Psychiatric symptoms in an individual with tuberous sclerosis

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Abstract: Tuberous sclerosis is a rare disorder with no specific treatment. In some cases psychological symptoms are the initial presenting symptoms, making the differential diagnosis difficult. We describe a patient with tuberous sclerosis who developed psychiatric symptoms and discuss the use of low-dose quetiapine to control her emotional and behavioral symptoms.

1. Case history

1.1 History

A 12-year-old female with tuberous sclerosis and associated psychiatric symptoms was admitted on February 6th, 2011 to the Kangning Psychiatric Hospital. The history of the development of her condition was as follows.

Born by normal delivery at full-term, her early childhood development was unremarkable. Facial erythema appeared when she was 3 years of age and subsequently expanded to cover the skin on her head and neck in elevated stripes; but it had never been painful so it was not treated. At the age of six she starting having frequent 30 to 60-second episodes (usually more than 12 times a day) during which her hands twitched, her head and neck were askew, she was non-responsive and she foamed at the mouth. After detailed assessments at several hospitals, a diagnosis of tuberous sclerosis was made. She was treated with 100 mg/d topiramate and 0.5g/d clonazepam for her seizures; these medications decreased the frequency of the seizures but did not eliminate them completely. She continued to have very brief seizures twice daily during which her eyes looked to one side and her hands twitched.

She completed the first two years of elementary school without trouble, but in the third year her scores in math and Chinese dropped significantly and she was no longer able to complete math problems that she had been able to complete in grades 1 and 2. At the same time she became introverted. Two years prior to the current admission (when she was 10 years old) her behavior changed; she became temperamental, attacked others with little provocation, and cried out repeatedly.

Three months prior to the current admission, she started treatment with 500 mg/d vigabatrin. This treatment gradually reduced her twitching and seizures (she had had none in the 6 weeks prior to admission), but in the month before admission she became increasingly moody, angry, impulsive and aggressive; this included biting her hands and scratching family members. Unable to manage this behavior, the family decided to admit her to a psychiatric hospital.

The patient’s mother had condyloma acuminatum during pregnancy, but there was no family history of mental disorders.

1.2 Physical and mental examination

At the time of admission her height and weight were 159 cm and 70 kg. She had normal vital signs and normal consciousness. Covering the head and neck she had elevated red erythema which did not fade when pressed. She was treated with 100 mg/d topiramate and 0.5g/d clonazepam for her seizures; these medications decreased the frequency of the seizures but did not eliminate them completely. She continued to have very brief seizures twice daily during which her eyes looked to one side and her hands twitched.

She had normal vital signs and normal consciousness. Covering the head and neck she had elevated red erythema which did not fade when pressed. She had depigmented spots of 0.5cm × 0.5cm scattered on the skin of her torso. On her abdomen and thighs there were streak-shaped pigmentation similar to striae gravidarum. On the second joint of her ring finger of the right hand there was a 0.5cm × 0.5cm painless nodule which was hard in texture, had clear border lines, and could not be moved. She had a supple neck and did not have abnormalities in her lungs or heart. Her abdomen was extended resembling pregnancy; she was not cooperative with the examination of her liver and
spleen but no abnormalities were detected.

Her consciousness was clear but she was uncooperative, crying and shouting during the examination. Her speech and mannerisms were age inappropriate, similar to those of a much younger child. There were no evident hallucinations or delusions. She had poor attention. Her memory, ability to do simple calculations, comprehension, judgment and overall intelligence were all impaired. She had immobile facial features and labile emotions. She was self-centered and stubborn. She was capable of basic self-care but was impulsive, destructive and aggressive. She had no insight into her condition and had only passively accepted the need for psychiatric help.

Electrolytes and liver and renal function tests were normal. Serum calcium level was 2.68 mmol/L. She had a normal electroencephalography and a normal echocardiography, but the computerized tomography of her head showed several nodular calcifications of different sizes bilaterally distributed under the ependymal or the lateral ventricle. An abdominal ultrasound revealed a fatty liver and hamartomas in both kidneys. On the Wechsler Intelligence Scale for Adults her scores were 49 for verbal intelligence and 62 for performance intelligence.

1.3 Management

She was diagnosed as having a mental disorder due to a medical condition (tuberous sclerosis). Taking into consideration the patient's young age, obesity, and the intracerebral nodules, we decided to provide symptomatic treatment with quetiapine, an antipsychotic that has relatively little effect on prolactin, body weight and the extrapyramidal system. The low starting dose of 25mg/d was gradually increased to 200mg/d and she was maintained on her antiepileptic medication (vigabatrin). This regimen lead to improvement in her disruptive and argumentative behavior so she was discharged two weeks after admission. She continued this dosage and was seen as an outpatient each month. At the time of the last follow-up in the end of October 2011 her condition had stabilized and she was able to undertake simple self-care at home.

2. Discussion

Tuberous sclerosis is an autosomal dominant disease with an incidence of between 2 to 10 cases per 100,000 individuals. The three major clinical symptoms are lipoadenoma, epileptic seizures, and cognitive impairments\(^1\). In some cases psychological and emotional changes are the most prominent symptoms,\(^6\) causing high levels of distress to both the patient and the patient's family members. There is no specific treatment for the disease, but a 20-month follow-up study of 113 patients\(^6\) reported that antipsychotic medications can improve the mental symptoms and stabilize the mood of individuals with tuberous sclerosis.

In this case the sequence of the development of symptoms was as follows: skin lesions, epilepsy, cognitive decline, changes in temperament, and, finally, impulsive and aggressive behavior. These symptoms and the associated findings on physical examination confirmed the diagnosis of tuberous sclerosis. During the course of her illness direct damage from intracerebral nodules and frequent epileptic seizures resulted in brain hypoxic ischemia, which caused associated cognitive decline and psychiatric symptoms, thus the formal psychiatric diagnosis was ‘Mental Disorder due to Another Medical Condition (tuberous sclerosis)’. The patient did not have a family history of mental illness, but her mother had a condyloma acuminatum virus infection during pregnancy which could have led to genetic mutations in the fetus. This possibility could potentially be assessed by a sophisticated genetic mutation analysis.

Given the lack of effective treatments for the underlying organic condition, treatment of the secondary psychiatric condition was necessarily limited to suppression of the symptoms. The second-generation antipsychotic medication quetiapine proved reasonably effective in managing the patient’s psychiatric symptoms, at least for the first year of treatment. Other patients with this condition have also presented with psychiatric symptoms,\(^6\) so psychiatric clinicians who evaluate severely disabled young patients should be aware of this rare but serious condition.

Conflict of interest

The authors report no conflict of interest.

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