Asian Journal of Pharmaceutical and Health Sciences
www.ajphs.com

A young female with cognitive impairment & history of Epilepsy - A case report

Pranay Bajpai[1]*, Nipun Pauranik[2], Mukesh Dube[3], Dinesh Chouksey[4], Ajoy.k.Sodani[5], R.K.Jha[6]

1. PG-Resident,Dept. Of Medicine, SAIMS, Indore (M.P.)
2. Assistant Professor, Dept.of Neurology, SAIMS,Indore (M.P)
3. Senior Registrar, Dept. of Neurology, SAIMS, Indore (M.P.)
4. Senior Registrar, Dept. of Neurology, SAIMS, Indore (M.P.)
5. Professor, Dept. of Neurology, SAIMS, Indore (M.P.)
6. Professor & HOD, Dept. Of Medicine, Sri Aurobindo Medical College (SAIMS), Sanwer Road, Indore - 453555 (M.P.), India.

ARTICLE HISTORY

Received: 08.04.2014

Accepted: 25.05.2014

Available online: 30.08.2014

Keywords:

Tuberous sclerosis,Benign Hamartomatous tumors, Neurofibromas, Angiofibromas.

*Corresponding author:

Email : niru2011ms@gmail.com
Tel.: +91-9861354573, 9437293322

ABSTRACT

Tuberous sclerosis (TS) Epiloia Or Bournervlle's Disease is a neuro-cutaneous syndrome characterised by abnormalities of both the integument and central nervous system (CNS) with an estimated frequency of 1/6000. It involves alterations to ectodermal and mesodermal cell differentiation and proliferation, causing benign hamartomatous tumors, neurofibromas and angiofibromas in the brain and other vital organs including the kidney, heart, eyes, lungs, skin and mucosa. It also affects the central nervous system and produces neurological dysfunctions such as seizures, mental retardation and behavior disorders.We report a case of a 18year/female brought to OPD of Department of Neuromedicine by her family members with complaint of family members with complain of repeated fight with family members always angry, moody and stubborn. She become irrational at times. She undergone ophthalmology examination which show Multiple retinal nodular hamartomas lesions in left eye, further MRI of Brain reviled Subependymal Giant Cell Astrocytoma of left Frontal Horn with white matter radiation lines suggestive of Tuberous Sclerosis Complex.

INTRODUCTION

Tuberous sclerosis (TS) Epiloia Or Bournervlle's Disease is a neuro-cutaneous syndrome characterised by abnormalities of both the integument and central nervous system (CNS) with an estimated frequency of 1/6000 (1-4). 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 which consist of 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 chromosome9q34, and TSC2, on chromosome 16p3). (5) Discovered in 1997, TSC1 is located on chromosome 9q34 and produces a protein called hamartin. TSC2, discovered in 1993, is located on chromosome 16p13 and produces a protein called tuberin. Although inheritance is autosomal dominant, 60-70% of cases occur through spontaneous mutations. Definite TSC is diagnosed when either 2 major features (out of a total of 11) or one major feature with 2 minor features (out of a total of 9) are present (6). Tuberous sclerosis has no cure, but treatment as medicine, educational and occupational therapy can help relieve symptoms.

CASE REPORT

An 18 year old female full term normal vaginal delivery cried after birth with normal developmental milestones, brought to neurology OPD by her family members with complain of repeated fight with family members always angry, moody and stubborn. She become irrational at times. Attenders also give history multiple admission in rehabilitation center for the same On taking a detail history her family member give history of poor school performance with history of unable to perform simple mathematical calculation also history of seizure disorder since the age of 3yrs with a frequency of episodes being seven to eight in a month all of same simeology. These seizure episode continue till the age of 14yrs she is seizure free since. There is no history of similar complain in the family. On general clinical examination

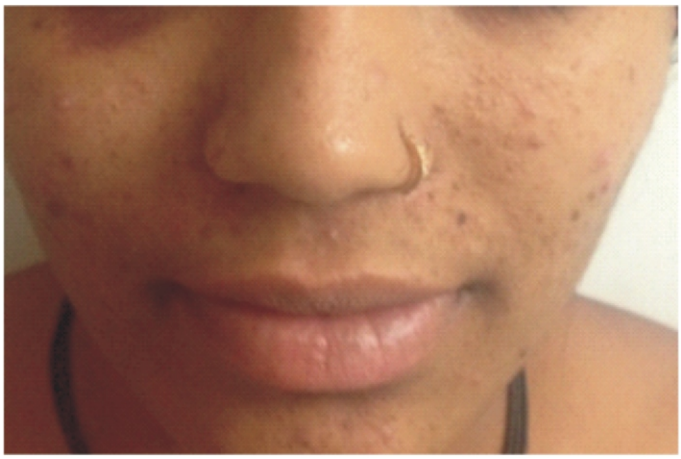


Fig.1 Hyperpigmented lesion on the cheek and raised from the skin surface-Adenoma sebaceum

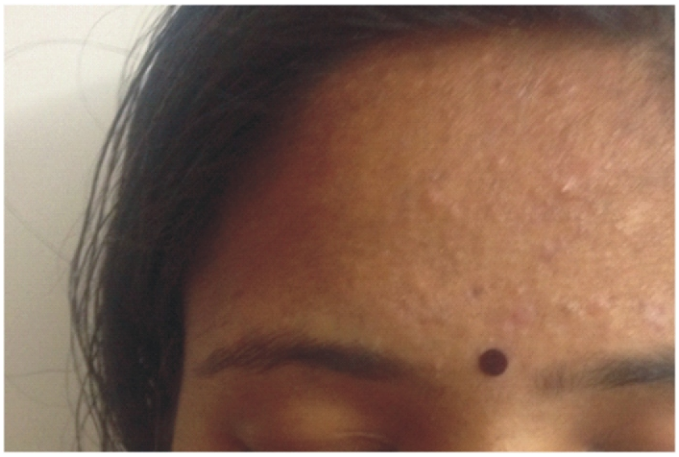


Fig.2 Depigmented lesions on the forehead-Ash leaf spots

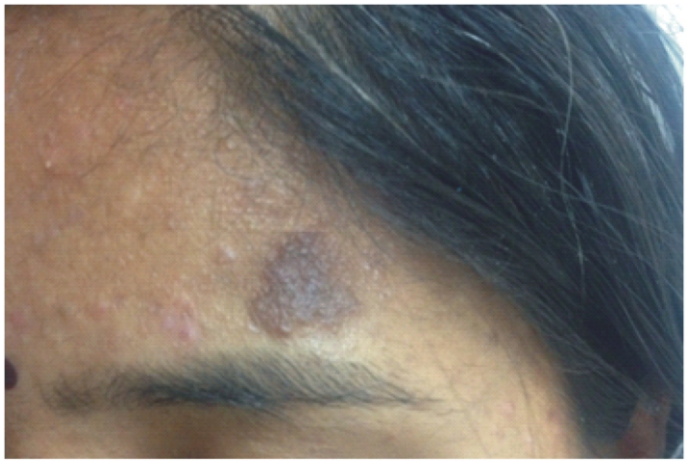


Fig.3 Shagreen patches observed over left eyebrow region

adenoma sebaceum (Fig.1). Ash leaf spots were seen on the forehead of the as depigmented lesions (Fig.2). Shagreen patches were also observed over left eyebrow region (Fig.3). Nontraumatic ungual or periungual fibroma note under finger nail (fig.4). Her MMSE (Mini Mental State Examination) score was 24/30 rest of neurological examination was normal, further her Psychoanalysis and IQ was found to be 10yr compared to her age.

She undergone detail ophthalmology examination which

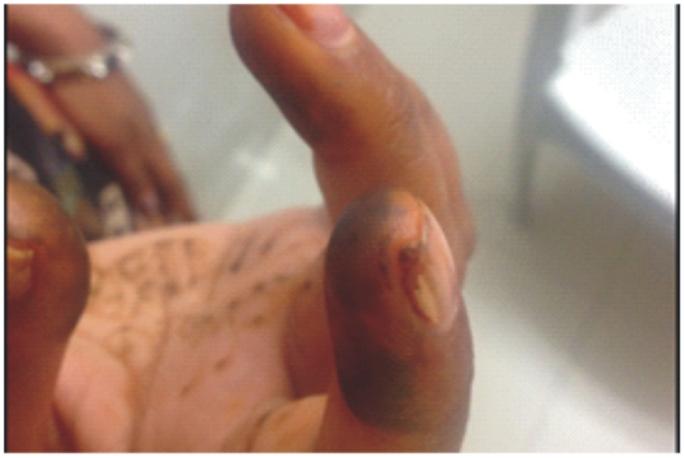


Fig.4 Nontraumatic ungual or periungual fibroma note under finger nail

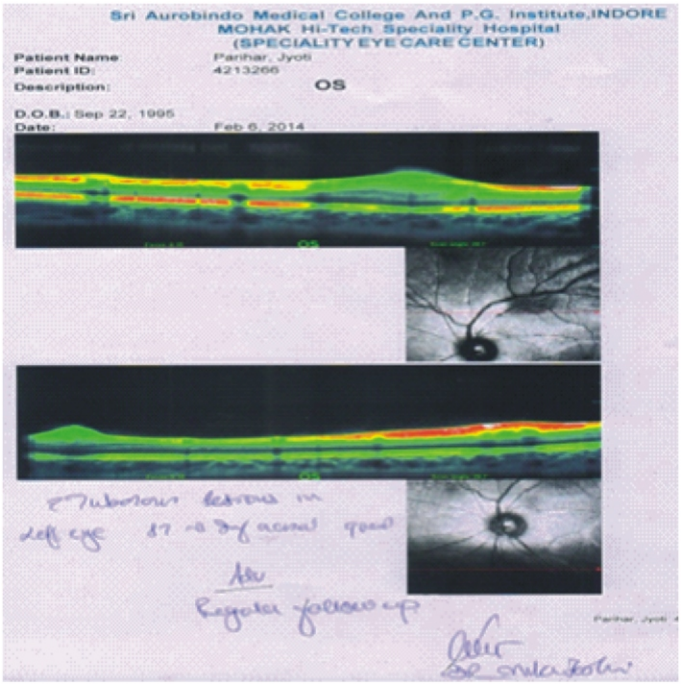
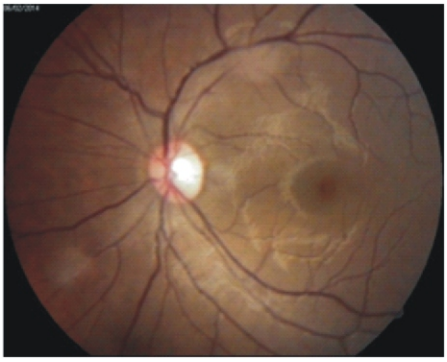


Fig.5-a Optical coherence tomography & **5-b** Retinoscopy showing Hamartomas lesions in left eye



show Multiple retinal nodular hamartomas lesions in left eye on retinoscopy examination which were further confirm by Optical coherence tomography (fig.5-a,b), further an Iris freckle was also noted (Fig.6).She undergone EEG during sleep and awake which was normal(Fig.7). MRI of Brain was performed which reviled

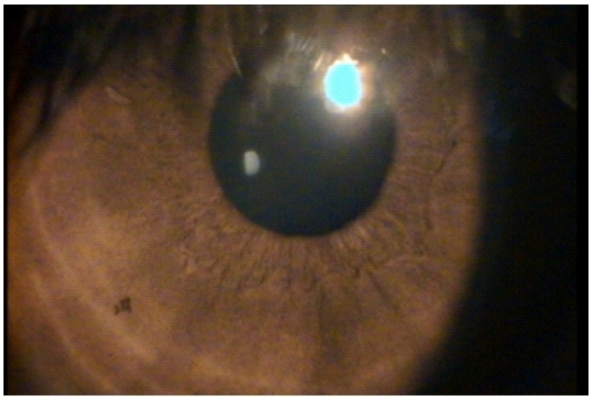


Fig. 6 Iris freckle as noted

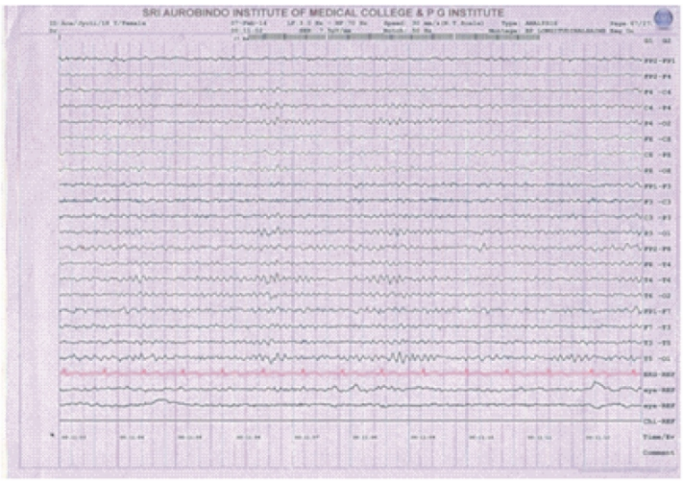


Fig.7 EEG during sleep and awake

Subependymal Giant Cell Astrocytoma of left Frontal Horn with white matter radiation lines (Fig.8) these findings were suggestive of Tuberous Sclerosis Complex.

Our patient fulfilled Six major criteria i.e. adenoma sebaeceum or facial angiofibromas, hypopigmented macules on the forehead, shagreen patches, Nontraumatic ungual or periungual fibroma note under finger nail, cortical & subcortical tubers and subependymal nodules, and one minor criteria i.e. Cerebral white matter "migration tracts". Keeping in view the dermatological lesions, low IQ of the patient and above described diagnostic criteria ; definite diagnosis of Tuberous Sclerosis with Epilepsy in remission was made.

DISCUSSION

Tuberous Sclerosis is an important genetic disorder that affects the patient and the family in various ways. Multiple research projects are being done around the world regarding further work up of the genes involved and treatment strategies. Now, due to an understanding of its pathogenesis, multiple drug therapies are available for certain manifestations of the disease. (7) But the patient, along with symptomatic control of seizures, should also be offered special schooling, and occupational therapy. Surgery, including dermabrasion and laser treatment, may be useful for treatment of skin lesions.

Multiple cases have been reported highlighting involvement of different organs in TSC. In 1998, a panel of international experts revised the diagnostic criteria for tuberous sclerosis complex at the TSC Consensus Conference in Annapolis,

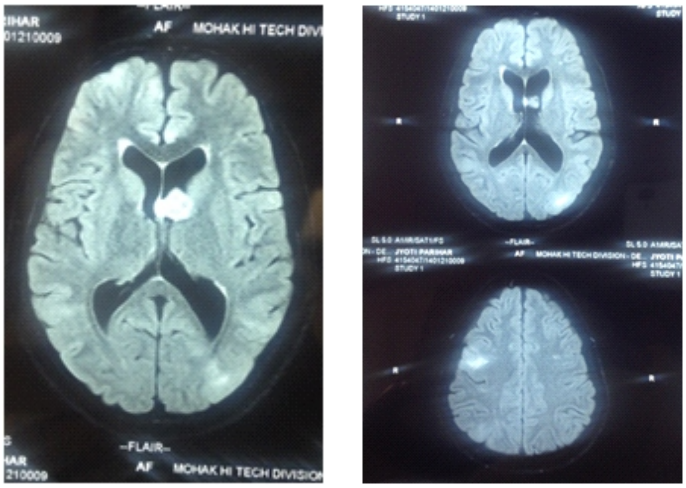


Fig.8 MRI Brain showing Subependymal Giant Cell Astrocytoma of left Frontal Horn with white matter radiation lines

Table 1. Diagnostic Criteria for Tuberous Sclerosis Complexsis Complex

MAJOR CRITERIA	
1.	Facial angiofibromas or forehead plaque
2.	Nontraumatic ungual or periungual fibroma
3.	Hvpomelanotic macules (more than three)
4.	Shagreen patch (connective tissue nevus)
5.	Cortical tuber
6.	Subependymal nodule
7.	Subependymal giant cell astrocytoma
8.	Multiple retinal nodular hamartomas
9.	Cardiac rhabdomyoma, single or multiple
10.	Lymphangiomyomatosis
11.	Renal angiomyolipoma
MINOR CRITERIA	
1.	Multiple randomly distributed pits in dental enamel
2.	Hamartomatous rectal polyps
3.	Bone cysts
4.	Cerebral white matter "migration tracts"
5.	Gingival fibromas
6.	Nonrenal hamartoma
7.	Retinal achromic patch
8.	"Confetti" skin lesions
9.	Multiple renal cysts.

Maryland (8),(9). The revised criteria (Table 1) reflect an improved understanding of the clinical manifestations of TSC. 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.

TS is thought to result from sporadic mutation in the majority of patients, since most patients have no family history of the disease (10),(11).

The triad of symptoms of TS, as described by Vogt (12) , 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 (13). 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. Subependymal nodules are detected in 95% of patients. Subependymal giant cell astrocytomas appear inhomogeneous, with intense enhancement after the administration of contrast material.(14)

CONCLUSION

TSC is a lifelong condition, therefore individuals should be regularly monitored by an experienced clinician. However, in a patient presenting with an incomplete triad of tuberous sclerosis, diagnosis may be possible with the help of imaging studies.

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 neurocutancous disease.Neurol Clin 2002; 20: 914-64.
5. Jozwiak J, Jozwiak S, Wlodraski P. Possible mechanism of disease development in tuberous sclerosis. Lancent Oncol 2008; 91(1):73-79.
6. Roach E, Sparagana S. Diagnosis of tuberous sclerosis complex. J Child Neurol 2004; 19: 643-9.
7. Yates JR. Tuberous sclerosis. Eur J Hum Genet 2006; 14: 1065-73.
8. E. Steve Roach, MD; Steven P. Sparagana, MD. Diagnosis of Tuberous Sclerosis Complex. J. Child Neuorl 2004; 19:643-649
9. Roach ES, Gomez MR, Northrup HII: Tuberous sclerosis complex consensus conference: Revised clinical diagnostic criteria. J. Child Neuorl 1998;13:624-628
10. Bourneville DM. Sclerose tubereuse des circonvolutions cerebrales: idotie et epilipsie hemiplegique. Arch Neurol 1880; 1:8191.
11. Winship IM, Connor JM, Beighton PH. Genetic heterogeneity in tuberous sclerosis: phenotypic correlations. J Med Genet 1990; 27: 418421.
12. Vogt H. Zur pathologie und pathologischen anatomie der verschiedenen idiotieformer. Monatsschr Psychiatr Neurol 1908; 24:106150.
13. O'Callaghan FJ, Osborne JP. Advances in the understanding of tuberous sclerosis. Arch Dis Child 2000; 83:140142.
14. Kunwarpal Singh, Amritpal Singh, Sukhdeep Kaur, Kulvinder Singh, CL Thukral. "Tuberous sclerosis: case report with review of literature". Journal of Evolution of Medical and Dental Sciences 2013; Vol. 2, Issue 45, November 11; Page: 8752-8759.