

## Tuberous Sclerosis in a Young Female- A Rare Case Report

Dr.Rajesh Kishore Debbarma, Dr.Kaushik Chakma

**Abstract:** Tuberous sclerosis complex Syndrome (TSCs) is an autosomal dominant disorder affecting multiple organs; caused by mutations of either the TSC1 or TSC2 gene encoding hamartin and tuberin respectively. It is characterized by the development of benign tumours affecting different body systems. The most common visible manifestations of TSC are facial angiofibromas and the formation of hamartomas in multiple organ systems leading to morbidity and mortality. We report a case of 22 year old girl in Tripura with Tuberous sclerosis complex syndrome presented with facial angiofibromas, angiomyolipomas of the bilateral kidney, subependymal nodules, subependymal giant cell astrocytoma.

**Key words;** facial angiofibromas, angiomyolipomas of the bilateral kidney, subependymal nodules, subependymal giant cell astrocytoma

### I. Introduction

Tuberous sclerosis first came to medical attention when dermatologists described the distinctive facial rash (1835 and 1850). Later it was presented by von Recklinghausen (1862) who identified heart and brain tumours in a newborn. However, Desire-Magloire Bourneville (1880) is credited with having first characterized the disease, coining the name tuberous sclerosis, thus earning the eponym Bourneville's disease. The neurologist Vogt (1908) established a diagnostic triad of epilepsy, idiocy, and adenoma sebaceum (an obsolete term for facial angiofibroma).<sup>1</sup>

As the manifestations of the disease are variegated in nature, the term Tuberous Sclerosis Complex (TSC) is now widely used. It is an autosomal dominant neurocutaneous syndrome, characterized by the development of benign tumors such as neurofibromas and angiofibromas located anywhere in the body (skin, central nervous system, heart, kidneys etc). TSC are due to mutations of the TSC1 and TSC2 genes, which intervene in cell cycle by differentiation, migration and proliferation. Though it was first identified as an autosomal dominant disorder 60- 70% cases can be due to spontaneous mutations<sup>2,3</sup>. The incidence of tuberous sclerosis is uncertain. The point of prevalence of TSC ranges from 1:6,000 to 1:10,000 individuals, and the diagnosis is usually established between 4-10 years of age or in puberty<sup>4</sup>. Tuberous Sclerosis Complex manifests with variable signs and symptoms together with angiofibromas distributed on the face and forehead. Sometime it can have a butterfly distribution. The most important neurological problems are mental retardation, seizures, autism and learning difficulties. The diagnostic criteria of TSC have been divided into major and minor features.<sup>5</sup>

#### Diagnostic criteria for tuberous sclerosis complex(TSC)

Major features	Minor features
1. Facial angiofibromas or forehead plaque 2. Non-traumatic ungula or periungual fibroma 3. Hypomelanotic macules (three or more) 4. Shagreen patch (connective tissue nevus) 5. Multiple retinal nodular hamartomas 6. Cortical tuber 7. Subependymal nodule 8. Subependymal giant cell astrocytoma 9. Cardiac rhabdomyoma, single or multiple 10. Lymphangioma/leiomyomatosis 11. Renal angiomyolipomas	1. Multiple, randomly distributed pits in dental enamel 2. Hamartomatous rectal polyps 3. Bone cysts 4. Cerebral white matter radial migration lines 5. Gingival fibromas 6. Nonrenal hamartoma 7. Retinal achromic patch 8. Confetti' skin lesions 9. Multiple renal cysts

Patients with TSC might have a delay in the diagnosis as some findings might be unrecognized during childhood by medical practitioners and some disease manifestations may not occur until adulthood. In the study

of Seibert et al, 56% of the patients were diagnosed in adulthood and two-thirds of these patients had symptoms in childhood.<sup>6</sup>

We herein report a case of 22 years old girl who presented with mental retardation, seizure disorder and facial angiofibromas, which on evaluation was found to be a case of tuberous sclerosis complex. The importance of recognition of features of this rare syndrome is stressed.

#### CASE REPORT

A 22 year old girl reported to the Medicine Department of AGMC & GBP Hospital, Agartala, Tripura with chief complaint of Seizure off & on since 3 days. On questioning it found that seizure was started when the patient was 5 yrs of age, 2-3 episode per day, all attacks are similar type, each episode of seizures last for about 15-30 seconds followed by unconsciousness for a period of 2-3 mins and frequency of seizure occur 3-4 wks interval and she is under regular treatment for the seizure. Parents gave a history of having difficulty in learning at school. She studied up to class one but drooped out due to poor performance. Psychological assessment has been done and Intelligence quotient (IQ) score is 31. No family history of similar illness.

On examination of the patient revealed multiple dome shaped papular lesions of brown coloured of about 10-15 mm size, seen over the nasolabial fold & cheeks suggestive of facial angiofibromas ("adenoma sebaceum") in typical butterfly pattern. [Figure 1].



Figure-1

On **Ultrasonography of whole abdomen** shows Multiple intra renal complex echogenic masses are seen involving ant. and posterior cortex of both the kidneys, max. measuring upto 4.06× 6.06 cm in size (rt kidney)- Feature Suggestive of- Multiple angiomyolipoma involving both kidneys (Figure-2)



Figure-2

On **CECT Scan of Brain** shows Subependymal giant cell astrocytoma (SEGA) with multiple subependymal calcified nodules (SENs) over the bilateral

Lateral ventricles -suggestive of Tuberos Sclerosis.(Figure-3)

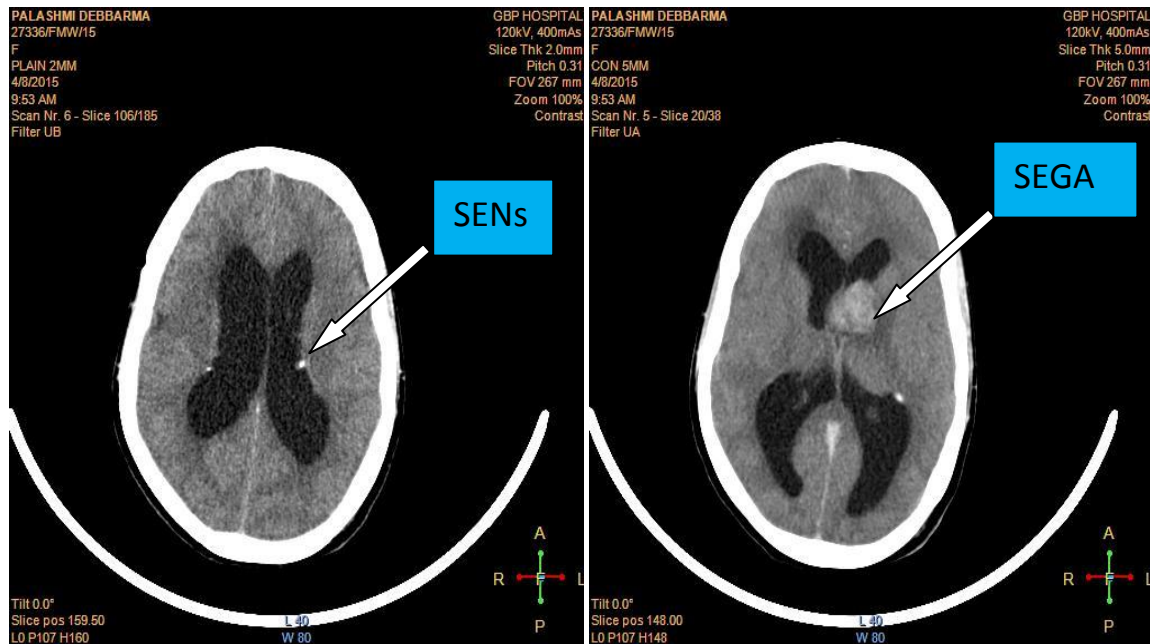


Figure-3

CHEST X-RAY (PA VIEW) - Normal study

ECHOCARDIOGRAPHY- Normal study

## II. Discussion

Patients with Tuberos sclerosis complex (TSC) range from intellectually normal to severely mentally retarded. TSC is often associated with mental retardation (in 70% of cases) and epilepsy (90%). Facial angiofibromas are observed in 70% of all cases, respectively.<sup>7</sup>In addition to mental retardation, multiple behavioural problems including sleep disorder, hyperactivity, attention deficit, aggressiveness, and autism have been found in children with TSC.<sup>8</sup> Seizures are the most common neurologic symptom of TSC occurring in 92% of patients.<sup>9</sup> The prevalence of learning disabilities varies from 38% to 80%, and when it does exist it tends to be moderate or severe in degree. Children with infantile spasms and hypo arrhythmia are reported to be more severely affected than those with any other form of epilepsy. Our case reported with mental retardation and epilepsy.

Tuberous sclerosis complex is characterized by very common neurocutaneous manifestations thus a careful skin examination of patients suspected to have TSC is mandatory. As revealed in the study of Jozwiak et al, the frequencies of patients with facial angiofibromas were 75% respectively.<sup>10</sup> Our case also presented with skin manifestation. As multiple organs are involved, there is wide variability in presentation. Neurologic symptoms and complications due to the development of subependymal nodules(SGAs) and subependymal giant cell astrocytomas (SEGA) are common in patients with TSC<sup>11</sup> as we found both in our case in a contrast CT scan of brain.

Two types of renal lesions occur in patients with tuber sclerosis; angiomyolipomas and renal cysts. They may be found independently or together: they may be unilateral, bilateral, single or multiple. Angiomyolipomas are benign in nature and asymptomatic but spontaneous rupture and subsequent hemorrhage in to retro peritoneum may occur and are the cause of chronic renal failure that may prove fatal.<sup>12</sup> Our case reported with angiomyolipomas of the bilateral Kidney.

It is estimated that nearly one million people are known to suffer from tuberous sclerosis.<sup>10</sup> It is an underestimated figure as many cases remain undiagnosed due to variegated clinical presentation. Intervention programs, including special schooling and occupational therapy may benefit individuals with special needs and developmental issues. Surgery, including dermabrasion and laser treatment, may be useful for treatment of skin lesions. There is no cure as such for tuberous sclerosis complex. Drug therapy for some of the manifestations of TSC is currently in the developmental stage. Prognosis of the disease depends on the severity or multiplicity of organ involvement. About a quarter of severely affected infants are thought to die before age 10 years, and 75% die before age 25 years; however, the prognosis for the individual diagnosed late in life with few cutaneous signs depends on the associated internal tumors. We treated the patient with anticonvulsant drug and patient was

referred to neurosurgeon for further treatment. Debulking of tumour and serial MRI scanning was advised but because of financial constrain it was not possible.

### **III. Conclusion**

It is not uncommon for patients with TSC to have symptoms or signs that do not lead to immediate diagnosis. In some cases, diagnosis is delayed for prolonged periods of time. Clinicians including child and adult neurologists, dermatologists, nephrologists and cardiologists should be aware of the myriad potential presenting symptoms and signs of TSC. Early diagnosis is very important to improve quality of life by thorough clinical and radiological evaluation, continuous monitoring of symptoms, family planning, genetic counseling, parents & other family members should be clinically examined including skin examination under woods UV light, eye examination for retinal phakomas, Chest x-ray, MRI brain scan & USG abdomen should be performed.

### **References**

- [1] Curatolo (2003), chapter: "Historical Background".
- [2] Hung CC, SuYN, ChienSC, LiouHH, ChenCC,ChenPC,et al. Molecular and clinical analyses of 84 patients with tuberous sclerosis complex. *BMC Med Genet.* 2006; 7:72.
- [3] Inoki K, Guan KL. Tuberous sclerosis complex, implication from a rare genetic disease to common cancer treatment. *Hum Mol Genet.* 2009;18:R94-100.
- [4] Cutando A, Gil JA, López J. Oral health management implications in patients with tuberous sclerosis. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod.* 2000;90:430-5.
- [5] TS Cheng. Tuberous sclerosis complex: an update Review Article Hong Kong J. *Dermatol. Venereol.* (2012) 20, 61-67.
- [6] Seibert D, Hong CH, Takeuchi F, Olsen C, Hathaway O, Moss J, et al. Recognition of tuberous sclerosis in adult women: delayed presentation with life-threatening consequences. *Ann Intern Med* 2011;154:806-13.
- [7] Curatolo P. Seizures. In: Curatolo P, eds. *Tuberous sclerosis complex: from basic science to clinical phenotypes.* London:McKeith Press, 2003: 46-76
- [8] Schwartz RA, Fernández G, Kotulska K, Józwiak S. Tuberous sclerosis complex: advances in diagnosis, genetics, and management. *J Am Acad Dermatol.* 2007;57:189-202.
- [9] Gupta S, Bhowate R, Degwekar SS. Clinical and radiological findings related to tuberous sclerosis complex: a case report. *J Contemp Dent Pract.* 2008;9:85-91.
- [10] Jozwiak S, Schwartz RA, Janniger CK, Michalowicz R, Chmielik J. Skin lesions in children with tuberous sclerosis complex: their prevalence, natural course, and diagnostic significance. *Int J Dermatol* 1998;37
- [11] Curatolo P. Seizures. In: Curatolo P, eds. *Tuberous sclerosis complex: from basic science to clinical phenotypes.* London:McKeith Press, 2003: 46-76.
- [12] Gupta S, Bhowate R, Degwekar SS. Clinical and radiological findings related to tuberous sclerosis complex: a case report. *J Contemp Dent Pract.* 2008;9:85-91.