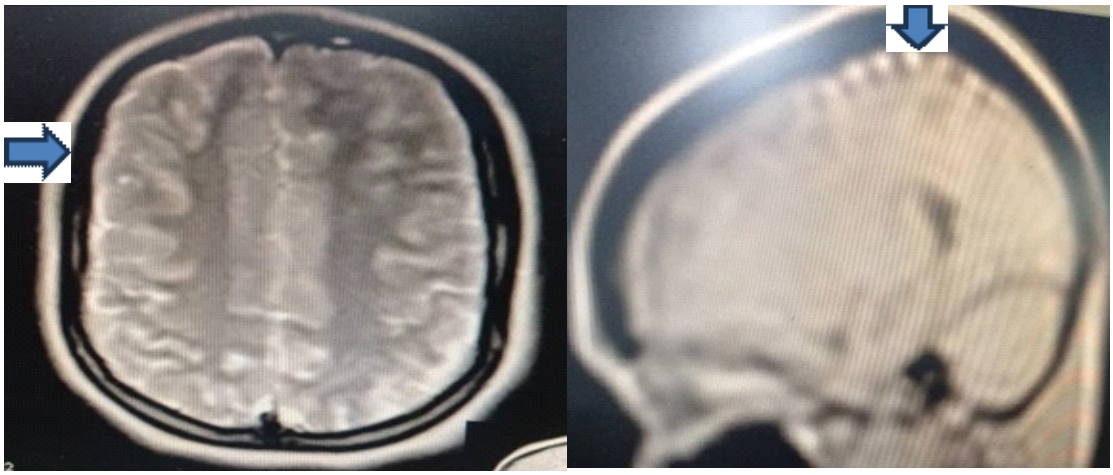

Figure 4. Cranial MRI (coronal and axial views) with cortical tubers

DISCUSSION

Tuberous Sclerosis Complex (TSC) typically manifests with a triad of seizures, intellectual disability, and skin lesions. However, this case represents an atypical presentation with isolated cutaneous findings and normal neurological function. Such cases highlight the phenotypic variability of TSC, particularly in patients with *TSC1* mutations, which are often associated with milder disease severity.[1]

Cutaneous findings are often the first indicator of TSC and can serve as a diagnostic clue in the absence of neurological symptoms. In this case, the early recognition of dermatological features prompted comprehensive evaluation, leading to timely diagnosis and management. The absence of seizures and cognitive impairment underscores the need for heightened awareness of atypical presentations.

Most of the cases of TSC reported in Nigeria had neurological symptoms in addition to cutaneous manifestation.[11,12,13] There is evidence from the literature that more than two-thirds of the TSC patients would have either epilepsy or cognitive impairment or both.[6] It is not certain why our patient did not have neurological symptoms despite having cortical involvement, but there is a possibility she could still develop them in the future. The phenotypic variability of this disorder is interesting and will likely influence the overall outcome of this disorder, with those with absent systemic complications inclined to having better outcome. Apart from cutaneous symptoms, our patient did not have either renal or cardiac complications.

Early diagnosis and multidisciplinary management are crucial to monitor for potential complications and ensure optimal long-term outcomes. For the management of skin lesions, topical rapamycin has proven effective in reducing facial angiofibromas, with improved cosmetic outcomes in patients.[1,2] Where laser therapies are available, they can significantly improve the appearance of angiofibromas in these patients.[14] The other aspects of skin care for these patients will involve emphasis on skin protection, especially from trauma, to prevent secondary infections and scarring

Although our patient does not have neurological complications such as seizures yet, regular neurological follow up is still necessary. If seizures develop, immediate commencement of anti-seizure medications may be warranted, and for refractory cases, mTOR inhibitors such as everolimus should be prescribed. Periodic brain imaging (MRI scans) is essential for monitoring subependymal giant cell astrocytoma (SEGA) or hydrocephalus, may require surgical treatment.[10]

Although our patient did not have renal involvement, the standard of investigation for renal care is renal ultrasonography or MRI to exclude angiomyolipomas or cyst.[15] In terms of treatment, MTOR (mammalian target of rapamycin) inhibitors have been shown to be effective in treating growing angiomyolipomas. If bleeding or renal dysfunction

occurs, embolization or surgery may be contemplated.[16]

Other systemic complications such as cardiac and pulmonary complications can also occur in TSC and should be looked out for. Symptomatic cases may need medical or surgical treatment, [17,18] whereas asymptomatic cases would benefit from regular monitoring of the renal function.

It is not unusual for patients with TSC to have developmental and behavioural disorders, even for patients with normal cognitive function. So, the goal is to identify subclinical learning disabilities or behavioural issues. [19]Collaboration with schools and special education services can optimize learning environments.[20] Presence of behavioural issues may be addressed with medications such as selective serotonin reuptake inhibitors (SSRIs).[21]

Another important aspect of care for TSC is the need to educate families about the genetic nature of this condition. It is inherited in autosomal dominant pattern with 50% chance of transmission to the offspring.[2]Conversations should also be held around reproductive issues with emphasis on preimplantation genetic testing and various options for family planning.[22]

Periodic evaluations, including clinical examinations, imaging, and laboratory tests, should be tailored based on the patient's age and organ involvement,[5] but long-term follow-up is vital to monitor for new or progressing manifestations of TSC. [23,24]

CONCLUSION

This case highlights an atypical presentation of TSC in an adolescent where cutaneous lesions exist with preserved cognitive function despite the presence of cortical tubers. This underscores the importance of recognizing dermatological signs as potential indicators of TSC, even in the absence of neurological symptoms. Thus, this report adds to the growing body of literature on the phenotypic variability of TSC and the need for heightened clinical vigilance in atypical cases.

Recommendations

Management of TSC is individualized and focus should be on addressing the patient's clinical manifestations, monitoring for potential complications, and providing supportive care. Early diagnosis, a multidisciplinary approach, and patient education are effective strategies for managing TSC especially in settings with limited resources.

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