

Tuberous Sclerosis with ADHD in Siblings: Case Report**Rita Hajela¹, Abdul Hameed², Seema Rai³**¹Assistant Professor, ²Senior Resident, ³Assistant Professor

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Abstract: Here we represent case of tuberous sclerosis with ADHD in two siblings aged 7 female and aged 5 male. They presented with seizures of two years duration and one month duration both showing features of ADHD and elder showing signs of mental retardation along with cutaneous manifestations and were diagnosed on basis of typical MRI and CT findings along with clinical features. Elder sister was already on Levitracetam but seizures were not controlled. Both the children were put on sodium valproate and seizures were controlled. They were also put on atomoxetine and their behavior improved to some extent. They are under follow up. Rapamycin the recently recommended drug, was neither available nor affordable by parents. Parents were offered genetic counseling and were explained prognosis and long-term management.**Keywords:** Tuberous sclerosis, TSC, Autism, ADHD, Neuro cutaneous disorder, Vogt triad, Bourneville disease, cortical tubers, sub cortical tubers, sub ependymal nodules.

INTRODUCTION

Tuberous Sclerosis or Tuberous sclerosis complex (TSC), also known as Bourneville disease[1] is a neuro cutaneous disorder, characterized by development of multiple benign tumours of nervous tissue, skin and eyes (originating from embryonic ectoderm [2]). Classically it presents in children with Vogt triad of Seizures, mental retardation and adenoma sebaceous, but due to its variable manifestation a set of diagnostic criteria have been developed[3]. Tuberous sclerosis is a rare genetic disorder with multi system involvement. It is an autosomal dominant disorder in familial cases, in others it is a sporadic mutation and in rare cases both the parents are normal and disease manifests in children through gonadal mosaicism[4-5]. Two mutations have been suggested through various studies as TSC1 on chromosome 9q32-34 and TSC 2 on chromosome 16p13.3 identified as hamartin and tuberlin respectively[6]. The incidence is reported as 1 in 6000-10000 cases.

CASE REPORT

Two children of different sex, born out of Non consanguineous marriage, reported with uncontrolled seizures lasting for 2 years and one month

respectively(Figure1). Parents belonged to a poor socioeconomic status. The elder female 7 years old daughter developed seizures, abnormal hyperactive behavior with mental retardation 2 years back and the symptoms were worsening since then. When the younger child, 5 years old son started showing similar behavior on attainment of similar age and developed seizures parents got scared and brought them to hospital. MRI brain of elder female child revealed presence of Multiple cortical and sub cortical tubers in both cerebral hemispheres along with sub ependymal nodules (Figure2) she also showed features of ADHD and mental retardation, there were multiple skin lesions also. However there was no involvement of heart, kidney or eyes till date. Plain CT head of 5 years old younger male child revealed multiple sub cortical tubers and small calcified nodules along ependymal lining of both lateral ventricles (Figure 3). His IQ was near normal but behavior showed features of ADHD. Skin showed multiple hypo pigmented lesions (Figure 4). Parents also have a third female child 2 years old who was investigated, but was normal and showed normal development till date. She is under follow up and repeat investigations are planned for appearance of any symptoms or signs.



Fig-1: Showing three siblings

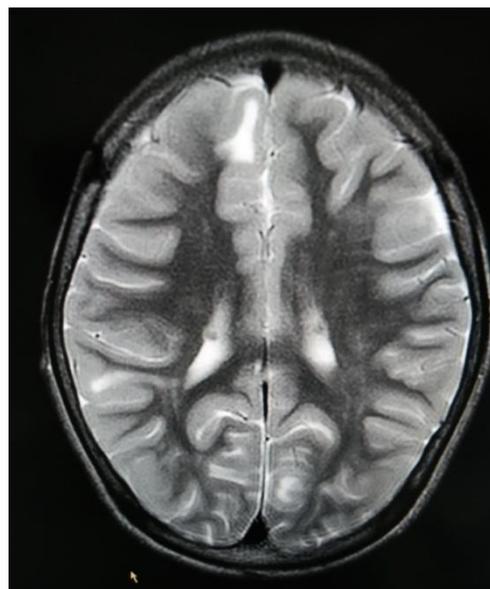


Fig-3: Multiple ill defined hypodensities in subcortical white matter of both cerebral hemispheres , small calcified nodules are seen along ependymal lining of both lateral ventricles

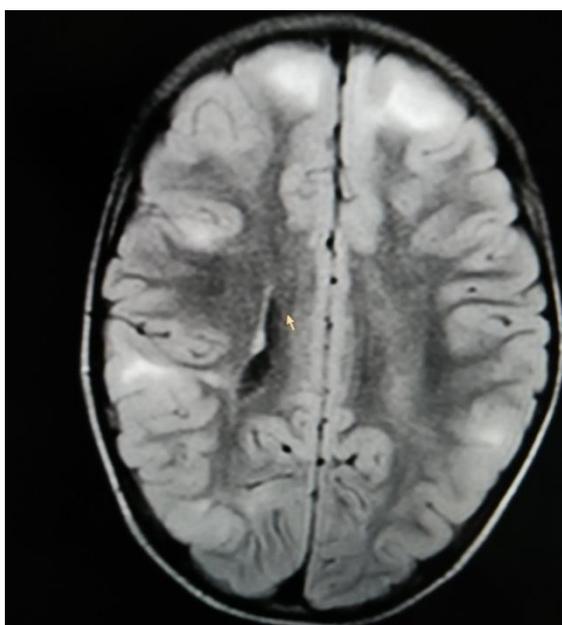


Fig-2: Showing Multiple cortical and subcortical tubers in both cerebral hemispheres along with subependymal nodules suggestive of Tuberous sclerosis



Fig-4: Hypopigmented macule -skin lesion in Tuberous sclerosis

DISCUSSION

The revised clinical diagnostic criteria for diagnosis of TSC are following

Major features		Minor features	
1	Hypo melanotic macules (≥ 3), at least 5 mm diameter)	1	Confetti skin lesions
2	Angio fibromas (≥ 3) or fibrous cephalic plaque	2	Dental enamel pits (≥ 3)
3	Ungual fibromas (≥ 2)	3	Intraoral fibromas (≥ 2)
4	Shagreen patch	4	Retinal achromic patch
5	Multiple retinal hamartomas	5	Multiple renal cysts
6	Cortical dysplasia including tubers and cerebral white matter radial migration lines radiation lines	6	Nonrenal hamartomas
7	Subependymal nodules		
8	sub ependymal giant cell astrocytoma		
9	Cardiac rhabdomyoma		

10	Lymphangioliomyomatosis		
11	Angiomyolipomas(≥ 2)		

Definite Clinical diagnosis is made when two major or one major and two minor features are present where as when one major and two minor features are present a probable case of TSC is considered and a follow up may reveal further features[7].

In our case two major features of cortical tubers and sub ependymal nodules were present along with minor feature of skin lesions. Children may or may not develop other features with follow up and aging .Both the parents were normal and there was no family history suggestive of disease in any blood relations. As both parents are normal chances of cases being presentation of autosomal dominance are ruled out. As two siblings of different sex are having similar disease starting at same age, chances of it being sporadic mutation is also statistically insignificant. Disease occurring at similar age with similar presentation in two consecutive children showing phenotypically similar morphologic facial features; they seem to be a case of expression of gonadal mosaicism, in which parents will be normal. However, we could not do genetic study as it was neither available at our place nor affordable by parents[8].

Seizures were immediately controlled once the children were put on sodium valproate. Seizure in TSC have responded well to Sodium valproate in other studies also [9]. The treatment presently recommended is topiramate and oral Rapamycin [10] but the drug was neither available nor affordable by poor parents. Genetic counseling, long term follows up and seizure free productive life is the goal in these cases. However Prognosis remains guarded and depends upon the system involvement size, site and progression of tubers and its effects.

CONCLUSION

TS have no predilection of sex and since siblings are affected with clinical features starting at almost similar age, gonadal mosaicism is the likely cause instead of sporadic mutation. or autosomal dominant inheritance. Both the cases had ADHD with TSC.

REFERENCES:

1. <http://www.rarediseases.org/rare-diseases/tuberous-sclerosis> accessed on September 29, 2015
2. Tuberous Sclerosis fact Sheet, http://www.ninds.nih.gov/disorders/tuberous_sclerosis/detail_tuberous_sclerosis.htm accessed on September 29, 2015
3. Northrup H; e Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 international tuberous sclerosis complex consensus conference Pediatric Neurology 2013; 49: 243-254.
4. Evans JC, Curtis J; The radiological appearance of tuberous sclerosis. The British journal of Radiology. 2000; 73:91-9.
5. Yvonne Baron, James barkovich A; MR imaging of tuberous sclerosis in neonates and young infants, AJNR 1999 20: 907-91.
6. Shepherd CW, Houser OW, Gomez MR; MR findings in tuberous sclerosis complex and correlation with seizure development and mental impairment AJNR Am J Neuro radiol 1995; 16:149-155.
7. Datta AK, Mandal S, Bhattacharya S; Autism and mental retardation with convulsion in tuberous sclerosis: a case report, Cases Journal 2009; 2:7061.
8. <http://www.casesjournal.com/content/2/1/7061> accessed on September 29, 2015.
9. Nath J, Dubey A, Pavan R; Analysis of twenty pediatric cases of tuberous sclerosis complex: Are we doing enough. Indian J Dermatol Venereol Leprol 2015; 81:23-8.
10. [http://www.tsalliance.org/documents/ADHD and TSC](http://www.tsalliance.org/documents/ADHD_and_TSC) accessed on September 29/9/2015.
11. Wataya-Kaneda M, Tanaka M, Nakamura A, Matsumoto S, Katayama I; A novel application of topical rapamycin formulation, an inhibitor of mTOR, for patients with hypomelanotic macules in tuberous sclerosis complex. Arch Dermatol 148(1):138-9.