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Case Report

Tuberous Sclerosis: An Overview of All Aspects of the Disease Based on a Pediatric Case

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ABSTRACT

Background and Importance: Tuberous sclerosis, also known as Bourneville's disease is a rare autosomal dominant disease affecting multiple systems. In this case report, we emphasize the importance of clinical criteria instead of genetic analysis in diagnosing tuberous sclerosis and the need for rigorous follow-up of patientsto prevent complications.

Case Presentation: Here we present a case of a 10-year-old boy presenting with intractable seizure and hypo-pigmented patches on his face and back of trunk. In neuroimaging evaluation, subependymal giant cell astrocytoma was diagnosed. Further, hisabdominal ultrasound showed multiple hamartomatous lesions in the liver and bilateral kidney. His cardiology and dental evaluation were normal. The dermatologist diagnosed a shagreen patch on the back of his trunk. Based on the latest clinical diagnostic criteria, he was diagnosed with a case of tuberous sclerosis and has been on the rigorous follow-up ever since.

Conclusion: Since tuberous sclerosis is a multisystem disease, early diagnosis is necessary to prevent acute symptoms and prevent long-term complications. Here we emphasize the need to use clinical criteria instead of genetic study for early diagnosis of tuberous sclerosis.

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Highlights

• Tuberous sclerosis is a rare genetic multiorgan disease.Early diagnosis and management of tuberous sclerosisaim to prevent complications.

• Here we discuss the case of a 10-year-old boy who presented with a seizure disorder and hypopigmented patches on his face and body.

• Further evaluation showed subependymal giant cell astrocytoma in his brain and multiple hamartomatous lesion in the liver and kidney.Hypopigmented patches on his body were later identified by a dermatologist as shagreen patches.

• Based on the tuberous sclerosis complex consensus conference 2012 criteria, a diagnosis of tuberous sclerosis was established.

• We hereby emphasize diagnosis based on clinical criteria rather than time-consuming and expensive genetic tests for diagnosis of tuberous sclerosis.Frequent and regular follow-up of such patients helps to deal with complications and improve the patient's quality of life.

Plain Language Summary

Tuberous sclerosis is a rare genetic multiorgan disease. Early diagnosis and management help to deal with complications and help the child to lead a normal life. Here we present the case of a 10-year-old boy presenting with a seizure disorder and multiple skin lesions. Further evaluation showedan intracranial brain tumor and multiple lesions in his liver and kidney. Based on the latest diagnostic criteria, he was diagnosed withtuberous sclerosis and was followed up with the regular screening of his blood parameters and imaging studies and lived his normal life. Only a few isolated case reports exist regarding tuberous sclerosis. All the reports highlighted the importance of clinical criteria in the diagnosis of tuberous sclerosis, mitigating the need for expensive and time-consuming genetic tests and the need for regular follow-up, similar to our case. Early diagnosis, management of acute complications, and anticipation and treatment of complications help patients to live a normal life despite such a rare and multisystem dreadful disease.

Background and Importance

Tuberous sclerosis is a rare disease with an incidence of 1 in 10000 livebirths [1]. The termtuberous sclerosis was coined by Bourneville in 1880. However, Recklinghausen was the first to describe the disease in 1862 [2]. It is a neurocutaneous disease characterized by the abnormal migration of glial tumor in the cerebral hemisphere and retina [3]. Sherlock coined the term EPILOIA described by the triad of Epilepsy (EPI), Intellectual Disability (LOI), and an association with adenoma sebaceum (A).The usual age of presentation is late childhood [4]. We highlighted the importance of clinical criteria in the diagnosis of tuberous sclerosis which mitigates the need for expensive and time-consuming genetic tests and the need for regular follow-up. At the same time,the management of acute complications and anticipation and treatment of complications have been addressed that help these patients live a normal life despite such a rare and multisystem dreadful disease.

Case Presentation

We present the case of a 10-year-old boy who presented with multiple episodes of generalized tonic-clonic seizures. His mother also presentsa history of poor performance in school. He was started on sodium valproate and evaluated with Magnetic Resonance Imaging (MRI) brain. Electroencephalogram (EEG), routine blood investigations,serum electrolytes, renal function tests, liver function tests and routine examination of urine were normal.The patient continued to have seizures even with an antiepileptic,therefore Lacosamide was added. His brain MRI showed abilateral sub-ependymal enhancing lesion of size 1x1.4x1cm (Figure 1). His EEG showed abnormal bilateral epileptic spikes.

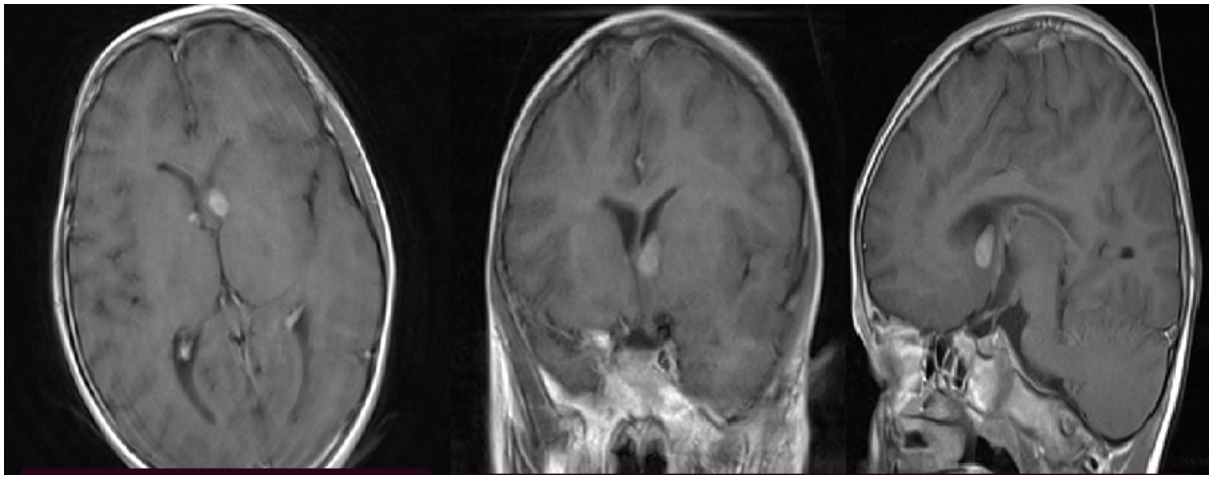

Figure 1. Axial,coronal,and sagittal contrast Magnetic Resonance Imaging (MRI) brainimages showing a subependymal-enhancing lesion (Lt>Rt)

Blood parameters indicated low Hemoglobin (Hb) 8g/dL and hematocrit of 14. Red Blood Cells (RBC) were observed in urine with the absence of any casts or White Blood Cells (WBC). A detailed abdominal ultrasound showed multiple hamartomas in the liver and bilateral kidney (Figure 2 & 3).

His cardiac and ophthalmology evaluation was normal. He was referred to dermatologists due to multiple

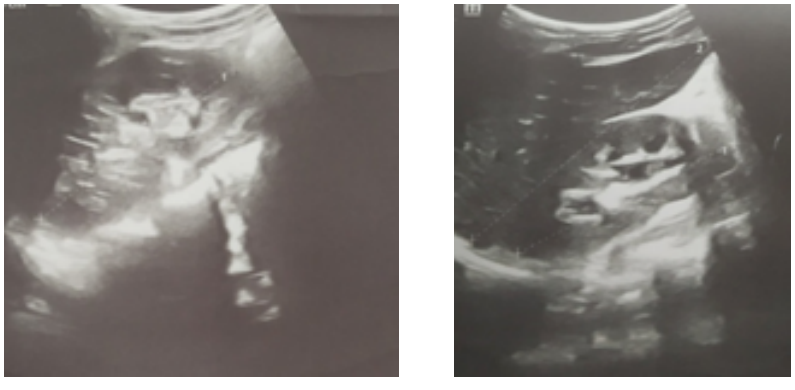

Figure 2. Ultrasound images of multiple angiomyolipomatous lesion of bilateral kidney

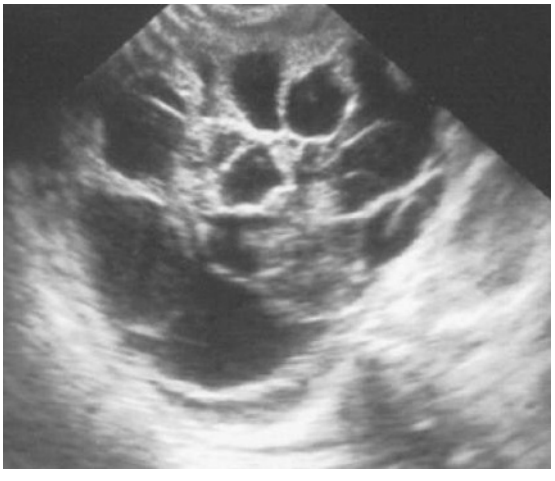

Figure 3. Ultra sound grey scale images of liver mesenchymal hamartomas

white macular patches on the face (Figure 4) and the back of the trunk. An apparent lesion of the orange peel of 3x5x2 cm was observed on the back of his trunk which indicated a shagreen patch (Figure 5).

With the effective diagnosis of tuberous sclerosis,he was also referred for dental evaluation. However, no gingival hypertrophy or dental abnormalities were found. His orthopantomogram (OPG) showed no bony lesion. An effective diagnosis of tuberous sclerosis was made. The child's seizure was well controlled on two antiepileptics and his hematuria resolved with steroid therapy. He was under regular follow-up forthe past year.

Discussion

Tuberous sclerosis is characterized by unusual tumor growth known as hamartomas in different organs [5]. Genetically, the abnormal gene tuberous sclerosis complex (TSC) 1 encodes hematin and is located in 9q34 and TSC 2 encodes tuberin locates in 16p 13.3 [6].The clinical diagnosis of tuberous sclerosis is definite if two features of major criteria or one major criterionare combined with two or more minor criteria. While a possible diagnosis of tuberous sclerosis is made if one major criterion or two or more minor criteria are present according to the recommendations of The Second International Tuberous Sclerosis Complex Consensus Conference 2012 [7].

Major criteria

1. Hypo melatonin macules (three or more, at least five mm diameter)

2. Angiofibroma (three or more) or fibrous cephalic plaque

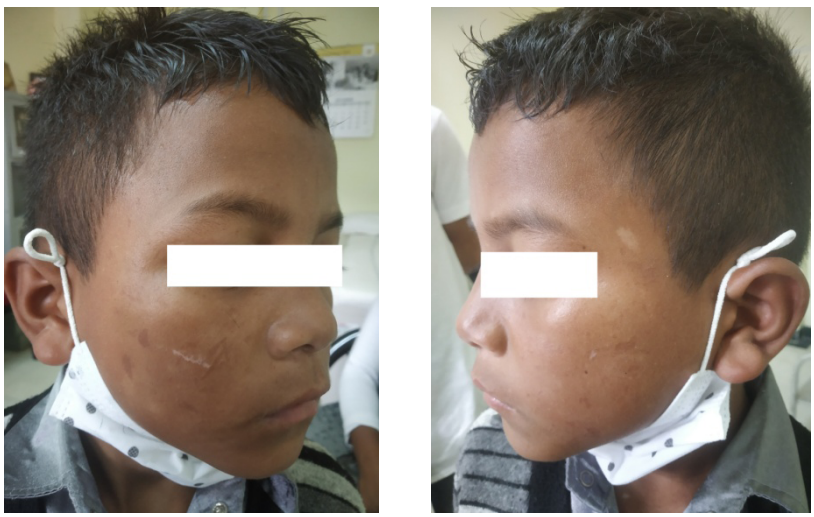

Figure 4. Multiple hypomelanotic macules on face

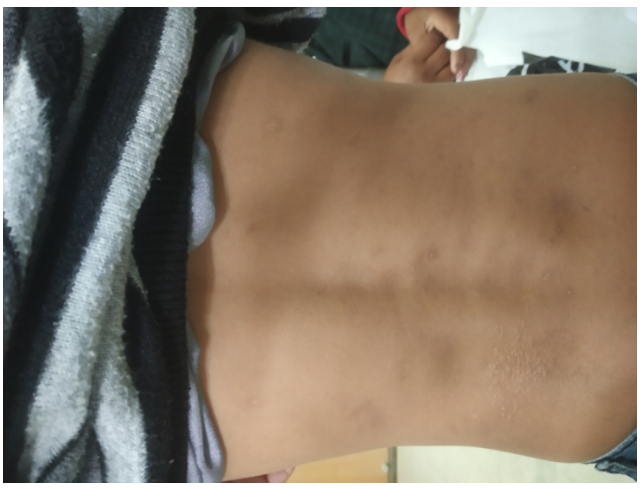

Figure 5. Orange peel appearance hyper pigmented lesion on the back of trunk

3. Ungual fibroma (two or more)

4. Shagreen patch

5. Multiple renal hamartomas

6. Cortical dysplasia

7. Subependymal nodules

8. Subependymal giant cell astrocytoma

9. Cardiac rhabdomyoma

10. Lymphangioleiomyomatosis (LAM)

11. Angiomyolipoma (two or more)

Minor criteria

1. Confetti skin lesion

2. Dental enamel pits (three or more)

3. Intraoral fibroma (two or more)

4. Retinal achromatic patch

5. Multiple renal cysts

6. Non-renalhamartoma

The criteria were updated in 2021.The term"cortical dysplasia" was changed from major criteria to "multiple cortical tubers and/or radial migration lines" because the former was too vague and non-specific. Second,"sclerotic bone lesions" was omitted from minor criteria [8].

In our case, the child had multiple hypomelanotic patches onthe face and trunk,shagreen patch on his back, subependymalhamartoma, and multiple renal hamartomas, thus satisfying 4 major criteria. He also has multiple liver hamartomas which are included in the minor criteria.

A patient diagnosed with tuberous sclerosis should undergo regular follow-up and be managed at the early stage of complications. Abdominal MRI is recommended to checkthe progression of renal angiomyolipoma every one to three years and yearly monitoring of renal parameters. For the treatment of acute clinical hematuria, treatment options include embolization, steroid therapy mechanistic Target of Rapamycin (mTOR) inhibitors,and nephrectomy. Annual screening of MRI brain for sub-ependymal giant cell astrocytoma,and annual neuropsychiatry evaluation for TSC Associated Neuropsychiatric Disorders (TAND) are required. Patientswith suspected or known seizure disordersare evaluated annually withan Electroencephalogram (EEG). Dermatological examination, cardiac evaluation, and dental examination should be done annually [9]. Tuberous sclerosis is a rare disease and only a few cases are mentioned in the literature. This is a unique case where we diagnosed tuberous sclerosis based on clinical criteria, managed the acute seizure and hematuria, and followedup the patient for early detection of the complication.

Conclusion

Tuberous sclerosis is a rare genetic disorder affecting the multiple systems, thus early diagnosis, regular surveillancefor complications and screening and counseling of family members can help in early detection and prevention of complications. We also emphasize the clinical criteria for diagnosis of tuberous sclerosis rather than genetic analysis.

Ethical Considerations

Compliance with ethical guidelines

Written informed consent was obtained from the patient and the identity of the patient was not disclosed compatible with the ethical guidelines.

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Authors' contributions

Conception and design, data analysis and interpretation: Tamajyoti Ghosh; Data collection: Tamajyoti Ghosh; Drafting the article, critically revising the article, reviewing the submitted version of the manuscript, approving the final version of the manuscript: Both authors.

Conflict of interest

The authors declare no conflict of interest.

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