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NAVIGATING THE MULTIFACETED NATURE OF TUBEROUS SCLEROSIS COMPLEX IN A YOUNG FEMALE: A CASE REPORT

Radio-Diagnosis

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ABSTRACT

Tuberous sclerosis is an autosomal dominant neurocutaneous disorder with a broad spectrum of clinical manifestations affecting multiple organs. This case report presents a detailed study of a 25year old female patient who exhibited an intricate constellation of symptoms and signs related to TSC (Tuberous Sclerosis Complex). The patient's clinical presentation included headache, giddiness, breathlessness, seizures, angiofibromas on the centrofacial areas, shagreen plaques and periungual fibromas. Radiological assessments revealed multiple subependymal nodules, SEGA (Subependymal Giant Cell Astrocytoma), cortical tubers, LAM (Lymphangioleiomyomatosis), bilateral renal angiomyolipomas (AML), sclerotic bone lesions in body, pedicle and spinous process of vertebrae. This case underscores the importance of a comprehensive and multidisciplinary approach to diagnose TSC, as it encompasses various clinical domains such as radiology, neurology, dermatology and nephrology. Insights gained from this rare case contribute to the better understanding of TSC and may aid in improving the care and outcomes of affected individuals.

KEYWORDS

Tuberous sclerosis, SEGA, subependymal nodules, angiomyolipomas, Tuberous Sclerosis Complex.

INTRODUCTION

Tuberous sclerosis is a rare genetic disorder characterised by the formation of noncancerous tumours in various organs, including the brain, skin, heart, lungs, kidneys and bones, presents a myriad of clinical manifestations that can manifest with varying severity in affected individuals [1] [2]. The clinical spectrum of TSC is remarkably wide, with symptoms ranging from benign skin abnormalities to life threatening complications such as seizures, intellectual disabilities and renal complications. Understanding the diverse clinical manifestations is essential for providing comprehensive care and tailored treatment approaches.

Furthermore, TSC is primarily driven by mutations in the TSC1 gene located on 9th chromosome encoding hamartin or TSC2 gene located on 16th chromosome encoding tuberin [3]. These are tumour growth suppressor proteins, which regulate the mechanistic target of rapamycin(mTOR) pathway [4]. This intricate genetic foundation adds another layer of complexity to TSC, as mutations can vary in type and location, leading to variable phenotypic expressions. To comprehensively address the multifaceted nature of TSC, a thorough exploration of the clinical features, radiological imaging findings and the underlying molecular pathway is imperative. TSC represents a challenging puzzle within the realm of medical genetics and neurology.

This case report of 25year old female patient who was referred to the department of radiodiagnosis, GMC Miraj for MRI Brain, aims to unravel the layers of complexity surrounding the TSC, shedding light on its diverse clinical presentation and imaging findings.

Case Report

Here in we report a case of 25year old female patient, who presented with complaints of chronic intermittent headache, giddiness, breathlessness, back ache and decreased appetite for 1 month, was referred to the department of radiodiagnosis, GMC Miraj for MRI brain. The patient presents a previous medical history marked by generalised tonic-clonic seizures, which commenced at the tender age of 2 years, with the most recent episode occurring approximately a decade ago.

On general physical examination, vital signs were found to be normal. Multiple well defined variable sized erythematous firm nodules noted over face, particularly on the central region – angiofibromas. Multiple well-defined raised skin coloured thick and rough plaques noted over back - shagreen patch. Firm small nodules noted in relation to nail beds-periungual fibromas in fingers and toes.

Contrast enhanced MRI brain scan done using Hitachi Airis Elite machine in our institution revealed multiple variable sized round to oval calcified hyperintense T1WI and hypointense T2WI lesions along the walls of bilateral lateral ventricles of brain- subependymal nodules and multiple cortical tubers in bilateral cerebral hemispheres and multiple well defined sclerotic lesions in diploic space of cranium.

NECT brain scan done using Siemens Somatom Definition AS 128 slice CT scan showed multiple hyperdense calcified subependymal nodules along the walls of bilateral lateral ventricles and multiple hypodense cortical tubers in bilateral cerebral hemispheres. NECT scan of the abdomen showed multiple variable sized renal masses containing macro fat consistent with angiomyolipomas. NECT scan of spine showed multiple well defined sclerotic lesions in body, pedicle and spinous process of vertebrae.

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

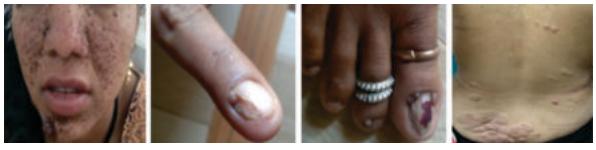

Figure 1. Clinical photograph of the patient showing angiofibromas predominantly involving centrofacial region, Periungual fibromas and Shagreen patches

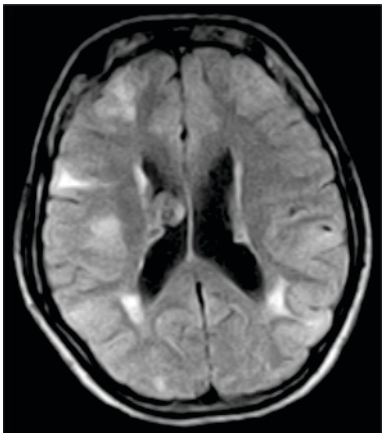

Figure 2. MRI, Axial FLAIR image showing cortical and subcortical tubers in right frontal lobe and bilateral parietal lobes.

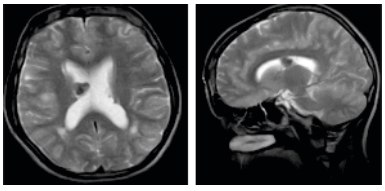

Figure 3. MRI, T2W axial(A) and Sagittal (B) images showing Calcified subependymal nodules

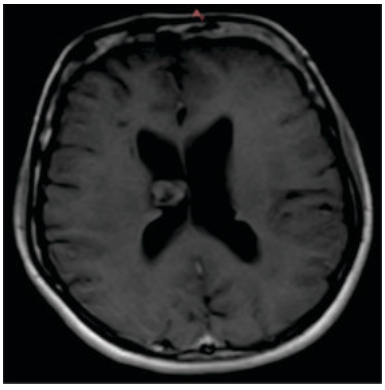

Figure 4. MRI, Axial FatSat contrast enhanced image showing Subependymal nodule along the wall of right lateral ventricle.

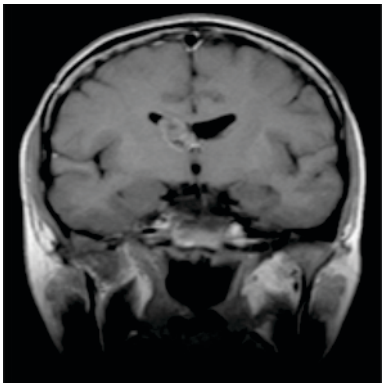

Figure 5. MRI, Coronal FatSat contrast enhanced image showing Subependymal Giant cell Astrocytoma in frontal horn of right lateral ventricle.

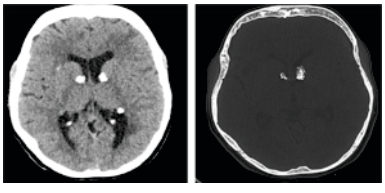

Figure 6. CT, Brain and bone window axial images showing calcified Subependymal nodules along the walls of bilateral lateral ventricles and multiple bony islands in diploic space of frontal bone.

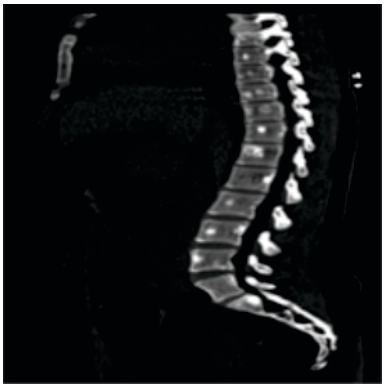

Figure 7. CT Spine, Bone window sagittal image showing calcified multiple bony islands in body , pedicle and spinous process of vertebrae.

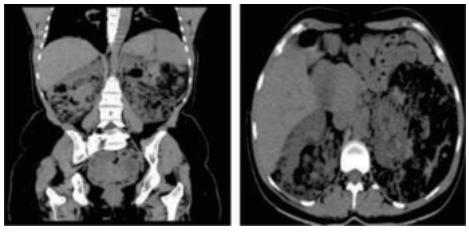

Figure 8. NCCT, Abdomen coronal and axial images showing multiple angiomyolipomas in bilateral kidneys.

DISCUSSION

Tuberous sclerosis complex is an autosomal dominant multisystem disorder consequent to mutation in either the TSC1 gene or the TSC2 gene. The TSC1 gene is located on long arm of chromosome number 9 and the TSC2 gene is located on short arm of chromosome number 16. Hamartin encoded by TSC1 gene and Tuberin encoded by TSC2 gene, regulate mTOR pathway, normally by keeping RHEB in an inactive state. In TSC, mutation of hamartin/tuberin cause disinhibition of RHEB and subsequent overactivation of mTOR pathway which leads to uncontrolled cell proliferation and hamartoma formation in various organs.

Tuberous sclerosis patients usually present in childhood with classic triad of seizures, intellectual disability and adenoma sebaceum [5]. However, this classic triad is present only in 30% of patients. Therefore, diagnostic criteria have been developed and revised by Tuberous sclerosis complex consensus group [6]. It includes genetic criteria and clinical criteria. The definitive diagnosis of TSC is considered if pathogenic mutations are present or when 2 major or 1 major and 2 minor features are present. The possible diagnosis of TSC is considered when 1 major or more than or equal to 2 minor features are present.

Major features:	Minor features:
1. Hypomelanotic macule (>2 in number, >4 in diameter)	1. Dental enamel pits
2. Angiofibromas or fibrous cephalic plaque (>2).	2. Intraoral fibromas.
3. Ungual fibromas (>1)	3. Retinal achromic patch
4. Multiple retinal hamartomas	4. Multiple renal cysts.
5. Shagreen patch	5. Nonrenal hamartomas
6. Cortical dysplasia	
7. Subependymal nodules	
8. SEGA	
9. Cardiac rhabdomyoma.	
10. LAM.	
11. Angiomyolipomas.	

In several instances, diagnosis is made incidentally; hence, the recognition of clinical features, the performances of radiological imaging and genetic testing are considered essential for achieving a timely diagnosis [6] [7].

Multidisciplinary and symptomatic management is imperative due to the extensive array of clinical manifestations witnessed in patients with TSC [5]. Regular follow up is deemed necessary to prevent complications that can jeopardize organ functions : Brain MRI every1-3 year; echocardiogram every 1-3 year in patients with rhabdomyomas; electrocardiogram every 3-5 year; high resolution chest CT every 5-10 year in females older than 18 year; dental examination twice a year; skin examination once a year; detailed ophthalmic examination once a year in patients with vision concerns or retinal lesions(sooner if they are receiving treatment with vigabatrin).

CONCLUSION

Tuberous sclerosis is a complex genetic disorder with diverse clinical manifestations affecting multiple organs. Early diagnosis and multidisciplinary approach to management are crucial to optimizing the quality of life for patients with TSC. This case report of a 25year old female with its intricate constellation of imaging findings and clinical features contributes to the growing body of knowledge surrounding TSC. It serves as a reminder of the diverse and complex nature of this neurocutaneous disorder. It reinforces the necessity of a comprehensive approach for diagnosis. By pooling knowledge from such cases, we can continue to improve the care and outcomes of individuals affected by TSC.

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