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Review Article

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Prenatal Diagnosis and Follow-Up of Fetal Cardiac Tumors

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Abstract

We gathered and simplified the available articles and case reported about the prenatal characteristics and postnatal outcome of Prenatal diagnosed fetal cardiac Tumors and outlined a recommended management algorithm from previous trials.

Keywords: Prenatal Diagnosis, Cardiac Tumors, Fetus, Neonate, Rhabdomyoma, Fibroma, Management Algorithm

Primary prenatal cardiac tumors are rare; their incidence varies between 0.0017 and 0.028% [1-10].

The five most common histological types of congenital primary cardiac tumors include rhabdomyoma secondary to tuberous sclerosis TSC (86%), followed by teratomas and fibromas. Hemangiomas and hamartomas were rarely reported [11].

Rhabdomyoma

Rhabdomyoma in the setting of tubular Sclerosis (TSC) represents the predominant etiology of fetal cardiac tumors, especially those who present with multiple masses usually a genetic disorder associated with brain and kidneys masses as well [5,9]. Definitive Diagnostic criteria of TSC include Two significant features or one prominent feature with ≥ 2 minor features (Table-1) [12]. The confirmation may require DNA analysis for the TSC1 and TSC2 genes. In addition, Antenatal MRI will be necessary for the fetus who fulfills the diagnostic criteria (Table 2).

Table 1: Common differential diagnoses for fetal cardiac masses identified during routine pregnancy ultrasound

Malignancies
• Primary
- Rhabdomyoma (secondary to tubular sclerosis)
- Fibroma (secondary to neurofibromatosis)
- Teratoma
- Thymic tumors
- Lymphomas
- Germ cell tumors
• Metastatic
Vascular
• Arteriovenous malformation: Hemangioma & hemangioendothelioma
• Ascending aortic aneurysm
Chromosomal anomalies:
• Trisomy 21
• balanced Robertsonian Translocation.

Table 2: Diagnostic feature of Tubular Sclerosis

Major features of TSC	Minor features
• Hypomelanotic macules (≥3, at least 5-mm diameter) • Angiofibromas (≥3) or fibrous cephalic plaque • Ungual fibromas (≥2) • Shagreen patch • Multiple retinal hamartomas • Cortical dysplasias* • Subependymal nodules • Subependymal giant cell astrocytoma • Cardiac rhabdomyoma • Lymphangioleiomyomatosis (LAM)† • Angiomyolipomas (≥2)†	• "Confetti" skin lesions • Dental enamel pits (>3) • Intraoral fibromas (≥2) • Retinal achromic patch • Multiple renal cysts • Nonrenal hamartomas

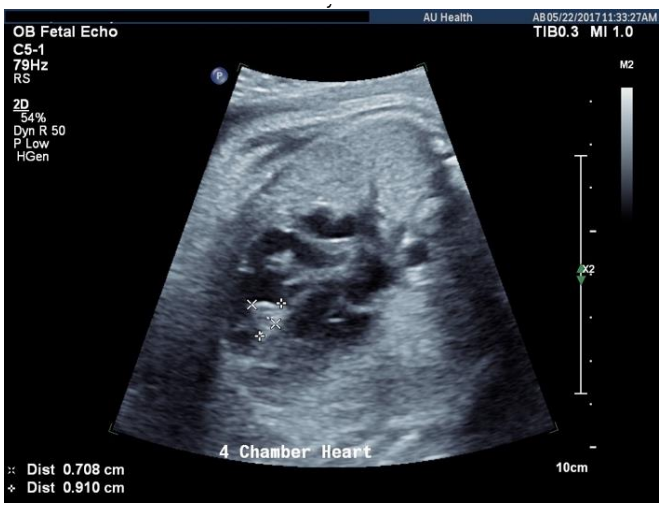

Figure 1: Fetal cardiac four-chamber ultrasound findings associated with cardiac Rhabdomyomas.

Teratoma

The second common cardiac tumor in fetuses is a teratoma. It often arises from the pericardium, although there are reported cases of intraventricular occurrence of this type of tumor [6,10,12,13]. Almost all teratomas lead to pericardial effusion. These tumors may also compress the heart and lungs interrupting their proper development. Teratomas typically contribute to significant pericardial effusion, which leads to further complications of pulmonary hypoplasia and a congenital heart defect. These complications usually carry a poor prognosis, are not good candidates for surgery, and most die within the first week of life.

Fibroma

Fibroma represents 12% of Fetal cardiac masses [5]. Fibroma usually presents as a single tumor arising from the ventricles. The initial diagnosis of cardiac fibroma can be made by the fetal echo ± MRI, but always the confirmation will be postnatal. Large sizes can also cause complications of cardiomegaly with congestive heart failure and significant pericardial effusion. Generally, primary benign cardiac tumors have a low tendency for rapid growth, but Cardiac Fibromas have a virtually unpredictable outcome, as we highlight below.

Diagnosis

Most of the Fetal cardiac masses are asymptomatic or can lead to significant hemodynamic disturbances and even can cause death in utero or the neonatal period [9-15].

Early Prenatal diagnosis allows for monitoring of the progress of these tumors and, if needed, intra-utero interventions and tailed management options, including the appropriate time and mode of delivery and planned management in the postnatal period [15-18].

The differentiation of the different histological types of cardiac tumors is primarily based on the specific echocardiographic findings such as appearance, size, cystic component, locations, and the number of tumors detected. In addition, the small size, slowly growing tumor makes it very challenging for the echocardiogram to detect the tumor in its early beginnings. These represent the two significant challenges in the early perinatal detection of cardiac tumors.

The diagnosis is usually made by accidental sonographic detection of Perinatal solitary or multiple compact fetal cardiac masses on Four chamber view of the sonographic exam. The Timor's size

usually ranges from 40-55 mm, but it may reach larger sizes. The patient should be referred to an echocardiographic examination to evaluate the number & location of the tumor, the presence of fetal hydrops, heart failure, obstruction of the left ventricular outflow tract, and arrhythmia. Assessing size and growth progression every two weeks for 32 weeks of gestational age is crucial.

Follow Up

After the initial examination, echocardiographic follow-up examinations should be performed every two weeks until 32 weeks of gestation and weekly after that. Serial echocardiographic ultrasound imaging is necessary to follow cardiac tumors and evaluate the tumor's progression, development of heart failure, or left ventricular outflow obstruction. It also helps in tracking the severity and rate of progression of pericardiac effusion, which is important to tailor the decision of termination or timing of delivery. Postnatal and prenatal confirmation of the diagnosis is mandatory. It is always recommended to assess cardiovascular functions in the fetus using an echocardiographic Cardiovascular Profile Score (CVPS) [19,20]. The CVPS of 7 points or less is diagnostic of congestive heart failure. Live newborns should be followed up to establish the need for medical or surgical therapy. The neonates are not candidates for surgery: if they have multiple massive or small tumors that did not cause significant hemodynamic disturbances.

Outcome

Generally, primary benign cardiac tumors have a low tendency for rapid growth [21,22].

Yinon et al. 2010 published retrospective studies conducted at the Department of Pediatric Cardiology at the Medical University of Lodz to evaluate the outcome of prenatal diagnoses of cardiac tumors in pregnancies over 16 years (1993–2009) [23]. An echocardiographic examination was done on any pregnant patient with abnormal four-chamber views. Forty fetuses were identified to have single or several cardiac tumors in association with fetal hydrops (18%), ventricular obstruction (30%), and arrhythmia (13%). All three fetuses with fibroma have survived. Three cases out of 33 patients with rhabdomyoma chose to terminate the pregnancy, four intrapartum death, and 26 (79%) stayed. On follow-up, 95% of all cases with rhabdomyoma were free of cardiac symptoms, but 88% had tuberous sclerosis—all three fetuses with teratoma presented with hydrops and zero survival. In addition, congestive heart failure was diagnosed in 5 fetuses (CVPS of 5.8 points), whereas 18 fetuses remained without congestive heart failure (mean CVPS was 8.88 points).

The rhabdomyoma carries a virtually benign perinatal outcome with a survival rate reaching up to 80%. Chao et al., 2008 published a meta-analysis of 138 cases of fetal cardiac rhabdomyoma and believed the strong predictors of an adverse outcome were tumor dimensions ≥ 20 mm, fetal arrhythmia, and hydrops [24]. Yinon et al. l, 2010, also the same risk factors (hydrops and tumor size) were confirmed, but fetal and neonatal mortality were reported with larger tumor dimensions (> 40 mm) except the fetuses with fibroma [23]. With large fibromas ≥40 mm, all fetuses with a fibroma survived in this study. Yinon et al. l 2010, added that tumor histology, in addition to the tumor size, are mainly relevant predictor factors for outcome fetuses with cardiac tumors [23].

Niewiadomska et al. 2010, has evaluated prenatal and postnatal outcomes of 23 cases with prenatal fetal cardiac tumors to determine whether ultrasonographic characteristics of the tumors (single or multiple, with or without associated heart failure) affect survival [25]. He concluded that there is no difference in the survival rate between neonates with a prenatal diagnosis of single and multiple tumors and fetuses with or without congestive heart failure. He outlines an algorithm for managing cardiac tumors according to his findings [Figure (2)].

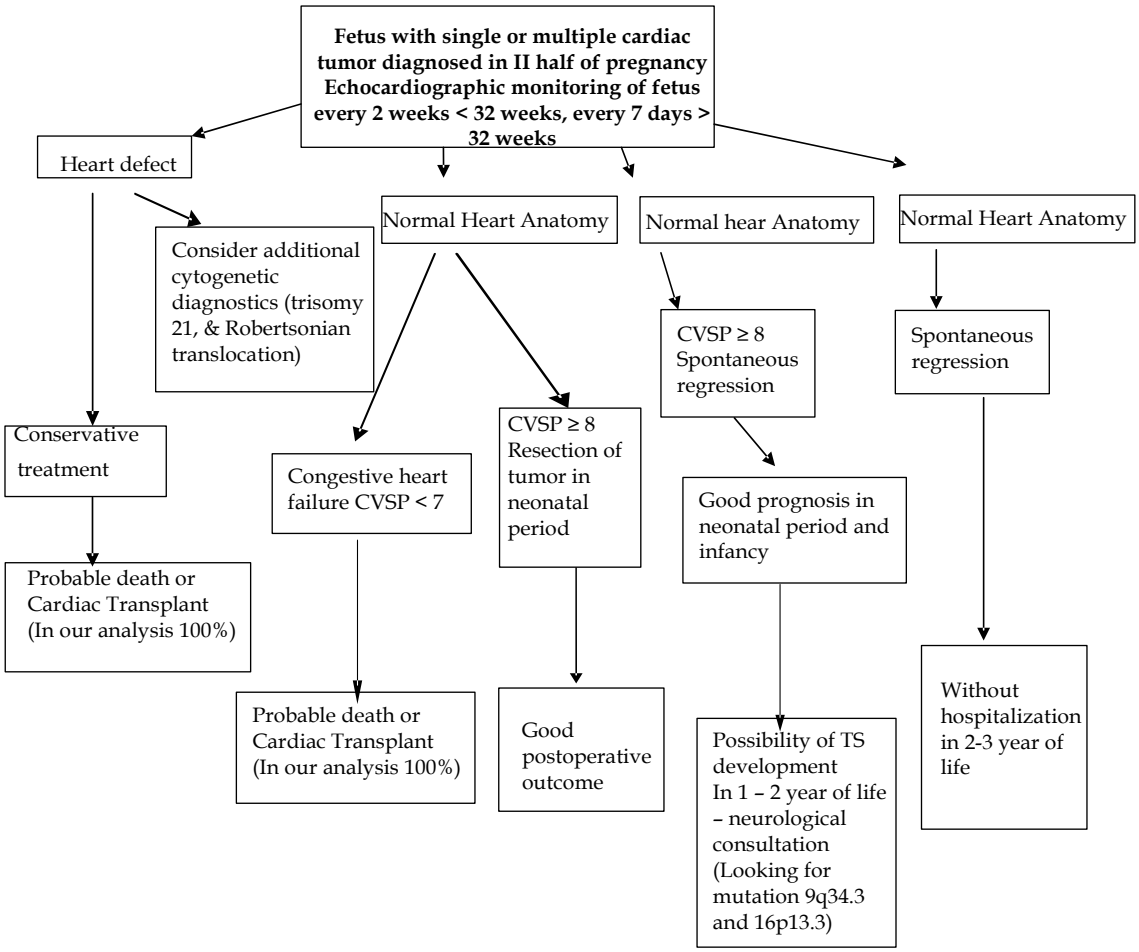

Figure 2: Management algorithm, [Niewiadomska-Jarosik et all 2010]. Quoted after permission from the author

Patients with cardiac fibroma have virtually unpredictable outcomes as they do not regress postnatally but tend to grow further after birth, unlike rhabdomyoma. Surgical debulking should be considered in cases with significant mass effects on cardiovascular blood flow because the infant may require heart transplantation [11]. Fibromas have also been associated with ventricular tachycardia and arrhythmia-related sudden death.

The reported cases with cardiac fibroma were all delivered at term with transient cyanosis at birth and treated with prostaglandin. We don't have reports of their long-term outcome. In another case, the tumor remains stationary in size, and the child remains asymptomatic at two years of age. In another case, the fibroma caused left ventricular inflow and transient left main bronchus obstruction. One of the cases reported ventricular tachycardia developed in early infancy, which was successfully controlled with oral amiodarone treatment. Unfortunately, the tumor has grown progressively from 3.2 cm at birth to 7 cm at 15 months, and the child may eventually require a heart transplant.

The mortality rate (Fetal or neonatal) is associated mainly with cardiac anomalies in early pregnancy, earlier delivery, larger tumor size, obstructive cardiac outflow, heart failure, and fetal hydrops at presentation. Surgical debulking of the tumor was performed in 5/12 neonates with single tumors [25].

Management

Postnatally, the treatment should be tailored to each case based on the symptomatology and the degree of cardiovascular dysfunctions. Asymptomatic lesions require no surgical interventions, and the newborns should be observed for partial or total tumor regression over time [21,22,26]. DNA analysis to confirm or exclude TSC is mandatory for those who presented with multiple tumors (cardiac and none cardiac), especially if it fits the diagnostic criteria of TSC. Clinical symptoms are likely to occur in these cases with massive inoperable tumors; the only therapeutic option is heart transplantation [27]. The treatment of choice for persistent or progressively growing cardiac tumors is surgical debulking. The candidates for debulking are those who present with hemodynamic

instability [21,22,27-32]. Regrettably, cases with severe hemodynamic instability may not be candidates for surgery as they may not be able to withstand it. Therefore, the cardiological and cardiosurgery consultation is recommended to identify those who develop hemodynamic instability. They also should estimate the surgery risk for the patient with congestive heart failure. Surgical debulking should aim to restore the heart's normal structural anatomy and achieve the best cardiac function possible, which may not always be synonymous with total tumor resection [21]. Niewiadomska-Jarosik et al. l, 2010, have outlined a management algorithm based on the outcomes of their study [figure (2)] [25-43].

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