Acute Psychosis and Epileptic Encephalopathy as a Preliminary Symptom Leading to the Diagnosis of Tuberous Sclerosis Complex in an Adolescent

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Abstract

Introduction: Tuberous sclerosis complex (TSC) is an autosomal dominant, variably expressed multisystemic disease. TSC-associated neuropsychiatric disorders (TAND) present at multilevel, and probably are underestimated in terms of both assessment and treatment.

Case: We present a 16-year-old boy with epilepsy and psychosis, presenting with auditory hallucinations and grandiose delusions. He did not benefit from risperidone treatment. He had generalized seizures and his electroencephalogram showed generalized periodic epileptiform activity alternating with attenuation periods. Hypopigmented macules on examination combined with neuroimaging findings including cortical and subcortical tubers with radial bands lead to the diagnosis of TSC.

Discussion: There is an age-related variation in the expression of TAND in terms of behavioral, intellectual, psychosocial and psychiatric levels. Acute psychosis with epileptic encephalopathy may be a presenting feature in adolescence, and should be managed in parallel with antiepileptic treatment.

Keywords

Acute psychosis, Adolescent, Tuberous Sclerosis, Epileptic encephalopathy

Introduction

Tuberous sclerosis complex (TSC) is a multi-systemic disease with an autosomal dominant inheritance involving many organs and systems. Characteristic skin lesions are hypopigmented macules, angiofibromas, shagreen patches and ungual fibromas [1]. Central nervous system (CNS) involvement is present in approximately 90% of individuals with a variety of pathological lesions including cortical or subcortical tubers, subependymal nodules, giant cell astrocytomas, white matter migration lines leading to epilepsy, cognitive problems, and neuropsychiatric disorders [2-4]. Psychiatric comorbidities, although consistently prevalent in different studies, are often under-diagnosed [5]. TSC manifests a range of neuropsychiatric problems at various levels with behavioral, intellectual, psychosocial components, which are collectively termed as TSC-associated neuropsychiatric disorders (TAND). Predominant psychiatric diagnoses in childhood include autistic spectrum disorders (40-50%), attention deficit hyperactivity disorder (30-50%), whereas in adolescence and adulthood anxiety and mood disorders are more common [6]. About half of the patients with TSC have varying degrees of intellectual disability, which may additionally challenge both the diagnosis and management of psychiatric manifestations [6].
Here we present a teenage boy who has been followed for intractable epilepsy for 4 years and psychiatric complaints for 2 years. He presented to our hospital with grandiose delusions, auditory hallucinations and generalized convulsions.

**Case Report**

A 16-year-old adolescent was referred to our hospital for delusions. His first complaints were seizures at the age of 12. Seizures were generalized tonic clonic in nature and resistant to phenytoin, levetiracetam, carbamazapine and vigabatrin. Before the diagnosis of epilepsy his school grades were average and he didn’t have any behavioral problems. Following the seizures he became aggressive, he had a dramatic drop in grades and he dropped out of school. His physical and sexual development were normal. Two years later his impulsive and aggressive behaviors gradually increased with accompanying delusions and hallucinations started. Commanding auditory hallucinations, visual hallucinations and grandiose delusions showed a prominent progression in the last two months. Grandiose delusions were fleeting and mostly religious. Some days he claimed to be a prophet, a fireman or a world-class soccer player. He was admitted to the child and adolescent psychiatry clinic when he was on risperidone 2 mg, phenytoin 300 mg, carbamazapine 1200 mg, levetiracetam 2000 mg, and vigabatrin 3000 mg treatment for almost two years. There was no family history of epilepsy, a psychotic or a bipolar disorder.

Diminished eye contact, decreased personal hygiene, decreased speech, decreased attention, incongruent affect, grandiose delusions, auditory and visual hallucinations were predominant features in his mental examination. Physical examination revealed hypopigmented macules and extrapyramidal signs. There were no ungual fibromas at finger or toe nails.

Electroencephalogram (EEG) showed generalized periodic epileptiform activity alternating with attenuation periods (Figure 1A). Cranial magnetic resonance imaging (MRI) showed cortical tubers and radial band formation.

**Discussion**

Psychotic symptoms are hallmarks of schizophrenia, but psychosis is also observed in mood disorders (such as bipolar disorder), epilepsy, brain tumors, central nervous system infections and intoxications [7]. Our patient had EEG abnormality and associated epileptic seizures.

Although lacking an established pathophysiology and consistency, epilepsy is considered as a risk factor for psychosis. According to a recent meta-analysis, pooled prevalence of psychosis in epilepsy is 5.6%, and 7% in temporal lobe epilepsy [8]. This rate is found to be 7.8 times higher than in people without epilepsy [8]. Psychosis in epilepsy generally exhibits mood instability, anxiety, hallucinations, delusions and confusion. It can be classified according to the temporal relationship to the seizures as ictal, postictal, and interictal psychosis. Ictal psychosis is associated with a focal onset status with altered consciousness. Postictal psychosis begins after a seizure following a lucid interval of a few days. Interictal psychosis is not strictly related to seizures, can be short-lasting or chronic [9]. Patients with intractable and early-onset seizures, with secondary generalization of seizures, using certain anticonvulsant drugs, and who had temporal lobectomy are suggested to have an increased risk of psychosis [10]. Our patient had uncontrolled seizures, ongoing EEG abnormalities and exposure to multiple antiseizure medications which might be at least partially responsible for his psychiatric problems. However, clinical amelioration of seizures and psychotic findings without a significant improvement in EEG patterns suggests that psychiatric symptoms might be an independent component and epileptic encephalopathy is not the only underlying pathophysiology of psychosis in this patient.

Neuropsychiatric problems in TSC are common. A new terminology, TAND, covers difficulties in behavioral, psychiatric, intellectual, academic, neuropsychological, and psychosocial levels. More than 90% of patients with TSC are likely to have some of these challenges, however due to under-recognition, the treatment gap is high, supposedly 70% [11, 12]. Psychiatric problems may be missed/overlooked in this population due to the high rate of associated intellectual disability. In TSC although there is a correlation between infantile spasms and autistic spectrum disorders and cognitive
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impairment, there is still a need for further analysis to enlighten the mechanisms underlying association between TSC and psychosis.

There is not a specific treatment for psychosis seen in TSC [13, 14]. In literature, a case was reported responding well to risperidone without side effects [13]. Our patient’s psychotic symptoms progressed while he was on risperidone and he had extrapyramidal side effects. Although risperidone plasma concentration was unknown at presentation, his other medications were enzyme inducers and might have decreased plasma level of risperidone, nevertheless extrapyramidal side effects were observed and switching to olanzapine ameliorated his psychotic findings.

In conclusion, we suggest that the diagnosis of TSC should be considered when an organic etiology is suspected as the underlying cause for psychosis in older children and adolescents. TSC may manifest a wide range of psychiatric and behavioral difficulties. It is important to detect this phakomatose to evaluate the patient’s multisystemic condition. There are ongoing studies with mTOR inhibitors on TAND [6]. This may lead to a specific treatment modality for psychiatric disorders in TSC highlighting the importance of proper diagnosis.

References