

# Tuberous Sclerosis Complex - A Case Report

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## ABSTRACT

Tuberous Sclerosis Complex (TSC) is an Autosomal Dominant genetic disorder characterized by the growth of numerous benign tumors in many parts of the body caused by mutations on either of two genes, TSC1 and TSC2. A case of an 8 year old female child who fulfilled 5 major criteria of Tuberous Sclerosis Complex is reported. TSC patients, besides receiving symptomatic treatment, should also be offered special schooling and regular follow up by expert physician.

**KEY WORDS:** Tuberous sclerosis, facial angiofibromas, adenoma sebaceum, ash leaf macules, shagreen patch , cortical tubers , subependymal nodules.

## INTRODUCTION

Tuberous Sclerosis or Tuberous Sclerosis Complex (TSC) is an Autosomal Dominant genetic disorder characterized by the growth of numerous benign tumors in many parts of the body; including the brain, skin, heart, lungs, eyes, kidneys and other organs, leading to significant health problems like seizures, intellectual impairment, autism or developmental delay<sup>(1)</sup>. TSC is caused by mutations on either of two genes, TSC1 mapping to 9q34 and TSC2 to 16p13.3, which encode for the proteins hamartin and tuberin respectively<sup>(2,3)</sup>. These proteins act as tumor growth suppressors, agents that regulate cell proliferation and differentiation<sup>(3)</sup>. Tuberous sclerosis is most common single gene disorder with estimated incidence 1 in 5800. Spontaneous genetic mutations occur in 75 % of patients<sup>(3)</sup>. TSC occurs in all races and ethnic groups, and in both genders<sup>(1,3)</sup>. Definite TSC is diagnosed when either 2 major features (out of a total of 11) or one major feature with 2 minor features (out of a total of 9) are present<sup>(3,4)</sup>. Tuberous sclerosis has no cure, but treatment as medical, educational and occupational therapy can help relieve symptoms.

## CASE REPORT

An 8 year old female child brought to the pediatric OP with the history of one episode of Seizure 5 day's back, which is GTCS type, which lasted for 5 minutes associated with deviation of mouth, frothing & loss of consciousness, not associated with bladder & bowel incontinence. There was no history suggestive of head injury, fever, ear discharge, delayed cry at birth, delayed milestones and contact with TB. The child had past history of seizures, with first episode

occurred at 5 yrs of age and she was on AED (phenytoin sodium) since then. There is no significant family history of seizures. But her father is having hyperpigmented nodules over face, a roughened raised patch over lumbosacral region.

On examination she is conscious, coherent, oriented to time, place and person.

There are tiny red papules over face (facial angiofibroma), hypopigmented patches (Ashleaf macules) over chest and back. A roughened raised lesion (Shagreen patch) is also present at the thoracolumbar region. There are no signs of cranial nerve involvement. Motor examination is normal. Fundus examination is normal. Her lab investigations include Hb of 8.0 gms %, WBC count is of 9,000 cells/ mm<sup>3</sup>, ESR of 30 mm during first hour. Her CXR and X-ray skull are normal. CT Brain showed 1. Cortical tubers noted in the right parietal region, left temporal region, left frontal region, 2. Sub ependymal nodules with calcifications. Her ultrasound Abdomen is normal with no renal involvement & 2D Echocardiogram is also normal.

With her past history of seizures and the presence of neurocutaneous markers on physical examination like angiofibromas, ashleaf macules, shagreen patch, family history of similar lesions present in her father and CT brain showing cortical tubers noted in the right parietal region, left temporal region, left frontal region and sub ependymal nodules with calcifications, the final diagnosis of Tuberous Sclerosis Complex is made.



Figure: 1 Ashleaf macules



Figure: 2 Subependymal nodules



Figure: 3 Cortical Tubers.

## DISCUSSION

Tuberous Sclerosis an important genetic disorder characterized by seizures, mental retardation and adenoma sebaceum (EPILOA)<sup>(5)</sup> affects the patient and the family in various ways. It may affect any organ. It is mainly recognized by lesions in the skin, brain, retina, kidney, heart & lungs. Epilepsy is most common medical disorder in 80 to 90 % of patients developed during their life time, majority have seizures during 1st year, one third of the them develop infantile spasms. Seizures and Mental retardation are due to disturbed histogenesis in the brain. Neurons are decreased in number and Astrocytes are large, bizarley shaped<sup>(6)</sup>. 50 % of patients have normal intelligence and cutaneous manifestations found in 96 % of patients. Cortical tubers, the most characteristic lesions of TS can be detected on MRI in 95% of patients<sup>(6)</sup>. Cortical tubers range from 2 to 30 in number, mostly in supratentorial region<sup>(7)</sup>. Calcified cortical tubers seen in 50%<sup>(7)</sup>. Subependymal nodules are found in 95% of patients<sup>(6)</sup>. Subependymal Giant Cell Astrocytomas in 15% of patients.

A diagnosis of Tuberous sclerosis can be made on individuals who harbor at least 2 major or one major plus 2 minor features are present. Individual with one major plus one minor is said to be probable TS, individual with one major or two minor is possible TS<sup>(1,4)</sup>.

**Major Features:** Cortical tuber, Subependymal nodules, subependymal giantcell astrocytoma, Facial angiofibroma or forehead plaque, Periungual fibroma (20%), hypomelanotic macules (>3)<sup>(2)</sup>, Shagreen patch, Multiple retinal hamartomas, Cardiac rhabdomyoma(50-60%), Renal angiomyolipoma , Pulmonary lymphangiomyomatosis<sup>(1,3)</sup>.

**Minor Features :** Cerebral white matter migration lines , Multiple dental pits >14 (100%)<sup>(5)</sup>, Gingival fibromas , Bone cysts , Retinal Acromatic patch , Confetti skin lesions , Non renal hamartomas , Multiple renal cysts , Hamartomatous rectal polyps<sup>(1,3)</sup>.

The patient, along with symptomatic control of seizures, should also be offered special schooling, and involvement of different organs in TSC. In majority, there was probable diagnosis with one major plus and one minor positive feature. In our case, the interesting feature was the presence of 5 major criteria, making it a very conspicuous presentation of TSC. Histologically, it consists of giant cells with abundant esinophilic cytoplasm that resembles gemistocytic astrocytes. Positive staining with GFAP is seen in most cases & supports the concept that subependymal astrocytomas are astrocytic.

**Consent:** A written consent had been taken from the child's parents.

**Conflict of Interest:** None. Source of funding: None

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