

Acute onset psychosis in a patient of tuberous sclerosis: A rare entity

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ABSTRACT

The Tuberous Sclerosis Complex (TSC) is a multisystem autosomal dominant condition occurring due to mutations in the TSC1 or TSC2 genes affecting around 1 in 20,000 people. TSC is inclusive of tumours of skin, kidney, brain, lung and heart as well as neurological conditions like seizures, autism spectrum disorder and intellectual disability. An array of neuropsychiatric illness known as TSC-associated neuropsychiatric diseases (TAND) are identified in around 90% of people with TSC. Among them, psychosis has been reported only in around 2.3% of cases globally and rarely from India. The Indian data of psychosis in patients of TSC is very sparse. Hereby, we report a case of a 20-year-old male who presented with symptoms of acute psychosis, catatonia and drug induced extrapyramidal symptoms (EPS) and MRI brain showed features suggestive of tuberous sclerosis complex.

Keywords: Tuberous sclerosis complex, Catatonia, Acute psychosis, Adenoma sebaceum, Cortical tubers, Subependymal Giant cell astrocytoma.

1. INTRODUCTION

Tuberous sclerosis complex (TSC), an autosomal dominant genetic condition occurring due to mutations in either TSC1 (encoding hamartin) or TSC2 (encoding tuberin). It has an incidence of about 1 in 20,000 people or 1 in 6,000 to 10,000 live births (Zamora and Aeddula, 2022). It is commonly diagnosed in childhood as majority of individuals present with dermatological manifestations and neurological abnormalities like childhood onset epilepsy, developmental delays in their early childhood. It is a multi-system disorder causing tumours of brain, kidney, heart, skin and lungs (Crino et al., 2006). This disorder involves various systems and the clinical representation is quite distinguishable including sub ependymal giant cell astrocytoma, cortical tubers, cardiac rhabdomyosarcoma occurring prenatally, renal angiomyolipoma, facial angiofibromas, hypomelanotic macules, adenoma sebaceum and pulmonary lymphangiomyomatosis (Henske et al., 2016). Apart from above mentioned abnormalities, an array of neuropsychiatric illness known as TSC-associated neuropsychiatric diseases (TAND) are identified in around 90% of people with TSC. There are six tiers of TAND expressions that have been identified: Intellectual, psychiatric, academic,

neuropsychological, behavioural and psychosocial. At psychiatric level, only 2.3% of TSC patients experience psychosis, compared to cases of attention deficit hyperactivity disorder (ADHD; 30–40%), autism spectrum disorders (ASD; 40–50%) and anxiety and depressive disorders (27–56%) (De-Vries et al., 2020). Hereby the indexed patient is a male who is 20 years old with acute onset psychosis with catatonia with drug induced extrapyramidal symptoms (EPS) with predominant visual hallucinations suspecting an underlying brain pathology and MRI brain showed features suggestive of tuberous sclerosis.

2. CASE DESCRIPTION

A patient who is 20 years old, having history of delayed milestones and poor academic performance with family history of Alcohol dependence syndrome and Cannabis use disorder in father presented to psychiatry OPD with fearfulness, suspiciousness, refusal to eat, hallucinatory behavior and disorganized behavior for 4 days. Previously he was diagnosed with childhood-onset epilepsy and intellectual disability with behavioral disturbances for which he was regularly receiving oral anticonvulsants and antipsychotics. On examination, there were a few catatonic symptoms in the form of staring, posturing and grimacing as well as extrapyramidal side effects such as marked cogwheel rigidity, hypersalivation, slowness of movements and postural tremors in upper limbs. Additionally, adenoma sebaceum was noticed on face over nose, nasolabial folds and cheeks. On mental status examination, he predominantly had visual hallucinations along with delusions of reference and persecution, cognitive functions were impaired. On assessment, intellectual quotient (IQ) was 41, suggesting a moderate intellectual disability, Modified Simpson Angus Scale (MSAS) score was 12 suggested severe degree of movement disorder, Bush-Francis Catatonia Rating Scale (BFCRS) score was 14. All basic investigation (CBC, LFT, KFT, TFT, S. electrolytes, RBS, ECG) were within normal limits. MRI brain done in view of visual hallucinations showed the presence of subependymal nodule, subependymal giant cell astrocytoma and cortical tubers, which were suggestive of tuberous sclerosis (Figure 1) which prompted a neurosurgery reference. No active surgical intervention was advised as no entrapment of nearby structure was seen; rather 6 monthly MRI was advised to check the progress of the tumour in future. His acute symptoms resolved over a week after treatment with inj. Promethazine, oral trihexyphenidyl 4 mg and oral Olanzapine 5 mg which was later titrated to 15 mg. After 2 months of continued treatment the caregiver reported overall improvement in psychotic and behavioral symptoms.

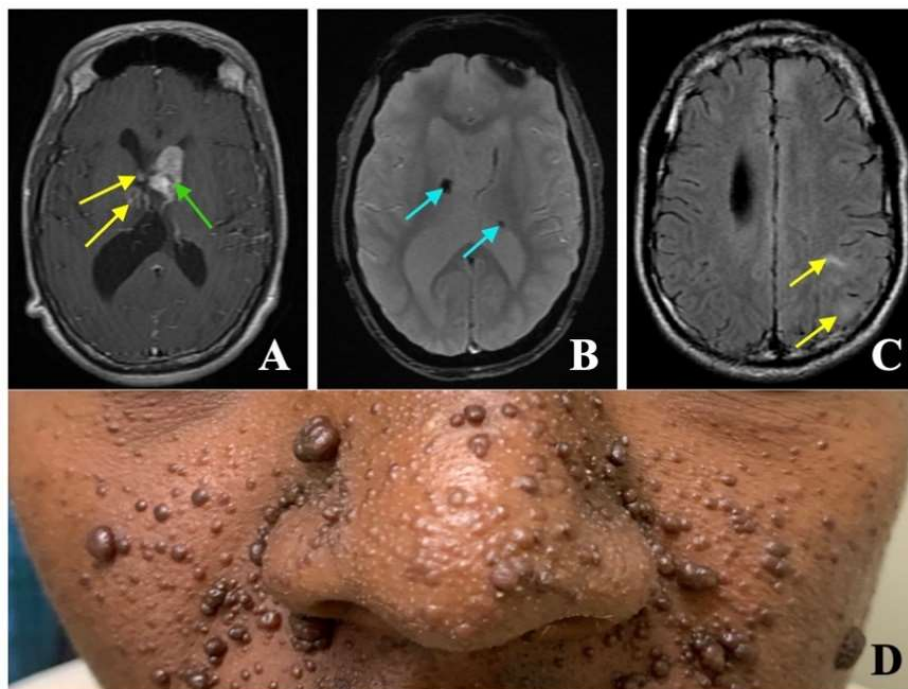


Figure 1 A) Contrast enhanced axial images shows Subependymal Giant Cell Astrocytoma (SEGA) (green arrow)-Enhancing lobulated solid cystic lesion appearing to arise from the septum pellucidum, Calcified subependymal nodules (yellow arrows)-peripherally enhancing altered signal intensity focal lesions in the subependymal region of bilateral lateral ventricles. B) GRE axial image shows blooming (blue arrows) represents calcified subependymal nodules. C) Flair axial images show cortical tubers (yellow arrows)-triangular and linear hyperintense areas in the cortex and juxtacortical region in left high parietal lobe. D) Facial angiofibroma (Adenoma sebaceum)

3. DISCUSSION

Tuberous sclerosis complex is usually diagnosed in childhood due to its early clinical presentation. Vogt in 1908 described a “classic triad” of tuberous sclerosis including seizures, adenoma sebaceum and mental retardation. Despite the obvious “clinical triad”, the clinicians find it challenging to diagnose a case of tuberous sclerosis complex. As per studies, this triad is present in just 29% of people who have been diagnosed with TSC and 6% of these patients do not exhibit all three symptoms (Staley et al., 2011). Therefore, in certain circumstances, a bad prognosis is the result of a misdiagnosis or a delay in diagnosis. So, it's important to get a full diagnostic workup including brain imaging during the progression of illness. Identifying TAND is also very challenging for clinicians. Although Intellectual disability is seen in around 50% of patients with TSC but cognitive impairment is not always present. The distribution of cognitive ability is bimodal, with one-third of the population having profound and half of the population having normal IQ (David et al., 2009). Psychosis however is reported only in 2.3% patients of TSC globally, compared to other psychiatric manifestations. The Indian data of psychosis in patients of TSC is very sparse. The major CNS pathological manifestations of tuberous sclerosis include cortical tubers being the hallmark feature of TSC along with SEN and SEGA (Holmes and Stafstrom, 2007). Due to their slow growth and lack of invasiveness, SEGA are best treated by surgical removal, which has been linked to great clinical outcomes and low morbidity and death. In contrast, the tumour is more likely to affect and invade neighbouring structures like the hypothalamus, genu of internal capsule and basal ganglia. Therefore, if discovered at later stages, performing a surgical resection is likely to be linked with increased rate of morbidity (Roth et al., 2013). Presence of SEGA in contrast enhanced MRI in our patient prompted a neurosurgical reference. Since no mass effect or midline-shift was noticed, surgical resection was not advised; rather 6 monthly MRI was advised to check further progression of the tumour in the future. After 2 months of continued treatment the caregiver reported improvement in psychotic and behavioural symptoms.

4. CONCLUSION

Therefore, this case highlights the fact that although rare, but Tuberous Sclerosis can present as acute psychosis in adolescent and early childhood and thus it should be suspected in patients having complex neurological manifestations, such as marked visual hallucinations, catatonia and epilepsy.

Contribution of Authors

Uniform contributions have been put into the study by each author.

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Informed Consent

Informed consent was taken from the patient and informant for conducting the study.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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