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Tuberous sclerosis: Paper presentation

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Abstract: *Tuberous Sclerosis complex also called as Bournville Disease is a rare Autosomal Dominant genetic Disorder caused by mutations in TSC1 and TSC2 gene. It is a disorder involving brain, skin, kidneys, heart, eyes and lungs Presenting in late childhood so early diagnosis is often challenging. . Here, we report a case of a15 year female child with tuberous sclerosis.Multiple research work is still in progress regarding treatment and early diagnosis.*

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I. Introduction :

Tuberous sclerosis complex is a rare genetic disorder with estimated prevalence of 1 in every 95,136in general population[1]. Although it is a autosomal dominant disease about 80% cases are caused by de novo Mutation[2].

It is a neurocutaneous syndrome characterised by development of multiple benign tumours in various parts of body. It commonly involves brain, skin , retina and other viscera like kidney and heart. TSC 1 and TSC 2 are tumour suppressor genes which encodes for Harmartin and Tuberin respectively. It is mutation in these genes responsible for tumerogenesis and hamartoma formation in multiple systems which accounts for pathogenesis and morbidity in this disease. The clinical triad of Adenoma sebaceum, intellectual disability and Epilepsy characterises Tuberous Sclerosis. Here we present a case report of 15 year old female patient with characteristic clinical and radiological features of tuberous sclerosis complex.

II. Case Report:

A 15 year old female resident of Solapur presented to the hospital in emergency under medicine with complaints of one episode of convulsion 1 hour back. She is a known case of epilepsy since age of 5 years on antiepileptic medications. Patient presented with complaints of generalized tonic clonic convulsions lasting for 2 min and relaxation phase for 10 min. Patient lost her consciousness in between. Convulsions were associated with uprolling of eyeballs, urinary incontinence and frothing there was no evidence tongue bite.

Episode of GTCS was controlled by injection levetiracetam 500 mg iv stat. Patient was in post-ictal confusion for 6 hours. There was no history of fever, altered sensorium, vomiting, loose motion. She was born of non consanguineous marriage full term normal vaginal delivery. Patient has 4 siblings and there is no history of any seizure disorder or skin lesions in family members. In past history, patient has first seizure when she was 5 years old for which she was started on Tab sodium valproic acid 200 mg bd since then. Later patient had multiple episodes breakthrough seizures. Patient was reported to be intellectually disabled. Patient had limited social interactions. Patient only interacted in few words and small sentences. Developmental milestones were not significantly delayed.

On general examination, patient is conscious, alert vitally stable. On physical examination there were multiple hyperpigmented papules over nasolabial region with characteristic distribution of butterfly shape (Adenoma sebaceum). Patient has 7 hypomelanotic whitish macules of size 5-7 mm on both lower limbs and one 5*2 cm size on lateral aspect of right mid- thigh. There was no evidence of any Shagreen patch. Dentition was normal no evidence of any caries. On cardiovascular examination heart sounds were normal no murmur. On detailed Central nervous system examination cranial nerve examinations normal, motor system normal, no sensory system within normal limits, no bowel bladder normal, deep and superficial reflexes normal.

Investigations showed normal complete blood count, RFT and LFT. Chest X ray normal and ECG is within normal limits. Fundus examination revealed no abnormalities. On CT head plain Multiple subependymal calcified nodules seen. CT Abdomen and Pelvis and HRCT Thorax revealed no significant abnormality. Serum

valproate levels were below therapeutic range. Dose of sodium valproate increased and therapeutic monitoring advised.

III. Discussion:

Tuberous sclerosis is a rare autosomal dominant genetic disorder characterised by mutations in the TSC1 and TSC2. It is a disorder of cellular differentiation and proliferation. Most of the cases present in early childhood with multiple episodes of seizures varying from focal to GTCS. Cutaneous manifestations are often the first clue towards suspicion of diagnosis of Tuberous sclerosis and they often present late in childhood so poses challenge in the early diagnosis of disease. Cutaneous lesions have variable presentationsThese lesions usually appear after 5 years of age and may be mistaken for acne. But these show wide variation in age of onset and severity and their progression[3].Most of the cases appear to present with variable presentation and remain undiagnosed. Cutaneous lesions may have cosmetic issues, so recent trial support the use of topical 0.1% Rapamycin on facial angiofibromas[4].Rapamycin is mTOR inhibitor. It is used in management of angiofibromas and angiomyoliomas as a newer treatment in the management of tuberous sclerosis.[6]Diagnostic Criteria for TSC is as elaborated in the table below(Table 1.1). Definite TSC can be diagnosed when two major or one major plus two minor features are present.[5]

In our patient 3 major criterions were fulfilled Adenoma Sebaceum, >3 hypomelanotic macules and subependymal calcifications and nodules. Patient has multiple episodes of GTCS which were refractory to antiepileptics. Frequent dose adjustments were required for its management. In our patient dose of sodium valproate was increased and seizure control achieved.Patient relatives also counselled regarding the disease entity and prognosis. TSC is a lifelong condition regular surveillance for different symptoms and early treatment are associated with better health and quality of life and favourable outcomes for patients.[7]

Major criterion	**Minor Criterion**
1) Cortical Tuber	1)Cerebral white matter migration lines
2) Subependymal nodule	2) Multiple dental pits
3) Facial angiofibroma	3)Hamartomatous rectal polyps
4) Ungual fibroma	4)Bone cysts
5) Shagreen patch	5)Retinal achromatic patch
6) Lymphangioleomyomatosis	6)Confetti skin lesions
7) Renal angiomyolipoma	7)Nonrenal hamartomas
8) Cardiac Rhabdomyoma	8) Gingival fibromas
9) Retinal Hamartomas	9)Multiple renal cysts
10)Multiple hypomelanotic macules(>3)	

Table 1.1 Criterion For Diagnosis of TSC

IV. Conclusion:

Tuberous sclerosis is a rare autosomal dominant genetic disorder involving multiple systems with variable expression. Although it presents most commonly with neurologic manifestations like epilepsy and mental retardation it is the characteristic dermatologic manifestations which are the cornerstones for early diagnosis. Early diagnosis demands great degree of suspicion and it is most often difficult in resource limited countries. There is currently no specific treatment available for TSC and lot of research is still going on for the same. All patients with TSC should undergo CT head, HRCT thorax ,USG abdomen and 2 D echocardiography to asses other lesions and complications.

Skin lesions can be managed by surgical dermabrasions. Despite variable expression, genetic counselling should be offered to all family members of patients. Thus TSC is an important cause of significant morbidity and should be considered as a differential in children presenting with convulsions.

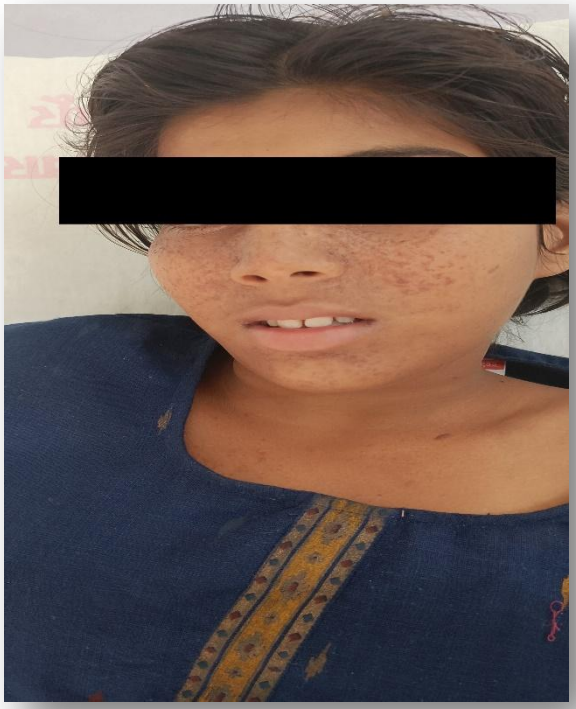

Figure 1.1 Adenoma Sebaceum

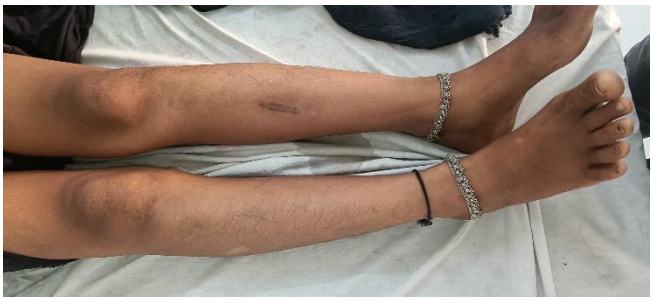

Figure 1.2 Multiple Hypomelanotic macules

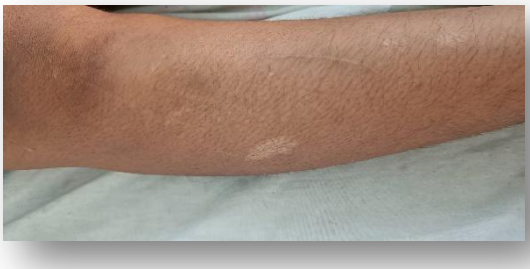

Fig 1.3 Hypomelanotic Macule

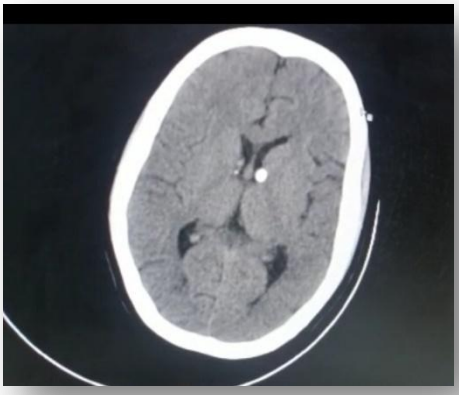

Fig 1.4CT Head showing subependymal nodule with calcifications

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