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Case Report

Case report on tuberous sclerosis

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ABSTRACT

Tuberous sclerosis is a genetic multisystem disorder characterized by widespread hamartomas in several organs, including the brain, heart, skin, eyes, kidney, lung and liver. The affected genes are TSC1 and TSC2, encoding hamartin and tuberin respectively. Most features of tuberous sclerosis become evident only in childhood, limiting their usefulness for early diagnosis. We report a case of 3months old female child with seizures and hypo-pigmented skin lesions. The case is rare as it is documented in a family affected continuously in three generations involving four members.

Keywords: Genetic disorder, Hypo-pigmented skin lesions, Seizures, Tuberous sclerosis

INTRODUCTION

Tuberous sclerosis (or) tuberous sclerosis complex (TSC) or Bourneville disease, first described by Desiree Magloire Bourneville in 1880.[1] It is a rare genetic disorder of autosomal dominant inheritance, variably expressed, multisystem disorder that can cause circumscribed benign, non-invasive lesions in various organs such as the skin, eyes, kidneys, brain, heart and lungs leading to significant health problems like seizures, intellectual disability, autism or developmental delay.[2,3] TSC is caused by mutations on either of two genes, TSC1 and TSC2, which encode for the proteins hemartin and tuberin respectively. These proteins act as tumor growth suppressors, agents that regulate cell proliferation and differentiation.[4]The disorder affects about one in ten thousand persons in the general population and has an estimated incidence of one case per 6,000 live births. Thus, it is the second most common neurocutaneous syndrome after neurofibromatosis. TSC has no predilection for gender or race or ethnicity. Cutaneous findings are usually the first clue that patient has TSC, but other features may lead to diagnosis. Definite TSC is diagnosed when either 2 major features (out of total 11) or one major with 2 minor features (out of total 9) are present (Table 1). TSC has no cure, but treatment as medicines for symptomatic relief, educational therapy can help to relieve symptoms.[4]

CASE REPORT

A 3 months old female child was brought to Hospital, with complaints of involuntary movements of left hand and fingers since one day. On first day child had involuntary clonic movements of left hand and fingers lasting for about 5minutes. Child was alert and was smiling at mother during the time of involuntary movements. Baby was born to non-consanguineous marriage with birth history of term, Normal Vaginal Delivery (NVD), cried immediately after birth and birth

weight was 3kgs. Immunization history includes single dose of Bacillus Calmette-Guerin (BCG), Diphtheria (DPT) and two doses of Oral Polio Vaccine (OPV) vaccination was given. There was no history of loss of eye to eye contact, excessive cry, fever, vomiting, loose stools, cough, cold, convulsions previously, decreased urine output or cry during micturition. History of pentavalent vaccine administration 20days back to the child. There was a family history (Figure 1) of angiofibromas over the face of his mother, grandmother and sibling since their birth (Figure 2).

Table 1: Major and Minor Criteria of tuberous sclerosis complex.

Major Criteria	Minor Criteria
Cortical tuber	Cerebral white matter migration line
Subependymal nodule	Multiple dental pits
Facial angiofibroma or forehead plaque	Gingival fibromas
Ungual or periungual fibroma (nontraumatic)	Bone cysts
Hypomelanotic macules (>3)	Retinal achromatic patch
Shagreenpatch	Confetti skin lesions
Multiple retinal hamartomas	Nonrenal hamartomas
Cardiac rhabdomyoma	Multiple renal cysts
Renal angiomyolipama	Hamartomatous rectal polyps
Pulmonary lymphangioleimyomatosis	
Sub ependymal gaint cell astrocytoma	

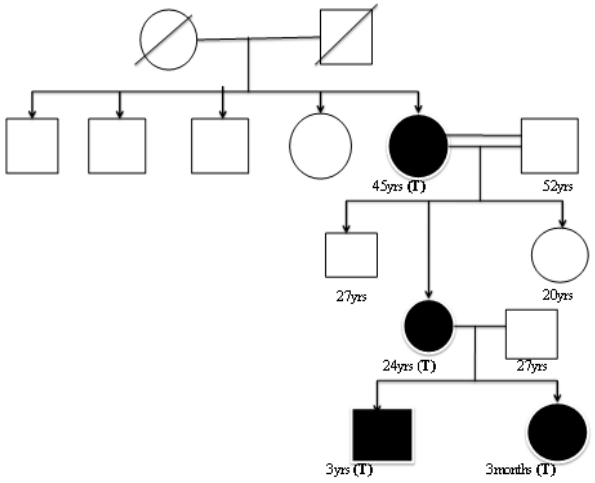

Figure 1: Pedigree of family with Tuberous sclerosis 'T' indicates Tuberous sclerosis.

Baby mother had 4-5attacks of convulsions at her younger age; she did not develop any further attacks. Grandmother had no convulsions documented till now. Sibling had similar history i.e., convulsions and admitted in hospital at 6months of his age and was diagnosed with tuberous sclerosis and was on Syrup VALPROATE and Syrup LEVITRACETAM. Sibling CT scan brain revealed periventricular calcification with some healed granulomas and had frequent episodes of convulsions, behavioral problems and developmental delay.

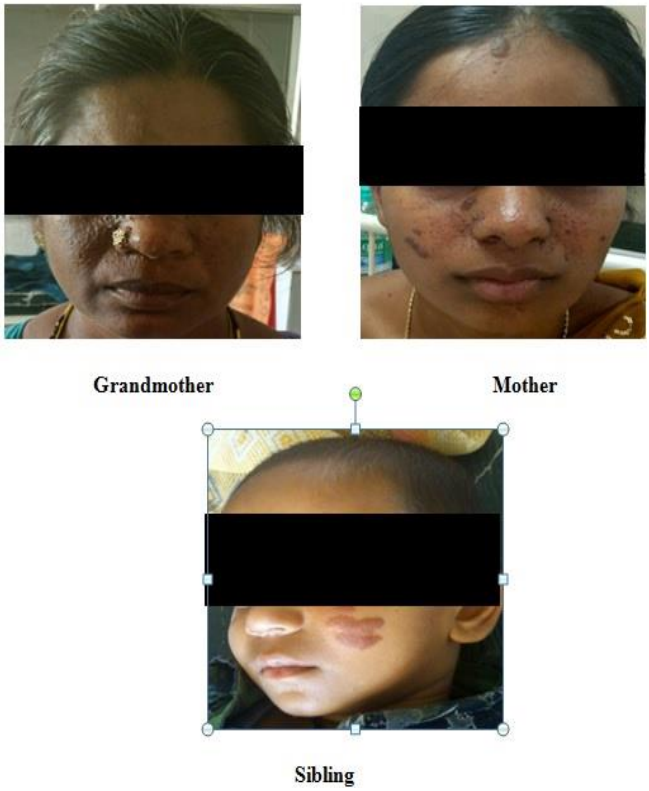

Figure 2: Facial Angiofibromas in grandmother, mother and sibling.

On examination child was conscious, afebrile and alert. Baby had multiple hypomelanoate macules (ash leaf) over back (Figure 3), trunk, chest, abdomen, thigh and gluteal region; flat occiput is present. Detailed CNS, RS, CVS, P/A examination revealed no abnormalities. Investigations showed Hb-11.3g/dl; WBC-9,800cells/cc mm; Platelets-2.4lakhs/cc mm; Differential count-P48, L50, E2; RBS-99mg/dl; Serum Na+- 145mmol/lit; Serum K+- 4.8mmol/lit. CT scan Brain showed minimal cerebral edematous frontal lobe. US abdomen was normal.

Treatment include loading dose of Injection PHENYTOIN 20mg/kg/dose i.e., 100mg in 3cc normal saline followed by Injection PHENYTOIN 5mg/kg/day i.e., 13mg twice daily; continuous IV fluids Isolyte-P was started. On the day of admission convulsions was documented again in the form of clonic movements of both upper limbs and followed by starring look. From day 5 of hospital admission only Syrup PHENYTOIN 5mg/kg/day i.e., 0.5ml twice daily was given. After complete observation baby was free of convulsions for 4days and discharged with Syrup PHENYTOIN 0.5ml twice daily.

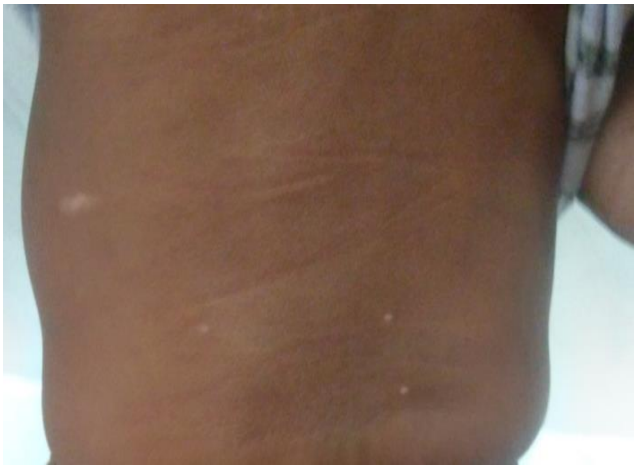

Figure 3: Hypomelanoate macules (ash leaf) over back.

DISCUSSION

Tuberous sclerosis is an autosomal dominant disorder that affects the patient and the family member in various ways. It is a disorder of cellular differentiation and proliferation that can affect the brain, skin, kidneys, heart and other organs.[5] The term tuberous sclerosis of the cerebral convolutions was used more than a century ago to describe the distinction findings at autopsy in some patients with seizures and mental sub normality. The term tuberous describes the potato like consistency of gyri with hypertrophic sclerosis. Population based studies in UK reported a frequency of 1 in 12,000 to 1 in 14,000 children under 10years of age and at a birth rate of 1 in 12,000 were affected by tuberous sclerosis. The wide range of organs affected by the disease implies an important role TSC1 and TSC2 genes, encoding hamartin and tuberin, in the regulation of cell proliferation and differentiation.[5,6] Recent studies, carried out on small families, indicated that mutation of TSC1 account for 15-30% of the families. In preponderance of mutation of TSC2 is even higher in sporadic cases, where mutations of TSC1 are found in 10-20% of families.[6]

In a series of patients reported by the mayo clinic more than 90% had skin lesions, about 90% had symptoms of cerebral pathology, 70-90% had renal abnormalities and about 50% had retinal hamartomas. CNS complications in TSC include epilepsy, cognitive impairment, challenging behavior and autism. Progress in structural and functional imaging has lead to further characterization of brain lesions such as cortical tubers, sub-ependymal nodules, sub-ependymal gaint cell tumors and white matter abnormalities. Epilepsy associated with TSC generally begins during first year of life and in most patients, in infantile spasm. Children with cognitive impairment are significantly more like to have an autistic spectrum disorder and attention deficit hyperactivity disorder. Seizures related sleep disorders such as prolonged sleep latency and night walking are routinely seen. Hypomelanotic macules are the most common dermatological manifestation, best seen under ultraviolet light (wood's lamp) particularly on the trunk and buttock. Hypomelanotic macules can be the only skin lesion in infants, if the child also have focal seizures or infantile spasms, a diagnosis of tuberous sclerosis should be considered.[6]

Renal complications are the most frequent cause of tuberous sclerosis related death. Multiple bilateral angiomyolipomas are more commonly seen in adults, especially in women's. Their frequency low in children i.e. 16% of patients below the age of 2years can be affected. Retinal complications can be found at any age, they have been described in small children and even in new born babies. Cardiac rhabdomyomas, pulmonary lymphangiomyomatosis and hepatic angiomyolipomas are less frequently observed.[6]

Usually the diagnosis is made when two major features or one major and two minor features can be shown (Table 1). Genetic testing enables patients with TSC to know exactly what mutation caused the disorder.[7] Once diagnosis is made, scrupulous, regular, age-dependent screening for behavioral, cognitive and neurodevelopmental dysfunction is strongly recommended.[6]

The management of TSC is symptomatic. However, the discovery of mammalian target of rapamycin (mTOR) pathway Upregulation in tuberous sclerosis associated tumors presents new possibilities for treatment strategies. Sirolimus makes the dysregulated mTOR pathway return to normal in cells that lack TSC1 or TSC2. Several results from in-vitro or in-vivo animal studies suggest that sirolimus or its analogues might be effective in the treatment of various manifestations of tuberous sclerosis (e.g. skin lesions, lymphangioleiomyomatosis, renal angiomyolipomas, renal-cell- carcinoma, or even polycystic kidney disease).[8]

CONCLUSION

Tuberous sclerosis is one of the neurocutaneous syndromes inherited in autosomal dominant fashion with almost complete penetrance with variable expressivity, affecting almost all organs. In our case patient and sibling had 2 major and 1 minor criteria, grandmother and mother had 2 major criteria for diagnosis. There is no cure for TSC, but symptomatic therapy is provided. As TSC is a lifelong condition, regular follow-ups, age-dependent screening for behavioral, cognitive and neurodevelopmental dysfunction is strongly recommended to enhance the quality of life for patients with TSC.

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REFERENCES

1. Shrestha S, Shrestha S, Ojha AR; Case report on Tuberous Sclerosis. Journal of Kathmandu Medical College, 2013;2(6);208-10.
2. Syed KB; Tuberous Sclerosis. J Pak Med Assoc. 2010;60(8):683-85.
3. Ishii M, Asano L, Kamiishi N, Hayashi Y, Daisuke Arai et al. Tuberous sclerosis diagnosed by incidental computed tomography findings of multifocal micronodularpneumocyte hyperplasia: a case report. Journal of Medical Case Reports. 2012;352(6):1-5.
4. Chandrakala, Patil S, Guruprasad KY. A Case Report of Tuberous Sclerosis in Two Generations. Journal of the association of physicians of India. 2014:62:60-64.
5. Behnes CL, Schutze G, Engelke C, Bremmer F, Gunaean B. 13-year-old tuberous sclerosis patient with renal cell carcinoma associated with multiple renal angiomyolipomas developing multifocal micronodularpneumocyte hyperplasia. BMC Clinical Pathology. 2013;13(4):1-5.
6. Curatolo P, Bombardieri R, Sergiuszjazwaiak. Tuberous sclerosis. 2008;372:657-68.
7. Hung CC, Su YN, Hwang Ys, Kim KJ.Mutational analysis of TSC1 and TSC2 in Korean patients with tuberous sclerosis complex. Brain Dev. 2006;7:72.
8. Rauktys A, Lee N, Lee L, Dabora SL. Topical rapamycin inhibits tuberous sclerosis tumor growth in a nude mouse model. BMC Dermatol. 2008;8:1.

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