Cardiac Rhabdomyoma with Tuberous Sclerosis - A Case of Unresponsive Seizures

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ABSTRACT

Tuberous sclerosis is a multisystemic disorder inherited in autosomal dominant pattern. It can be diagnosed as early as intra-uterine period of life but clinically may remain asymptomatic until late childhood or adulthood. We here report a case of TSC with cardiac rhabdomyoma presenting as unresponsive tonic seizures in a 10-year-old with behaviour abnormality.

Keywords: Tuberous Sclerosis, Cardiac Rhabdomyoma, Seizures

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Introduction

Tuberous sclerosis is a genetic disorder with occurrence of 1 in 10000 live births. It involves gene defects in TSC1 on chromosome 9 coding for hamartin and TSC2 gene on chromosome 16 coding for tuberin, which are tumour suppressors which act by inhibiting activation of MTOR protein. Hence defect in these genes lead to growth of benign tumours in various organ systems, like cerebral tubers, cardiac rhabdomyoma, adenoma sebaceosa. It can also present differently in a same family with mild or severe symptoms.

The hallmark of TSC is CNS involvement. The most common neurological manifestations being generalised tonic-clonic seizures, cognitive impairment and autism spectrum disorders.

Case Presentation

A 10-year-old female child presented with unresponsive seizures 4-5 episodes per day (including sleep seizures) for 2 years. Seizures were of tonic type (unlike classic GTCS seen in TSC), lasting for 20-30 seconds, associated with random eye movements and loss of consciousness. There was no aura and post-ictal confusion. There was no familial history of seizures.

Medical history revealed cardiac rhabdomyoma diagnosed at the age of 8 years with complaints of palpitations. Child was also taken to a psychiatrist an year ago for hyper-active behaviour and poor concentration (no medical documentation). Academic performance was not up to the mark.

Antenatal, birth and postnatal history was uneventful.

On examination child was well built, conscious, coherent and co-operative. afebrile, vitals were stable, no pallor, icterus, cyanosis, lymphadenopathy, oedema and clubbing.

Anthropometry was within normal limit [Ht:131cms (10th-25th centile) Wt.: 28kgs (25th-50th centile)]; Head to toe examination revealed multiple hypopigmented macules and ash-leaf patches noted over the trunk and lower limbs (Figure 1) with shagreen patch over the lumbo-sacral region.

Blood work up for seizure was normal except mild elevation in liver enzymes SGOT (36U/L) & ALP (214U/L). ECG showed sinus tachycardia, 2D-ECHO showed myxomatous mitral valve, with mild MR and TR. MRI brain revealed calcified granuloma in right posterior parietal lobe (Figure 2a) and sub-ependymal nodules (Figures 2b & 2c).
Immediate family members were screened, mother, maternal aunt, and maternal grandfather had skin lesions in mother (Figures 3a & 3b). Mother also has ungual fibromas (Figure 3c).

Pedigree

Management

Child was previously treated with VALPROATE but the dosing was not appropriate, during the hospital stay the dosing was adjusted and Tab. Clobazam was added. Although IQ and DQ assessment of the child were found to be normal, with a detailed history and behavioural assessment child was diagnosed to have ADHD, for which she was started on Tab. ATOMOXETINE. Cardiologist opinion was taken for rhabdomyoma and regular follow up for every 2 years is advised. Dental examination revealed no enamel pits or oral lesions. Fundus examination was normal and regular follow-ups were advised by the ophthalmologist.

Mothers MRI, CT abdomen, 2D ECHO was normal. Fundus examination of the mother and family members was normal.

Figure 1. Showing multiple hypopigmented macules (ash-leaf patches) over the trunk and legs.

Figure 2a. Showing calcified granuloma in right posterior parietal lobe. 2b & 2c showing sub-ependymal nodules.
The child was discharged after 3 days of seizure free period.

**Discussion**

The cardiac rhabdomyoma is considered a hamartomatous proliferation frequently associated with tuberous sclerosis of the brain, sebaceous adenomas, and various hamartomatous lesions of the kidney and other organs.

The association of tuberous sclerosis and cardiac rhabdomyoma is important and has usually been explained by strong clinical association. Molecular evidence of this association have now been identified as the TSC2 gene missense mutation (E36; 4672 G>A, 1558 E>K TSC2).

Cardiac rhabdomyomas occur chiefly, but not exclusively, in the pediatric age group; a 45-year single-institution review found rhabdomyoma to account for 58% of cardiac neoplasms in 64 pediatric patients (age < 18 years) who presented for surgical evaluation of a cardiac tumor.

Typically 12 out of 15 children with cardiac rhabdomyoma had tuberous sclerosis the clinical presentation consisted of heart failure or a cardiac murmur in six patients each and arrhythmia in three patients. However in our case the cardiac lesion remained silent but periventricular calcifications of the tubers resulted in unresponsive seizures.

Treatment for TSC is only symptomatic. Seizure disorders are treated with antiepileptic drugs. Behavioural disorders are treated with proper counselling and behavioural therapy. Other associated systemic masses are treated accordingly with either medical management or surgical interventions. According to recent studies EVEROLIMUS is an effective drug in treating refractory seizures and also reducing the volume of the lesions. Proper genetic counselling is about the risk of inheritance is also a major part of treatment.

**Follow-Up Protocol for Diagnosed Cases:**

Based on 2012 International tuberous sclerosis complex conference:

- MRI is advised every 1-3 yrs. till 25yrs of age.
- Annual renal function, blood pressure, USG abdomen (or CT/MRI).
- Echocardiogram every 1–3 years in asymptomatic patients until regression of cardiac rhabdomyomas is documented,
- 12-lead ECG every 3–5 years (for drug toxicity effects).
- High-resolution chest CT every 5–10 years in asymptomatic females 18 years of age and older, and every 2–3 years in patients with lung cysts.

There is no screening protocol when cardiac Rhabdomyoma is an initial presenting feature.

**Conclusion**

The common reasons for unresponsive seizures in children include improper compliance, adherence for therapy and reconsideration of diagnosis and add-on anti-epileptic is often warranted. It is often missed to consider that the natural history of the disease itself being progressive, could result in improper seizure control. There are various time ascertained protocols to screen for lesions in various organ-systems. It is not new to detect rhabdomyoma incidentally in about 50 percent of the patients with tuberous sclerosis. But Our case here emphasizes the need for meticu-
lous screening for tuberous sclerosis when the initial presentation is Cardiac Rhabdomyoma alone. Patients recognised earlier in life with proper counselling and medication are found to have a lesser incidence of developmental delay and mental retardation and other complications. Hence showing the need for proper intervention for all cardiac rhabdomyomas for the cause.

End Note

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