CASE REPORT

A Case of Tuberous Sclerosis Triad with Psychiatric Manifestation

Prosenjit Ghosh¹, Monu Doley², Anshuman Gogoi³

ABSTRACT

Tuberous sclerosis (TS) is a rare disorder of genetic origin, caused by mutations in the genes TSC1 and TSC2. It is characterized by benign tumors with multisystem involvement resulting in dermatological, nephrological, neurological and psychiatric manifestations. We are presenting a case of a 21 years old male with tuberous sclerosis presenting with dermatological manifestations, seizures, intellectual disability and psychiatric manifestations including delusions and hallucinations, developing extrapyramidal symptoms after antipsychotic administration. Neuroimaging showed characteristic subependymal calcified nodules. With appropriate anticonvulsant and antipsychotic medications he showed clinical improvement.

Keywords: Extrapyramidal symptoms, Intellectual disability, Psychosis, Seizure, Subependymal nodules, Tuberous sclerosis, Vogt’s triad. Indian Journal of Private Psychiatry (2019): 10.5005/jp-journals-10067-0027

INTRODUCTION

Tuberous sclerosis (TS) complex is a genetically determined multisystem disorder that may affect any human organ system. It was initially described by Rayer in 1835 and then by von Recklinghausen in 1862.¹ Bourneville coined the term tuberous sclerosis to describe the brain pathology. Two genes causing TSC have been identified: TSC1 (9q34) and TSC2 (16p13.3). Their protein products hamartin (TSC1) and tuberin (TSC2) form a complex that regulates the PI3-kinase/AKT pathway to control cell size and proliferation. Loss of these cellular functions is central to the pathogenesis of hamartomas associated with TSC.² Its incidence is 1 in 6,000–10,000 live births.³

International Tuberous Sclerosis Complex Consensus Conference (2012) recommended genetic and clinical criteria for diagnosis of tuberous sclerosis. The genetic criterion consists of a pathogenic mutation in the TSC1 or TSC2 genes. The clinical criteria consist of 11 major and 6 minor (Table 1) criteria. Clinically, definite diagnosis: 2 major features or 1 major with ≥2 minor features, possible diagnosis: 1 major feature or ≥2 minor features.¹

The classical Vogt’s triad consists of: epilepsy, low intelligence and adenoma sebaceum (epiloia) (Reddy et al.).⁴ Tuberous sclerosis complex is associated with significant psychiatric comorbidities like anxiety, depression, aggression, ADHD, disruptive behavior and are frequently reported.⁵ However, comorbidities like cases of psychosis, schizophrenia, bipolar disorder, auditory hallucinations, alcoholism are less frequently reported.⁶

Here, we are presenting a casereport of tuberous sclerosis complex with comorbid psychosis presenting with antipsychotics induced extrapyramidal symptoms (EPS).

CASE DESCRIPTION

A 21-year-old male from rural background presented to Psychiatry Department of Silchar Medical College and Hospital on 15-04-2019 during emergency hours with a history of insidious onset of abnormal behaviors for 5 months, which were exacerbated in the preceding couple of weeks, without any major life-event or

Table 1: Clinical criteria of tuberous sclerosis

<table>
<thead>
<tr>
<th>Major features</th>
<th>Minor features</th>
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<tbody>
<tr>
<td>Hypomelanotic macules (≥3, at least 5 mm diameter)</td>
<td>“Confetti” skin lesions</td>
</tr>
<tr>
<td>Angiofibromas (≥3) or fibrous cephalic plaque</td>
<td>Dental enamel pits (≥3)</td>
</tr>
<tr>
<td>Ungual fibromas (≥2)</td>
<td>Intraoral fibromas (≥2)</td>
</tr>
<tr>
<td>Shagreen patch</td>
<td>Retinal achromic patch</td>
</tr>
<tr>
<td>Multiple retinal hamartomas</td>
<td>Multiple renal cysts</td>
</tr>
<tr>
<td>Cortical dysplasias*</td>
<td>Nonrenal hamartomas</td>
</tr>
<tr>
<td>Subependymal nodules</td>
<td></td>
</tr>
<tr>
<td>Subependymal giant cell astrocytoma</td>
<td></td>
</tr>
<tr>
<td>Cardiac rhabdomyoma</td>
<td></td>
</tr>
<tr>
<td>Lymphangioleiomyomatosis (LAM)†</td>
<td></td>
</tr>
<tr>
<td>Angiomyolipomas (≥2)†</td>
<td></td>
</tr>
</tbody>
</table>

*Includes tubers and cerebral white matter radial migration lines
†A combination of the two major clinical features (LAM and angiomyolipomas) without other features does not meet criteria for a definite diagnosis

¹-³Department of Psychiatry, Silchar Medical College and Hospital, Silchar, Assam, India
Corresponding Author: Prosenjit Ghosh, Department of Psychiatry, Silchar Medical College and Hospital, Silchar, Assam, India, Phone: +91 9435072563, e-mail: p_ghosh72@yahoo.com
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A Case of Tuberous Sclerosis Triad with Psychiatric Manifestation

was no family history of any neurological or psychiatric disorder.

he did not have any formal training in painting. There

of hypergraphia. For a major part of the day he scribbled and drew

of self-care without assistance. He spoke minimally but with history

2–3 times per month. He walked independently, could follow simple

in 11 years of age lasting 2–3 minutes. Clusters of attacks occurred

as poor academic performance, he was dropped out from school.

at 6 years of age, but due to problem in coping up with peer groups as well

was evident over his lower back and thighs. He also had multiple

as a case of tuberous sclerosis and was put on tab phenytoin 300 mg per day in divided
dose and oral multivitamin and was discharged on 16-01-2012 with

However, starting from 2017, he started having occasional

breakthrough seizures while on the previous medication. His latest

seizure attack had been on 01-04-2019, i.e., two weeks prior to this

presentation.

Mental state examination revealed inadequate eye contact,
poor personal hygiene, blunted affect with delusion of persecution

and auditory hallucinations. He was provisionally diagnosed

as a case of other mental disorders due to brain damage and
dysfunction and to physical disease (F06 according to ICD-10).

Tab phenytoin was stopped, and he was initiated with tab sodium

valproate 800 mg per day in divided doses, tab risperidone (3 mg)

and trihexyphenidyl hydrochloride (2 mg) once daily and tab

lorazepam 2 mg at bedtime.

After a few days patient was bought again to SMCH psychiatry

OPD with complaints of agitation, restless feeling, increased anger,
tremulousness of hands, decreased oral intake, increase salivation,
slowness of daily activities, along with fearfulness and hearing

of voices. These symptoms appeared after taking medication

prescribed on 15-04-2019 for 5–7 days. So, he was admitted in male

psychiatry ward for detailed evaluation.

Further evaluation following admission revealed that he

was born of a nonconsanguineous marriage, was delivered

vaginally at home following an uneventful labor with no postnatal

complications. He showed delay in developmental milestones—
walking without support at 2 years of age, speaking monosyllables

at 3 years of age. He used to remain aloof and self-absorbed in

his childhood. He was admitted in primary school at 6 years of

age, but due to problem in coping up with peer groups as well

as poor academic performance, he was dropped out from school.

At 9 years of age, he started developing small nodules over his nose

and gradually multiple nodules appeared all over his facial region

along with multiple hypopigmented lesions on his body (3 in back,

2 in upper thighs). Along with this he had first episode of seizure

in 11 years of age lasting 2–3 minutes. Clusters of attacks occurred

at 2–3 weeks intervals. He developed brief staring spells, occurring

2–3 times per month. He walked independently, could follow simple

commands, could feed himself, could perform daily routine activities

of self-care without assistance. He spoke minimally but with history

of hypergraphia. For a major part of the day he scribbled and drew

scenic pictures and human figures when provided with pencils

and paper. He did not have any formal training in painting. There

was no family history of any neurological or psychiatric disorder.

But his father had a few nodules on his face and nasal bridge in a

scattered fashion.

Physical examination findings were like this: blood pressure =

110/70 mm Hg, pulse rate = 82/minute. There was pallor, but no

icterus, cyanosis, nail abnormalities, or palpable neck or axillary

lymph nodes. He had bilateral fine hand tremors, bradykinesia,

angiofibromatous nodules over whole of oro-facial region including

nose and forehead. Hypopigmented lesions (total 5 in number)

were evident over his lower back and thighs. He also had multiple

crinkled skin lesions (Shagreen patches) over his back.

Mental state examination revealed average built, poor

hygiene, decreased psychomotor activity, with the patient being

uncooperative, and rapport could not be established. Speech was

slurred, was of low tone, and was irrelevant at times. Mood was

fearful with moderately apprehensive, appropriate, reactive, labile

affect with a wide range. Thought revealed delusion of persecution,

which was encapsulated and well-systematized. Auditory

hallucination was present. His intelligence was low (IQ = 60) with

impaired abstract thinking, judgement and reasoning and insight

being grade I (Figs 1 to 3).

Routine laboratory investigation findings were within normal

range except low Hb (7.8 g/dl).

Among radiological findings, CT-scan brain showed multiple

subependymal calcified nodules bilaterally in the region of body of lateral

ventricles (Fig. 4). Chest X-ray, ECG and USG whole abdomen

showed no abnormality. Ophthalmological findings were normal.

Provisionally the patient was diagnosed according to ICD-10

criteria as other mental disorders due to brain damage and
dysfunction and to physical disease (TSC) with mild mental

retardation (F06 with F70) with acute drug induced EPS.

He was started with IV infusion fluids, injectable multivitamin,

trihexyphenidyl hydrochloride 4 mg orally per day in divided doses

and sodium valproate 800 mg orally per day in divided doses.

Patient’s restless agitated behavior decreased and gradually his

hand tremors and bradykinesia along with slurring of speech

decreased. He was then discharged with tab olanzapine 10 mg, tab

sodium valproate 800 mg in divided doses and tab trihexyphenidyl

hydrochloride 2 mg. On first follow-up visit after 10 days, his

psychotics symptoms were found to be improved but not

significantly. He was seizure free. However, he again developed EPS.

He was then advised tab risperidone 2 mg and tab trihexyphenidyl

2 mg per day along with sodium valproate in the earlier dose.

Fig. 1: Facial angiofibromas (adenoma sebaceum)
Later, after around 6 weeks he developed a breakthrough seizure episode when he was again brought to our OPD. By that time his psychotic symptoms showed improvement. His valproate dose was increased to 1,000 mg per day in divided doses. In subsequent visits, the risperidone dose was gradually reduced. Now he is maintaining well with risperidone 0.5 mg per day, valproate 1,000 mg per day, seizure free. Now he is more concerned with body dysmorphism, mainly facial. Patient and attendant were counselled regarding this.

**DISCUSSION**

Early diagnosis of TS is important through clinical, radiological evaluation. Regular monitoring of the individual is very important, as it affects all the system of the body. In this case, development of symptoms is in sequences as follows—skin lesion at 9 years of age, first seizure episodes at 11 years of age followed by cognitive decline, changes in temperament, behavior and finally psychotic symptoms. Psychotic symptoms are not uncommon in children with tuberous sclerosis; a study on 90 children reported more than 50% having psychotic behavior.\(^7\) About 62% of patients with TS have some form of epilepsy.\(^6\) In a range of 38% (Webb)\(^9\) —64% (Gillberg)\(^5\) presented with intellectual disability and cognitive impairment. A study by Ebrahimi-Fakhari et al.,\(^10\) the majority of patients presented with CNS involvement—cortical dysplasia in 51.5%, subependymal nodules in 47.7% and seizure disorder overall in 69.8%.\(^11\) Dermatological manifestations like angiofibroma, shagreen patches are recognized manifestation in adults\(^15\) as in this case report.

TS affects both patient and family physically and psychologically. It is considered a rare disorder. There is no specific treatment for the disease but a 20th month follow-up study of 113 patients reported that antipsychotic medication can improve the mental symptoms and stabilize the mood of individuals with TS (Chung et al.).\(^3\) Current guidelines on the management of epilepsy in TS emphasizes greatly on early recognition and prompt treatment of epilepsy.\(^12\) Multiple drug therapies are ongoing and research projects are being carried out in the world for further workup of the genes involved and treatment strategies.

**CONCLUSION**

Psychological intervention and pharmacotherapy combined brought seizure and psychotic process under control in this case. Patient was on regular follow-up. Patient reported feeling of anxiousness, body dysmorphism. Reassurance was given. As the patient was hypergraphic, he was encouraged to culture his skills in a better way. As he is having mild intellectual disability, cognitive enhancement training is advised. Parents were made to understand about the disease and be aware of the emotional needs of the child. Further, they were advised to continue the medication and warning signs of seizure and abnormal behavior was explained. Necessity of regular follow-up visit was also explained.

**REFERENCES**


