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Case Report

Incidental diagnosis of tuberous sclerosis in a child with falciparum malaria

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ABSTRACT

Tuberous sclerosis complex is a rare genetic disorder inherited in autosomal dominant fashion. It is a multisystem disorder involving brain, skin, kidneys, heart, eyes and lungs which becomes apparent only in late childhood, limiting the usefulness of early diagnosis in infancy. Here, we report a case of a 14 year female child presenting with seizure, mental retardation and typical skin manifestations.

Keywords: Adenoma sebaceum, Neurocutaneous syndrome, Tuberous sclerosis

INTRODUCTION

Tuberous Sclerosis is a genetic disorder characterized by the growth of numerous benign tumours in many parts of the body; including the brain, heart, lungs, eyes, kidneys, skin and other organs, leading to significant health problems like seizures, intellectual disability, autism or developmental delay. TSC is caused by mutations on either of two genes, TSC1 and TSC2, which encode for the proteins hamartin and tuberin respectively. These proteins act as tumour growth suppressors, agents that regulate cell proliferation and differentiation.[1]

CASE REPORT

Here is a 14 years female Hindu child, product of a non-consanguineous marriage presented with complain of fever with chills and rigors since 10 days along with icterus and 2-3 episodes of vomiting per day since 5 days. There was history of multiple seizures (2-3 episodes per month) since age of 8 year of generalised tonic clonic type.

She was found to be moderate to severely mentally retarded and her developmental milestones were delayed. At present her mental age was 5-6 year with SMR stage 1. She experienced her first seizure episode at the age of 8 year. There was no history of seizure in other family members.

On physical examination child was conscious, there was severe pallor with icterus .There were multiple red nodules over nose and cheeks which appears like adenoma sebaceum (Figure 1) along with multiple hypo pigmented macules (ash leaf macules) on trunk.

Investigations showed macrocytic anaemia (Hb 2.1gm/dl, WBCs 4520/mm^3, platelets 81000/mm^3). MP card test was positive for falciparum malaria. Total billirubin was 3.9mg/dl with direct being 0.6 mg/dl, SGOT 476 U/L and SGPT 382U/L. chest X-ray was normal. The child was transfused with 2 units of packed cell volumes along with antimalarial drugs, icterus improved. The child transfused with 1 unit whole blood and bone marrow aspiration done

which shows megaloblastic anemia. She was started on sodium valproate for seizures.

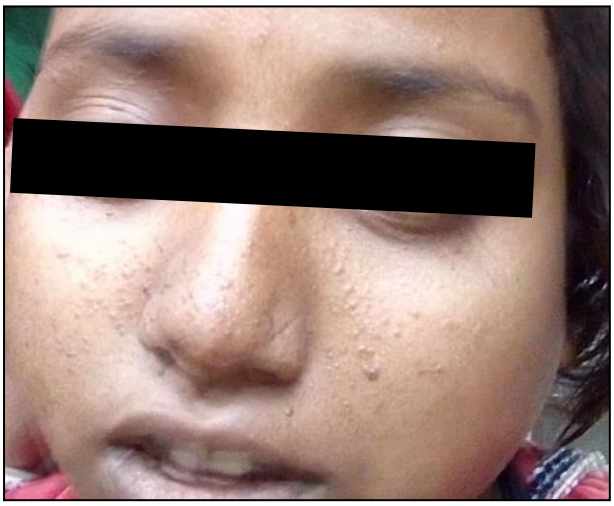

Figure 1: Adenoma sebaceum.

CT head showed multiple calcified sub-ependymal nodules along frontal horn of bilateral lateral ventricles, temporal horn right lateral ventricle and floor of 4th ventricle (Figure 2, 3). EEG shows generalised epileptic form activity. On fundus examination no anomaly was found.

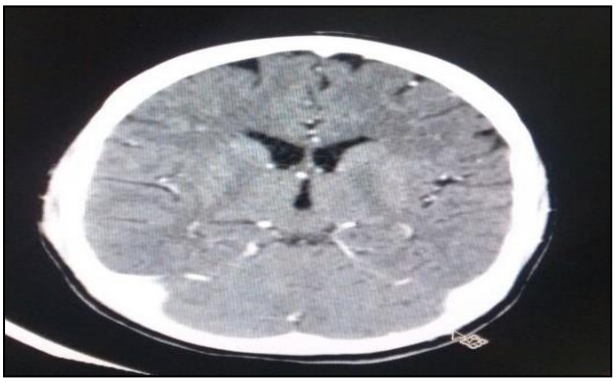

Figure 2: CT scan of head showing subependymal nodule in lateral horn.

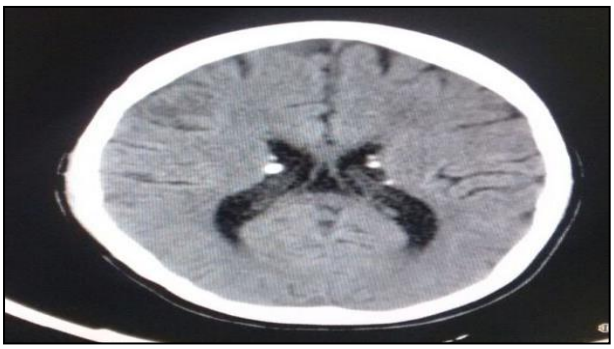

Figure 3: CT scan of head showing subependymal nodule in temporal horn.

Summarizing her past history, extensive physical signs and investigations, the final diagnosis of Tuberous Sclerosis Complex with malaria was made. She remained seizures free for 10 days and was ultimately discharged on sodium valproate 200 mg thrice a day along with oral antibiotics and multivitamin and advice for follow up. Vigabatrin could not be started due to financial aspects

DISCUSSION

Tuberous sclerosis complex is a multisystem genetic disorder of variable phenotypic expression, with an incidence of about 1 in 5800 live births worldwide. The disorder results from a mutation in the TSC1 gene in chromosomal region 9q34 or the TSC2 gene in chromosomal region 16p13 and is inherited in an autosomal dominant fashion, although up to two thirds of cases result from spontaneous genetic mutation.[2] Manifestations of tuberous sclerosis can become apparent in persons of any age, but most patients have clinical symptoms before they are aged 10 years. The disease develops as an abnormal growth of ectodermic cells producing tumors extending to areas of the head, heart, brain, eyes, skin and kidneys.[3]

The most common and earliest skin finding in TSC is multiple hypo pigmented macules (also called ash leaf spots). Adenoma sebaceum is a hamartoma composed of connective and vascular elements and is properly termed an angiofibroma they are pathognomonic of TSC. Angiofibromas form discrete pink papules on the malar region of the face in a “butterfly distribution” in 70% of TSC patients.[4,5] The shagreen patch is found in the lumbosacral region characteristically present as an irregularly shaped roughened raised lesion with orange peel consistency.

The major neurologic manifestations of tuberous sclerosis complex are seizures, autism, developmental delays, including mental retardation, and behavioral and psychiatric disorders. Seizures are present in about 80-90% of patient which varies from subtle focal seizure, infantile spasm, to generalized seizure. The intracranial features of TSC are cortical or subcortical tubers, sub ependymal nodules, sub ependymal giant cell astrocytoma’s, and white matter radial migration lines. Tubers are most commonly found in the cerebrum, 90% being present in the frontal lobes.[6]

Pulmonary lymphangio-leiomyomatosis probably affects 1-3% of patients with tuberous sclerosis. A cardiac rhabdomyoma can be discovered using echocardiography in approximately 50% of TSC patients. Patients with tuberous sclerosis complex (TSC) can develop a number of renal lesions, the most common being angiomyolipomas and cysts.[7]

Definite TSC can be made when two major or one major plus two minor features are demonstrated.[8] Our patient had three major criteria (sub ependymal nodules in CT

scan head, facial angiofibroma, hypomelanotic macules more than three in number, which fits in the diagnosis of Tuberous sclerosis. She had history of multiple seizures needing antiepileptic drug. Late diagnosis is very common in our part of world due to the paucity of facilities.

Seizures are managed with an anticonvulsant medication like vigabatrin (infantile spasm), lamotrigine (generalized seizure). But young children with TSC who have early onset of focal seizure or spasm, develops intractable seizure later that responds poorly to antiepileptic drug. Alternative non-pharmacological treatment which includes vagus nerve stimulation, use of ketogenic diet, and resective epileptic surgery. Use of Inhibitors of the mammalian target of rapamycin (mTOR) in regression of astrocytoma's, angiofibromas and angiomyoliomas are newer modalities in the management of tuberous sclerosis.[9] The prognosis of TSC depends on the severity or multiplicity of organ involvement. About a quarter of severely affected infants are thought to die before the age of 10% and 75% before 25 years. However, in the case of individuals diagnosed late in life with few cutaneous signs, prognosis depends on the associated internal tumors and cerebral calcifications.[10]

CONCLUSION

TSC is a lifelong condition; therefore individuals should be regularly monitored by an experienced clinician. TSC must be included in the differentials of children presenting with seizures, mental retardation and peculiar skin manifestations.

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