Nonsurgical device closure of isolated ostium secundum atrial septal defect in a case of genetically proven tuberous sclerosis

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ABSTRACT

Tuberous sclerosis (TSC) is an autosomal dominant multisystem disease associated with multiple cardiac Rhabdomyomas; however, congenital cardiac malformations are very rare in TSC. A 5-year-old girl with classical features of TSC had an associated large secundum atrial septal defect (ASD). The left to right shunt through the ASD was augmented by the multiple left ventricular masses. Nonsurgical closure of the ASD avoided the neurological and cardiac complications that may occur due to cardiopulmonary bypass during open-heart surgery. This first novel interventional report in TSC stresses on the value of such catheter interventions to mitigate risks in complex cardiac associations.

Key words: *Amplatzer septal occluder, Atrial septal defect, Cardiopulmonary bypass, Rhabdomyomas, Tuberous sclerosis*

Tuberous sclerosis (TSC) is a rare multisystem genetic disease that causes benign tumors in the brain, kidneys, heart, liver, eyes, lungs, and skin. Cardiac rhabdomyomas, the most common primary cardiac tumors in infancy and childhood have a clear association with TSC. This tumor often presents as multiple tumors within the walls of the left and right ventricles and less frequently in the atria. Their partial or complete spontaneous regression has been well documented [1]. Congenital heart diseases (CHDs) are extremely rare in TSC and equally rare are their associations with cardiac rhabdomyomas [1-8]. When they occur together, the cardiac tumors may alter the hemodynamics of the underlying CHD depending on their location. To the best of our knowledge, there are no reports of transcatheter closure of secundum atrial septal defect (ASD) in a case of genetically proven TSC harboring a tumor mass inside the heart.

CASE REPORT

A 5-year-old girl, born as a 2nd child of nonconsanguineous parents in a family with no history of CHD was diagnosed to have osmium secundum ASD and multiple ventricular rhabdomyomas in the heart in infancy. Following 1 episode of typical febrile seizures at 2 years of age, she was investigated with computed tomographic brain imaging, which showed multiple cortical and subependymal tubers. She had mild effort intolerance and history of recurrent respiratory infections. There was no family history of TSC.

On examination, she had numerous adenoma sebaceum (Fig. 1). She was underweight (14 kg) for her age but had normal neurodevelopment. On physical examination, she was comfortable, alert and active girl with normal oxygen saturations (98%) on room air. On cardiovascular examination, there was cardiomegaly, normal first heart sound, wide fixed split second heart sound, and 3/6 Ejection systolic murmur at the pulmonary area. She has no neurological deficits.

Echocardiography showed a 10 mm osmium secundum ASD shunting left to right with right atrial and right ventricular volume overload. A couple of tumor masses attached to the left ventricular side of interventricular septum near the apex were increasing the left to right flows. Her electrocardiogram showed normal sinus rhythm, right axis deviation, and r SR pattern in V1 lead. Her brain scan showed numerous subependymal and cortical calcified tubers (Fig. 2). The abdominal ultrasonography showed normal

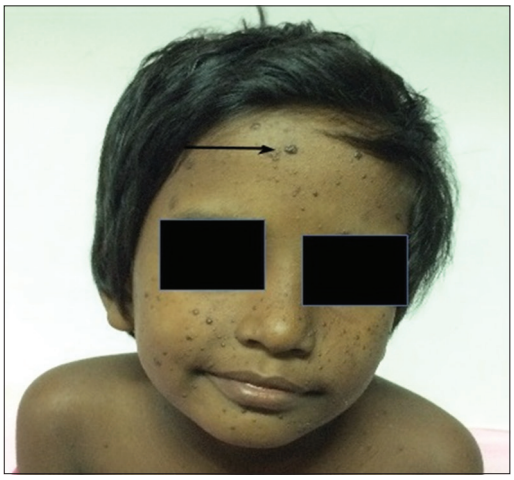

Figure 1: Multiple facial angifibromas

kidneys and a small liver hemangioma. Genetic studies with next generation sequencing were positive for mutations in TSC2 genes (Fig. 3). As the cardiac surgical correction of the ASD carried the risks of cardiopulmonary bypass (CPB) in view of the presence of neurological tubers and cardiac tumors, a nonsurgical alternative was considered and the defect was closed by a 12 mm amplatzer septal occluder device (St. Jude Medical, Plymouth, MN) in the cardiac catheterization suite. On a follow-up at 6 months, echocardiography showed stable device position, normal size of right sided chambers, and partially regressed cardiac tumors confined to the left ventricular apex (Fig. 4).

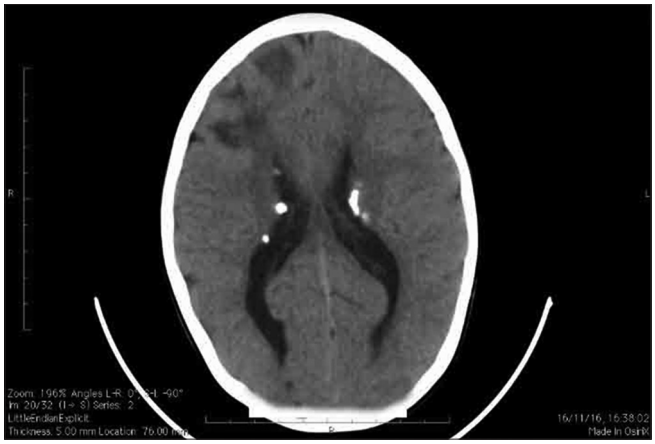

Figure 2: Calcified subependymal nodules on computed tomography brain

DISCUSSION

TSC is a relatively common autosomal dominant disease with a prevalence of 1/10000; two-thirds do not have family history due to de novo mutations. Two tumor suppressor genes TSC1 mapped on chromosome 9q34 coding for protein named hamartin and tuberin mapped on chromosome 16p13 coding for protein named tuber in have been identified [9,10]. Rhabdomyomas are hamartomas rather than true neoplasms and are the most common primary intracardiac tumor in children.

Nearly 92% of rhabdomyomas were multiple, occurring with equal frequency in both ventricles; atria were involved in only 30% of patients. These tumors are often seen in infancy, but a

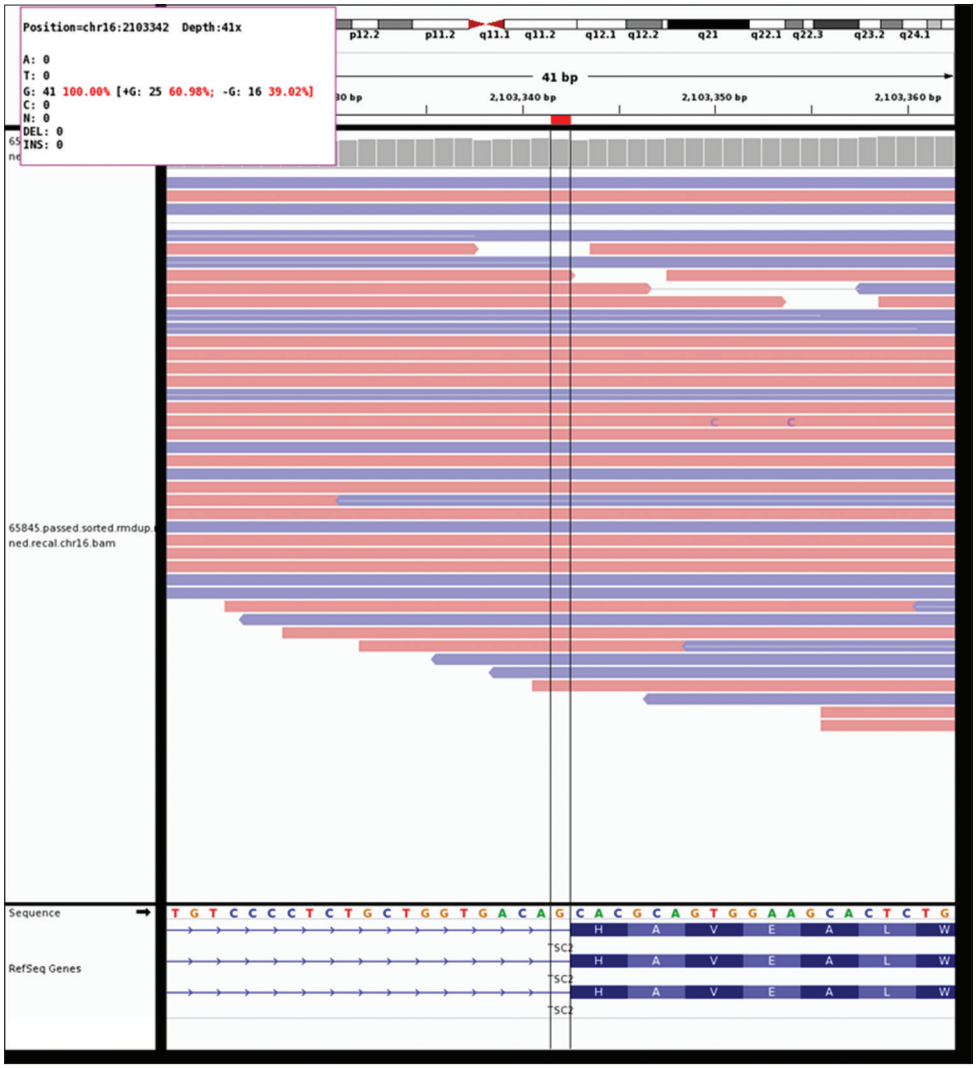

Figure 3: Heterozygous 3' splice site variation in intron 3 of Tuberous sclerosis 2 gene (chr16:2103342;G>G/A; Depth:71x) that affects the invariant GA acceptor slice site of exon 4 (c.226-1G>G/A; ENST00000219476

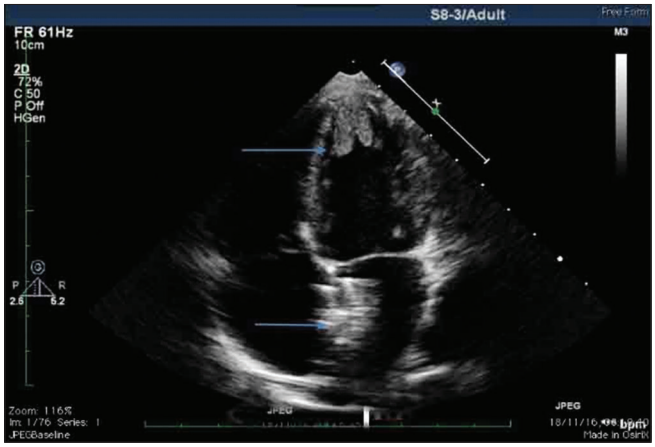

Figure 4: Rhabdomyoma at the apex and atrial septal defect occluder

majority tends to shrink and even disappear with age [1]. When they are multiple, they are often associated with TSC. Most cardiac rhabdomyomas were asymptomatic and incidentally detected on echocardiogram. Congenital cardiac malformations are very rare in TSC, whether or not it is associated with rhabdomyomatosis [1-8]. The previous listed associations include tetralogy of fallout in one patient [4], discrete subaortic stenosis in one [7], ventricular septal defect in three [3,5], coarctation and aortic stenosis in one [5]. Even though TSC is widely prevalent and CHDs occur at a frequency of 8/1000 at birth, the rare association between the two is not fully understood.

The location and size of the cardiac tumor may influence the hemodynamics of the underlying CHD. Rhabdomyomas very rarely need surgery as they often decrease in size or disappear completely unless they are obstructing or inducing severe cardiac arrhythmias [1]. In our patient with an ASD, the left to right shunt was augmented by impaired left ventricular relaxation contributed by the tumor mass. We highlight the rare association of isolated secundum ASD in a patient with TSC, which was managed nonsurgical by transcatheter method and has not been reported in literature previously. Neurological complications of CPB can render an otherwise perfect open heart surgery less meaningful. Various causative mechanisms have been postulated for neurological injury after CPB including embolization of gaseous and particulate matter, cerebral hypoperfusion, and inflammatory response to CPB [11]. The harmful effects of CPB in a patient with cardiac tumors, and history of epilepsy was mitigated by adoption of nonsurgical device closure of the defect in this patient.

CONCLUSION

We highlight the rare association of isolated secundum ASD in a patient with TSC, which was managed nonsurgical by transcatheter method. Corrective surgery on CPB is risky due to seizures and cardiac tumors, and the risk was avoided by nonsurgical intervention in our patient.

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