TUBEROUS SCLEROSIS COMPLEX: A CASE REPORT
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HOW TO CITE THIS ARTICLE:

ABSTRACT: Tuberous sclerosis is a multisystemic genetic disease. A case of 28 year old male is reported here with 7 major and 3 minor criteria for diagnosis of Tuberous sclerosis complex along with some unusual and rare features of the disease.

KEY WORDS: Tuberous sclerosis, shagreen patch, Koenen's tumour.

INTRODUCTION: Tuberous Sclerosis complex (TSC) was first described in 1880’s as "Bourneville’s disease" named after the French physician Desire-Magloire Bourneville (1840-1909).¹ Rayer gave the first complete description of tuberous sclerosis in 1835.² Sherlock³ coined the name 'epiloia', the diagnostic triad composed of epilepsy, low intelligence and adenoma sebaceum.

Tuberous sclerosis is a multisystem genetic condition whose key features include multiple facial angiofibromas, hypopigmented macules, seizures, cardiac rhabdomyoma, and renal lesions with prevalence from 1/10,000 to 1/30,000.⁴ The presence of two major or one major plus two minor features meet the diagnostic criteria for definite tuberous sclerosis complex.⁵

CASE REPORT: A 28 year old male born of non consanguineous marriage presented with multiple eruptions over face since 12 years. He had H/O head ache and convulsion on & off since 2 to 3 years every 2 – 3 monthly. Patient was mentally retarded with low IQ. No positive family history present. No H/O of fever, urinary complaint, joint pain or abdominal pain was present.

On examination, multiple hyperpigmented small shiny papules with few nodular lesions over nose, alae of nose, cheeks and forehead, characteristic of adenoma sebaceum [Figure 1(a)]. Pedunculated skin tags were present over chest, back, buttocks, genital area, groin and scalp. Over the right arm 3 - 4 ash-leaf macule were present. Multiple shagreen patches over back [Figure 1(b)], abdomen, buttocks, back of thigh, back of left knee joint and arm. Dermal nevus was present over right buttock [Figure 1(c)]. Nail showed Periungual Koenen's tumour over middle finger of left hand and fourth toe of left feet [Figure 2]. Small depression over upper and lower incisor was seen. Oral cavity does not reveal any fibroma or other pathology.

CT scan head showed subependymal calcified tubers in left parietal region with Right sided cerebral atrophic changes [Figure 3(a)]. ECG and ECHO showed LVH. Fundoscopy showed chorioretinal atrophy and bilateral retinal hematomata on right side close to the macula, suggestive of TS.

Abdominal sonography showed multiple echogenic lesions in bilateral kidney suggestive of multiple angiomyolipomas, few cysts in left kidney and Angiomyolipoma in right lobe of liver. X-rays of hands and feet showed multiple cysts [Figure 3(b)].

DISCUSSION: Major features of TS includes facial angiofibromas, fibrous plaques over forehead, hypomelanotic macules (greater than three), shagreen patches, periungual fibromas, multiple retinal nodular hamartomas, cortical tubers, subependymal nodules, subependymal giant cell astrocytoma,
cardiac rhabdomyoma, lymphangioleiomyomatosis, and renal angiomyolipoma. Minor features include multiple dental enamel pits, hamartomatous rectal polyps, bone cysts, cerebral white matter radial migration lines, gingival fibromas, nonrenalhamartoma, retinal achromic patch, confetti skin lesions, and multiple renal cysts. The presence of two major or one major feature plus two minor features meet the diagnostic criteria for definite tuberous sclerosis complex [Table 1].

Mutations in one of two genes, TSC1 on chromosome 9q34, and TSC2 on chromosome 16p13, respectively, encoding for hamartin and tuberin, accounts for this disorder. Both genes are transmitted in an autosomal dominant fashion. TSC2 mutations account for the majority of sporadic cases, and these individuals usually show a more severe phenotype that includes renal lesions and neurologic deficits. The presence of germlinemosaicism has also been confirmed; however, there are no standard peripheral molecular tests for detection.

Skin lesions, which are found in 70-80 percent of cases, are important features for early diagnosis. Multiple facial angiofibromas, which are observed in approximately 80% of affected individuals, may appear within the first 2 years of life. The angiofibromas are firm, discrete, red-brown, telangiectatic papules, 1-10 mm over nasolabial furrow, eyelids, cheek and chin.

Ash leaf-shaped or thumbprint-shaped and guttate or confetti-like macules are ovoid, white or hypopigmented, 1-3 cm in size, present over trunk or limbs since birth.

Shagreen patches appear as irregular thickened, skin-colouredleathery plaques that are frequently located on the lumbosacral region and represent a type of connective-tissue nevus. It develops at age of 2 years and occurs in approximately 50 percent of affected individuals. Multiple shagreen patches over abdomen, buttocks, back of thigh, back of left knee joint and arm was present in our case which is an unusual finding not reported till date.

Our patients had all the lesions bilaterally, a few case reports in which one of the feature of the disease was found unilaterally.

Periungual fibromas are smooth, firm, skin-coloured papules that are distributed around the nail folds appear in late childhood and may be the sole cutaneous finding in some individuals. Other cutaneous lesions include pedunculated, skin-coloured papules (molluscum pendulum), cafe-au-lait macules and gingival fibromas.

Histopathologically most of the lesions are hamartomas, and in many organs the cells resemble embryonic cells, suggesting that defect occurs at an early stage of life. Most of the cutaneous lesions show excess of collagen. The angiofibromas consist of hyperplastic blood vessels and sebaceous glands of immature hair follicles, in addition to increased collagen synthesis.

Various ocular and neurologic manifestations occur in tuberous sclerosis including retinal hamartomas, punched-out areas of retinal depigmentation, seizure disorders, mental retardation, learning disabilities, autism, attention-deficit disorders, and psychoses. Epilepsy is the most common neurologic symptom and may affect 80-90 percent of TS individuals. Supratentorial brain lesions, which are found in 90 percent of individuals, include cortical tubers, subependimal nodules, subependimal giant-cell astrocytomas, white matter linear migration lines, and transmantle cortical dysplasia. Cortical tubers represent anomalous glial proliferation and migration and are thought to have epileptogenic foci.

Cardiac, renal, and other organ anomalies may occur in TS. Cardiac rhabdomyomas can be detected in 50 percent of affected infants and may spontaneously involute during the first few years.
of life. Renal lesions are noted frequently on screening and the majority of these lesions are angiomyolipomas. Renal cysts are less common, and renal-cell carcinomas may occasionally occur.

A multidisciplinary treatment approach is necessary to assess for neurodevelopmental, ophthalmologic, renal, and other organ system involvement. Neuroimaging, cutaneous and ophthalmologic examination, renal ultrasonography, echocardiography, and chest computed tomography should be done at time of diagnosis. Periodic monitoring, which includes neuroimaging, neurodevelopmental assessment, and renal ultrasonography should be done at least every 1-3 years. The cosmetic appearance is improved by removing angiofibromas with pulse-dye vascular laser (wavelength 585nm) or by carbon dioxide laser. Surgical treatment may be required for relief of symptoms in other organs.

The life expectancy of severely affected infants is poor, 3% die in first year, 28% under 10 years and 75% before 25 years. The prognosis for older children or young adults with mild disease is unpredictable.

For proper genetic counselling mutation studies should be carried out on the affected child. Both genes are studied in sequence Prenatal diagnosis is possible with DNA technology, provided mutation in the affected child is known. The patient was referred to neurophysician and given antiepilepsy drugs, was counselled and advised for laser therapy for adenoma sebaceum. Children of affected parent should be offered a skin examination for ash-leaf macule, renal & liver ultrasound and cardiac ultrasound at mutual consultation.

**CONCLUSION:** Case was fulfilling seven major criteria and 3 minor criteria along with other unique features like, multiple shagreen patches, molluscum pendulum, few cysts in left kidney and angiomyolipoma in right lobe of liver.

**REFERENCES:**

CASE REPORT


<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Case</th>
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<tbody>
<tr>
<td>1 Facial angiommas</td>
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<tr>
<td>2 Ash-leaf macule</td>
<td>+</td>
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<tr>
<td>3 Shagreen patch</td>
<td>+</td>
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<tr>
<td>4 Periungual Fibromas</td>
<td>+</td>
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<tr>
<td>5 Retinal nodular hamartomas</td>
<td>+</td>
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<tr>
<td>6 Renal angiomyolipoma</td>
<td>+</td>
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<td>7 Cortical tubers</td>
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<table>
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<th>Minor Criteria</th>
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<tr>
<td>1 Dental Pits</td>
<td>+</td>
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<td>2 Bone cysts</td>
<td>+</td>
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<td>3 Multiple renal cysts</td>
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Table 1: Diagnostic criteria for Tuberous sclerosis

Figure 1(a): Adenoma sebaceum, (b) Shagreen patches over back, (c) Dermal nevus over right buttock.
Figure 2: Koenen’s tumour over (a) middle finger of left hand, (b) fourth and fifth toe of left feet.

Figure 3(a): CT scan head shows subependymal calcified tubers in left parietal region with right sided cerebral atrophic changes, (b): Multiple cysts on X-ray of hands.

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