A case report on Antenatal Diagnosis of Cardiac Rhabdomyoma with Tuberous Sclerosis complex

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Abstract

Cardiac rhabdomyoma is the most common cardiac tumor in fetal and newborns, which is associated with tuberous sclerosis. It is often detected by echocardiography and regular ultra sonography in the second trimester of pregnancy. Tumor size in this disease varies and fetal hydrops and pericardial effusion are unusual. The size, number, and location of the tumors can produce a mass effect that may result in malfunctioning of blood flow and further cause organ dysfunction (heart failure and arrhythmias). Early diagnosis of cardiac rhabdomyoma is crucial for effective treatment. This case report illustrated the case of antenatal cardiac rhabdomyoma with tuberous sclerosis. Cardiac masses were detected before birth in ultrasound and postnatally all these tumors were excised.

Keywords: Rhabdomyoma, Tuberous Sclerosis.

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Introduction

Cardiac rhabdomyoma is a benign non-vascular homogeneous, hyperechogenic hamartomoustumor of myocardium. It is most common in fetus and neonates, with a high incidence associated with tuberous sclerosis[1]. The coexistence of cardiac rhabdomyoma with tuberous sclerosis was first

documented in a newborn infant in 1862[2]. The postnatal phase of foetal cardiac rhabdomyoma hits around 1 in 40000 individuals[3]. However, the reported incidence in prenatal period was 0.12%, and it ranged from 0.02 to 0.17% in live newborns[4]. It is caused by genetic variation during the formation of striated muscle, leading to cardiac rhabdomyoma. Therefore, the etiology of the disease is not clearly understood. Cardiac rhabdomyoma is seen in serial ultrasound examinations between 20 and 30 weeks of pregnancy[5]. Although it may be seen in all myocardial locations, it is more usually found in the septum or ventricles[3]. Tuberous sclerosis complex (TSC) is an autosomal dominant inherited disease that results in neuro cutaneous syndrome that affects the brain, skin, heart, kidney and other organs[2]. According to studies, 30% of TSC cases are hereditary, while the other 70% are caused by de-novo mutations that inactivate the TSC1 and TSC2 genes, which encode proteins, (1) tuberin and (2) hamartin[3,4]. In absence of required medical treatment, cardiac rhabdomyoma could disrupt the heart function of growing fetus. Prostaglandin E is used in the management of duct potency in hemodynamically unstable neonates.

1. Case Study

A 28-year-old mother, gravida two, para one, at her 37.2 weeks of gestation underwent an elective caesarean section (C- section) contemplating her previous C-section and Rh-negative gestation. An indirect coombs test was performed to confirm Rh-negative situation in the current gestation. This demonstrated that the mitral valve was obstructed by the largest cardiac mass. In addition, a minor atrial septal defect (ASD) was detected. Ultrasound showed dilatation of the pulmonary artery, left atrium, and left ventricles, as seen in figure 1.

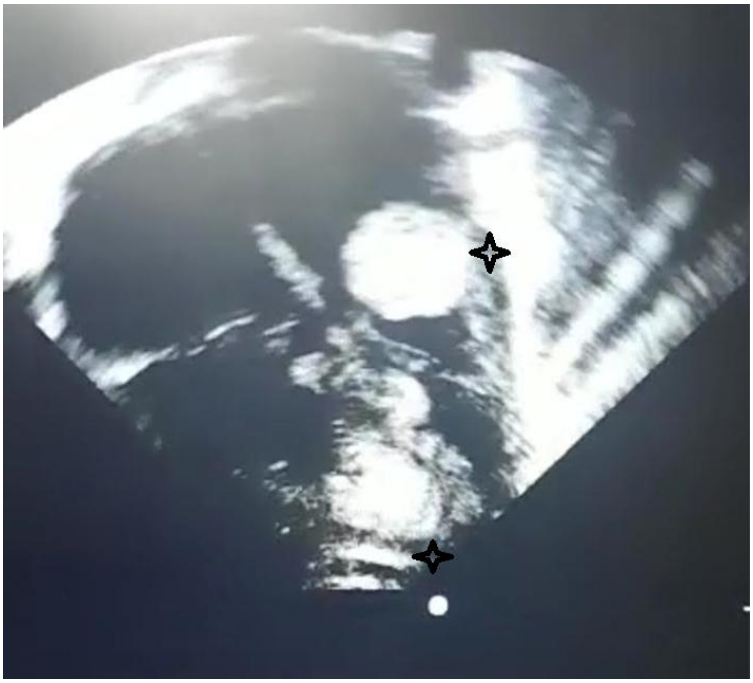


figure 1. Multiple cardiac masses shown in ultrasound obstructing the mitral valve, small atrial septal defect (ASD) was also detected.

Antenatally administrated corticosteroid to the mother as the child was premature. Female child with birthweight 2.4 kg was born. The child needed resuscitation at birth and was shifted to NICU. In NICU baby was euthermic, euglycemic, with acrocyanosis with heart rate of 154/min, respiratory rate of 68/min with sub-coastal retractions, inter-coastal retractions, and supra sternal retractions were seen with saturation of 92% , was taken on BCPAP with peep of 5cm. Systemic examination showed cardiovascular system (CVS) first heart sound (S1) and second heart sound (S2) were heard with a tumour plop on auscultation. Postnatally echo screening was done, multiple tumours were observed including a large tumour of 12×13 mm in size where the left atrium mass was attached to the posterior mitral valve between the left atrium and left ventricle. It was diagnosed that antegrade flow was restricted through the anterior mitral valve, resulting in mild mitral regurgitation. Additionally, a 2.6 mm tumor 2 was observed on the lateral posterior mitral valve. A tumor 3 (3×8 mm) attached to the lower left ventricular surface was also detected. Tumor 4 (9x7 mm), infiltrating myocardium and filling the apex with the right ventricle. Tumor 5 was measured at 4 mm and was found to attach with the lower right ventricular septum. A 8×8 mm tumor 6 was also detected that was attached to an inter atrial septum and in the right atrium, without obstructing tricuspid valve.

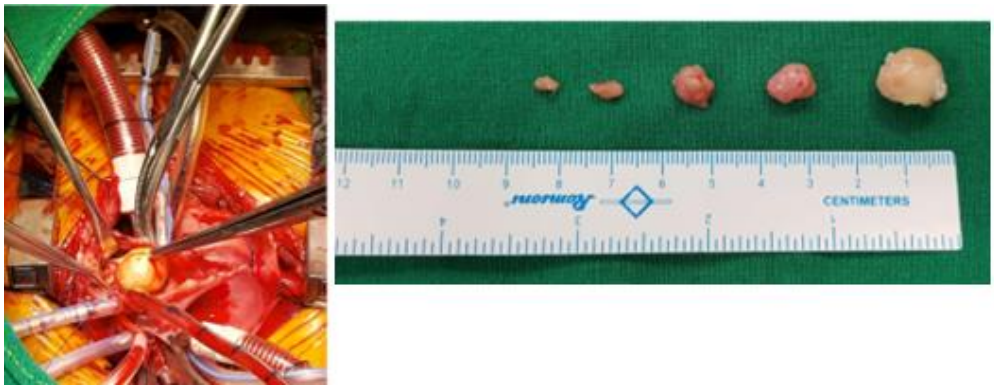


Figure 2.
Cardiac surgery to operate cardiac masses, five tumours excised in surgery shown as per their sizes.

There were two hypopigmented patches similar to ash leaf Macules noted at the anterior part of the abdomen and lateral aspect of the trunk shown in figure 3.Considering the diagnosis, milrinone and sirolimus injections were provided to reduce the risk of heart failure and the spread of tumors to other organs. Even after early intervention the child further deteriorated needing for mechanical ventilation and cardiothoracic surgery was performed with multiple tumor excisions from heart. During the surgery, well circumscribed, white to yellow masses ranging from 0.4 to 1.4 cm were observed, as shown in Figure 2. Five tumours out of six were excised as the one with smallest size were difficult to excise. These five tumours are shown in Figure 2 as per their size. Furthermore, microscopic examination of excised tumors revealed that the cells were large, round to polygonal, with clear cytoplasm and well-defined nodules, with spider cell appearance serving as a pathognomonic feature, as shown in Figure 4, mitotic activity was absent, fibrosis and calcification was rare in the observation.Postoperatively, the baby was shifted to intensive care unit. However, 6-8-hour post-surgery, the baby had an episode of cardiac arrest, and there was no reversal of circulation found, and eventually she succumbed to death.

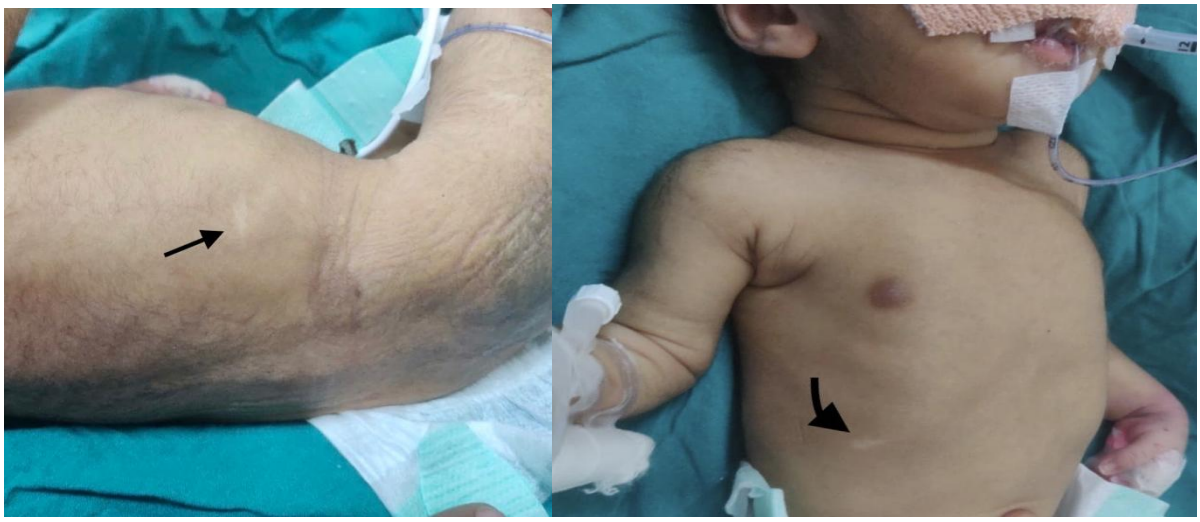


Figure 3. Ashleaf macules over the anterior and lateral aspect of the abdomen.

Discussion

Cardiac tumors are very rare in neonates, rhabdomyoma being the commonest, accounting for up to 60% of cases involving left atrium, left ventricle, lateral posterior mitral valve, lower left ventricular surface, right ventricle apex, lower right ventricular septum, inter atrial septum, and right atrium. .Prenatal diagnosis of rhabdomyoma indicates that baby may have postnatal manifestations of tuberous sclerosis. Their spontaneous regression has been documented, circumference decreases by ~2 mm month due to their hamartomous nature.

Clinical profile varies from still-birth to intrauterine myocardial infarct (due to coronary artery compression). Occasionally, they cause fetal hydrops or arrhythmias on fetal heart requiring serial ultrasound monitoring. Institutional Delivery with pediatric cardiology and surgery facilities, is recommended.

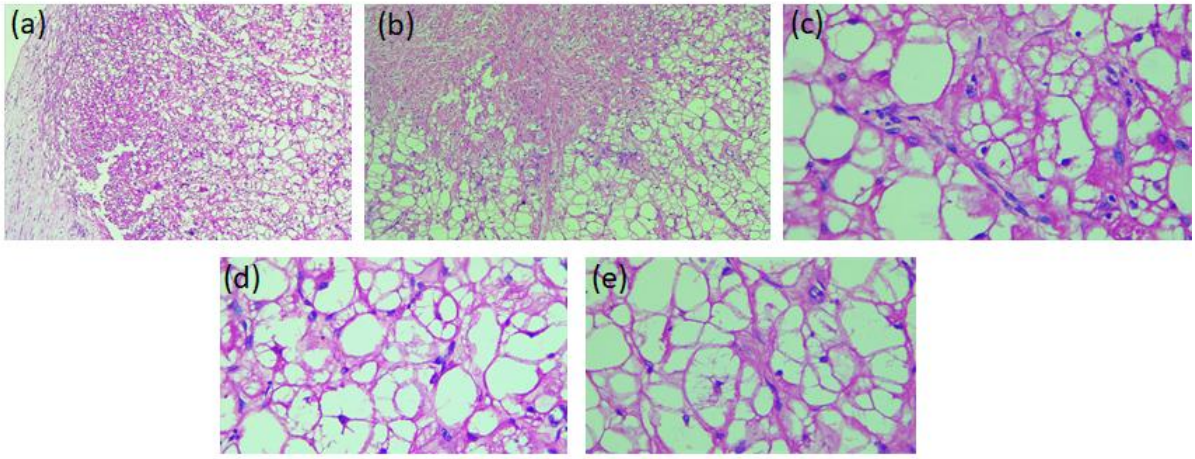
Serial ultrasound evaluation, MRI and in some cases, angiography may be indicated. Definitive indications for surgery include cardiac outflow obstruction, persistent arrhythmias, cardiac failure and cardiogenic emboli. Orthotropic cardiac transplantation is indicated if neonate presents with severe myocardial ischemia.

Pathologically, rhabdomyomas are single or multiple, non-capsulated soft lesions which show intracavitary extension with almost obliteration of cavity. Microscopically, they consist of discrete masses of large, rounded vacuolated cells predominantly with peripherally placed nuclei (spider cells). Glycogen is present in cytoplasm, concentrated towards periphery. Cross-striations are observed in few cells at periphery. Electron microscopy shows myofibrils with z-bands, and clusters of leptofibrils with striations at a periodicity of ~1600 nm.

Allele loss in hamartomas from patients with tuberous sclerosis, for markers spanning chromosome 16q13.3 in region of TSC2 gene and chromosome 9q34 in region of TSC1 gene, has been found supporting their role as growth suppressor. Mouse model of cardiac rhabdomyoma has been generated by loss of TSC 1 gene, which developed dilated cardiomyopathy with enlarged ventricular myocytes similar to spider cells.

Well-conducted studies estimate that about two-thirds of cases of tuberous sclerosis are mutations, remaining are familial in autosomal-dominant pattern. For proper diagnosis and genetic counselling, mutation studies should be carried out on affected child. Prenatal diagnosis is possible with DNA technology.

Figure 4. Microscopic examination, lower magnification in (a) (b) (c) showed well circumscribed, typically multiple, white to yellow masses. Higher magnification (d) and (e) showed spider cell



appearance

Aggarwal et al., discussed a case study where parents were diagnosed, and the father was found to have a history of adenoma sebaceum, axillary freckling, and multiple café-au-lait spots, which indicated tuberous sclerosis[6]. This suggested early prenatal diagnosis might be required during the pregnancy. Though the child needed resuscitation at birth and was started on tumor regressive drug sirolimus the child deteriorated further needing for surgical intervention[7,8]. Similarly, Aggarwal et al., case report showed death of new-born after 36 hours of survival[6].

2. Conclusion

In most affected fetuses, cardiac rhabdomyomas are benign. An early prenatal identification of cardiac rhabdomyomas is essential for effective fetal treatment planning and reducing the risk of infant mortality. Cardiac rhabdomyomas are the first manifestations of tuberous sclerosis; thus, thenewborn should be examined carefully. The association between tuberous sclerosis and cardiac rhabdomyomas raises substantial concerns for the quality of life of infants who survive the removal of a tumour. The reported case showed benign form of 6 tumorsbut some of them are large masses. This study indicated that placement of these tumors is crucial and can make them lethal. Although tuberous sclerosis is thought to be inherited autosomally, there is no family history in this reported case, thus it might be sporadic. This study advised for the termination of pregnancy when any sign of tuberous sclerosis is detected during parental check-ups.

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