TUBEROUS SCLEROSIS: CASE REPORT WITH REVIEW OF LITERATURE
Kunwarpal Singh1, Amritpal Singh2, Sukhdeep Kaur3, Kulvinder Singh4, C.L. Thukral5

HOW TO CITE THIS ARTICLE:

ABSTRACT: Tuberous sclerosis (TS) Epiloia Or Bournerville’s Disease is one of the important neurocutaneous syndrome characterized by abnormalities of both the integument and centre nervous system (CNS) with an estimated frequency of 1/6000 (1-4). We report a case of a 10 yr old male child who presented to the department of dermatology with complaint of multiple nodular lesions on the face. He was referred to the department of radiodiagnosis for imaging evaluation and was diagnosed as a case of tuberous sclerosis.

INTRODUCTION: Von Recklinghausen first described tuberous sclerosis in 1862. Desire-Magloire Bourneville (a French physician) coined the term sclerose tubereuse, from which the name of the disease has evolved. Sherlock coined the term EPILOIA encompassing the clinical triad of tuberous sclerosis (Epi: epilepsy, Loi: low intelligence, A: adenoma sebaceum). As the manifestations of the disease are variegated in nature, the term tuberous sclerosis complex (TSC) is now widely used. It is an autosomal dominant inherited disease, being associated with at least two separate chromosomes (TSC1, found on chromosome 9q34, and TSC2, on chromosome 16p3).

Clinical diagnosis is easy when the patient presents with classical triad of seizures, mental retardation and adenoma sebaceum. However, in a patient presenting with an incomplete form of tuberous sclerosis, mistakes in the diagnosis are possible. We report a case of 10 years old male child who presented with dermatological lesions and on evaluation was found to be a case of tuberous sclerosis. The importance of recognition of features of this rare syndrome is stressed.

CASE REPORT: A 10 year old male child presented with a chief complaint of multiple nodular lesions on the cheeks. On clinical examination, lesions were hyperpigmented and raised from the skin surface known as adenoma sebaceum (Fig.1). Ash leaf spots were seen on the forehead of the child as depigmented lesions (Fig.2). Shagreen patches were also observed at the lower back in the lower lumbar region appearing as light yellow colored thickened nodules (Fig.3). Child was performing poorly in the school and he was unable to solve simple mathematical calculations. There was no history of seizures. Routine biochemical investigations were normal.

MRI of the brain was done which showed multiple small nodular lesions along the ependymal surface of both the lateral ventricles appearing hypointense on T2WI (Fig. 4) and isointense on T1WI (Fig. 5). Some of the lesions showed blooming on T2FFE sequence (Fig. 6) and showing calcification on NCCT images (Fig. 7). Post contrast T1WI sequences showed moderate to avid enhancement of the nodular lesions; however the calcified lesions did not enhance (Fig.8).

There was also evidence of multiple ill defined scattered areas of increased signal intensity on T2WI and FLAIR images in the cortical and subcortical locations of bilateral cerebral hemispheres (Figs. 9-12). Few thin linear subcortical hyperintensities were also observed extending medially upto the ependyma of the lateral ventricle (Fig. 11).
USG abdomen of the patient was done using high frequency (7-11Mhz) linear probe; which showed multiple small anechoic cysts in both the kidneys cortical in location (Figs.13, 14) which were further confirmed on MRI abdomen using BFFE coronal and T2W_RT SPIR axial sequences as hyperintense cystic lesions bilaterally. (Figs 15, 16).

USG of the right eye showed a curvilinear echogenic focus in the vitreous chamber along the posterior coat which was probably retinal hamartoma (Fig.17).

Our patient fulfilled five major criteria i.e. adenoma sebaceum or facial angiofibromas, hypopigmented macules on the forehead, shagreen patches in the lower back, cortical & subcortical tubers and subependymal nodules, and two minor criteria i.e. migration lines and multiple renal cysts. Retinal lesion was not included in the criteria as it was a single lesion. Keeping in view the dermatological lesions, low IQ of the patient and above described diagnostic criteria; definite diagnosis of tuberous sclerosis was made.

**DISCUSSION:** TSC is a dominantly inherited disorder affecting multiple organs. In 1998, a panel of international experts revised the diagnostic criteria for tuberous sclerosis complex at the TSC Consensus Conference in Annapolis, Maryland. The revised criteria (Table 1) reflect an improved understanding of the clinical manifestations of TSC and its genetic and molecular mechanisms. Consequently, the revised criteria require TSC-associated lesions of two or more organ systems or at least two dissimilar lesions of the same organ to confirm the diagnosis. TS is thought to result from sporadic mutation in the majority of patients, since most patients have no family history of the disease.

The triad of symptoms of TS, as described by Vogt, consists of seizure, adenoma sebaceum (facial angiofibroma), and mental retardation. Not all patients have this classic triad, however, and half of all patients are of normal intellect and a quarter do not have seizures. Although facial angiofibromas are commonly described as the hamartomatous lesions of TS, which may involve virtually any organ. A diagnosis of TS is definite when two major features or one major and two minor features exist, probable if one major and one minor feature are present, and possible when more than two minor features or only one major feature is present.

**Imaging:** Overall, CT reveals intracranial abnormalities in 85% of patients with tuberous sclerosis. Cortical tubers are often seen as low-attenuating peripheral lesions. Subependymal nodules appear as localized projections into the ventricular cavity and may enhance after the intravenous contrast administration, although contrast enhancement is more difficult to recognize calcified lesions. In 10-15% of patients, subependymal nodules may transform into giant cell astrocytomas. These tumors are benign and usually occur at or near the foramen of Monro. They show inhomogeneous enhancement pattern. Angiomyolipomas often have low attenuation values if they contain sufficient fat, but they are indistinguishable from other renal tumors if they contain little or no lipid.

Cystic lesions are well characterized at CT as fluid density hypodense lesions. The CT chest findings reveal interstitial thickening, alveolar destruction, and honeycomb; these are pathologically indistinguishable from lymphangioleiomyomatosis (LAM).

MRI is the imaging modality of choice for evaluating intracranial lesions of tuberous sclerosis. Cortical tubers, or hamartomas, are the most characteristic lesions of tuberous sclerosis; they are detected on MRIs in 95% of patients. The appearance of cortical tubers on MRIs varies with
patient age. In neonates and young children, the cortical tubers and subependymal nodules are hyperintense on T1-weighted images and hypointense on T2-weighted images. In older children and adults, the cortical and subependymal lesions are isointense or hypointense on T1-weighted images. They are hyperintense relative to gray matter, as well as white matter, on T2-weighted images, depending on the presence of calcification. Enhancement of cortical and subcortical lesions is uncommon and occurs in fewer than 5% of the cases. Enhancement of subependymal nodules is common, and it is better visualized on MRI.

MRI depicts several distinct patterns of white matter lesions, including straight or curvilinear radial cerebral bands, wedge-shaped abnormalities, nonspecific conglomerate lesions, and cerebellar radial bands. White matter lesions in older children and adults typically are isointense or hypointense on T1-weighted images compared with white matter and hyperintense on T2-weighted images compared with gray matter and white matter. A small percentage of white matter lesions enhance after the administration of contrast material.

Subependymal nodules are detected in 95% of patients. Subependymal giant cell astrocytomas appear inhomogeneous, with intense enhancement after the administration of contrast material.

On ultrasonography, a finding of multiple angiomyolipomas with a high fat content is highly suggestive of tuberous sclerosis appearing highly echogenic. Renal cysts are another primary manifestation of renal involvement. Cysts almost always are multiple; typically, they are bilateral. Cysts are anechoic and may be indistinguishable from findings in autosomal dominant polycystic kidney disease.

CONCLUSION: Clinical diagnosis is easy when the patient presents with classical triad of seizures, mental retardation and adenoma sebaceum. However, in a patient presenting with an incomplete form of tuberous sclerosis, mistakes in the clinical diagnosis are possible and imaging helps in the diagnosis.

REFERENCES:
CASE REPORT


• **Major features**
  - Facial angiofibromas or forehead plaque
  - Nontraumatic ungual or periungual fibroma
  - Hypomelanotic macules (more than three)
  - Shagreen patch (connective tissue nevus)
  - Cortical tuber
  - Subependymal nodule
  - Subependymal giant cell astrocytoma
  - Multiple retinal nodular hamartomas
  - Cardiac rhabdomyoma, single or multiple
  - Lymphangiomatomatosi
  - Renal angiomyolipoma

• **Minor features**
  - Multiple randomly distributed pits in dental enamel
  - Hamartomatous rectal polyps
  - Bone cysts
  - Cerebral white matter "migration tracts"
  - Gingival fibromas
  - Nonrenal hamartoma
  - Retinal achromatic patch
  - "Confetti" skin lesions
  - Multiple renal cysts

**Table 1. Diagnostic Criteria for Tuberous Sclerosis Complex**
CASE REPORT

Fig.1 Show hyperpigmented lesion on the cheek and raised from the skin surface—Adenoma sebaceum

Fig.2 Show depigmented lesions on the forehead—Ash leaf spots.

Fig.3 Show light yellow colored thickened nodules at the lower back—Shagreen patches

Fig.4 T2WI axial sequence of brain show multiple small hypointense nodular lesions along the ependymal surface of both the lateral ventricles

Fig.5 On T1WI axial sequences the lesions appears isointense
Fig. 6 On T2WFFE axial sequences the lesions show some blooming.

Fig. 7 NCCT brain axial sequence shows calcification in few of the lesions.

Fig. 8 Post contrast T1WI sequences showed moderate to avid enhancement of the nodular lesions.

Figs. 9, 10, 11 and 12 T2WI axial and FLAIR axial sequences show multiple ill-defined scattered areas of increased signal intensity in the cortical and subcortical locations of bilateral cerebral hemispheres.
Fig. 13 and 14 USG using high frequency (7-11 Mhz) linear probe shows multiple small anechoic cysts in both the kidneys in the cortical location.

Fig. 15 and 16 MRI of the abdomen using BFFE coronal and T2W_RT SPIR axial sequences shows small hyperintense cystic lesions in both the kidneys.

Fig. 17 USG of right eye using high frequency (7-11 Mhz) linear probe shows a curvilinear echogenic focus in the vitreous chamber along the posterior coat-probably retinal hamartoma.

AUTHORS:
1. Kunwarpal Singh
2. Amritpal Singh
3. Sukhdeep Kaur
4. Kulvinder Singh
5. Associate Professor, Department of Radiodiagnosis, Sri Guru Ram Das Institute of Medical Sciences and Research.
6. Professor and Head, Department of Radiodiagnosis, Sri Guru Ram Das Institute of Medical Sciences and Research.