Case Report

Tuberous sclerosis: A case study and update

Akhand MI

Introduction

A tuberous sclerosis is a rare genetic disorder included in neurocutaneous syndrome. It was first described by Von Reclinghausen in 1862 and in 1880, Bourneville used the term Sclerosis tuberose for the potato-like lesions in the brain. It is inherited as autosomal dominant but 60% cases are sporadic owing to new mutation. Incidence varies from 1 in 10,000 to 1 in 100,000 of 75% cases having positive family history but rarely detectable when the child is born.

The cardinal features of Ts are Skin lesions, Mental retardation from birth and Epilepsy starting usually before 2 yrs of age. Cutaneous symptoms include depigmented or hypomelanotic macules, presenting at birth, persisting throughout life. Most macules are leaf-shaped, resembling the leaf of the European Mountain Ash tree.

Adenoma sebaceum, a facial angiofibroma, shagreen patch, connective tissue hamartoma and Cafe-au-lait spots, small fibroma resembling course Googe flesh. There are also some ophthalmic and visceral symptoms including Phakoma in the retina, Renal tumor and cyst, Rhabdomyoma of heart, Lung cyst, Haemangioma of liver and spleen.

There is no method for prenatal diagnosis. Diagnosis is established by Clinical exam, CT/MRI of brain, EEG etc. Treatment is symptomatic comprising seizure control and management of other complications if any.

Case study

Nasreen Akhter, an 8 yrs old girl, first issue of her parents, born full term with uneventfully perinatal period to a non-consanguous uneducated lower social parents brought to our paediatric OPD from Rana vola, Uttara, Dhaka, with the complaints of repeated convulsion characterised by brief symmetrical muscular contraction of the face, head & limbs with loss of body tone and tendency to fall causing injury since her 4 yrs of age. She also had irrelevant talks, activity and behavior for the same period. She is self directed home-bound girl showing preference to play with inanimate objects other than playmates.

She had two hospital admissions between the ages 1 to 2 yrs for febrile convulsion. She has no hearing or visual problem other than mild bilateral squint but she is unable to talk adequately still now.

All parameters of milestone were delayed since birth. There is no family history of such illness.

Clinically she is hyperactive, showed prancing and parqueting movements with myoclonic type of seizures of early childhood.

Adenoma sebaceum was evident on both cheeks, around the nose & forehead exempting the upper lip, sizes varying from pin head to pea & two shagreen patches over lumbo-sacral region. Formal intellectual assessment was not possible & clinical assessment suggested moderate mental retardation.

Fundus occuli examination, Renal function tests, USG of Abdomen, CXR, ECG and Echocardiogram examinations are found normal findings. But cranial EEG reveals brief bursts of spike activity generalized all over the tracing. Skull radiography shows...
intracerebral calcifications of size (1.5 x 1.3) cms. on both views. Non-contrast a scan of brain shows multiple calcifications of varying sizes in the sub-ependymal locations of the lateral ventricles. Superficial CSF spaces are normal but Rt. lateral ventricle Frontal horn is dilated due to compression over the Foramen Monro by the adjacent large calcified mass. Brain-stem and cerebellum shows no abnormality.

Discussion
Tuberous sclerosis eponymically is called pringle disease when only dermatological findings are found, Bourneville disease when the Ns is only affected and West syndrome when skin lesions are associated with infantile spasm, hypo-arrhythmia and MR³. Vogt first emphasized the classic triad of seizure, mental retardation and adenoma sebaucium. Adenoma sebaucium are not the adenoma of sebaceous gland but are small hamartomas arising from nerve elements of the skin along with hyperplasia of connective tissue & blood vessels. These are not present at birth but become clinically evident in over 90% cases by the age of 4 yrs³. At first the facial lesions are the size of pin head or a millet seed & red in colour, distributed symmetrically on the nose & cheeks in butterfly fashion. May involve forehead & chin but rarely affect the upper lip. The lesions gradually increase in size and become yellowish & glistening.

Shagreen Patch, a conn-ctive tissue hamartoma usually become evident after 1 st decade of life & found in the lumbo sacral region. These are yellowish brown elevated plaques resembling pigmented skin or orange peel. Cafe-au-Iait spots, are small fibromas, look like course goose flesh.

Seizures and mental retardation are the indications of diffuse encephalopathy. Infantile myoclonic spasm with or without hypo- arrhythmia, are the characteristics seizures of young infant. Older children has generalized tonic-clonic or partial complex seizures. There is a close relationship between the onset of seizures at young age and mental retardation. smalley et al, in have autism and mental retardation.

Brain is usually normal in size but several hard nodules occur in the surface of the cortex. The limbs of the Lateral Ventricle is frequently the site of numerous small nodules that project (nto the ventricular cavity as "Candle Guttering" These nodules consists of clusters of atypical glial cells in the center and giant cells in the periphery. Malignant changes may occur as a progression to form a glioma or spongioblastoma, Glioblastoma & ependymoma¹.

Retinal hamartoma, a phacoma observed in 50% of well studied cases of Ts, Visceral
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abnormality observed includes Hypernephroma, renal cysts, Renal Angiomyolipoma, Rhabdomyosarcoma, Lung cyst, haemangioma of Uver & spleen and sclerotic lesion in small! bones of hands and feet.

Cytogenetically Ts is complicated and not due to single gene defect on one chromosome. Chromosome 16 p 13, 3 with a gene product called tuberine appears a major site but 11 q-22,23 and possible linkage to chromosome 9 are implicated.

There is no method for prenatal diagnosis but clinical diagnosis is possible at most ages. In infancy three or more macules of 1 cm or more size suggests the diagnostic. Involvement may result in difficulties in the diagnosis of Ts. Gomez defined the primary and secondary diagnostic criteria.

Table-1, Diagnostic Criteria for TS3

<table>
<thead>
<tr>
<th>Primary diagnostic criteria</th>
<th>Secondary diagnostic criteria</th>
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<tbody>
<tr>
<td>One of the following criteria:</td>
<td>Two of the following criteria :</td>
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<tr>
<td>Facial adenoma sebaceous,</td>
<td>Infantile spasms,</td>
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<tr>
<td>Penangangial or subungal</td>
<td>Hypereosinophilic macules,</td>
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<tr>
<td>fibroma,</td>
<td>Shagreen Patch,</td>
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<tr>
<td>Cortical or subependymal tuber,</td>
<td>Single retnal hamartoma,</td>
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<tr>
<td>Multiple retnal hamartomas,</td>
<td>Intra ventricular or parasiticeral</td>
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<td></td>
<td>nodular calcification,</td>
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<td></td>
<td>Bilateral renal angiomyolipoma,</td>
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<tr>
<td></td>
<td>Cardiac rhabdomyoma.</td>
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Important laboratory studies includes: small calcifications within the substance of brain on skull x-Ray, calcified subependymal tubers are better visualized by CT scan and sonogram (in Infant), angiogram are often diagnostic. Renal cyst may be associated with albuminuria or azotemia. IVU are also diagnostic of renal lesions. Chest radiograph may reveal pulmonary lesion or Rhabdomyoma with cardiomegaly. ECG findings are variable but echocardiogram is diagnostic. CSF is normal except when large intracerebral tumor is present. EEG are often abnormal, specially in patient with clinical seizures. Finding of EEGare slow wave activity, arrhythmia, focal or multifocal spike or sharp wave discharge and generalized spike & wave discharge.

There is no specific treatment. Symptomatic management includes, anti convulsants for seizures, shunting for hydrocephalus, behavioral & educational strategies for mental retardation infantile myoclonic spasm often responds to corticosteroid. Focal and generalized seizures are treated with anticonvulsants. Cosmetic surgery for facial adenoma or large shagreen patches. Progressive cystic renal involvement often responds to surgical decompression. Cardiac Rhabdomyoma and CCF are managed medically with cardiotonic, diuretics, obstructive intracavitary tumors require surgical excision of tumor and progressive pulmonary involvement by respiratory therapy.

Prognosis

Mild or solely cutaneous involvement often follows a static course where as those with full blown syndrome have progressive coJJrse with increasing seizures and dementia. Brain tumor, status epilepticus, renal insufficiency, cardiac failure or progressive pulmonary impairment can lead to death3. Most patient die within a few years after the onset of these complications & severely affected individuals generally die before the age 30'.

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