Case Report

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Tuberous Sclerosis Spectrum

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Abstract

Tuberous sclerosis complex (TSC) is a relatively rare autosomal dominant disorder characterized by widespread benign tumor formation in a variety of organs. Mutations in either TSC1 or TSC2 tumor suppressor gene are responsible for TSC. The gene products of TSC1 and TSC2, also known as hamartin and tuberin, respectively, form a physical and functional complex and inhibit the mammalian target of rapamycin complex 1 (mTORC1) signaling. The mTORC1 pathway is an evolutionarily conserved growth promoting pathway. mTORC1 plays an essential role in a wide array of cellular processes including translation, transcription, trafficking and autophagy. In this review, we will discuss recent progresses in the TSC-mTOR field and their physiological functions and alterations of this pathway in pathophysiology.

Our case is 9 years male child presented to us with skin lesion prominent on face.

Keywords: Tuberous sclerosis; Shagreen patch; Adenoma sebaceum.

Introduction

Von Recklinghausen first described tuberous sclerosis in 1862. Desire-Magloire Bourneville (a French physician) coined the term sclerose tubereuse, from which the name of the disease has evolved. Sherlock coined the term EPILOIA encompassing the clinical triad of tuberous sclerosis (Epi: epilepsy, Loi: low intelligence, A: adenoma sebaceum). 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 inherited disease, being associated with at least two separate chromosomes (TSC1, found on chromosome9q34, and TSC2, on chromosome 16p3).[1] The disease is transmitted either through genetic inheritance or as a spontaneous genetic mutation. The incidence of tuberous sclerosis is 1 in 6000 births, and about two thirds of cases are sporadic, occurring in the absence of a family history of the disorder.[2]

Clinical diagnosis is easy when the patient presents with classical triad of seizures, mental retardation and adenoma sebaceum. However, in a patient presenting with an incomplete form of tuberous sclerosis, mistakes in the diagnosis are possible. We herein report a case of 19 years old male who presented with seizures and on evaluation was found to be a case of tuberous sclerosis. The importance of recognition of features of this rare syndrome

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is stressed.

Case Summary

A 9 years male, presented to our OPD de of hospital with complaints of skin lesions over face .

His past history was significant as he was reported to be mentally retarded (mental age is 7yrs now with DQ 77%).

On physical examination vitals were normal. Examination of skin revealed multiple nodular lesions on face, depigmented spots on the back,a large skin lesion on left pinna and yellowthickened area over the lower back (Fig 1 to 4).

1. Multiple small nodular lesions over face-Adenoma sebaceum (Figure I)
2. Depigmented spots, 2-3 cm over back - Ash leaves (Figure II)
3. A heap of tissue over left pinna-hamartoma (Figure III)
4. A yellowish thickened area over lower back-Shagreen patch (Figure IV)

Muscle tone andreflexes were normal and

Figure I: Adenoma Sebaceum

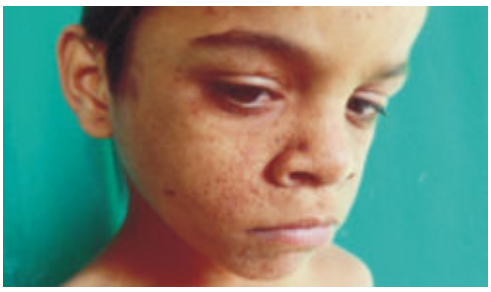


Figure II: Ash Leaf

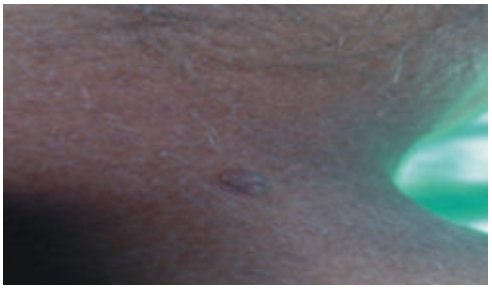


Figure III: Hamartoma

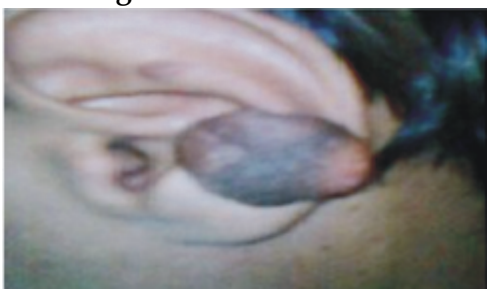


Figure IV: Shagreen Patche

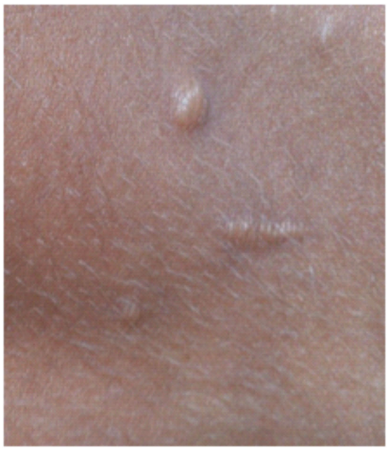
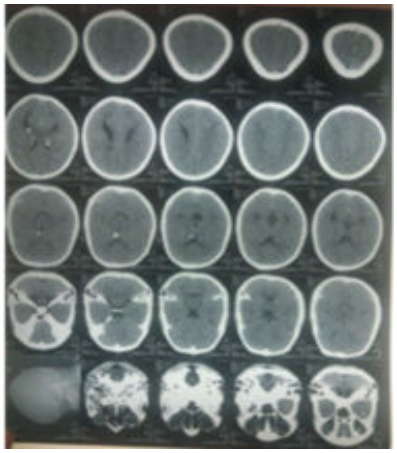


Figure V: Subependymal Calcification



no sensory deficit waspresent. His had poor past memory and was unable to perform simple arithmetic sums. Restof examination was unremarkable. His laboratory investigations revealed normal blood counts. Routine urinalysis was normal. Renal function tests, serum electrolytes and blood sugar level were normal. Abdominal

ultrasonography showed parenchyma of rightkidney replaced by multiple cysts andheterogenous high intensity masses consistentwith diagnosis of renal angiomyolipoma. CT of brain showed subependymal nodules. ECG and Echocardiography were normal. All clinical features suggested the classical picture of tuberous sclerosis. Molecular analysis of the gene TSC1 and TSC2 in chromosome 9 and 16 respectively could not be performed due to the availability constraints. Patient was discharged in stable condition on carbamazepine and levetiracetam with regular follow-up advice.

Discussion

Tuberous sclerosis shows a wide variety ofclinical expressions. Some individuals areseverely affected, while others have very few features. Tuberous sclerosis is characterized bythe development of unusual tumor-like growths (hamartomas) in brain, skin, retina and viscera. As multiple organs are involved, there is wide variability in presentation. Arguably the mostimportant hamartomas are cerebral corticaltubers, which are regions of abnormal corticalarchitecture with distinctive large neuronal cells. These hamartomatous swellings resemble potatoes and hence, referred to as tubers. Cortical tubers cause some of the most important clinical manifestations of tuberous sclerosis: epilepsy, mental retardation, and abnormal behavior including autism (mosaicism).[3,4,5,6]

Epilepsy occurs in 80-90% of all patients; with a positive correlation with subnormal intelligence.[7]

Cutaneous lesions are present in ninety six percent of the patients. These include facialangiofibroma (adenoma sebaceum), subungualfibromas, and shagreen patches. Two types of renal lesions occur in patients with tubersclerosis: angiomyolipomas and renal cysts. They may be found independently or together: they may be unilateral, bilateral, single or multiple. Angiomyolipomas are benign in natureand asymptomatic but spontaneous rupture and subsequent hemorrhage in to retroperitoneum may occur.[8]

In the heart, the most frequent and characteristic type of tumor is cardiacrhabdomyomas. Incidence of cardiacrhabdomyomas in children with tuberous sclerosis is higher than in adult patients with tuberous sclerosis. It has been suggested that such lesions tend to regress in early infancy and adolescence.[9]

The present patient had tuberous sclerosischaracterized by classical features: seizures, mental retardation, and facial angiofibromas. Incomplete forms of tuberous sclerosis may present with acute complications such as hematuria, retroperitoneal hemorrhage orpneumothorax.[10]

It is estimated that nearly one million people are known to suffer from tuberous sclerosis. 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. Drug therapy for some of the manifestations of TSC is currentlyin 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. This presentation aims at considering the rarity of the disease and listing it in the differential diagnosis of children presenting with seizures, skin manifestations and mental retardation.

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