

CASE REPORT

TUBEROUS SCLEROSIS: CASE REPORT WITH REVIEW OF LITERATURE

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ABSTRACT: Tuberous sclerosis (TS) Epiloia Or Bournerville's Disease is one of the important neuro-cutaneous syndrome characterised by abnormalities of both the integument and central 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)⁵.

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.⁶

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. These were 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 calcification on NCCT images (Fig.7). Post contrast T1WI sequences showed mild to moderate 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).

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USG abdomen of the patient was done using high frequency (7-11Mhz) linear probe; which showed multiple small anechoic cysts in both the kidneys in the cortical 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. (Figs15,16).

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.⁷ 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^{8,9}. 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 diagnosis¹⁰. TS is thought to result from sporadic mutation in the majority of patients, since most patients have no family history of the disease^{11,12}.

The triad of symptoms of TS, as described by Vogt¹³, 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 seizures¹⁴. Although facial angiofibromas are commonly described as the hamartomatous lesions of TS, hamartomas 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 honeycombing; these are pathologically indistinguishable from lymphangioleiomyomatosis (LAM)

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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.¹⁵

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:

1. Haslam RHA. Neurocutaneous syndromes. In: Behrman RE, Kliegman RM, Jenson HB (eds). Nelson text book of Pediatrics. 17th edn. W B Saunders company. Philadelphia 2004.pp. 1837-38.
2. Berg B O. Neurocutaneous syndromes. In: Maria BL (ed) Current Management in Child Neurology. B C Decker. Hamilton 1999.pp. 278-80.
3. Kulkarni ML. Tuberous sclerosis. In: Parthasarthy A (eds). IAP Textbook of Paediatrics. 2nd edition. Jaypee Brothers New Delhi: 2003.pp. 569.
4. Kandt R S. Tuberous sclerosis complex and neurofibromatosis type I: the two most common neurocutaneous disease. *Neurol Clin* 2002; 20: 914-64.
5. Jozwiak J, Jozwiak S, Wlodarski P. Possible mechanism of disease development in tuberous sclerosis. *Lancet Oncol* 2008; 91(1):73-79.
6. Yasir illahi, Salma tanveer, Ahmed khurshid pasha, Awais naeem, Nasima ali. Tuberous

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- sclerosis. classical presentation in a male patient. Nishtar medical journal January - March 2010; Vol 2, No. 1.
7. Brigid A. Staley, MPH, Emily A. Vail, MD, Elizabeth A. Thiele, MD, PhD. Tuberous Sclerosis Complex: Diagnostic Challenges, Presenting Symptoms, and Commonly Missed Signs. Pediatrics Vol.127 No.1 January 1.2011; pp.e117-e125.
 8. E. Steve Roach, MD; Steven P. Sparagana, MD. Diagnosis of Tuberous Sclerosis Complex. J. Child Neurol 2004; 19:643-649
 9. Roach ES, Gomez MR, Northrup HII: Tuberous sclerosis complex consensus conference: Revised clinical diagnostic criteria. J. Child Neurol 1998;13:624-628.
 10. Hymann MH, Whittemore VH: National Institutes of Health consensus conference: Tuberous sclerosis complex. Arch Neurol 2000;57:662-665.
 11. Bourneville DM. Sclerose tubereuse des circonvolutions cerebrales: idiotie et epilepsie hemiplegique. Arch Neurol 1880; 1:81-91.
 12. Winship IM, Connor JM, Beighton PH. Genetic heterogeneity in tuberous sclerosis: phenotypic correlations. J Med Genet 1990; 27:418-421.
 13. Vogt H. Zur pathologie und pathologischen anatomie der verschiedenen idiotieformer. Monatsschr Psychiatr Neurol 1908; 24:106-150.
 14. O'Callaghan FJ, Osborne JP. Advances in the understanding of tuberous sclerosis. Arch Dis Child 2000; 83:140-142.
 15. Anne G. Osborn. Diagnostic Neuroradiology. Elsevier 2012. pp. 93-98.

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| <ul style="list-style-type: none"> • Major features |
| <ul style="list-style-type: none"> • Facial angiofibromas or forehead plaque |
| <ul style="list-style-type: none"> • Nontraumatic unguial or periungual fibroma |
| <ul style="list-style-type: none"> • Hypomelanotic macules (more than three) |
| <ul style="list-style-type: none"> • Shagreen patch (connective tissue nevus) |
| <ul style="list-style-type: none"> • Cortical tuber |
| <ul style="list-style-type: none"> • Subependymal nodule |
| <ul style="list-style-type: none"> • Subependymal giant cell astrocytoma |
| <ul style="list-style-type: none"> • Multiple retinal nodular hamartomas |
| <ul style="list-style-type: none"> • Cardiac rhabdomyoma, single or multiple |
| <ul style="list-style-type: none"> • Lymphangiomyomatosis |
| <ul style="list-style-type: none"> • Renal angiomyolipoma |
| <ul style="list-style-type: none"> • Minor features |
| <ul style="list-style-type: none"> • Multiple randomly distributed pits in dental enamel |
| <ul style="list-style-type: none"> • Hamartomatous rectal polyps |
| <ul style="list-style-type: none"> • Bone cysts |
| <ul style="list-style-type: none"> • Cerebral white matter "migration tracts" |
| <ul style="list-style-type: none"> • Gingival fibromas |
| <ul style="list-style-type: none"> • Nonrenal hamartoma |
| <ul style="list-style-type: none"> • Retinal achromic patch |
| <ul style="list-style-type: none"> • "Confetti" skin lesions |
| <ul style="list-style-type: none"> • Multiple renal cysts |
| <ul style="list-style-type: none"> • Table 1. Diagnostic Criteria for Tuberous Sclerosis Complex |

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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

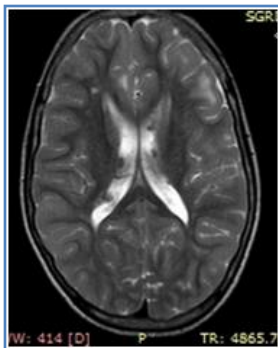


Fig.4 T2WI axial sequence of brain show multiple small hypointense nodular lesions along the ependymal surface of both the lateral ventricles

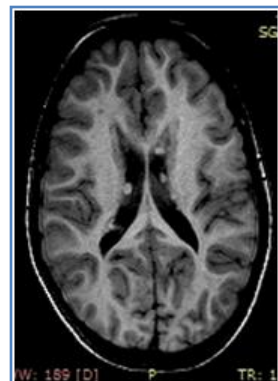


Fig.5 On T1WI axial sequences the lesions appears isointense

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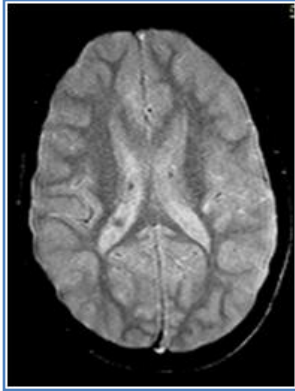


Fig.6 On T2WFFE axial sequences the lesions show some blooming

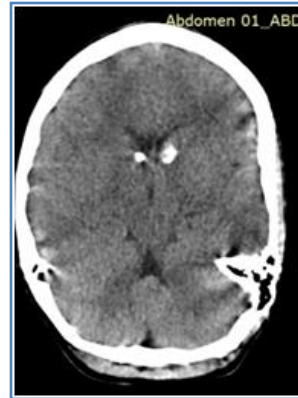


Fig.7 NCCT brain axial sequence shows calcification in few of the lesions.



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

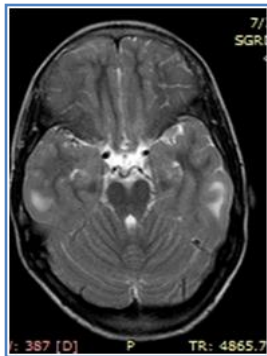


Fig 9

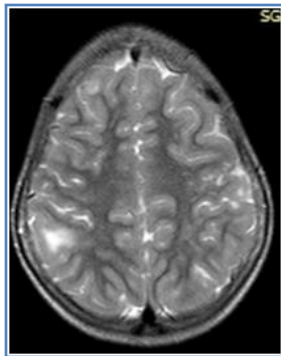


Fig 10

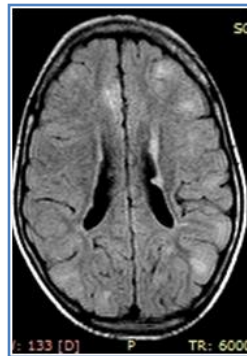


Fig 11

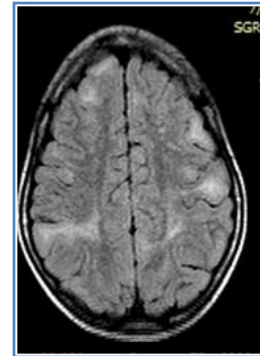


Fig 12

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.

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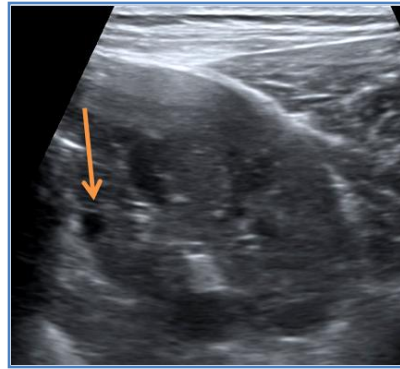
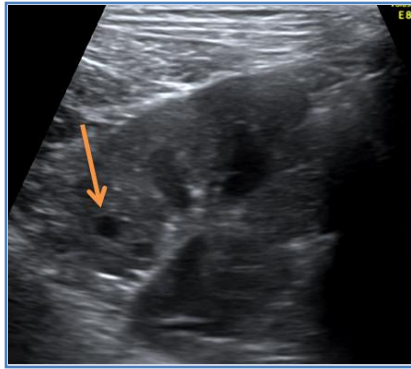


Fig. 13 and 14 USG using high frequency (7-11 Mhz) linear probe shows multiple small anechoic cysts in both the kidneys in the cortical location

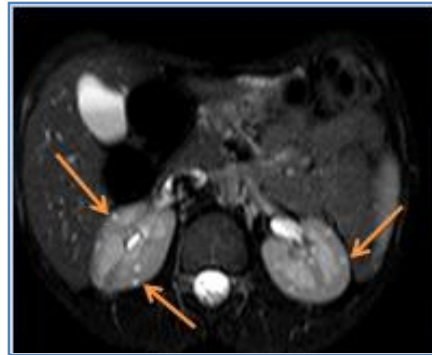


Fig. 15 and 16 MRI of the abdomen using BFFE coronal and T2W_RT SPIR axial sequences shows small hyperintense cystic lesions in both the kidneys.



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.

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