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Case Report

Navigating Tuberous Sclerosis in a 41-Year-Old Patient: Clinical Insights and Management

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ABSTRACT

Tuberous sclerosis complex is a rare genetic disorder that is characterized by the presence of non-cancerous tumors in different organs, primarily affecting the brain, skin, kidneys, heart, and lungs. This condition is caused by mutations in either the TSC1 or TSC2 genes, which disrupt the mTOR pathway. The clinical manifestations of TSC can vary greatly, ranging from mild skin abnormalities to more severe neurological problems such as epilepsy, cognitive impairment, and autism spectrum disorders. Tumors and cystic lesions of the kidneys can be the associated abnormalities of the renal tract. While in most cases, they can be asymptomatic, adverse effects on renal function have also been reported. The case study details a 41-year-old woman who received a belated diagnosis of TSC. She had a history of seizures over the past 26 years, with a physical examination revealing classic TSC features such as facial angiofibroma, enamel pits, and periungual fibromas. The patient also had a background of learning difficulties. She was diagnosed with advanced renal failure which was picked up when she presented with pedal oedema. She ended up on dialysis a few months following the presentation. Treatment for TSC typically targets specific symptoms, with antiepileptic medications prescribed for seizures and surgical interventions for sizable tumors. Regular monitoring is essential to detect potential complications early on. The case emphasizes the significance of prompt diagnosis and comprehensive care in TSC to enhance patient outcomes and well-being. Given the disease's diverse nature, regular check-ups and tailored treatment strategies are vital for effective management.

Keywords: Angiofibromas, Enamel pits, Intellectual disability, Multiple hamartomas, Seizures, Tuberous Sclerosis Complex.

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INTRODUCTION

The uncommon autosomal dominant multisystem condition known as Tuberous Sclerosis Complex (TSC) is typified by the development of hamartomas in several human organs, such as the skin, brain, kidneys, lungs, and heart. Around two million individuals globally are impacted by TSC, which has a fatality rate of 1:8000 among live births, irrespective of the sexual characteristics. It exhibits a broad range of phenotypic characteristics that differ in intensity. Mutations in tumor suppressor genes TSC-1, responsible for encoding the hamartin protein located on the long arm of chromosome 9, or TSC-2, responsible for encoding the tuberin protein located on the short arm of chromosome 16, have been identified in cases of TSC. Most patients with TSC have central nervous system involvement, resulting in a variety of functional and structural abnormalities such as seizures, intellectual impairment, and behavioral disorders, as well as structural abnormalities like cortical tubers and subependymal nodules.[1,2]

The Vogt triad such as adenoma sebaceous-like facial angiofibromas, seizures, and cerebral impairments is the traditional childhood presentation. Three-quarters of individuals have facial angiofibroma and seizures; half have intellectual disabilities; only a small percentage of people have all three conditions. As a result, diagnostic standards have been developed to help with TSC diagnosis.[3,4] In over 80% of instances, the diagnosis is made in the early years of infancy, frequently as a result of the development of hypomelanotic macules or convulsions.[5] However, there is still a small group of patients for whom a diagnosis is not made until maturity. This is typically due to a lack of changes in the skin, kidneys, or lungs.[6] Here, we discuss the case of a patient diagnosed with TSC in their fourth decade of life with distinctive radiological and clinical features.

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CASE DETAILS

A 41-year-old lady presented to the Nephrology department with a seven-day history of facial puffiness, worsening pedal edema, and breathlessness. She was noted to be hypertensive with a BP of 210/110 mmHg. A general physical examination revealed pallor and bilateral pedal edema. She had multiple 2-4 mm brownish-black lesions on her face in keeping with facial angiofibroma and periungual fibromas on her fingers and toes. She had evidence of dental deformities (Figure 1).

Past medical history included a diagnosis of epilepsy at the young age of 10 years and she underwent a hysterectomy when she was 31 years old for menorrhagia. She had been on Phenytoin 100 mg twice a day, and Tab. Clobazam 5 mg once a day for epilepsy.

Blood tests revealed anemia with a Hemoglobin value of 5.9 gms/dL and TLC of 4100 cells/cu.mm, platelet count of 1.5 x 10^5 cells, Creatinine was 6.0 mg/dL, Potassium 4.8mmol/L, Sodium 138 mmol/L, Chloride 112 mg/dL, and serum albumin 3.8 mg/dL. Complete urine analysis showed 2+ of albumin. There were no prior medical records including blood tests or radiological imaging available.

She was admitted to the hospital for further management. She was given an infusion of IV Nitroglycerine and was initiated on IV Torsemide and oral antihypertensives namely Cilnidipine 20 mgs twice a day, Prazosin HCl 5 mgs twice a day, Clonidine 100 mcg thrice a day. Ultrasound of the abdomen showed no evidence of structural abnormalities in the kidneys but there was

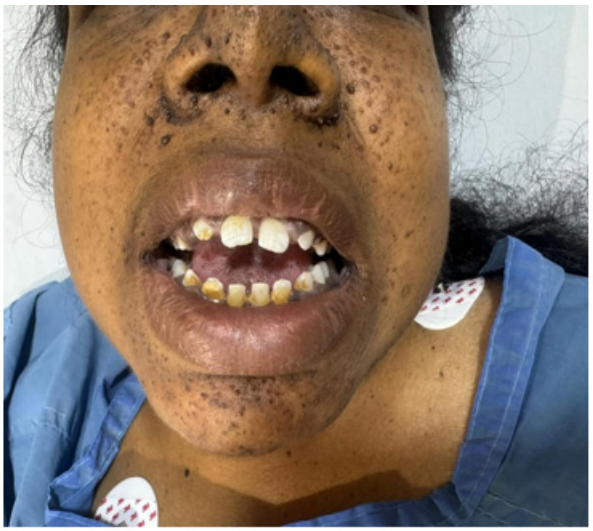

Figure 1 (a)

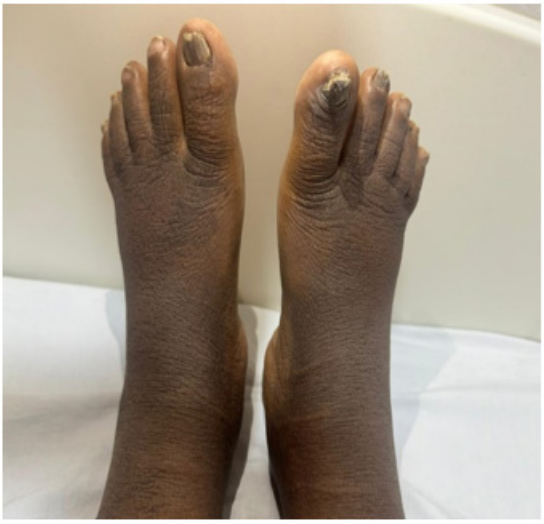

Figure 1 (b)

Figure 1 (c)

Figure 1: (a) depicts Angio-fibroma on the Face and multiple enamel pits and (b), and (c) show periungual fibroma on the hallux of both feet and right hand.

increased echogenicity, loss of corticomedullary differentiation and grade 3 renal parenchymal changes in keeping with chronic kidney disease. Urine spot protein, and Creatinine ratio was 5.5 in keeping with nephrotic range proteinuria. Renal biopsy was not done in view of likely chronicity of kidney disease. She became euvolaemic and the blood pressure was brought under control in a few days. She was given Iron supplements and Erythropoietin for anemia.

Her eGFR dropped to less than 10 mL/min/1.73m^2 over the next 3 months and she developed uremic symptoms. She had to be commenced on maintenance haemodialysis thrice a week.

DISCUSSION

Seizures, autism, and behavioral and mental issues are among the most common neurological manifestations of Tuberous Sclerosis. Seizures manifest in approximately 85% of individuals and typically commence during the initial year of life, presenting as mild focal seizures, infantile spasms, or generalized seizures.

The prevalence of TSC remains consistent across genders and races, although symptoms are often less severe in women.[7,8] Around 80% of cases are identified during childhood, yet some diagnoses may be postponed in childhood or adulthood, as the neurological and skin manifestations of the disorder tend to decrease over time. Dermatological indicators of TSC encompass facial angiofibroma, hypomelanotic macules (Ash leaf patches), shagreen patches, skin tags, and ungual hamartomas. Early diagnosis can save money and improve treatment outcomes for TSC patients.[9] Tuberous sclerosis can sometimes be difficult to diagnose due to its widely varied clinical characteristics. Only 35% of cases exhibit the traditional Vogt's trio, which includes seizures, mental impairment, and cutaneous angiofibroma.

Clinical manifestations of Tuberous Sclerosis Complex (TSC) arise from irregular cell growth, proliferation, and migration during fetal development.[10] The TSC1 and TSC2 genes are responsible for producing hamartin and tuberin, respectively, which play a crucial role in regulating the mTOR pathway. Dysregulation of this pathway can trigger hyperactivation, resulting in the development of noncancerous tumors or hamartomas in various organ systems.[11] TSC2 gene mutations are more common and are associated with more severe neurological symptoms compared to TSC1 mutations. In cases of familial inheritance, symptoms tend to be milder, with TSC1 mutations having a more significant impact.[12] Genetic testing of the patient confirmed the presence of a harmful mutation in the TSC2 gene.

The existence of clinical criteria or a family history may raise a diagnostic suspicion for TSC. The two primary diagnostic methods for TSC are genetic testing and the identification of clinical symptoms. Tuberous sclerosis complex may be passed down in an autosomal dominant manner, or individuals may acquire the condition due to a new pathogenic mutation. Computed tomography, magnetic resonance imaging, electrocardiograms, echocardiograms, and pulmonary function tests are further helpful diagnostic tools.[13] MRI and CT have been used as follow-up methods for individuals with TSC, which has helped to lower death and morbidity rates in addition to their diagnostic utility.

The degree or assortment of organ involvement affects the prognosis of TSC. It is estimated that 25% of seriously afflicted infants pass away before turning 10 and 75% before turning 25 years. On the other hand, the prognosis for those with late-life diagnosis and limited cutaneous indications is dependent on concomitant internal malignancies and cerebral calcifications.[14]

The patient in the case report had firm, brownish-black papules on both cheeks that protruded from the skin surface in keeping with facial angiofibroma. She had periungual fibromas and a neuro-cognitive dysfunction as well. Though renal impairment in Tuberous sclerosis is usually linked to the presence of renal hamartomas, angiomyolipomas, cystic lesions, the absence of these points to the likelihood of chronic glomerulonephritis which is an uncommon pathology.

CONCLUSION

Very few instances of the rare disease tuberous sclerosis complex are identified in adulthood. Understanding the disease's clinical characteristics can help raise suspicions about it and lead to an early diagnosis, both of which are essential for an enhanced diagnosis and the standard of living when treated appropriately. TSC can be accidentally detected through the evaluation of clinical characteristics and imaging data, regardless of the individual's age, without any deliberate effort or intention. The above case highlights the importance of measuring renal function despite the absence of structural renal tract abnormalities

In summary, the age-related clinical spectrum of TSC varies. Consequently, medical professionals need to be aware of the wide range of ways that TSC symptoms and indicators may manifest. In addition, screening are recommended for everyone suspected of having TSC to rule out the illness. Reducing the morbidity and death linked to this condition requires early detection.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

TSC: Tuberous Sclerosis Complex; **BP:** Blood Pressure; **EGFR:** Estimated Glomerular Filtration Rate; **CT:** Computed Tomography; **MRI:** Magnetic Resonance Imaging; **MTOR:** Mechanistic Target of Rapamycin; **TAND:** TSC Associated Neuropsychiatric Disorders.

AUTHOR CONTRIBUTIONS

Every author made a significant impact on the conception and layout, data collection, and creation of the manuscript. They also pledged to assume accountability for the complete report, engaging in its composition or thorough review of essential intellectual aspects, and presenting the final polished version for evaluation by the journal for publication.

ETHICAL CONSIDERATIONS

The authors have conscientiously ensured that ethical matters, including plagiarism, data falsification, and redundant publication, have been thoroughly considered and addressed.

PATIENT CONSENT

Consent was obtained from the Patient upon guaranteeing her to keep the personal information confidential and that anonymity would be preserved.

SUMMARY

The case study delves into the medical history of a 41-year-old female who received a belated diagnosis of Tuberous Sclerosis Complex (TSC), a hereditary condition that leads to benign tumors in various organs. The individual had a background of seizures, cognitive challenges, and was found to have kidney failure necessitating dialysis. Notable TSC indicators identified included facial angiofibroma, enamel pits, and periungual fibromas. Despite severe kidney dysfunction, the typical renal hamartomas were not present, indicating a potential underlying chronic glomerulonephritis. The analysis emphasizes the significance of early detection and consistent monitoring for effective TSC management, emphasizing the wide array of clinical symptoms and the necessity of holistic care to enhance patient prognosis.

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