IJMAHS

CASE STUDY

# Epiloia a forgotten name of Tuberous Sclerosis

Rajesh Rai[1], Kapil Jadhav[2], Vijay Dihora[3]

[1]Professor, [2,3]Resident, Department of Paediatrics, D. Y. Patil School of Medicine, Nerul, Navi Mumbai- 400614, Maharashtra

**Correspondence to: Vijay Dihora (vijaydihora@gmail.com)**

**ABSTRACT:**

Epiloia (Tuberous Sclerosis) is a rare neurocutaneous syndrome inherited as autosomal dominant fashion and associated with involvement of other systems like kidneys, heart, eyes and lungs. Manifestation of Tuberous Sclerosis becomes apparent only in late childhood, limiting the usefulness of early diagnosis in infancy. Here, we report a 3 year old male child, who presented with uncontrolled generalized tonic-clonic seizures with neuro cutaneous marker (ash leaf macules and adenoma sebaceum).

To create awareness among clinicians to not only treat convulsions in symptomatic child but should make efforts to find out other causes of convulsions by detailed history and thorough clinical examination especially beyond infancy.

A treatable condition if identified in time would help to plan a strategy for better outcome.

***Key words***: *Epiloia, Tuberous sclerosis, Bourneville's disease, Adenoma sebaceum, Shagreen patch*

## INTRODUCTION

Epiloia also called as Bourneville's disease, was first described by Desiree- Magloire Bourneville in 1880, is a rare genetic disorder of autosomal dominant inheritance with the prevalence of 1 in 6000 live births [1,2], affecting both sexes and all ethnic groups [3,4,5].

Tuberous Sclerosis complex (TSC) is caused by mutations of one or both the genes TSC1 and TSC2. The TSC1 gene, discovered in 1997, is on chromosome 9 (9q34) and produces a protein termed Hamartin. The TSC2 gene, identified in 1993, is on chromosome 16 (16p13.3) and produces the protein Tuberin [1, 5, 6]. These proteins act as tumor growth suppressors to regulate cell proliferation and the differentiation of nerve cell division to form new generations of cells which acquire individual characteristics.

The chances of mental retardation is higher in younger patients having signs and symptoms of Tuberos sclerosis.

## CASE REPORT

A 3 year old male child came with status epilepticus with history of multiple episodes of generalized tonic-clonic seizure since last three days with history of multiple hospital admissions for the same reason and was on antiepileptic drug (syrup valproate 35mg/kg/day) since the age of one year. He was born of a non-consanguineous marriage with uneventful birth history. There was no history of seizure in other sibling or family members; however his father had skin nodules over the face along with a hypopigmented macule over the trunk.

Child had tachycardia (heart rate 170 bpm) and tachypnea (respiratory rate 56 cycles/min.) with fever (temperature 102 F) with adequate blood pressure (94/60 mm Hg). The child was malnourished. There was history of global developmental delay with developmental quotient (DQ) of 66%. The child had multiple hyper-pigmented papules (adenoma sebaceum) (Figure - 1) over the nasolabial region with multiple hypo-pigmented lesions (Ash leaf macule) over chest and trunk (Figure - 2). CNS examination revealed hypertonia of both upper and lower limbs with brisk deep tendon reflexes and absent superficial reflexes: Babinski's sign was positive bilaterally. There was no signs of cerebellar involvement or meningeal irritation. Other systemic examination was within normal limits. Fundus examination of both eyes revealed no abnormality.

Computed tomography scan of brain showed multiple well-defined calcified nodular lesions seen in the bilateral subependymal region of the lateral ventricles (Figure - 3). Complete blood count showed leukocytosis with normal differential counts. Renal and liver function tests were within normal limits. An electroencephalogram (EEG), Two-Dimensional Echocardiogram (2D Echo) and USG abdomen was within normal limits. His serum

valproate level was within the therapeutic range, Lamotrigine 2 mg/kg/day was added after which the seizure frequency decreased though he had short seizures in-between. The dose of Lamotrigine was increased to 5 mg/kg/day which bought the seizure under control.

Counseling about the disease and prognosis was done before discharge, and patient is on regular followup in our OPD and is convulsion free.

## DISCUSSION

"Tuberous sclerosis" is the neurocutaneous syndrome is named for the firm whitish tuber like nodules arising from the cerebral convolutions with multisystemic involvement.

Tuberous sclerosis complex is a rare genetic disorder with heterogeneous presentation varying from severe mental retardation and incapacitating seizures to normal intelligence and an absence of seizure, often within the same family. The major neurological manifestations of tuberous sclerosis complex are seizures, autism, developmental delay and behavioral and psychiatric disorder. Seizure is present in about 80-90% of patient which begins during the first year of life; varies from subtle focal seizure, infantile spasm, to generalized seizure [3,7]. Seizures are managed with an anticonvulsant medication like Vigabatrin (infantile spasm), Lamotrigine (generalized seizure) [4], However young children with TSC who have early onset of focal seizure or spasm develop intractable seizure later that responds poorly to antiepileptic drug [3]. These are candidates for alternative non-pharmacological treatment which includes vagus nerve stimulation, use of ketogenic diet, and resective epileptic surgery [8].

TSC has dermatologic manifestations like hypomelanotic macule (90%), facial angiofibroma (75%) and Shagreen patch (20-30%) [4]. Hypomelanotic macules are present at birth and almost all lesions are evident within the first two years of life. Facial angiofibromas (adenoma sebaceum) are present as a “butterfly distribution” in the malar area as small pink to red dome-shaped papules during preschool years. However in our case it was most prominent over chin. Shagreen patch characteristically present in the lumbosacral region as an irregularly shaped roughened raised lesion with orange peel consistency. Adolescent pediatric children may have cosmetic issues, so recent trial support the use of topical 0.1% Rapamycin on facial angiofibromas [9].

Retinal lesion in TS is of two types mulberry tumors that arise from nerve head and phakoma which are retinal hamartomas of astrocytic origin but in our patient did not have any retinal lesions.

Approximately 50% of children with TS have rhabdomyomas of the heart. These may be numerous or located at the apex of the left ventricle, they tend to slowly resolve spontaneously even though they can cause congestive heart failure and arrhythmias [10]. Hamartomas or polycystic disease can cause pain, hematuria and in some cases renal failure by the involvement of kidneys in most patients: our patient neither renal nor cardiac involvement. Generalized cystic or fibrous pulmonary changes in the lung may lead to spontaneous pneumothorax [10] which was again not observe in this case.

Diagnostic Criteria for TSC is as given in the Table no 1 [2,3,5]. Confirmatory diagnosis of TSC require; Either 2 major criteria or 1 major with 2 minor criteria.

*Table. 1: Major and Minor Criteria of tuberous sclerosis complex*

| | Major criteria | Minor Criteria |
|---|---|---|
| 1 | Cortical tuber | Cerebral white matter migration lines |
| 2 | Subependymal nodule | Multiple dental pits |
| 3 | Facial angiofibroma or forehead plaque | Gingival fibromas |
| 4 | Ungual or periungual fibroma | Bone cysts |
| 5 | Hypo melanotic macules (>3) | Retinal achromatic patch |
| 6 | Shagreen patch | Confetti skin lesion |
| 7 | Multiple retinal hamartomas | Non renal hamartomas |
| 8 | Cardiac rhabdomyoma | Multiple renal cysts |
| 9 | Renal angiomyolipoma | Hamartomatous rectal polyps |
| 10 | Pulmonary lymphangioleiomyomatosis | |

Our patient had three major criteria (subependymal nodules in CT scan brain, facial angiofibroma and hypo melanotic macules more than three in number) which fit in the diagnosis of Tuberous sclerosis. He had intractable seizure requiring frequent adjustment of antiepileptic drug and doses (sodium valproate and Lamotrigine) and seizure were controlled. Dietary advice, hematinics and multivitamins were given.

The newer modalities in the management of tuberous sclerosis are inhibitors of the mammalian target of rapamycin (mTOR) which helps in regression of astrocytomas, angiofibroma and angiomyolipoma [11] which may be seen as a future modality of management before a surgical intervention.

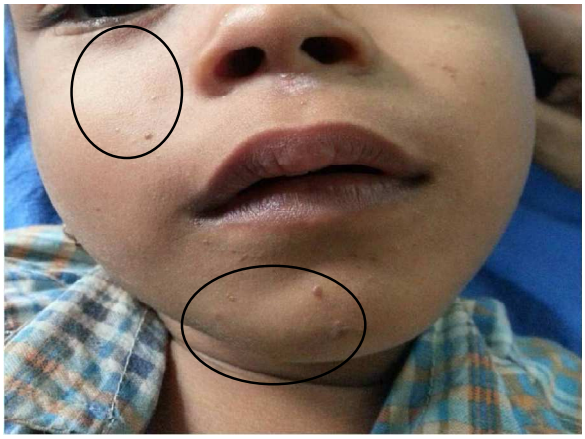

**Figure 1: Adenoma sebaceum over face**

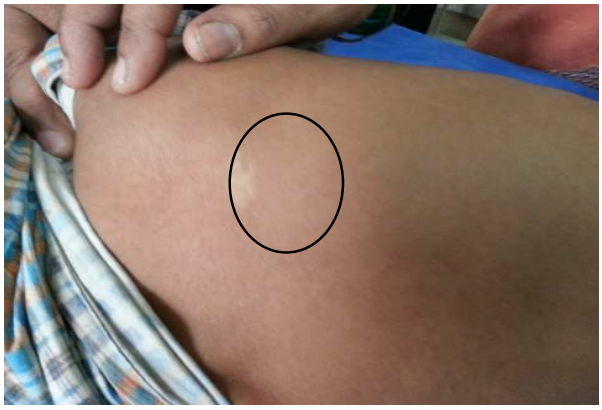

**Figure 2: Ash leaf macule over back**

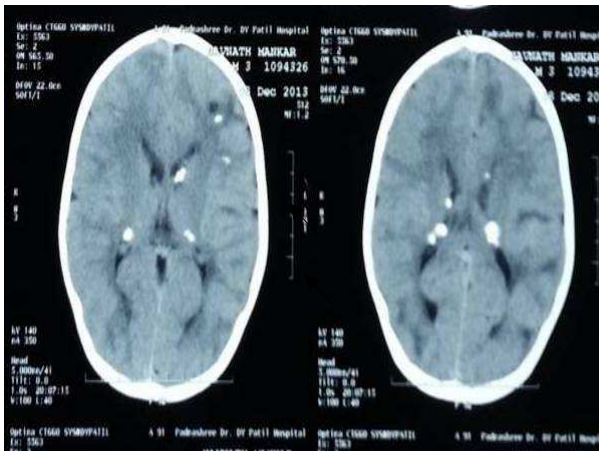

**Figure 3: CT scan of brain showing subependymal nodule.**

***Site this article as:*** Rajesh Rai, Kapil Jadhav, Vijay Dihora**,** *Epiloia a forgotten name of Tuberous Sclerosis,* Int J Medicine and Allied Health Sciences, 2015; 4: 419-421

## CONCLUSION

1. To conclude any child who presents with seizures, must be looked for skin lesions which can sometimes clinch the diagnosis as was in our case.
2. The age of presentation is inversely proportional to the severity of complication, thus early diagnosis is vital.
3. The aim of the management of TS is to prevent and treat the complication like intractable seizures and mental retardation at later age.
4. Counselling of parents is very important which include about the disease, its inheritance, prognosis and complication.
5. Management may change with newer modalities like mTOR which help this lesion regress.

## REFERENCES

1. Cutado A, Antonio J, Lopez J. Oral health management implecations in patients with tuberous sclerosis. Oral Surg Oral Med Oral Pathol Radiol Endol 2000; 90:430-5.
2. Damm DD, Tomich CE, White DK, Drummond JF. Intraosseous fibrous lesions of the jaws. Oral Surg Oral Med Oral Pathol Radiol Endol 1999; 87:334-40.
3. McCall T, Steven S, Salzman KL, Fults DW. Tuberous Sclerosis: a syndrome of incomplete tumor suppression. Neurosurg Focus 2006; 20(1):E3.
4. Leung AKC, Robson LM. Tuberous Sclerosis Complex: A Review. J Pediatr Health Care. 2007; 21:108-114.
5. Harper JJ, Trembath RC. Genetics and Genodermatosis. In: Neil Cox, Christopher Griffiths (eds.). 7th ed. Australia: Blackwell; 2004. p12.33-12.37
6. Office of Communications and Public Liaison National Institute of Neurological Disorders and Stroke National Institutes of Health. *Tuberous Sclerosis Fact Sheet*.
7. http://www.ninds.nih.gov/disorders/tuberous_sclerosis/detail_tuberous_sclerosis.htm (accessed March 10, 2015).
8. Finkelstein R. Advances in Tuberous Sclerosis Complex Research: The October 1, 2003, Child Neurology Society Workshop. J Child Neurol. 2004; 19:734.
9. Thiele EA. Managing Epilepsy in Tuberous Sclerosis Complex. J Child Neurol 2004;19:734.
10. Madke B. Indian Dermatol Online J. 2013; 4(1):54-57.doi: 10.4103/2229-5178.105488.
11. Haslam RHA. Neurocutaneous syndromes. In: Behrman RE, Kliegman RM, Jenson HB (eds). Nelson text book of Pediatrics. 17th edn. W B Saunders company. Philadelephia 2004.pp. 1837-38.
12. Krueger DA, Franz DN. Current Management of Tuberous Sclerosis Complex. Pediatr Drugs. 2008;10(5):299-313.