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NAVIGATING TUBEROUS SCLEROSIS IN A 41-YEAR-OLD PATIENT: CLINICAL INSIGHTS AND MANAGEMENT

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ABSTRACT:

Introduction: 1. Tuberous sclerosis complex (TSC) is a rare genetic disorder distinguished by noncancerous growths in different parts of the body, particularly in the brain, skin, kidneys, heart, and lungs. It is caused by mutations in either the TSC1 or TSC2 genes, which interfere with the mTOR pathway. The range of symptoms associated with TSC can vary greatly, from minor skin manifestations to serious neurological complications such as epilepsy, cognitive deficits, and autism spectrum disorders. **Case Nuances:** 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 and common neurological symptoms of TSC. **Discussion:** 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. **Conclusion:** 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.

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 an average of 1:8000 among live births, irrespective of sexual category. It exhibits a broad range of phenotypic characteristics that differ in intensity. 1. Mutations in the tumor suppressor genes TSC-1 and TSC-2, located on chromosome 9 and chromosome 16 respectively, lead to the development of TSC. TSC-1 encodes the hamartin protein, while TSC-2 encodes the tuberin protein. 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 traditional manifestation seen in childhood is referred to as the Vogt triad, consisting of seizures, facial angiofibroma resembling adenoma sebaceum, and cognitive deficits. 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 convulsions5. However, there is still a small group of patients for whom a diagnosis is not made until maturity. This is typically due to changes in the skin, kidneys, or lungs6. Within the context of our discussion, we explore the scenario of a patient who received a diagnosis of TSC during their fourth decade of life, showcasing unique Radiological and Clinical characteristics.

CASE DETAILS

1. A 41-year-old woman presented to the General Ward unit reporting symptoms including Pedal Edema, facial swelling lasting one week, unilateral headache, shortness of breath during physical activity, palpitations, and brownish-black lesions measuring 2-4 mm on the face and around the nose area for the past week. They were bilateral and symmetrical in nature. Teeth deformities were also seen. On examination, her blood pressure was measured at 210/110 mmHg, suggestive of de-novo Hypertension, the respiratory rate was measured at 13 cycles per minute, and her temperature was 98.6F. Her caretaker reported that she had been suffering from Seizures since 1998, and was on Tab. Phenytoin 100mg twice a day, and Tab. Clobazam 5mg once a day. She had shunted mental growth since childhood. She had a hysterectomy 10 years back.

On systemic examination, she was found to be having Edema over her legs, and her BMI was 30 (overweight, because of her shorter stature). She was given IV Nitroglycerine 5ml/hour to reduce the systolic blood pressure, Prazosin Hcl 2.5mg BD, and Sodium Bicarbonate 1000mg BD. After undergoing the Laboratory Investigations, her Hemoglobin was 5.9g/dL, Serum Chloride levels were slightly elevated (112mg/dL), her serum creatinine levels were higher than the normal levels (6mg/dL), and her urine analysis has shown that Pus Cells were found 6-8/HPF, epithelial cells are 4-6

cells/HPF. The Ultrasonography of the Abdomen has revealed hepatic congestion, cholelithiasis, bilateral contracted kidneys with grade III renal parenchymal changes, and minimal ascites. Based on the Clinical Findings and the Laboratory Investigations, the diagnosis was made as Tuberous Sclerosis.

The treatment given included IV Nitroglycerine 5ml/hour, Recombinant Human Erythropoietin-α 4000U given Sub-cutaneous weekly once, Prazosin Hcl 2.5mg two times a day orally, IV Torsemide 20mg given twice a day, Phenytoin and Clobazam same as the intermediate management given at the admission, Tab. Ferric Pyrophosphate with Vitamin C, B12, and Folic Acid is to be taken once a day, and IV Ferric Carbonate 500mg with 100ml of NS is given Immediately. On day 2 of her admission, she reported difficulty in passing stools and was given Syrup Lactulose 20ml twice a day. After 7 days of Hospital Stay, she was discharged with Tab Torsemide 20mg BD, Tab Prazocin 5mg BD, and Tab. Cilnidpine 20 mg BD, Cap. Multivitamin once a day, Tab. Clobazam 5mg OD, and Tab. Phenytoin 100mg BD. She was asked to follow up after one week.

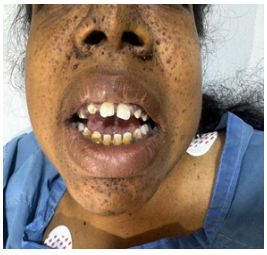

Figure 1 (a)

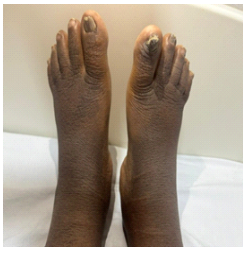

Figure 1 (b)

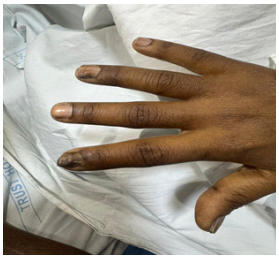

Figure 1 (c)

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

DISCUSSION

Seizures, autism, and behavioral and mental issues are among the most common neurological manifestations of Tuberous Sclerosis. Seizures are present in approximately 83-88% of patients and typically commence within the initial year of life. The spectrum of seizures experienced can vary from mild focal seizures and infantile spasms to generalized seizures.TSC is equally prevalent regardless of gender or race, but symptoms tend to be milder in women 7, 8. The majority of individuals, around 80%, receive a diagnosis of tuberous sclerosis during childhood. However, there are cases where the diagnosis is delayed until late childhood or adulthood, as the typical neurological symptoms and skin abnormalities associated with the disorder tend to diminish over time. Dermatological signs of tuberous sclerosis include facial angiofibroma, hypomelanotic macules (also known as Ash leaf patches), shagreen patches, skin tags, and ungual hamartomas. It is important to note that early diagnosis can have significant benefits, such as cost savings and improved treatment outcomes for patients with tuberous sclerosis. However, diagnosing this condition can be challenging due to its diverse range of clinical characteristics9. Only 35% of cases exhibit the traditional Vogt's trio, which consists of seizures, mental impairment, and cutaneous angiofibroma.

The clinical features of the Tuberous Sclerosis Complex (TSC) stem from abnormal cell growth, proliferation, and migration in the embryonic stage[10]. The TSC1 and TSC2 genes encode hamartin and tuberin, respectively, which are crucial for regulating the mTOR pathway. Disruptions in this pathway can result in hyperactivation, leading to the formation of benign tumors or hamartomas in different parts of the body[11]. Mutations in the TSC2 gene are more prevalent and are linked to more severe neurological issues compared to TSC1 mutations. In instances of familial inheritance, symptoms are typically less severe, with TSC1 gene mutations having a more pronounced effect[12]. A genetic examination of the patient revealed 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. If one of the parents has genetic mutations, the offspring may be in danger by as much as 50%. The two primary diagnostic methods for TSC are genetic testing and the identification of clinical symptoms. 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. 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 individual mentioned in this case report had identical, solid, brownish-black bumps on both sides of their face that projected outwards from the skin. The papules differed in size, ranging from thin and needle-like to larger and resembling broad beans. Consequently, the documented case met all the clinical diagnostic criteria outlined in the 2012 International TSC Conference Consensus Statement.

CONCLUSION

Very few instances of the rare disease tuberous sclerosis complex are identified in adulthood. Recognizing the clinical features of a disease can prompt suspicions and facilitate an early diagnosis, crucial for improving prognosis and enhancing the quality of life through appropriate treatment. TSC may be incidentally detected at any stage of life through the evaluation of clinical manifestations and imaging findings. 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 should be done on everyone suspected of having TSC to rule out the illness. Reducing the morbidity and death linked to this condition requires early detection.

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.

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