International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Diagnostic Features of Tuberous Sclerosis Complex: Case Report and Literature Review

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Abstract: ***Background: Tuberous sclerosis complex (TSC) is a rare genetic disorder characterized by the development of benign tumours in multiple organs, including the brain, kidneys, heart, and skin. Radiological imaging plays a crucial role in the diagnosis and management of TSC, providing insights into the extent and progression of the disease. Case Presentation: We present the case of a 17-year-old girl presented with new-onset seizures. Neuroimaging studies, including magnetic resonance imaging (MRI) of the brain, revealed multiple cortical tubers, subependymal nodules, which are characteristic radiological features of TSC. Conclusion: Radiological imaging is indispensable in the diagnosis and monitoring of tuberous sclerosis complex. Awareness of characteristic radiological findings, such as cortical tubers, subependymal nodules, and renal angiomyolipomas, is crucial for early detection and appropriate management of patients with TSC. This case underscores the importance of interdisciplinary collaboration between radiologists, neurologists, and geneticists in the comprehensive care of individuals with tuberous sclerosis complex.***

Keywords: Tuberous sclerosis complex (TSC); clinical diagnostic criteria; major features; minor features; subependymal nodules (SENs); renal angiomyolipoma (AMLs); cardiac rhabdomyomas

1. Introduction

Tuberous sclerosis complex (TSC) is a rare genetic disorder characterized by the development of benign tumours in multiple organs, including the brain, kidneys, heart, lungs, and skin. It is caused by mutations in either the TSC1 or TSC2 genes, leading to dysregulated cellular proliferation and differentiation. The prevalence of TSC is estimated to be 1 in 6,000 births, making it a relatively uncommon but clinically significant condition.

Clinical manifestations of TSC can vary widely, ranging from dermatological findings such as facial angiofibromas and hypomelanotic macules to more severe neurological and systemic complications. Neurologically, TSC is associated with the formation of cortical tubers, subependymal nodules, and subependymal giant cell astrocytoma (SEGA), which are key radiological features crucial for diagnosis and management.

Radiological imaging, particularly magnetic resonance imaging (MRI) and computed tomography (CT), plays a pivotal role in the diagnosis and monitoring of TSC. These imaging modalities not only aid in identifying characteristic lesions but also provide valuable information about lesion size, location, and progression over time. Early detection and accurate characterization of TSC-related lesions through radiological imaging are essential for timely intervention and management.

In this case report, we present the radiological findings of a patient with TSC, highlighting the characteristic features observed on MRI and other imaging modalities. Through this case, we aim to underscore the importance of radiological assessment in the comprehensive evaluation and management of tuberous sclerosis complex.

2. Case Report

A 17-year-old female presented to our neurology clinic with a history of recurrent seizures and developmental delay since early childhood. Her medical history included multiple hospital admissions for seizure management and developmental assessments.

Clinical Examination:
On examination, the patient appeared developmentally delayed with mild cognitive impairment. Neurological examination revealed no focal deficits. Dermatological examination showed facial angiofibroma and hypomelanotic macules, consistent with the characteristic cutaneous manifestations of TSC.

Based on these clinical features and radiology findings, this case was diagnosed as TSC.

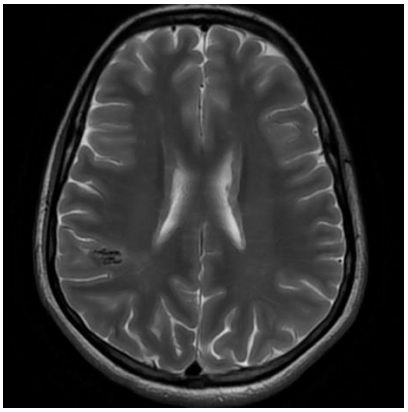

Figure 1: T2 axial section shows hypointense lesion noted in the left parietal region and hypointense subependymal nodules along left lateral ventricle margins.

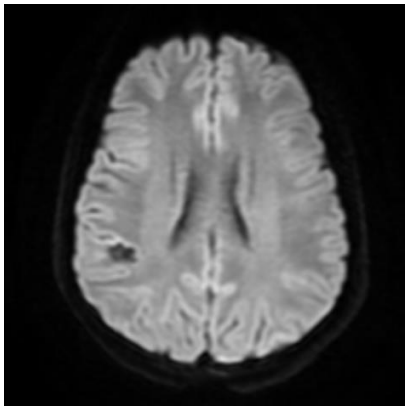

Figure 2: GRE sequence shows hypo intensity in the corresponding region confirming it a calcified cortical nodule.

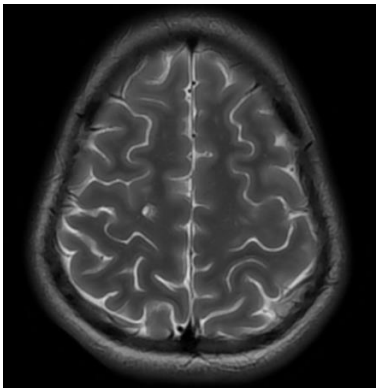

Figure 3: T2 axial section shows hyperintense lesion in right high frontal region.

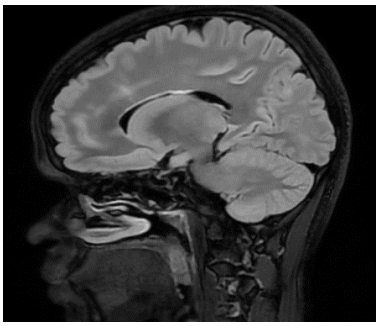

Figure 4: T2 FLAIR sagittal section showing multiple hyperintense radial bands along the bilateral frontal and parietal white matter regions.

3. Discussion

Tuberous sclerosis complex (TSC) is a genetic disorder characterized by the development of benign tumors or hamartomas in multiple organs, including the brain, kidneys, heart, lungs, and skin. Radiological imaging, particularly magnetic resonance imaging (MRI) and computed tomography (CT), plays a crucial role in the diagnosis, characterization, and management of TSC-related lesions.

Brain Imaging Findings:

1) **Cortical Tubers:**
   Cortical tubers are one of the hallmark radiological features of TSC. These lesions appear as areas of abnormal cortical thickening and hyperintensity on T2-weighted and FLAIR sequences of MRI. They are typically located in the cerebral cortex, often in the frontal and temporal lobes, and are associated with neuronal migration abnormalities and gliosis.
2) **Subependymal Nodules (SENs):**
   Subependymal nodules are small, non-enhancing lesions located along the walls of the lateral ventricles. They are best visualized on MRI and can occasionally show calcifications on CT scans. SENs are considered precursor lesions to subependymal giant cell astrocytoma (SEGAs), which are larger and may exhibit growth over time.
3) **Subependymal Giant Cell Astrocytoma (SEGAs):**
   SEGAs are low-grade tumours that arise from subependymal nodules and can obstruct cerebrospinal fluid flow, leading to hydrocephalus. MRI is crucial in monitoring the size and growth of SEGAs, as surgical intervention may be necessary if there is significant mass effect or hydrocephalus.

Other CNS Manifestations:

- **White Matter Lesions:**
  Diffuse white matter abnormalities may be observed on MRI in patients with TSC, reflecting underlying demyelination or gliosis associated with cortical tubers.
- **Epileptogenic Zones:**
  Cortical tubers and their associated abnormalities are often epileptogenic, contributing to the high incidence of epilepsy in patients with TSC. Identification of these lesions through imaging helps guide surgical planning for epilepsy management.

Abdominal Imaging Findings:

Renal Angiomyolipoma (AMLs):
Renal AMLs are common in TSC and can be detected by ultrasound, CT, or MRI. They typically present as hyperechoic or heterogeneous masses containing fat, smooth muscle, and blood vessels. Serial imaging is essential to monitor for growth and potential complications such as haemorrhage or renal impairment.

Cardiac and Pulmonary Imaging:

- **Cardiac Rhabdomyomas:**
  These benign tumors are frequently found in infants with TSC and can be detected prenatally or early in life using echocardiography. They often regress spontaneously but may require monitoring for potential complications such as arrhythmias or outflow tract obstruction.
- **Pulmonary Lymphangioleiomyomatosis (LAM):**
  LAM, characterized by the proliferation of smooth muscle cells in the lungs, primarily affects adult women with TSC. High-resolution CT is used to evaluate the extent of pulmonary involvement and guide management strategies.

Discussion Points:

- **Diagnostic Challenges:**
  While MRI and other imaging modalities are valuable in diagnosing TSC, the variability in lesion presentation and evolution poses diagnostic challenges. Clinicians must correlate imaging findings with clinical manifestations and genetic testing results for accurate diagnosis and management.
- **Monitoring and Management:**

Regular surveillance imaging plays a crucial role in monitoring disease progression, assessing treatment efficacy, and detecting potential complications in patients with TSC. Individualized management strategies, including pharmacotherapy and surgical interventions, are guided by radiological findings and multidisciplinary collaboration.

- **Research and Future Directions:**
  Advances in imaging techniques, such as functional MRI and diffusion tensor imaging, hold promise for better understanding the pathophysiology of TSC-related brain lesions and optimizing treatment approaches. Continued research is needed to elucidate the natural history of TSC and improve imaging protocols for early detection and intervention.

4. Conclusion

Any age group and ethnicity might be affected by TSC in both males and girls. Finding characteristics and making a diagnosis of TSC depend heavily on medical imaging. On the other hand, clinical characteristics are the primary cause of suspected TSC instances and patient illness investigation. We disclosed two instances of TSC. According to the literature, neurological symptoms, such as seizures, were frequently the first indicators of TSC that prompted an examination and diagnosis.

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