

Signs and Symptoms of Tuberous Sclerosis Complex

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Editorial

Tuberous Sclerosis Complex (TSC) is a multisystem disorder. Described in 1908 as a VOG tries, including adenoma sebaceum, epilepsy and mental retardation. Because TSC affects no two people in the same way, there is no sure way to predict where and how the disorder will manifest.

57 patients at the Child and Youth Health Care Institute of Vojvodina were diagnosed with TSC on the basis of hypomelanotic skin lesions and epileptic seizures (45.61%), hypomelanotic skin changes, cardiac rhabdomyomas and epileptic seizures (21.05%), hypomelanotic skin changes and neuroimaging (3.51%), epileptic seizures and neuroimaging (10.53%) and epileptic seizures and kidney changes (1.75%).

Tuberous Sclerosis Complex Features

Diagnosis is based on symptoms and signs presentation which are differentiated as major and minor clinical TSC characteristics (Table 1) [1-3].

Major features of TSC	Minor TSC Features
Facial angiofibromas or forehead plaque	"Confetti" skin lesions
Ungual fibroma (>2)	Multiple randomly distributed dental enamel pits (>3)
Hypomelanotic macules (>3 and >5 mm)	Radial migration lines in cerebral white matter
Shagreen patch	Rectal polyps (hamartomas)
Multiple nodular retinal hamartoma	Bone cysts
Cortical tuber	Gingival fibromas (>2)
Sub ependymal nodules	Nonrenal hamartoma
SEGA tumors (sub ependymal giant cell astrocytoma)	Achromic retinal patch
Cardiac rhabdomyoma	Renal cysts (multiple)
Lymphangiomyomatosis	-
Renal AML	-

Table 1: Differentiation of major and minor clinical TSC characteristics.

Neurological TSC Features

Several types of brain c may be seen in patients with TSC, including cortical tubers, Sub Ependymal Nodules (SEN), and SEGA tumors. Some individuals will have all of these changes, whereas others will have none. The vast majority of individuals with TSC, however, will have one of these abnormalities. Abnormal neurological findings result from their location, size, and growth [4-6].

Seizures occur in 60-90% of children with TSC, in three quarters of infants when they are manifested as epileptic spasms. 57.9% of children having TSC have the first attack during within first 6 months of life, 75% within the first year and 6.4% after the age of five. Multifocal or focal EEG changes are found in over 70% of patients with TSC. It is believed that the development of epilepsy after the first attack in TSC is 100%.

Mental retardation depends on the presence of epileptic seizures and the development of epileptic encephalopathy, as well as on the secondary damage to the localization of nodules, astrocytoma, or SEGA tumor or it can be a result of hydrocephalus.

Skin changes

The best recognised TSC cutaneous manifestation are hamathoma: Adenoma sebaceum, angiofibroma. They appear in early childhood and show progression during puberty and adolescence. Other skin lesions presents as: Hypomelanotic macules, unguinal and gingival fibromas, shagreen patch or forehead and face patches [7].

Cardiac findings

Cardiac manifestations of TSC are usually maximal presented at birth and during early in life (22/26GW). Rhabdomyomas are present in 50-60% of patients with TSC at birth. 50-85% of infants with isolated cardiac rhabdomyomas at birth will present other signs of TSC during later life. Patients with TSC and atrial or ventricular rhabdomyomas usually do not exhibit any symptoms. There might be signs of cardiac failure, hydrops or even fetal death. Rhabdomyomas involving the cardiac conducting system may predispose ventricular pre-excitation or other arrhythmias.

Ophthalmic findings

Ocular abnormalities are present in 50-80% of TSC patients. Analogous to hypomelanotic skin macules hypo pigmented areas of retina, iris, and even eyelashes are reported.

Renal findings

Renal manifestations are the second most common clinical features of TSC, manifesting as: autosomal dominant polycystic kidney disease, isolated renal cysts, Angiomyolipomas (AML), and renal cell carcinoma [8].

Polycystic kidney disease present in 2-3% of TSC patients, during early life causing hypertension, hematuria, nephrolithiasis or renal failure. They are present in patients with genetic abnormality affecting *TSC2* and *PKD1* gene. Usually asymptomatic renal cysts are present in 20% of male and 10% of female TSC patients.

AMLs are noted in as many as 80% of persons with TSC. They also can occur as isolated lesions in persons without TSC. They appear as multiple small AMLs studding the kidney surface of the kidney or as a larger lesion, giving symptoms if they are over 4-6 cm in their largest diameter. 75% AMLs over 6-8 cm diameter often cause hemorrhage. Large AML and renal cell carcinoma appear frequent in TSC patients.

Lung findings

Symptomatic pulmonary involvement are present exclusively in adult women (>30 years), in 40% as AMLs over 4-6 cm diameter. They mostly present as: multifocal micronodular pneumocyte hyperplasia, pulmonary cysts, and Lymphangioleiomyomatosis (LAM).

Dental findings

Large number of pitting of the dental enamel is present in permanent teeth of TSC patients. In the primary (deciduous) teeth they are present in 30% of affected children, rarely producing symptoms. Smaller numbers (<6) of dental pits is present in 10% of healthy controls. Gingival fibromas occurs in 70% of adults and 50% of children with mixed dentition, but only in 3% of TSC children with only primary teeth. Gingival fibromas associated with more than 10 dental pits are highly suggestive of TSC.

Other organs systems features

Gaster, intestine, and colon hamartomas and polyposis occur, almost without significant symptoms. Gastrointestinal hamartomas occasionally cause bleeding. Asymptomatic and non-progressive are hepatic cysts and AML are present in 24% of TSC patients, with, with female-to-male ratio 5:1.

Sclerotic and hypertrophic bone lesions may be found incidentally on radiography, occasionally palpable, or associated with nonspecific, vague, aching pains.

Arterial aneurysms, intracranial, aortal or axillary are very rare.

TAND-TSC associated neuropsychiatric disorders

Around 90% of TSC patients have a range of behavioral, psychiatric, intellectual, academic, neuropsychological and psychosocial difficulties. TAND-tuberous sclerosis complex-associated neuropsychiatric disorders bring together these multidimensional manifestations of the disorder [9].

Our Patients

57 patients at the Child and Youth Health Care Institute of Vojvodina were diagnosed with TSC on the basis of hypomelanotic skin lesions and epileptic seizures (45.61), hypomelanotic skin changes, cardiac rhabdomyomas and epileptic seizures (21.05), hypomelanotic skin changes and neuroimaging (3.51%), epileptic seizures and neuroimaging (10.53%) and epileptic seizures and kidney changes (1.75%).

Conclusion

Because TSC affects no two people in the same way, there is no sure way to predict where and how the disorder will manifest, but in children skin changes, seizures and cardiac rhabdomyoma are dominant clinical signs.

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