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Case Report

Tuberous Sclerosis in a Young Adult

Ikramullah Khan and Rifat Yasmin

Department of Dermatology, Pakistan Institute of Medical Sciences, Islamabad

Tuberous sclerosis is a genetic disorder of hamartoma formation in many organs, characterized by angiofibroma, Shagreen patch, periungual fibroma, ash-leaf macule, although not invariably, seen in association with epilepsy and mental retardation. We document a case of tuberous sclerosis in a young adult without CNS manifestations.
Key word: Tuberous sclerosis complex (TSC)

Introduction

Tuberous sclerosis complex (TSC) is known to be a genetic disorder affecting cellular differentiation, proliferation, and migration early in development, resulting in a variety of hamartomatous lesions that may affect virtually every organ system of the body. Clinically, TSC exhibits an autosomal dominant inheritance pattern, with a high spontaneous mutation rate.

Neurological and dermatological abnormalities are the most common physical findings, since brain and skin pathology occurs in as many as 90-95 % of affected individuals, but these show a wide variation in age of onset and severity. Physical findings can vary greatly since TSC can affect different organ systems in different ways at different times of the patient's life.

Three imaging procedures are usually undertaken: CT or MRI scans of the brain, renal ultrasounds, and echocardiograms[1, 2].

The goals of treatment for patients with TSC are the same as for all patients with a multisystem chronic disease: providing the best possible quality of life with the fewest complications from the underlying disease process, least adverse treatment effects, and minimal medications.[3]

Case Report

A 28 years old male presented through outpatient department of Pakistan Institute of Medical Sciences Islamabad, with complaint of papulonodular lesions on face since the age of 8 years, gradually increasing in size, along with hypopigmented patches on left leg and lower back.

Parents were not related, and there was no other family member having such complaint. There was no history of seizures or behavioral abnormality.

On examination, the adult was of average built, well oriented and was having normal intelligence. He had multiple reddish brown papules (Angiofibromas) on face (Figure 1), more so on chin and nasolabial folds, ranging in size from 1 to 10mm.There were hypopigmented macules (Ash leave macule) one on left leg (Figure 2) and other on lower back. However there were no other skin lesions.

On investigation patient was having normal biochemistry, Chest X-Ray, Echocardiography, ultrasound abdomen and CT scan brain excluding systemic involvement like kidneys, lungs, heart and CNS in disease process. Eye examination was also normal.

Biopsy of Angiofibroma was done which showed hyperplastic blood vessels and decreased total collagen content (Figure 3). The patient was diagnosed as a case of tuberous sclerosis according to the diagnostic criteria determined by a committee of the US National Tuberous sclerosis Association.

Patient was advised pulsed dye vascular laser treatment of his Angiofibromas, and was advised regular follow-up for monitoring, for possible systemic involvement. Genetic counseling of patient was also done.

Fig. 1: Angiofibromas on Face, More so on Chin and Nasolabial Fold

Fig. 2: Ash Leaf Macule on Left Leg

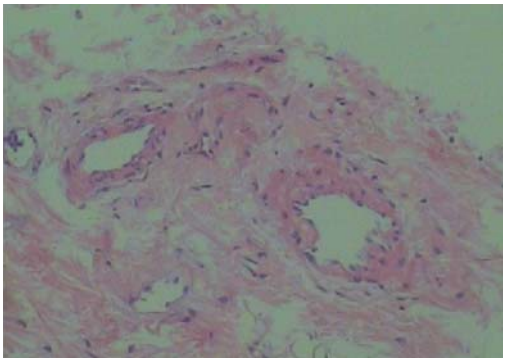

Fig. 3: Histopathology of Angiofibroma, showing Hyperplasic Blood Vessels

Discussion

Tuberous sclerosis shows a wide variety of clinical expressions. Some individuals are severely affected; while others have very few features.[4] Forme frustes are common. An accurate estimation of the course in an individual depends on the extent of 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. The most common cause of mortality and morbidity is the complications of neurological involvement, which are chiefly due to intractable epilepsy, status epilepticus, and subependymal giant cell astrocytoma with associated hydrocephalus. Renal complications are the next most frequent cause of morbidity and death. Less common are cardiac arrhythmias, congestive heart failure, and end-stage lung disease.

Most individuals present with parental concern about small raised tumors on the child's face. (In most cases, the parent draws the attention to the cutaneous stigmata.) Children with late onset and individuals with few skin signs may remain

undetected until adolescence. Mental retardation is observed in 60-70% of cases; however, if mental development is normal throughout childhood, subsequent worsening is uncommon. Ocular involvement includes hypopigmented spots in the iris, equivalent to the ash-leaf macule in the skin. Retinal phakomas are observed as whitish-gray nodular lumps.

Findings in other organs include cardiac rhabdomyomas, Aneurysms of thoracic and abdominal aortas,[5] Renal involvement is usually manifested by an angiomyolipoma, less commonly by renal cysts. Pulmonary changes include lymphangiomatosis with cyst formation.[6] Gastrointestinal tumors may be associated.

Patient is diagnosed according to Diagnostic criteria determined by a committee of the US National Tuberous sclerosis Association which has been revised. Crieteria has major and minor features which are following.

Major Features:

Facial angiomas and forehead plaque
Nontraumatic ungula and periungual fibroma
Hypomelanotic macules(>3)
Shagreen patch
Multiple retinal nodular hamartoma
Cortical tuber
Subependymal nodule
Subependymal giant cell astrocytoma
Cardiac rhabdomyoma
Lymphangioleiomyomatosis
Renal AML

Minor Features:

Multiple dental pits
Hamartomatous rectal polyps
Bone cysts
Cerebral white matter radial migration lines
Gingival fibromas
Nonrenal hamartoma
Retinal achromic patch
"Confetti" skin lesions
Multiple renal cysts

Diagnostic Criteria

Definite TSC- Either two major features or one major plus two minor Features.
Probable TSC- One major plus one minor feature
Possible TSC- Either one major feature or two or more minor features.

Evaluation of newly diagnosed patients should include a personal and family history and a clinical examination, including fundoscopy, cranial imaging[8] (eg, MRI[9], nonenhanced CT scanning), renal ultrasonography, and echocardiography in infants. Either CT scanning or MRI may need to be performed every 1-3 years, depending upon the level of clinical suspicion in a given child.

In a family with only one child affected, evaluation of parents is more important than siblings or relatives.

Histologically Angiofibromas show atrophic sebaceous glands with dermal fibrosis and dilation of some of the capillaries. The fibrosis occasionally has a glial appearance because of the large size and stellate shape of the fibroblasts. Elastic tissue is absent in the angiofibromas.

A multidisciplinary team approach is useful to address the many organ systems that may be affected.

Periodic monitoring is necessary, ranging from 1-3 years, depending on the internal tumors and their manifestations. Treatment plans should be determined on an individual basis.

References

1. Franz DN: Diagnosis and management of tuberous sclerosis complex. Semin Pediatr Neurol 1998 Dec; 5(4): 253-68.
2. Roach ES, DiMario FJ, Kandt RS, Northrup H: Tuberous Sclerosis Consensus Conference: recommendations for diagnostic evaluation. National Tuberous Sclerosis Association. J Child Neurol 1999 Jun; 14(6): 401-7.
3. The Tuberous Sclerosis Association: Clinical guidelines for the care of patients with Tuberous Sclerosis Complex. Available at: http://www.tuberous-sclerosis.org/professionals/guidelines.shtml. Birmingham, England; April, 2002.
4. Webb DW, Fryer AE, Osborne JP: Morbidity associated with tuberous sclerosis: a population study. Dev Med Child Neurol 1996 Feb; 38(2): 146-55
5. Jost CJ, Gloviczki P, Edwards WD, et al: Aortic aneurysms in children and young adults with tuberous sclerosis: report of two cases and review of the literature. J Vasc Surg 2001 Mar; 33(3): 639-42
6. Franz DN, Brody A, Meyer C, et al: Mutational and radiographic analysis of pulmonary disease consistent with lymphangioleiomyomatosis and micronodular pneumocyte hyperplasia in women with tuberous sclerosis. Am J Respir Crit Care Med 2001 Aug 15; 164(4): 661-8.
7. Roach ES, Gomez MR, Northrup H: Tuberous sclerosis complex consensus conference: revised clinical diagnostic criteria. J Child Neurol 1998 Dec; 13(12): 624-8
8. Altman NR, Purser RK, Post MJ: Tuberous sclerosis: characteristics at CT and MR imaging. Radiology 1988 May; 167(2): 527-32
9. Takanashi J, Sugita K, Fujii K, Niimi H: MR evaluation of tuberous sclerosis: increased sensitivity with fluid- attenuated inversion recovery and relation to severity of seizures and mental retardation. AJNR Am J Neuroradiol 1995 Oct; 16(9): 1923-8.