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Prenatal Diagnosis of Tuberous Sclerosis by Fetal Echocardiography With an Unusual Clinical Course After Birth

Maryam Moradian, MD [1,*]; Mohammad Dalili, MD [1]; Mahmood Merajie, MD [1]

[1]Rajaie Cardiovascular, Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Maryam Moradian, MD, Rajaie Cardiovascular, Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran. Tel.: +98-2123922170, E-mail: m.moradian@rhc.ac.ir.

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Introduction: The cardiac outcome in tuberous sclerosis patients is usually favorable, and cerebral manifestations determine the ultimate prognosis in these patients.
Case Presentation: Our tuberous sclerosis patient developed arrhythmia unexpectedly while his tumors were in regression, presenting a challenge to us as to whether or not opt for surgery.
Conclusions: This case report underscores the role of fetal echocardiography in the prenatal diagnosis of cardiac disease and illustrates rhabdomyomas in a tuberous sclerosis patient. Rhabdomyomas are histologically benign; however, they may cause severe arrhythmia even when they are regressing.

Keywords: Pediatric Cardiology; Preventive Cardiology; Fetal Echocardiography; Tuberous Sclerosis

1. Introduction

Fetal or neonatal cardiac rhabdomyomas are benign and smooth muscle tumors of the myocardium and consist of immature myocytes. These tumors are deemed the most common primary cardiac tumors in the pediatric age group. About 50-60% of rhabdomyomas are associated with tuberous sclerosis, an autosomal dominant disorder in which benign hamartomas develop in multiple organ systems, including the heart (1-3). We herein describe a patient who unexpectedly experienced arrhythmia during the spontaneous regression of his rhabdomyomas, which were originally detected via fetal echocardiography.

2. Case Presentation

A 30-year-old pregnant woman referred to our Echo Lab for fetal echocardiography while bearing a 35-week-old fetus because she and her older child (a 7-year-old girl) had tuberous sclerosis. She was diagnosed to have tuberous sclerosis after her first child was born with severe tuberous sclerosis. The woman had a history of two episodes of childhood seizure, which was controlled by drug therapy with no recurrence. She was of normal intelligence and was well-educated, so she suffered from a mild form of tuberous sclerosis. The diagnosis had been confirmed by brain CT scan, showing sub-ependymal nodules. The father was completely normal and was well-educated. The parents were not relatives. Their first child had been diagnosed to have severe tuberous sclerosis while being evaluated for developmental delay. The child had been identified as having delayed speech and language ability, mental retardation, uncontrollable seizures, and renal and brain tumors.

In our Echo Lab, fetal echocardiography was performed at the 35th week of gestation and revealed mild increase in the cardiothoracic ratio; enlargement of the right atrium (RA), left atrium (LA), and left ventricle (LV); deviation of the inter-atrial septum to the left; a large pedunculated homogenous mass in the LV cavity (2.2 cm × 2.7 cm); and two smaller masses in the right ventricle (RV). The LV mass occupied 85% of the LV cavity. The tumor seemed to have emerged from the apical portions of the interventricular septum. Color Doppler study showed moderate tricuspid and mild mitral valvular regurgitation as well as a bidirectional shunt via the foramen ovale. There was no LV or RV outflow tract obstruction. The fetal heart rate was 130 beats per minute, with no arrhythmia (Figure 1).

Implication for health policy/practice/research/medical education:
This case report highlights the role of fetal echocardiography in the prenatal diagnosis of cardiac disease and demonstrates rhabdomyomas in a tuberous sclerosis patient. Although benign, rhabdomyomas may cause severe arrhythmia, even when regressing.

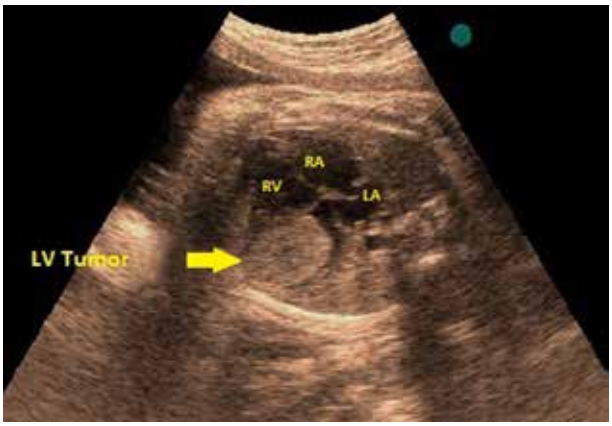

Figure 1. Fetal echocardiography in four-chamber view, showing a large homogenous left ventricular cavity mass (arrow)

Three weeks later, the male infant, weighing 3700 gr, was delivered via an uneventful Caesarian section. His APGAR scores at the first and fifth minutes were eight and nine, respectively. After four days, he was referred to our hospital for further evaluation. On admission, physical examination demonstrated normal neonatal reflexes and stable vital signs: respiratory rate of 30 per minute; heart rate of 100 beats per minute; mean blood pressure of 50 mm Hg; and normal limb pulses. The only pathologic finding was a grade III/VI systolic murmur at the apex and left sternal border. Transthoracic echocardiography (TTE) revealed the same findings as fetal echocardiography. The neonate's hemodynamic status was stable, so we decided to follow up his condition at regular intervals in the outpatient department (Figure 2).

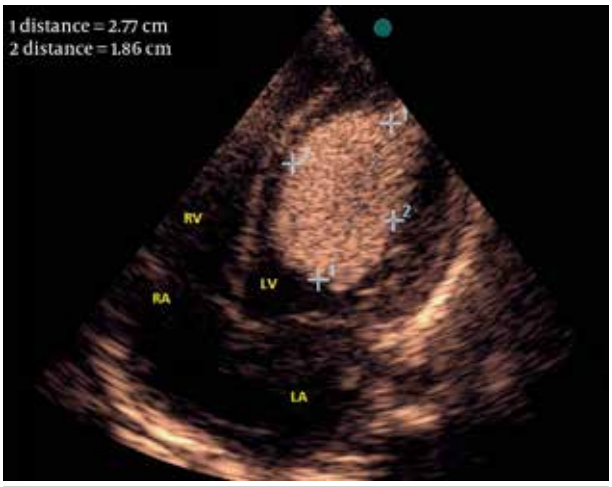

Figure 2. Transthoracic echocardiography of the child at two months old, showing a left ventricular tumor

During a one-year clinical follow-up, the child had normal growth and development and serial TTE showed a gradual reduction in the size of the tumors. Brain computed tomography revealed two subependymal tubers, but the child had no neurological symptoms until he was thirteen months old, when after an episode of gastroenteritis, he experienced his first attack of ventricular tachycardia (VT). The blood level of electrolytes was normal, and the arrhythmia could not be attributed to the electrolyte imbalance. The VT was sustained, and its QRS morphology was in favor of an LV origin (Figure 3).

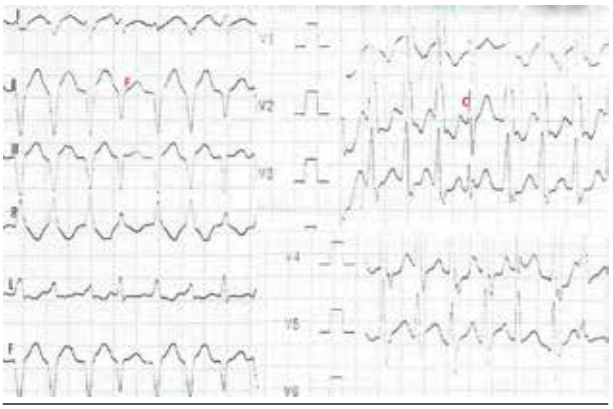

Figure 3. Surface 12-lead electrocardiogram, showing ventricular tachycardia with superior axis and right bundle branch block pattern. Fusion beat (F) and capture beat (C) confirm the diagnosis of ventricular tachycardia.

Capture and fusion beats during the arrhythmia and absence of response to Adenosine confirmed the diagnosis of VT. After reconsideration and substitution of a few drugs, the arrhythmia was finally controlled by a combination of Amiodarone and Esmolol. The child was discharged with a maintenance dose of oral Amiodarone and Propranolol. During a follow-up period of 22 months, despite a gradual decrease in the size of the tumors, the arrhythmia recurred due to a mild reduction in anti-arrhythmic doses. Accordingly, the anti-arrhythmic drugs were continued by their full doses. In the following evaluations, the RV tumors had disappeared completely and the LV tumor size had reduced significantly (Figure 4). Between VT attacks, electrocardiograms were normal.

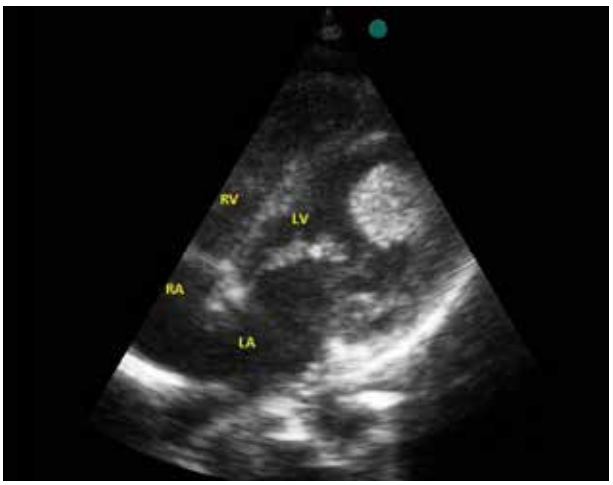

Figure 4. Transthoracic echocardiography in four-chamber view of the child at 22 months old, showing a reduced left ventricular tumor size

3. Conclusions

Fetal cardiac rhabdomyomas, albeit rare, are the most common fetal cardiac tumors. More than 60% of antenatally detected cardiac tumors are rhabdomyomas, and these are often associated with tuberous sclerosis (1, 4). Tuberous sclerosis is an autosomal-dominant, multisystem disorder with variable expressivity (1, 5). Rhabdomyomas are multiple, well-circumscribed, noncapsulated, white or gray-white intramural or intracavitary nodules that can occur anywhere within the heart and they most commonly involve the ventricles (2). According to the tumor's location, number, size, and degree of invasion, various symptoms such as mechanical obstruction of the outflow tract, heart failure, and arrhythmia may develop (5). Rhabdomyomas have been diagnosed by two-dimensional echocardiography in the fetus. Such prenatal detection has been made while screening fetal dysrhythmias, nonimmune hydrops, decreased fetal growth, and familial tuberous sclerosis (2). Other imaging modalities for the prenatal diagnosis of tuberous sclerosis are brain ultrasonography and MRI (6, 7). Postnatally, patients may not present obvious clinical findings, despite extensive cardiac involvement. Others may have only a murmur of valvular obstructive disease. Newborns and infants with large rhabdomyomas are often critically ill and present with respiratory distress, congestive heart failure, and low cardiac output. Sudden death has been attributed to arrhythmias in pediatric patients of all ages. These arrhythmias may be a result of either severe hemodynamic compromise or contiguous location of tumors to the conduction system. All major rhythm disturbances, including sinus bradycardia, atrial and ventricular tachycardias, and first- to third-degree atrioventricular block, have been reported (2).

Our patient was evaluated prenatally due to a positive family history of tuberous sclerosis. Fetal echocardiography showed multiple cardiac masses, in favor of rhabdomyoma. We, therefore, planned for safe delivery and close clinical follow-up. However, in spite of the usual course and while the tumors were decreasing in size, our patient experienced arrhythmia.

The treatment modalities of patients with cardiac tumors and arrhythmias are dependent on clinical symptoms. Surgical removal is indicated only for patients with refractory arrhythmia, which has poor response to medical management, or significant intracardiac obstruction. The cardiac outcome in tuberous sclerosis is usually favorable, and cerebral manifestations determine the ultimate prognosis in these patients (5). Our patient's arrhythmia occurred unexpectedly because the tumors were regressing at that juncture; we were faced with a challenge as to whether or not opt for the surgical removal of the tumors. Fortunately, we succeeded in controlling the child's arrhythmia after several drug trials. It is deserving of note that although cardiac rhabdomyomas are histologically benign tumors, they can result in mortality and morbidity (8).

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Authors' Contributions

Dr. Dalili contributed to the writing of the section on arrhythmia.

Financial Disclosure

The authors declare that they have no conflicts of interest.

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