



CLINICAL PRESENTATIONS OF TUBEROUS SCLEROSIS COMPLEX: TWO CASE REPORTS

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Tuberous sclerosis complex (TSC) which is also known as Bourneville Disease, cerebral sclerosis, epiloia, sclerosis tuberosa or simply tuberosa sclerosis is a rare genetic disorder which presents as benign growths in skin, brain and other viscera resulting in severe developmental, behavioural and systemic abnormalities. Virtually all the patients with TSC will show skin growths of variable sizes. Those children who manifest the skin lesions early in life also have history of seizures. The name tuberous sclerosis comes from the characteristic tuber or potato-like nodules in the brain, which calcify with age and become hard or sclerotic. This disorder has been known to exist ever since it was diagnosed by French physicians about a century back when it was known as epiloia or Bourneville Disease. Vogt in 1880 described the classical triad of mental retardation, intractable seizures and delayed development¹

Quite a few of the TSC patients show evidence of the disorder in the early years of life. But it is a disease which is known to remain dormant and subtle and may present later in life which is one of the reasons why this disease remains unnoticed and under or misdiagnosed in many patients for most part of their lives².

The physical manifestations of the disease are due to malformed tissues (hemartia), hamartomas which are benign growths like subependymal nodules or angiofibromas and very rarely malignant growths as hamartoblastomas. Most of the children show developmental³ and learning disabilities, intellectual impairment, problems with concentration in learning⁴.

Case 1:

15 years old female student of class 6 belonging to a village in the peripheral part of Ludhiana, Punjab. She was born at term at a private nursing home and appeared to be normal with no congenital

abnormalities. The parents observed proportionate physical growth but was seen to develop small areas of patchy discolouration (hyperpigmentation) as well as wart like peduncled growths on one side of the face extending to lateral and posterior aspect of neck by the time this child was 5 years of age. The growths seem disappear in certain areas temporarily. Multiple small growths which looked like skin tags continued to appear in crops. The child was observed to be moody, aloof and disconnected and showed minimal inquisitiveness as would be expected in a normal child in growing age group. She was admitted to a primary school in the village but her performance was barely passable. She began to have repeated episodes of seizures by the time she attained age 10 years. She was diagnosed to have TSC on the basis of skin manifestations, convulsions and CT scan findings which showed subependymal nodules, cortical and subcortical tubers which are classic intracranial manifestations of tuberous sclerosis.

Case 2:

29 years old married lady hailing from Saharnpur Uttar Pradesh presenting with history of hypertension, occasional seizures, dyspnoea and appearance of variable sizes of skin growths visible mostly on forehead, face, neck, upper back and both upper limbs. Examination of the face showed facial angiofibromas which had been present since childhood. She also manifested fleshy growths under and around the toe nails and to some extent in the nails of the fingers with the largest one in the left big toe showing evidence of haemorrhage. CT head showed few subcortical tubers in the vicinity of foramen magnum partially blocking it. Ultrasonography of the abdomen showed hamartomas in kidneys bilaterally. Chest Xray revealed multiple small cysts in both lungs.

DISCUSSION

Tuberous sclerosis is an autosomal dominant genetic disorder with variable expressivity and incomplete penetrance. Majority of the cases are sporadic genetic mutations, not inheritance, but are likely to pass on to the progeny. So far it has been mapped to two genetic foci, TSC1 which encodes for the protein hamartin is located on chromosome 9 q34 and TSC2 which encodes for protein tuberlin located on chromosome 16 p13.3. Hamartin and Tuberlin function as a complex which is involved in cell division and cell growth⁵.

TSC is known to occur in all races and both genders. It is a coincidence that both the observed cases in this study are females. Published data in literature⁶ puts the estimates of prevalence to be between 7 to 12 cases per 100,000 with majority (more than 50%) being undetected. The diagnosis has become easier and more specific with the advent of CT and ultrasound scanning. Prior to 1998, the diagnosis of TSC was mainly confined to severely affected individuals with learning disabilities, facial angiofibromas and seizures (Vogt's triad). TSC is capable of affecting most organ systems and tissues. In the central nervous system it may

present as brain tumours⁷ which are giant cell astrocytoma, cortical tubers or subependymal nodules. In the kidneys it may present as benign tumours like angiomyolipomas which are generally multiple and bilateral. Autosomal dominant polycystic kidney disease is occasionally seen to be associated with TSC. Pulmonary involvement may present as multiple cysts and lymphangiomyomatosis. There may be rhabdomyomas in the cardiac muscle which are easily picked up by echocardiography. Dermatological manifestations in the form of facial angiofibromas, periungual fibromas (Koenen's tumour), hypomelanotic macules, forehead plaques and shagreen patches are easily detectable. Retinal lesions called astrocytic hamartomas or phakomas which can easily get calcified are also seen in some cases of tuberous sclerosis. Although it is still considered to be rare, tuberous sclerosis is still a common disease when compared to many other genetic illnesses. Complete work up of the diagnosis of TSC and its variants is based on major and minor criteria^{8,9,10}.

REFERENCES

1. Curatolo P, Jóźwiak S, Nabbout R; TSC Consensus Meeting for SEGA and Epilepsy management. Management of epilepsy associated with tuberous sclerosis complex (TSC): clinical recommendations. *Eur J Paediatr Neurol*. 2012 Nov;16(6):582-6.
2. Paolo Curatolo, Roberta Bombardier and Sergiuz Jozwiak: Tuberous Sclerosis. *The Lancet*, 372 :9639, pp 657-668, Aug 2008
3. Harrison JE, Bolton, PF (1997). "Annotation: Tuberous sclerosis". *Journal of Child Psychology and Psychiatry* 38 (6): 603-614. doi:10.1111/j.1469-7610.1997.tb01687.x. PMID 9315970.
4. Ridler K, et al. (2006). "Neuroanatomical Correlates of Memory Deficits in Tuberous Sclerosis Complex". *Cerebral Cortex* 17 (2): 261-71. doi:10.1093/cercor/bhj144. PMID 16603714.
5. Northrup H, Au K (5 December 2005). "Tuberous Sclerosis Complex". *GeneReviews*. Retrieved 2 September 2007
6. O'Callaghan FJK, Shiell AW, Osborne JP, Martyn CN (1998). "Prevalence of tuberous sclerosis estimated by capture-recapture analysis". *Lancet* 351 (9114): 1490.
7. Ridler K, et al. (2004). "Standardized whole brain mapping of tubers and subependymal nodules in tuberous sclerosis complex". *Journal of Child Neurology* 19 (9): 658-665. PMID 15563011.
8. "Tuberous Sclerosis Fact Sheet". National Institute of Neurological Disorders and Stroke. 11 April 2006. Retrieved 3 October 2006.
9. "Summary of Clinical guidelines for the care of patients with Tuberous Sclerosis Complex" (PDF). Tuberous Sclerosis Association. April 2002. Retrieved 3 October 2006.

10. Roach E, Sparagana S . "Diagnosis of tuberous sclerosis complex". Journal of Child Neurology 19 (9): 643-9, 2004.