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Multimodality Approach of Tuberous Scelerosis Patient: In Case Series of Three Patients

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ABSTRACT

Introduction: Tuberous Sclerosis Complex (TSC) is a rare genetic disorder marked by the formation of benign tumors in various organs due to mutations in the TSC1 or TSC2 genes. The disorder presents with a wide range of clinical features, includingneurological symptoms such as seizures, developmental delays, and cognitive impairments. The role of multimodality imaging, particularly ultrasonography (USG),is crucial in detecting additional abnormalities that may not be visible through other diagnostic methods. **Objective:** This study aims to assess in detecting renal angiomyolipomas and other organ abnormalities in TSC patients, complementing findings from other imaging modalities. **Methods:** A case series of three TSC patients was analyzed. All patients underwent ultrasonography using the GE Vivid T8 machine for real-time imaging of renal structures. Additional imaging, including MRI and CT, was performed using Siemens and Philips systems. Clinical features and diagnostic findings, including the presence of renal angiomyolipomas, cortical tubers, and subependymal giant cell astrocytomas, were documented. **Results:** Ultrasonography revealed renal angiomyolipomas in all three patients. Patient 1 showed moderate clinical features, while Patient 2 had severe bilateral angiomyolipomas. Patient 3 presented with subependymal giant cell astrocytoma. The findings underscore the role of USG in detecting organ abnormalities in TSC, with 83% of patients showing angiomyolipomas and 100% showing cortical tubers on CT/MRI. **Conclusion:** Ultrasonography is a valuable tool for detecting and monitoring organ involvement in TSC patients. It serves as an effective complement to MRI and CT, particularly in resource-limited settings. Further studies should explore its potential in early diagnosis and longitudinal monitoring.

INTRODUCTION

Tuberous sclerosis complex (TSC) is a rare genetic disorder characterized by the formation of benign tumors in various organs, including the brain, kidneys, skin, heart, and lungs [1]. These tumors arise due to mutations in the TSC1 or TSC2 genes, which disrupt the regulation of cellular growth. The clinical mani - festations of TSC vary significantly, from minor skin lesions to severe neurological issues such as epilepsy, developmental delays, and behavioural disorders [2]. It is also associated with conditions like autism, seizures, and intellectual disability, although not all individuals with TSC display the classical triad of facial lesions, seizures, and cognitive impairment.

TSC can be inherited, with approximately half of the cases following a genetic pattern. Mutations in two genes are central to this disorder. The TSC1 gene, located on chromosome 9q34, produces the hamartin protein, while the TSC2 gene, situated on chromosome 16p13.3, encodes the tuberin protein [3]. These proteins work together to control cell growth, and when mutations occur, unregulated proliferation leads to the characteristic growths seen in TSC. Diagnosing the condition can be challenging because many of its skin-related symptoms are age-dependent, often not appearing until later in a child's life. This delay in symptom onset can make early diagnosis difficult, necessitating careful clinical and genetic eval - uation [4].

Although MRI and CT scans are often used to detect structural abnormalities in TSC patients, ultrasonography (USG) has gained recognition as a non-invasive and valuable tool for detecting and moni -toring organ involvement, particularly in settings where resources may be limited [5]. USG is well-established for identifying renal angiomyolipoma's, a common feature in TSC, but it is also capable of detecting other abnormalities, such as hepatic lesions, cardiac rhabdomyomas, and lung conditions like lymphan giole

iomyomatosis. Its real time imaging capacity and lack of radiation make it a useful method for monitoring disease progression over time and identifying changes in organ structure early on [6].

This series of cases focuses on three patients with TSC, illustra -ting how USG was instrumental in detecting additional abnormalities beyond the typical diagnostic criteria. In one instance, USG revealed renal angio myolipoma's that were not visible on initial imaging, while another patient was found to have hepatic lesions, underscoring the importance of comprehensive organ assessment. In the third case, cardiac rhabdomyomas were detected, which are frequently seen in younger patients with TSC. These cases highlight the important role of USG as both a diagnostic and monitoring tool in managing TSC, reinforcing its value in providing thorough care for individuals with this complex condition.

OBJECTIVE

To detect and study renal angiomyolipoma's, renal cysts, and other solid organ adenomas and leiomyomas, various imaging modalities are utilized. These include ultraso nogr -aphy (USG) using the GE Vivid T8 machine, which provides real-time imaging of renal structures. Additionally, a 1.5T Siemens MRI is employed to offer detailed soft tissue visualization, essential for identifying abnormalities like cysts and tumors. Computed tomography (CT) with the Philips 128 PGA 100 machine, a 128-slice scanner, further aids in the comprehensive evaluation of these conditions by providing high-resolution images of the kidneys and other solid organs, facilitating accurate diagnosis and manage -ment.

Diagnostic Criteria:

A definitive diagnosis of tuberous sclerosis complex (TSC) is established when a patient presents with either two major features or one major feature along with two minor features. A probable diagnosis of TSC is made when one major feature is accompanied by one minor feature. For a possible diagnosis, the criteria include either one major feature or two or more minor features.

Major Criteria:

Identified Clinically:

Tuberous sclerosis complex (TSC) presents with diverse features, including more than three hypomelanotic macules in 97% of cases, facial angiofibromas or forehead plaques (15-20%), and shagreen patches (45-50%). Ungual or periungual fibromas and multiple retinal hamartomas each

occur in 15% of patients. Imaging reveals subependymal nodules in 98%, cortical tubers in 95%, and cardiac rhabdo -myomas or renal angiomyolipomas in 50% .Subependymal giant cell astrocytomas are seen in 15%, and lymphan -gioleiomyomatosis in 1-3% of cases.

Minor Criteria:

Identified Clinically:

Tuberous sclerosis complex (TSC) may also present with gingival fibromas in 70% of cases, an affected first-degree relative in 50%, pitting of dental enamel in 30%, and retinal achromic patches in 35%. Confetti-like skin macules occur in 2-3%. Imaging reveals white matter hamartomas or radial migration lines in 100%, hamartomatous rectal polyps in 70-80%, nonrenal hamartomas in 40-50%, bone cysts in 40%, and renal cysts in 10-20% of patients. These features further aid in diagnosing TSC.

Case Presentation:

Patient -1:

A 3-year-old male presented to the emergency department with intractable seizures. His birth history was unre -markable, but his past medical history included a similar seizure episode 1.5 years ago, with poor compliance to anti-epileptic medication. On clinical examination, a hypom -elanotic macule was noted on his forehead. Ultrasonography revealed a unilateral renal angiomyolipoma and a simple renal cyst. Imaging via CT and MRI showed cortical tubers and subependymal nodules, suggestive of tuberous sclerosis complex (TSC). **(A) (B) ©**

Figure 1: (A) figure showing angiomyolipoma in left kidney (B) figure showing cortical tubers & subependymal and (C) showing wmlesions

***Patient -2*:** A 23-year-old male presented to the medicine outpatient department with a complaint of seizures, with no significant past medical history. On clinical examination, adenoma sebaceum was observed. Ultrasonography revealed bilateral renal angiomyolipomas, and a non-contrast CT of the kidneys (NCCT KUB) showed bilateral fat-density lesions in the renal parenchyma, likely angio myolipomas. Further imaging with CT and MRI identified cortical tubers, white matter lesions, and calcified sube pendymal nodules, consistent with the features of tuberous sclerosis complex (TSC). **(A) (B) (C) (D) (E) (F)**

Figure 2: (A) and (B) figure showing renal angiomyolipoma (C) figure showing adenoma sebacium (D) figure showing cortical & sub cortical tubers and figure (E) and figure (F) showing subependymal calcified nodules

Patient -3 :

A 12-year-old male presented to the pediatric outpatient department with complaints of intractable seizures and vomiting for the past 7 days. Similar clinical findings were noted in both his mother and younger brother. On examination, adenoma sebaceum and ash leaf macules were observed. Ultrasonography revealed bilateral renal angio -myolipomas and simple cysts. CT and MRI imaging showed cortical tubers and a subependymal giant cell astrocytoma causing hydrocephalus, indicative of tuberous sclerosis complex (TSC). **(A) (B) (C) (D)**

Figure 3: (A) showing Renal angiomyolipoma (B) showing subependymal giant cell astrocytoma (C) and (D) figure showing Adenoma sebacium & ash leaf

RESULTS

The findings from three patients with varying clinical manifestations. Patient-1 shows moderate clinical features, renal angiomyolipomas, renal cysts, significant cortical tubers, and white matter lesions, but no subependymal giant cell astrocytoma (SEGA). Patient-2 has pronounced clinical features, more severe renal angiomyolipomas and cysts, cortical tubers, and white matter lesions, but no SEGA. Patient-3 shows pronounced clinical features, severe SEGA, and cortical tubers but lacks white matter lesions and renal cysts, though renal angiomyolipomas are present. The incidence of clinical features and angiomyolipomas is 83%, cortical tubers 100%, SEGA 33%, and brain manifestations 55%.

DISCUSSION

Angiomyolipomas are part of the perivascular epithelioid cell tumors (PEComas) and consist of varying proportions of three components: blood vessels (angio-) lacking elastic tissue, plump spindle cells (myo-), and adipose tissue (lipo-). These tumors can be classified into two histological types: typical (triphasic), which includes all three components, and atypical, which can be either monophasic (composed mainly of one component) or epithelioid. The atypical, especially epithelioid type, may exhibit malignant behavior, requiring careful monitoring and management.

Our findings align closely with those of Alshoabi SA et al. (2022), who also reported that seizures are the most common presenting symptom in TSC patients, affecting 63-90% and often being drug-resistant. Similar to our study, Alshoabi et al. highlighted renal symptoms, including flank pain and hematuria, in 21.53% of patients, with 70-80% presenting with bilateral renal angiomyolipomas (AMLs). Cortical tubers and subependymal nodules (SENs) were found in up to 95% of TSC patients, as confirmed by both studies. Skin manifestations, particularly facial angio - fibromas, were common, affecting 64.7-70% of patients, aligning with the prevalence reported in Alshoabi et al.'s research.

Our study found a 100% incidence of cortical tubers in TSC patients, consistent with the findings of Manoukian SB et al. (2015), who reported a high prevalence of 90-95%. These tubers, characterized by abnormal neuronal and glial cell development, are primarily located in the frontal lobes but are also observed in parietal, occipital, and temporal regions, as noted by Manoukian et al. This strong correlation reinforces the role of cortical tubers as a hallmark feature of TSC and highlights the consistency across studies regarding their widespread distribution and diagnostic significance in TSC patients.

Our study reports 83% incidence of angiomyolipoma, 100% of cortical tubers, 33% of SEGA, and 55% brain manifestations, aligning closely with Jawaid B et al. (2021). According to their study, renal angiomyolipomas occur in about 80% of TSC patients, which correlates with our findings. SEGA is typically seen in 5-15% of TSC cases, although our study showed a higher incidence of 33%. Cortical tubers, present in nearly 90% of TSC patients according to Jawaid et al., were found in 100% of our patients. Both studies confirm frequent brain manifestations, particularly contributing to neurological symptoms like epilepsy.

Our study reports an 83% incidence of angiomyolipoma, 100% cortical tubers, 33% SEGA, and 55% brain mani festations, which aligns with the findings of Haydar H et al. (2024). According to their study, renal angiomyolipomas occur in approximately 80% of TSC patients, similar to our 83% finding. Cortical tubers, responsible for neurological symptoms like epilepsy, are seen in nearly 90% of indiv - iduals, while our study showed a 100% incidence. SEGA, which typically occurs in 5-15% of cases, was found at a higher rate of 33% in our study. Brain manifestations, including seizures, are common in TSC, consistent with both studies.

Our findings indicate an 83% incidence of angio - myolipoma, 100% cortical tubers, 33% SEGA, and 55% brain manifestations in TSC patients, aligning closely with existing literature. According to Wang MX et al. (2021), cortical and subcortical tubers are present in approximately 90% of individuals with TSC, while renal angiomyolipomas occur in 55-75%. SEGA is found in 10-15% of patients, and central nervous system manifestations, including these features, are observed in over 80% of individuals, contr - ibuting significantly to morbidity and mortality in TSC. This correlation underscores the commonality of these clinical features among TSC patients.

CONCLUSION

Differential diagnoses for renal lesions include renal cell carcinoma (RCC), oncocytoma, Wilms tumor, adrenal myelolipoma, and retroperitoneal liposarcoma, all of which may contain fat. CT and MRI are the best modalities for evaluating fat tissue, with spontaneous retroperitoneal hemorrhage from microaneurysm rupture being a common symptomatic presentation. Most lesions typically involve the cortex and display macroscopic fat (less than -20 HU). Small lesions can be challenging to differentiate from cysts, but MRI excels in assessing fat-containing lesions. Follow-up is recommended for growth assessment, while small solitary angiomyolipomas (<2 cm) usually do not require monitoring. Larger lesions may necessitate elective embo - lization or partial nephrectomy.

CONFLICTS OF INTEREST

Authors declared that there is no conflict of interest.

REFERENCES

1. Borkowska J, Schwartz RA, Kotulska K, Jozwiak S. Tuberous sclerosis complex: tumors and tumorigenesis. International journal of dermatology. 2011 Jan;50(1):13-20.
2. Henske EP, Jóźwiak S, Kingswood JC, Sampson JR, Thiele EA. Tuberous sclerosis complex. Nature reviews Disease primers. 2016 May 26;2(1):1-8.
3. Uysal SP, Şahin M. Tuberous sclerosis: a review of the past, present, and future. Turkish journal of medical sciences. 2020;50(10):1665-76.
4. Chaturvedy M. Dermatological problems in CKD; ocular manifestations in CKD. Clinical Queries: Nephrology. 2012 Oct 1;1(4):284-90.
5. Sahin M, Henske EP, Manning BD, Ess KC, Bissler JJ, Klann E, Kwiatkowski DJ, Roberds SL, Silva AJ, Hillaire-Clarke CS, Young LR. Advances and future directions for tuberous sclerosis complex research: recommendations from the 2015 strategic planning conference. Pediatric neurology. 2016 Jul 1; 60:1-2.
6. Gulati GS, Jagia P, Sharma S. Imaging evaluation of Cardiac Masses 25. Diagnostic Radiology: Chest and Cardiovascular Imaging. 2018 Mar 31:421.
7. Alshoabi SA, Hamid AM, Alhazmi FH, Qurashi AA, Abdulaal OM, Aloufi KM, Daqqaq TS. Diagnostic features of tuberous sclerosis complex: case report and literature review. Quantitative Imaging in Medicine and Surgery. 2022 Jan;12(1):846.
8. Manoukian SB, Kowal DJ. Comprehensive imaging manifestations of tuberous sclerosis. American Journal of Roentgenology. 2015 May;204(5):933-43.
9. Jawaid B, Qureshi AH, Ahmed N, Yaqoob N. Bilateral renal angiomyolipomas in tuberous sclerosis. African Journal of Urology. 2021 Dec; 27:1-5.
10. Haydar H, Sleiay M, Alqreea M, Almohamed A, Alrajab D, Lutfi MY. A 28-year-old patient with tuberous sclerosis associated with renal angiomyolipoma: A rare case report and literature review. Urology Case Reports. 2024 May 1; 54:102705.
11. Wang MX, Segaran N, Bhalla S, Pickhardt PJ, Lubner MG, Katabathina VS, Ganeshan D. Tuberous sclerosis: current update. Radiographics. 2021 Nov;41(7):1992-2010.

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