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Medicine

TUBEROUS SCLEROSIS: AN UNUSUAL CAUSE OF REFRACTORY SEIZURE IN EARLY CHILDHOOD.

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ABSTRACT **Background:** Tuberous Sclerosis also known as BOURNEVILLE DISEASE, this is an autosomal dominant disorder, it is caused by mutations in either the TSC1 gene, which maps to chromosome 9q34 and encodes a protein termed hamartin, or the TSC2 gene, which maps to chromosome 16p13.3 and encodes the protein tuberin. Hamartin forms a complex with tuberin, which inhibits cellular signalling through mTOR, and acts as a negative regulator of the cell cycle.

Introduction: We describe Tuberous sclerosis an unusual cause of refractory seizure in early childhood.

Diagnosis: Tuberous sclerosis is diagnosed mainly by clinical findings and imaging. (Computed Tomography and Magnetic resonance imaging).

Intervention: Several anti-epileptic drugs like phenytoin, levetiracetam, sodium valproate, Clobazam etc.,

Outcome: Patient experienced generalized tonic clonic convulsions even while he was on polytherapy with anti-epileptic drugs (phenytoin + levetiracetam + sodium valproate + clobazam) without any complications observed over follow up period.

Conclusion: It was concluded that combination therapy of anti-epileptic drugs could significantly reduce the frequency of seizures while not being able to eliminate them completely.

KEYWORDS : Tuberous Sclerosis, Refractory Seizures

INTRODUCTION:

This is an autosomal dominant disorder with an incidence of ~1 in 5000–10,000 live births. It is caused by mutations in either the TSC1 gene, which maps to chromosome 9q34 and encodes a protein termed hamartin, or the TSC2 gene, which maps to chromosome 16p13.3 and encodes the protein tuberin. Hamartin forms a complex with tuberin, which inhibits cellular signalling through mTOR, and acts as a negative regulator of the cell cycle. Patients with tuberous sclerosis may have seizures, mental retardation, adenoma sebaceum (facial angiofibroma's), shagreen patch, hypomelanotic macules, periungual fibromas etc., Skin lesions are present in 90% patients and may be seen at all ages. Ash-leaf spots (Hypopigmented macules) are generally detected in infancy/early childhood. Facial angiofibroma's formerly called adenoma sebaceum may be seen at any age but more common in late childhood or adolescence. Additional features like angiofibroma, subungual fibroma; cardiac rhabdomyoma; adenomatous small intestine polyps; pulmonary and renal cysts; cortical tuber; subependymal giant cell astrocytoma may also be present.

Case Presentation:

A 17-year-old male presented with h/o recurrent seizures. Seizure is characterised by generalised tonic clonic seizure lasting for 3-5 minutes associated with post ictal confusion for about 30 min to 1 hour. These GTCS usually occurs 1-2 episodes per week, in the last 1 month, sometimes may associated with tongue bite. Patient is known case of seizure disorder since the age of 9 years, and under anti-convulsant therapy for same. His parent's give history of recurrent seizures despite being on treatment. Also, they noticed learning difficulties because of which he had been dropped out of school at age of 10 years.

On General Physical Examination:

Multiple well defined reddish brown nodular growths were noted on the fore head/nose/cheeks in a butterfly pattern called as adenoma Sebaceum. Also, hypo-pigmented macule was seen over the chest called as ash leaf macule, shagreen patch seen over back.

All routine biochemical investigations including serum electrolytes and serum calcium were done and were normal. Following this the patient was subjected to radiological examination

NCCT brain was s/o Hypodense areas in sub-ependymal region of both ventricles indicating calcified tuberous lesions. Fundoscopy and USG(A+P) were found to be normal.

Management:

Patient was managed conservatively on multiple Antiepileptics like Phenytoin, levetiracetam, sodium valproate and clobazam. On this combined medication patient was seizure free for 2 days, later on patient was discharged on these medications.

Fig.1 Facial Angiofibroma

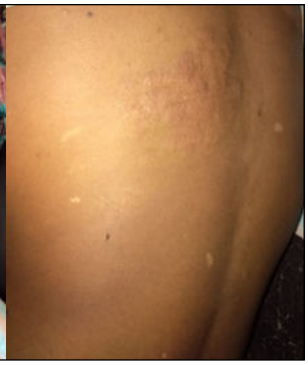

Fig.2 Shagreen Patch In Back

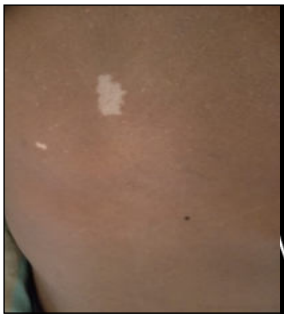

Fig.3: Hypomelanotic Macule

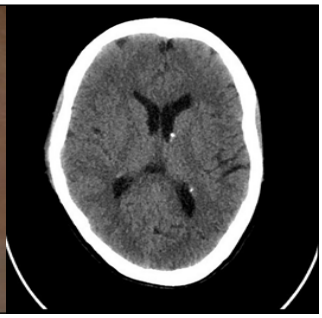

Fig. 4 : Subependymal Nodules On NCCT Brain

DISCUSSION:

Patients with tuberous sclerosis may have seizures, mental retardation, adenoma sebaceum (facial angiofibroma), shagreen patch, hypomelanotic macules, periungual fibromas, renal angiomyolipoma, and cardiac rhabdomyomas.

Epilepsy/cognitive disability/neurobehavioral abnormalities which are there in almost 80% patients with TSC are found to be the most common presenting complaints.

These patients have an increased incidence of subependymal nodules, cortical tubers, and subependymal giant-cell astrocytomas (SEGAs).

Some patients may also have Kidney Tumour like-Angiomyolipoma's; lymphangioleiomyomatosis; rare RCC with variety of histologic

appearances may also be present.

For diagnosis of tuberous sclerosis requires correlation between clinical findings and imaging.

Major Criteria:
Facial angiofibroma's, ungual fibroma, renal angiomyolipoma, pulmonary lymphangiomyomatosis, cortical tubers, Shagreen patch, Hypomelanotic macule, retinal hamartoma, cardiac rhabdomyoma, sub-ependymal giant cell tumour.

Minor Criteria:
Dental enamel pits, bone cysts, rectal polyps, gingival fibromas, retinal acromic patch. One major plus two minor/ two major criteria when fulfilled are diagnostic.

Patients frequently require anticonvulsants for seizures. SEGAs do not always require therapeutic intervention, but the most effective therapy is with the mTOR inhibitors sirolimus or everolimus, which often decrease seizures as well as SEGA size.

CONCLUSION:

Despite of taking polydrug therapy with phenytoin, levetiracetam, sodium valproate and clobazam the patient experienced generalized tonic clonic convulsions with a frequency of once / twice per month which was not followed by any complications during a follow up period. It can be henceforth concluded that the combination of phenytoin/levetiracetam/sodium valproate/clobazam can reduce the frequency of seizures but cannot eliminate them completely. Newer drugs like mTOR inhibitors like sirolimus or everolimus can be used to decrease seizure as well as Subependymal giant cell astrocytoma size.

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