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CASE REPORT

"Tuberous Sclerosis"- A Rare Cause of Seizure

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Abstract:
Tuberous sclerosis (TS) is one of the important neurocutaneous syndrome with a variety of clinical manifestations. We present a 19 years old boy with classical triad of Tuberous sclerosis who had seizure, mental retardation, facial angiofibromas and also having other features which cover the newer diagnostic criteria's. TS should be considered as a differential diagnosis in patient of seizure with mental retardation.

Introduction:
Tuberous sclerosis (TS) or Bourneville's disease is an autosomal dominant neuro-cutaneous syndrome classically characterized by a clinical triad of epileptic seizures, mental retardation, and skin lesions[1]. The disease has an incidence of 1:10,000 to 1:70,000 life births. TS affects both sexes equally and also in all races[2]. TS was first observed by Von Recklinshausen in 1862, but the first clear description of TS was given by Desire-Magloire Bourneville in 1880, who recognized the pathological features of white tumours or tubers and areas of sclerosis of cerebral gyri at post-mortem in patients with epilepsy and mental retardation. In 1908, Vogt reported the classical clinical triad of TS[3]. The name, composed of the Latin word *tuber* (potato like swelling) and the Greek word *skleros* (hard), refers to the pathological finding of thick, firm and pale gyri, called "tubers", in the brains during postmortem. TS is a multi-system genetic disease that causes benign tumors (Hamartomas) to grow in the brain and on other vital organs such as the kidneys, heart, eyes, lungs, skin with a variety of clinical manifestations[2,3]. We present here a young boy who had classical features of tuberous sclerosis.

Case report:
A 19 years old normotensive, non-diabetic male from Narshindi reported at department of Neurology, Dhaka medical college hospital, with the complaints of small rounded rashes over his cheeks and nose for 7 years and repeated generalized convulsions for 6 years. He is also mentally retarded from childhood and he quit school after class V because of very poor academic performance. On clinical examination, we found that there were numerous papular lesions (2-3mm) over the cheeks and nose (facial angiofibromas), hypopigmented macules (ash-leaf macule) over the trunk, a thickened leathery hypopigmented patch (shagreen patch) over the lumbosacral area and a periungual fibroma in the right thumb. His vital parameters were within normal

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limit. Systemic examination including the nervous system revealed no abnormality, except low IQ level. All routine and relevant investigations revealed normal findings, but CT scan of head showed calcified area in left temporal subcortical region and subependymal regions. This patient was diagnosed as a case of Tuberous Sclerosis on the back ground of clinical features (seizure, mental retardation and skin lesions) supplemented by CT scan findings. The patient was prescribed tablet carbamazepine 200mg twice daily with good control of seizure. Now he is on regular follow up.

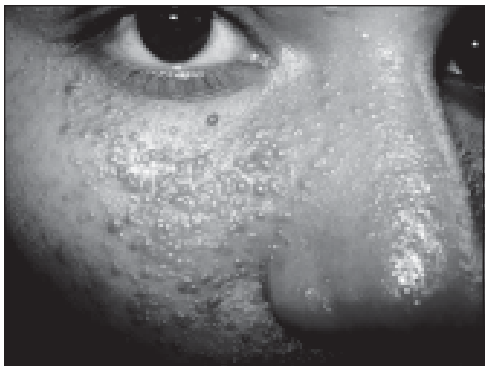

Fig.-1: *Facial angiofibromas (adenoma sebaceum).*

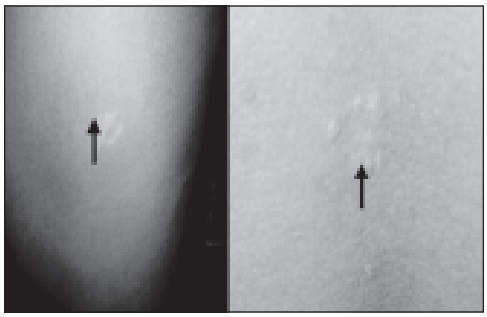

Fig.-2: *Ash leaf hypopigmented macules in the trunk (arrow).*

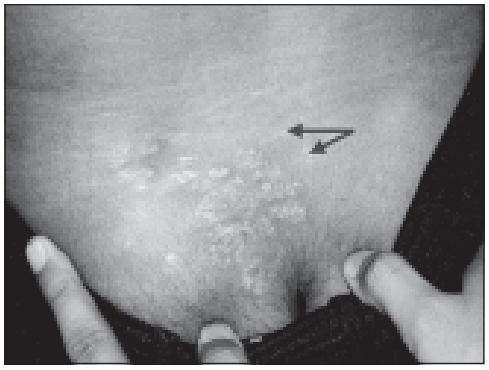

Fig.-3: *Shagreen patches in lumbosacral region (arrow).*

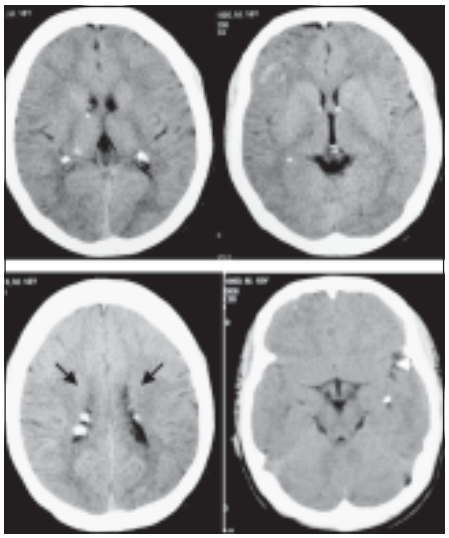

Fig.-4: *CT scan of head showing subependymal (black arrows) & subcortical (white arrow) calcified tubers.*

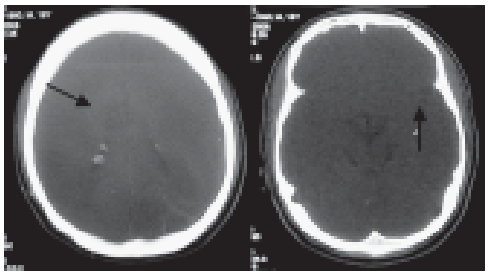

Fig.-5: *CT scan (bony window) of head confirmed the presence of calcifications (arrows).*

Discussion:

Tuberous sclerosis (TS) is one of the neurocutaneous syndrome characterized by the development of benign neoplasms (hamartomas) of the skin and the various internal organs. TS have an autosomal dominant inheritance pattern, with a high spontaneous mutation rate. Two distinct genetic loci responsible for TS have been identified: one on chromosome band 9q34 (also referred to as *TSC1*) and another on chromosome band 16p13 (*TSC2*)[4], although about two-third cases are sporadic due to new, spontaneous mutations in TSC1 or TSC2 and only one-third individuals inherit the disorder from a parent with TS[4].

Tuberous sclerosis is characterized by multiple hamartomas in one or many organs. The disease affects many organ systems other than skin and brain including the heart, kidneys, eyes, lungs and bones. These hamartomas are composed of varying amounts of mature adipose tissue, smooth muscle, and blood vessels[5]. The classic triad of mental retardation, seizures, and a papular facial nevus known as adenoma sebaceum is observed in less than 50% of patients. All components of this triad may not appear simultaneously or may not appear at all. So, the newer criteria for diagnosis of TS were defined at a consensus conference in 1998. According to these criteria, diagnosis requires the presence of two major features, or one major and two minor features[5].

Major features:

- Facial angiofibromas or forehead plaques
- Non-traumatic ungula or periungual fibroma
- Hypomelanotic macules (three or more)
- Shagreen patch (connective tissue nevus)
- Multiple retinal nodular hamartomas
- Brain cortical tuber
- Subependymal nodules
- Subependymal giant cell astrocytoma
- Cardiac rhabdomyoma
- Pulmonary Lymphangioleiomyomatosis
- Renal Angiomyolipoma[5]

Minor features:

- Multiple randomly distributed pits in dental enamel
- Rectal hamartomatous polyps
- Bone cysts
- Cerebral white matter radial migration lines
- Gingival fibromas
- Nonrenal hamartomas
- Retinal achromic patch
- Confetti skin lesions
- Multiple renal cysts[5]

This patient had six major features . Diagnosis of the disorder is based on a careful clinical examination in combination with computed tomography (CT) or magnetic resonance imaging (MRI) of the brain, which may show tubers in the brain, and other radiological investigations of the heart, liver, and kidneys, which may show tumors in those organs[6,7]. A Wood's lamp or ultraviolet light may be used to locate the ash leaf hypopigmented macules which are sometimes hard to see in pale or fair skin.

Mortality in tuberous sclerosis is due to cardiac, renal and cerebral pathologies. Sudden deaths may be seen following cardiac arrhythmias, intractable epilepsy, intracranial hemorrhages, obstructive hydrocephalus, aneurysm rupture and spontaneous pneumo-thorax. Subependymal tubers may convert into giant cell Astrocytoma in brain[8]. But there is no definite cure for TS. Treatment is mainly symptomatic. Antiepileptic drugs may be used to control seizures, and medications may be prescribed for behavioral problems. Special schooling and occupational therapy may benefit individuals with special needs and developmental issues[9]. Surgery including dermabrasion and laser treatment may be useful for treatment of skin lesions and excision of tubers.

Conclusion:

Tuberous Sclerosis is a life long condition and patient should accept this truth, but individuals need to be regularly monitored by a doctor to make sure that, they are receiving the best possible treatments.

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