

Tuberous sclerosis misdiagnosed as epilepsy

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Abstract

Tuberous sclerosis (TS) is a rare genodermatoses characterized by neurological symptoms and hamartomas in multiple organs including brain, skin, kidney, eyes, heart, lungs & G.I tract. The classic triad of epilepsy, adenoma sebaceum and mental retardation usually occurs in one third of the patients, thus requiring high index of suspicion to diagnose TS. Otherwise it may easily be misdiagnosed as epilepsy or neurofibromatosis. Here we present a case of tuberous sclerosis in 11 year old girl misdiagnosed as epilepsy because of her convulsions. A comprehensive medical history including family history, thorough physical examinations, clinical suspicion and neuroimaging are required to confirm the diagnosis.

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Introduction

Tuberous sclerosis complex (TSC) is an important neurocutaneous syndrome, inherited as an autosomal dominant trait with variable expression and a prevalence of 1/6000 newborn.¹ TSC is characterized by spectrum of signs and symptoms that present over a patients lifetime, including neurologic disorders, multisystem tumor growth and dermatologic manifestations. The disease is first described by Bourneville in 1880, is called epiloia (epi=epilepsy, loi=low intelligence, a=adenoma sebaceum)², has been revised to include other manifestations because many patients with tuberous sclerosis do not exhibit this triad.³ TS is extremely heterogeneous disease with a wide clinical spectrum varying from severe mental retardation and incapacitating seizure to normal intelligence and a lack of seizure, often within the same family.¹ The term tuberous sclerosis refers specifically to the presence of multiple sclerotic masses scattered throughout the cerebrum. The diagnosis of TSC is based on the identification of hamartomas in more than one organ system such as skin, brain, kidneys, heart and eyes.⁴ The presence of hamartomas in two different organ systems is considered by some clinicians to be sufficient for the diagnosis.⁵

Skin lesions occur in nearly all individuals & are important for diagnosis. Skin lesions include hypomelanotic macule (congenital white leaf shaped macule), focal poliosis, facial angiofibromas, shagreen patch plaque, periungual angiofibroma (kocnen tumour). TSC is caused by

mutations of either of two genes TSC1 (9q34) & TSC2 (16p13), which encode for the proteins hamartin and tuberin respectively. These proteins act as tumour growth suppressor, agents that regulate cell proliferation and differentiation.⁶ The availability of neuroimaging facilities like computerized tomographic (CT) scan and magnetic resonance imaging (MRI) has made it possible to demonstrate the presence of cortical hamartomas, white matter abnormalities and subependymal nodules in the brain as early as 6 weeks of age. The CT findings are characteristics, though MRI is the imaging of choice as the cortical tubers can be seen in 95% of patient.⁷ Wood's lamp examination accentuates the ash leaf macule. Definite TSC is diagnosed when either 2 major features (out of total 11) or one major feature with 2 minor features (out of a total of 9) are present.⁸ Tuberous sclerosis has no cure but treatment as medicine, educational and occupational therapy can help relieve symptoms. We are presenting here a 11 year female who had classical features of TS but was misdiagnosed as epilepsy due to seizure disorder.

Case Report

Shorna, a 12 year old girl, resident of Sonadanga, Khulna, got admitted to paediatrics department of KMCH on 19 June 2013 through emergency department with the complaint of convulsions for one day. She was a diagnosed case of epilepsy for the last 9 months and had been on antiepileptic

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medication. Currently she presented with one day history of generalized tonic clonic convulsions each lasting for 2-3 minutes, with relaxation period of 5-10 minutes. She did not regain consciousness in between. The convulsions were associated with urinary incontinence, frothing and uprolling of eye balls. No tongue bite was present. Such episodes were occurring repeatedly during the above mentioned period but the frequency was increasing day by day. There was no preceding history of fever, cough, diarrhoea or fall.



Figure-1. Adenoma sebaceum in the face

Convulsion was controlled by 2 doses of P/R Inj. Diazepam at an interval of 15 minute. She also developed multiple papulo-erythematous lesion over forehead and cheek for last 10 years and hypo pigmented macules mainly in trunk and abdomen.

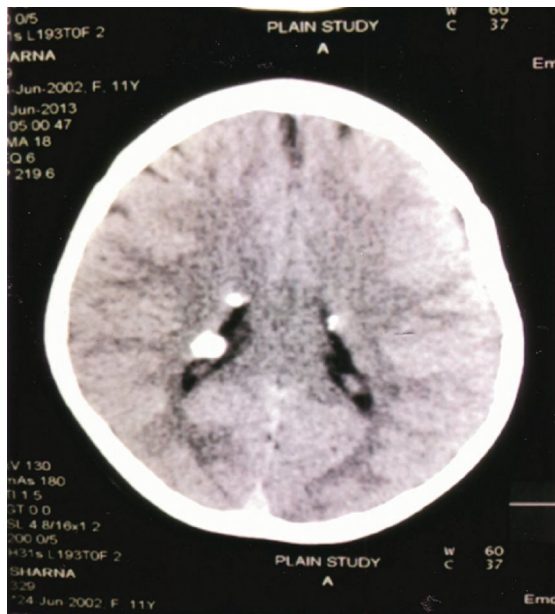


Figure-2. CT scan showing paraventricular calcified nodules

In past history, there was nothing significant. Birth history was uneventful. Her milestones of development were not delayed. During her period of convulsion she was irregularly treated with anticonvulsant drugs. But one important thing is that her mother died due to same type of illness. On physical examination she was found normal with stable vital signs. Physical signs include, facial adenoma sebaceum (Fig-1), ash leaves macules in trunk and abdomen. There was shagreen patch (resembling shark skin) on the dorsum of the left hand & subungual angiofibroma on the middle toe of the left foot. On conversation, her intelligence seemed normal. Lab investigations showed moderate anaemia. All other routine test including ultrasonogram of whole abdomen, ECG, showed normal but CT scan of brain showed calcified lesion in paraventricular region of parietal lobe (Fig-2). Fundoscopic examination showed normal. Summarizing her past history, physical examination and investigations, the final diagnosis of tuberous sclerosis was made. She was ultimately discharged on sodium valproate and advised for routine follow up.

Discussion

Tuberous sclerosis complex (TSC) is an autosomal dominant disorder, characterized by hamartomas in many organs.⁵ The condition was described by Von Recklinghausen in 1862.⁹ In 1880, Bourneville described the pathologic features of the sclerotic tubers found in post mortem patient with epilepsy and mental retardation and coined the term "Sclerose tubereuse".⁴ It is an inherited disease with almost complete penetrance but variable expressivity. Two thirds (65%) of cases are sporadic and are thought to represent new mutations. According to National Institute of Health (NIH) consensus conference, a permanent diagnosis of TSC can be made when two major features or one major feature plus two minor characteristics are demonstrated.¹⁰ Additional diagnostic categories include probable TSC, when one major feature plus one minor feature are present and possible TSC, when either one major feature or two or more minor characteristics are present.¹⁰ Major features (facial angiofibroma or adenoma sebaceum, periungual fibroma, hypomelanotic macule more than three, shagreen patch (connective tissue nevus), cortical tuber, subependymal nodule, subependymal astrocytoma, multiple retinal hamartomas, cardiac rhabdomyoma, lymphangiomyomatosis, renal angiomyolipomas) Minor features (Multiple pits in dental enamel, hamartomatous rectal polyp, bone cysts, cerebral white matters, gingival fibromas, non renal haemartomas, retinal

achromic pathc, confetti skin lesion, multiple renal cysts). The disease involves many organ in addition to skin and brain and it may assume a diversity of forms, the least severe of which is difficult to diagnose.¹¹ The clinical diagnosis is virtually certain if the triad of epilepsy, mental retardation and adenoma sebaceum is present.¹² It is the early stage of the disease and the forme fruste (least severe form) that proves difficult to diagnose and here the experienced dermatologist can be of great help. It is important to note that epilepsy and delay in psychomotor development are by no means diagnostic of tuberous sclerosis, since they occur in many diseases.

It is in this case and also in every seizable population with epilepsy or mental retardation, especially when the family history is unrevealing, a search for the dermal lesions or phakoma of the retina or gingival fibromas is rewarding. Seizure occurs in most patients as is the case of our patient.¹¹ Some children present with infantile spasm but the spectrum of the seizure disorder ranges from focal seizure to tonic clonic seizure, even status epilepticus. Seizures are seen, in approximately 70% patient with normal mental status as is our case.¹³ Neurological signs are considered uncommon, except when an intracranial neoplasm develop.¹³ Our patient had no evidence of focal neurological deficit though the CT brain scan revealed cerebral nodules. Prognosis for patients with TS varies with the severity of disease manifestation. The usual life span of patients with tuberous sclerosis varies. Infants with cardiac rhabdomyomas may require surgical excision of the tumor early in life. But many mildly affected patients survive until their 50s or 60s. Standard anticonvulsant therapy usually suppresses the seizure tendency.¹³ TSC is a lifelong condition. In evaluating the case of epilepsy or mental retardation one should be vigilant that this may be case of tuberous sclerosis. Therefore individuals should be regularly monitored by an experienced clinician. In conclusion, we like to say that our case of tuberous sclerosis is an addition to the few reported case.

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