The Journal of Medical Research

Case Report

JMR 2015; 1(4): 112-114
July- August
ISSN: 2395-7565

www.medicinearticle.com

A case of tuberous sclerosis presented with profound intellectual disability, intractable seizure, suspected abuse and Pica

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Abstract

Background: Tuberous sclerosis complex is a neurocutaneous syndrome inherited as autosomal dominant manner. It presents with CNS, dermatological manifestations and other systemic involvement. **Methods:** A case of male adolescent of 13 years age who presented in tertiary care OPD with strong family history of intellectual disability. The history obtained from his parents and necssary investigation work up has been done. A multidisciplinary team examined the patient and some unique features has been obtained. **Results:** The uniqueness of the case is it presents with profound intellectual disability, there is difficult to treat epilepsy due to combination of complex partial seizure with secondary generalization and myoclonus, eating disorder in the form of pica has been noted, spreading leg infection raises the possibility of child abuse and neglect. **Conclusions:** The appropriate treatment approach lies in judicious history taking. Parental counseling, the safety of patient should get the priority. Medical management should be combined with behavioural therapy, parental therapy and psychosocial rehabilitation. Genetic testing is necessary and multidisciplinary approach is required by a team comprising of but not limited to psychiatrists, clinical psychologist, special educator, pediatrician, physician, surgeons, dermatologist and ophthalmologist.

Keywords: Tuberous sclerosis, Intellectual disability, Intractable seizure, Neglect and abuse, Pica.

INTRODUCTION

Tuberous sclerosis complex (TSC) is a rare, multi-system genetic disease that causes benign tumours to grow in the brain and on other vital organs such as the kidneys,heart,eyes, lungs and skin. It usually affects CNS & results in a combination of symptoms including seizures, development delay, behavioural problems, skin abnormalities & kidney disease.The disorder was previously known as epiloia or Bourneville's Disease but only 30-40% presents with all three of the triad (epilepsy, low intelligence and adenoma sebaceum) and 59% met diagnostic criteria of Roach *et al* [1]. TSC is caused by defects or mutations on two genes i.e TSC 1 (chromosome 9, hamartin)and TSC 2 (chromosome 16, tuberin). It is inherited as autosomal dominant disorder affecting 1 to 2 million individuals worldwide with prevalence of one in 6000 newborn [2].

CASE REPORT

Mr. AS, 13 years old male patient (Fig 2) is suffering from recurrent intractable since childhood. He was born by caesarian section without significant antenatal and perinatal history. The parents were concerned about his delay in development and attacks of seizure at the age of two months and consulted pediatrician. After careful history it was obtained that the patient had recurrent complex partial seizures with myoclonus associated with screaming, sialorrhea, frothing from mouth and self-injurious behaviour. He was unable to walk properly which is associated with frequent abnormal movement of his limbs. There is increased restlessness associated with throwing of arms and legs to and fro. There is presence of a visible lesion in the back & and there are spreading leg infections (Fig 3) and referred to dermatologist. The parents informed that he ingests all sorts of dirty and inedible objects which he gets within his reach. In 2005, at the age of three years he was admitted and a multidisciplinary team diagnosed the case as Tuberous sclerosis presented with profound intellectual disability with epilepsy, Adenoma sebaceum and fibroma on the back. His father has similar skin lesions. He has two other siblings (4 yrs and 5 yrs) having similar skin lesions.

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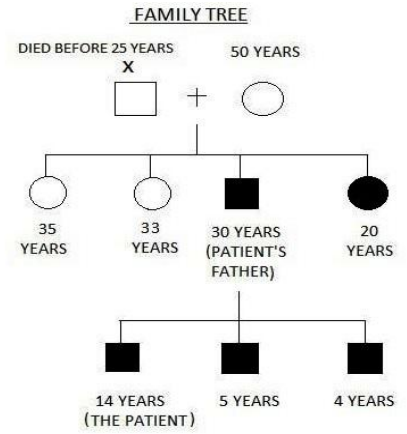

Fig 1: Characteristic autosomal dominant pattern of inheritance

The opthalmological examinations found Retinal lesions, called astrocytichamartomas (or "phakomas"), which appear as a greyish or yellowish-white lesion in the back of the globe on the ophthalmic examination. But the characteristic calcification was missing. Non retinal lesions which are common in TSC like coloboma and angiofibromas of the eyelids were also not found. Fundus examination didn't show papilledema related to hydrocephalus [3].

The characteristic dermatological abnormalities found are hypomelanic macules, fibroma in back (Fig 4) reddish spots or bumps of facial angiofibroma called Adenoma sebaceum.and small fleshy tumours called ungual or subungual fibroma that grow around and under the toe and finger nails. Shagreen patches appearing as flesh-colored soft plaques, though characteristically found in the lumbosacral area, found here in the upper back with i.e in thoracolumbar region with pebbly surface (Fig 5) [4].

Table 1: Investigation Findings

1A. Routine blood count: TLC=19500 DLC=$N^{68}L^{22}M^{6}E^{4}B^{0}$ ESR=75mm/1^{st} hour FPG=78 S. urea, creatinine, LFT, TFT 1B. USG of whole abdomen= bilateral renal cortical cysts with lipomatous growth SOL (suggestive of possible angiolipoma which is found in 70-80% cases)	2. X-ray 2A. Chest X ray:- Evidence of patchy pneumonitis in costophrenic region, bilaterally. Progressive replacement of the lung parenchyma with multiple cysts by lymphangioleiomyomatosis (LAM) can be expected and will be searched in subsequent follow up with HRCT thorax as plan of management. 2B. Xray left knee joint:- soft tissue swelling without any osteoporotic changes, bony injuries or joint affection.
3. Echocardiography: (i) SitusSolitus (ii) AV/SA concordance (iii) Small mass 10x10 mm arising from interventricular septum could be cardiac rhabdomyoma can be discovered using echocardiography in approximately 50% of people with TSC. However, the incidence in the newborn may be as high as 90% and in adults as low as 20%.	3. IQ: - IQ is 19 which indicate Profound Mental Retardation.
1. CT scan:- (i) Candledip calcification (ii) Gliosis at right fronto-parietal region- possibly sequele of haemorrhage.	2.MRI: Periventricular hypointensities, suggestive of calcification and tubers are found and favouring for Tuberous Sclerosis [5]. Haemorrhagic area is seen in right high parietal region with smallvessels around it.

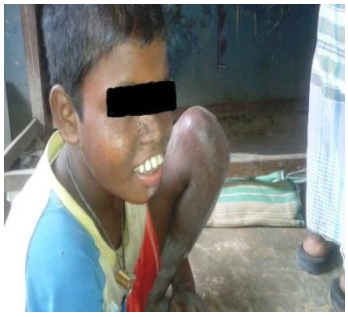

Figure 2: The subject

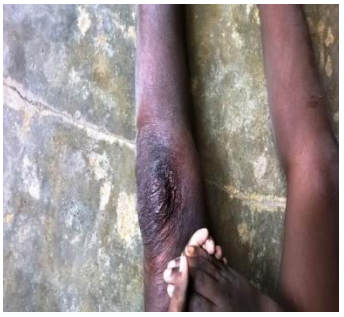

Figure 3: Spreading leg infection

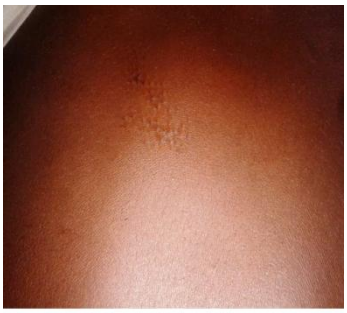

Figure 4: Shagreen patches in back

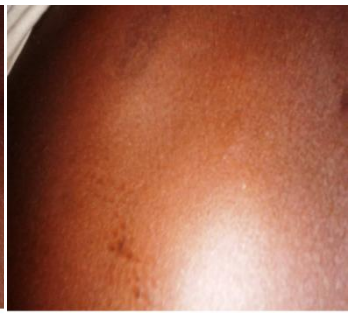

Figure 5: Fibroma on the Back

DISCUSSION

The overall incidence of intellectual disability is approximately 40% with a range of 38-80%. The index case is having profound intellectual disability which is not common found in 31% in one sample [6]. The most frequent behavioral disorders found in tuberous sclerosis, apart from intellectual disability are autism or autistic like behavior (36%), hyperactive or impulsive behavior (26%), and aggressive or destructive behavior (48%) [7].

In literature patient with tuberous sclerosis with secondary generalized seizure, infantile spasm and autistic features has been mentioned [8]. The poor control of seizure due to combination of complex partial seizures with myoclonus is unique in this case unlike those commonly found which is responsive to oxcarbazepin (900 mg/d) e, levetiracetam (1000 mg/d) and clonazepam (3 mg/d) in divided doses. An association between temporal lobe lesions with autistic features has been mentioned in case series [9]. The behavioural abnormalities get reduced with effective control of seizures an early initiation with antiepileptic drugs reduces the possibility of developmental non progression.

During examination of the patient, the spreading infection in lower limbs and back is noted. The possibility of neglect and abuse can't be ruled out. Cellulitis being treated with intravenous antibiotics and he responded well. The child helpline being called for and parental counseling has been arranged. Patient is also taking non-edible items including earthen materials, wooden pieces, matchsticks and cigarette butts. Four percent of cases of TSC were documented to have pica. The pica should be searched in adult presentation of Tuberous sclerosis complex with history of epilepsy. In all cases of pica possibility of Iron deficiency anemia and lead poisoning should be suspected [10].

CONCLUSION

There is no cure for TSC, although treatment is available for a number of symptoms. Antiepileptics are used to control seizures. Specific medications may be prescribed for behaviour problems. Intervention programs including special schooling and occupational therapy may benefit the individuals. Surgery may be needed in case of complications especially for renal tumors. Respiratory insufficiency may be treated with supplemental oxygen therapy or lung

transplantation if severe. As TSC is a lifelong condition, individuals need to be regularly monitored by doctor to make sure they are receiving the best possible treatment.

The abuse and neglect are associated with severe intellectual disability and more common in institutional set up than in domestic care. However caregiver burnt out may be attributed to physical abuse and mostly remain concealed. It is important for clinician, mental health professionals to search for it and reporting is mandatory for protection of human rights of mentally ill and the safety of victim [11].

Acknowledgement-

The authors are indebted to parents and the subject of the case report for the cooperativeness and giving permission to publish the case report.

Consent-

Written informed consent had been taken from the father as the patient is having profound intellectual disability.

Ethical clearance-

Has been taken from Institutional review committee for Ethical clearance for research work, Murshidabad Medical college and Hospital.

Conflict of interest – Nil

Funding - Nil

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