INTRAUTERINE FETAL DEATH WITH INTRACARDIAC RHABDOMYOMA

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Congenital heart disease is estimated to occur in 8 to 9 cases per 1,000 live births [1,2]. Among them, congenital cardiac tumors are estimated to occur in 1–2 per 10,000 patients, and over 90% of these are benign [3–5]. Hence, congenital cardiac tumors account for most sonographic cardiac abnormalities.

Of these congenital cardiac tumors, rhabdomyoma is the most common, accounting for up to 60% of all fetal cardiac lesions [6]. It may occur as a single lesion or as multiple lesions, usually within the ventricles. Congenital cardiac rhabdomyoma tumors are often visualized by echocardiography as a pedunculated mass that may obstruct ventricular flow.

There is a very strong association between fetal cardiac rhabdomyomas and tuberous sclerosis. Around 50% to 80% of fetuses with rhabdomyomas have tuberous sclerosis [7,8]. In addition, this cardiac tumor is the commonest childhood cardiac neoplasm and is almost always multiple and ventricular [9]. Its presence increases the frequency of mental retardation and convulsions by up to 80%. The diagnosis of intrauterine tuberous sclerosis is, however, difficult. Definitive antenatal diagnosis using DNA probes or linked markers may be useful, but such examinations are usually not available in most hospitals. Therefore, prenatal diagnosis is usually based on appropriate family history and visualization of characteristic tumors on fetal cardiac sonography [9,10].

We present an interesting case of fetal multiple lesion-type congenital myocardial rhabdomyomas and a review of the literature. This report presents data, including sonographic images, autopsy report and chromosome studies, that may add further insight into this rare fetal tumor.

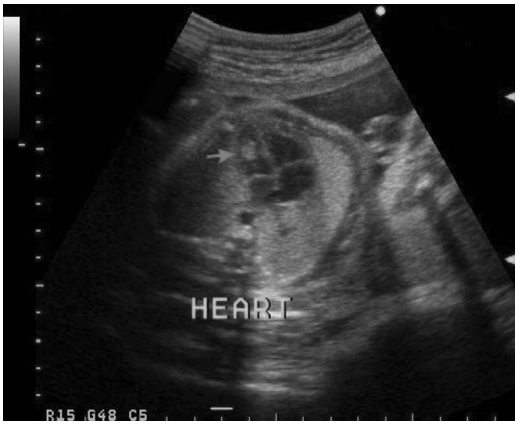

Figure 1. Rhabdomyoma (arrow) measuring 8 × 6 mm within the left ventricle.

A 25-year-old, gravida 1, para 0, patient had an unremarkable antenatal history, including the first-trimester triple test and nuchal translucency. Amniocentesis was performed at 16 weeks and revealed a 46,*XY* karyotype. There were no significant findings in the patient's past medical, surgical or family history. Most importantly, there was no family history of tuberous sclerosis.

At 29 weeks, sonographic evaluation of the fetus revealed symmetrical biometric measurements of the fetal head, abdomen and long bones that were consistent with the estimated gestational age. However, fetal echocardiography revealed a homogeneous, solid, echogenic mass measuring 8 × 6 mm within the left ventricle (Figure 1). The heart rhythm was normal. There was no evidence of pericardial effusion or ascites. Fetal aortic and umbilical artery Doppler studies were appropriate for the gestational age. Intracranial and renal anatomies were unremarkable. Hence, cardiac rhabdomyoma was suspected on the grounds of the intracardiac sonographic finding.

The patient was followed closely. Intrauterine fetal death was discovered 1 week later without signs of

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abdominal pain or vaginal bleeding. The pregnancy was medically terminated using intravaginal misoprostol. A dead fetus was delivered 12 hours later. Gross examination revealed generalized ecchymosis with mild edematous change of the umbilical cord (Figure 2). No other gross abnormalities were noted.

Upon the patient's consent for fetal autopsy, the procedure was performed with autopsy results confirming our diagnosis of multiple intracardiac rhabdomyomas (Figures 3–6). No other renal or brain tumors were found.

The differential diagnosis of a fetal intracardiac tumor should include that of rhabdomyoma, teratoma, sarcoma, myxoma, and fibroma. Rhabdomyoma is by far the commonest and accounts for up to 60% of all intracardiac tumors. Rhabdomyomas are often multiple, well-circumscribed tumors that can occur anywhere in the myocardium. They may originate from the atria or the free wall of the ventricular myocardium, but most frequently originate from the ventricular septum. Tumor size is variable, with some tumors being only a few millimeters in diameter. The clinical presentation of intracardiac rhabdomyomas depends on their number, size, and position. Their presentation ranges

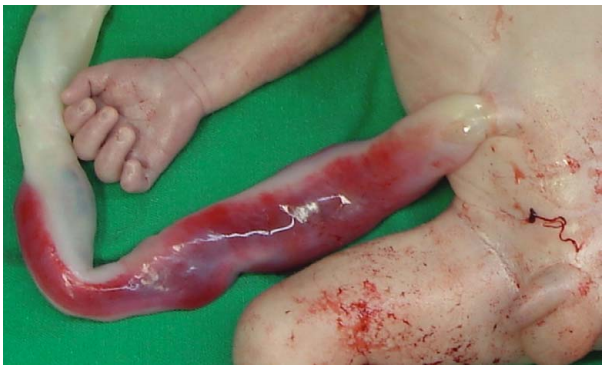

Figure 2. Ecchymosis and mild edematous change of the umbilical cord.

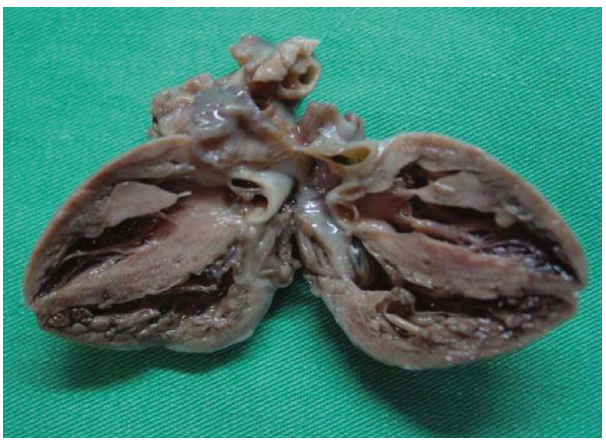

Figure 3. The absence of intracardiac tumor on autopsy.

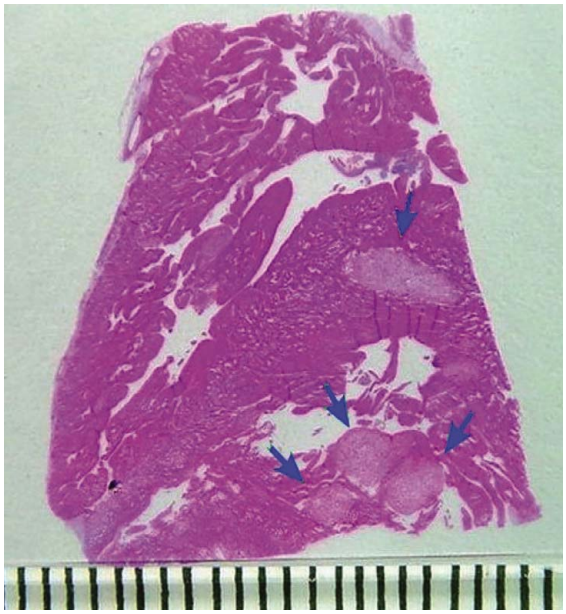

Figure 4. Multiple nodular lesions of varying sizes (arrows) within the myocardium (hematoxylin and eosin, original magnification).

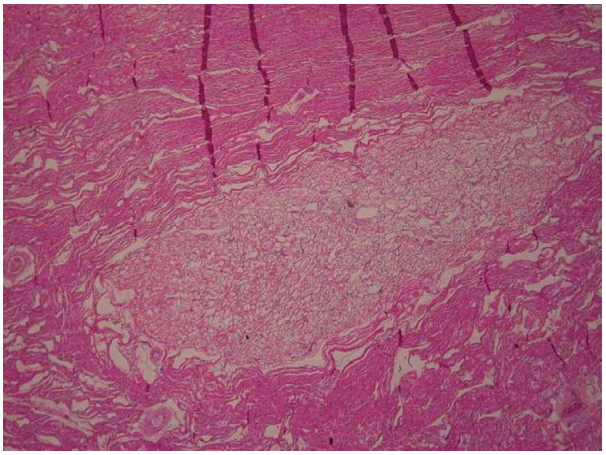

Figure 5. Nest of pale rhabdomyoma cells in the myometrium (hematoxylin and eosin, ×100).

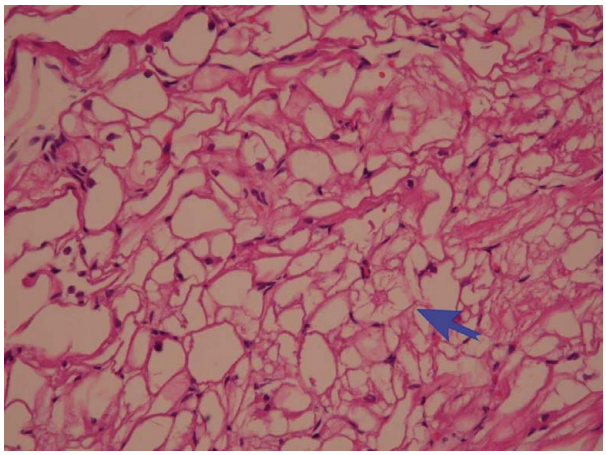

Figure 6. Vacuolated rhabdomyoma cells of varying sizes with characteristic spider appearance (arrow; hematoxylin and eosin, ×400).

from symptom-free, congestive cardiac failure, low cardiac output secondary to intracardiac flow obstruction, and arrhythmias, to sudden death.

Tuberous sclerosis is an autosomal dominant disorder complex characterized by the development of distinctive benign tumors in multiple organ systems, including the skin, brain, heart, lungs, kidney and liver [11]. Mutations in at least two different genes have been identified. One such gene is located on chromosome 9 (*TSC1*) and the other on chromosome 16 (*TSC2*). The *TSC1* gene, mapped to chromosome 9q34, has 21 coding exons and two leader exons, and encodes a 130 kDa (1,164 amino acids) protein named hamartin. The *TSC2* gene, mapped to chromosome 16p13.3, has 41 coding exons and one leader exon, and encodes a 198 kDa (1,807 amino acids) protein named tuberin [11]. *TSC2* mutations are more common (70%) than *TSC1* mutations (30%). Furthermore, approximately 70% of the mutations are *de novo* [12].

It is estimated that 50–86% of those affected with tuberous sclerosis have rhabdomyomas [13,14]. Rhabdomyomas are usually small, multiple (> 90%), miliary nodules measuring less than 1 mm. Hence, a search for these extracardiac hamartomas should be performed in all cases of intracardiac tumors.

Crawford et al suggested that the presence of intracardiac rhabdomyomas can help identify tuberous sclerosis on an antenatal basis [15]. Subsequently, other investigators confirmed that the prenatal diagnosis of intracardiac rhabdomyomas is preliminary evidence that the fetus will have other postnatal manifestations of tuberous sclerosis. However, many tuberous sclerosis cases are results of *de novo* mutations, making a diagnosis based on family history unproductive.

Most fetuses with intracardiac rhabdomyomas associated with tuberous sclerosis are asymptomatic. Occasional arrhythmias may be detected by fetal heart rate monitoring [5]. After birth, the outcome of intracardiac rhabdomyomas remains uncertain. Some series suggested a poor outcome with a high mortality rate [16–18]. Recent reports have described spontaneous regression of these tumors [19–24]. In a fetus with an intracardiac rhabdomyoma, serial sonographic evaluation is indicated to determine the presence of fetal cardiac decompensation and fetal hydrops. A careful family history may reveal tuberous sclerosis, if this disease is not already obvious in the index case. Appropriate genetic counseling should be offered to the parturient patient and other family members. The absence of a family history does not exclude tuberous sclerosis in the fetus, as many cases represent *de novo* mutations. Delivery of the neonate not presenting with significant hemodynamic compromise should be managed expectantly and monitored for tumor regression. Serial sonographic evaluation and magnetic resonance imaging can be used; in some cases, angiography may be indicated. Surgery is often not necessary, even with massive tumor size, as tumor regression has been documented [19–24]. However, when cardiac outflow obstruction, persistent arrhythmias, cardiac failure or cardiogenic emboli are present, surgical resection may be lifesaving [17–19]. Delivery at a tertiary institution complete with pediatric cardiology and surgery services is recommended.

In conclusion, we have presented a case of fetal intracardiac rhabdomyoma and reviewed the literature. Intracardiac rhabdomyoma is closely associated with tuberous sclerosis. When an intracardiac tumor is detected prenatally, hamartomas should be looked for in other organs. Magnetic resonance imaging may help delineate other fetal hamartomas, especially those originating from the brain and kidney. In addition, amniocentesis for chromosome karyotype and cordocentesis for specific DNA probe examination may be arranged.

In our case, the intracardiac rhabdomyoma was detected by sonography without the presence of other hamartomas. The patient was regularly followed for fetal cardiac outflow obstruction and arrhythmia. Magnetic resonance was not arranged in time before fetal death. Cordocentesis can detect the presence of *TSC1* and *TSC2* gene mutations using specific DNA probes. As the fetus did not have multiple organ hamartomas and intracardiac rhabdomyomas often regress after birth, serial sonography was preferred over the more invasive cordocentesis.

Fetal autopsy revealed that the intracardiac rhabdomyomas were of multiple nodular type, though these lesions were not grossly evident on autopsy. This finding was not compatible with the prenatal sonographic finding of a single intraventricular mass. This feature was seen in our case as a solitary sonographic intracardiac tumor and turned out instead to be multi-lesional. In addition, multiple intracardiac rhabdomyomas are often only associated with those affected with tuberous sclerosis, which was not true in our case. Altogether, the value of performing magnetic resonance imaging in delineating multi-lesion rhabdomyomas is questionable.

Multiple miliary intracardiac rhabdomyomas were the only finding upon pathology. Although rhabdomyoma may lead to cardiac outflow obstruction, this was not likely to be the cause of fetal death in our case, as the grossly non-evident tumors were not large enough to lead to cardiac outflow obstruction. Arrhythmia is another complication of an intracardiac rhabdomyoma. We suspect that fetal death was the result of arrhythmia.

Cord accident may often be the cause of sudden intrauterine fetal death. Ecchymosis of the umbilical cord with mild edematous change may be compatible with cord accident. Thus, cord accident may well be another possibility of the fetal death.

To conclude, fetal intracardiac tumors are rare and should be cared for in a tertiary institution. Close antenatal follow-up may help reduce morbidity and mortality. Pediatric cardiologists and cardiovascular surgeons can offer further care and emergent surgical management should the fetus survive to term.

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