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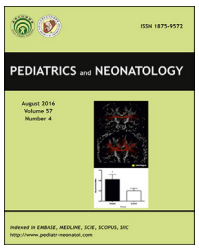

REVIEW ARTICLE

Fetal Primary Cardiac Tumors During Perinatal Period

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Fetal primary cardiac tumors are rare, but they may cause complications, which are sometimes life threatening, including arrhythmias, hydrops fetalis, ventricular outflow/inflow obstruction, cardiac failure, and even sudden death. Among fetal primary cardiac tumors, rhabdomyomas are most common, followed by teratomas, fibromas, hemangiomas, and myxomas. Everolimus, a mammalian target of rapamycin inhibitor, has been reported to be an effective drug to cause tumor remission in three neonates with multiple cardiac rhabdomyomas. Neonatal cardiac surgery for the resection of primary cardiac tumors found by fetal echocardiography has been reported sporadically. However, open fetal surgery for pericardial teratoma resection, which was performed successfully via a fetal median sternotomy in one case report, could be a promising intervention to rescue these patients with large pericardial effusions. These recent achievements undoubtedly encourage further development in early management of fetal cardiac tumors. Owing to the rarity of fetal primary cardiac tumors, relevant information in terms of prenatal diagnosis, treatment, and prognosis remains to be clarified.

1. Introduction

Primary cardiac tumors are rare in all age groups with an incidence of 0.0017–0.027% at autopsy.[1] In infantile population, the incidence of primary cardiac tumors was reported to be 0.25%.[2] Even though fetal primary cardiac tumors (FPCTs) are infrequent, they are incidentally disclosed by widely used prenatal echocardiography.[3] Most FPCTs are benign; although fetal malignant and metastatic cardiac tumors have also been described, they are much rarer. FPCTs can be categorized into benign tumors (rhabdomyomas, teratomas, fibromas, hemangiomas, and myxomas) and malignant tumors (rhabdomyosarcomas and fibrosarcomas). In addition, Isaacs[4] also included oncocytic cardiomyopathy in the category. No significant differences were seen between the incidence of FPCTs and that of the infantile groups (0.11% *vs.* 0.08%).[4] Although the incidences of various types of tumors varied from fetuses to neonates

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and children, cardiac rhabdomyomas, teratomas, and fibromas remained the three most common types.[5] Nevertheless, fetal information was always limited (Figure 1). Murmurs, cyanosis, arrhythmias, and cardiac failure are the major presenting signs of FPCTs during the perinatal period.[4] Fetuses with certain cardiac tumors may also present with hydrops fetalis and ventricular outflow/inflow obstruction.[7] Neonatal cardiac surgery for the resection of primary cardiac tumors found by fetal echocardiography and open fetal surgery for pericardial teratoma resection have greatly encouraged further development in early management of fetal cardiac tumors. Owing to the rarity of FPCTs, relevant information regarding prenatal diagnosis, treatment, and prognosis remains to be clarified.

2. Definitions

The concept of FPCTs has to been differentiated from a series of terms of cardiac tumors, including congenital cardiac tumors, fetal cardiac tumors, pericardiac teratomas, and malignant fetal cardiac tumors. Concepts that require further clarification may also include primary pericardial tumors, pericardial cysts, and primary malignant pericardial tumors in the pediatrics summarized by Restrepo et al.[8]

FPCTs that are described here represent the following: (1) primary (other than secondary); (2) fetal (not postnatal as for the time of onset or investigation, but intervention might be postponed or extended to the postnatal period); (3) cardiac and pericardial, as diffuse growth of cardiac tumor cells may infiltrate the myocardium, epicardium, and endocardium as well as the (intra)pericardium; and (4) both benign and malignant. It seems that no secondary (metastatic) cardiac tumor has been developing either from the fetuses *per se* or from their mothers. In addition, congenital cardiac tumors might be interpreted as primary cardiac tumors in both fetuses and neonates,[9] *i.e.*, with a larger age range than the fetal ones.

3. Fetal primary cardiac tumors

3.1. Rhabdomyoma

Cardiac rhabdomyoma is the most common type of FPCT with an incidence of 60%.[10] Zheng[11] found only three cases of fetal cardiac rhabdomyomas in regular examinations of more than 4,800 pregnant women. Cardiac rhabdomyomas are usually benign, and involve the left and right ventricles and ventricular septum. They often grow into the intracavity of the cardiac chambers, growing either intramurally or extracardiacally. Of all cases, 90% of the cardiac rhabdomyomas are multiple tumors. Hydrops fetalis, obstruction of the ventricular outflow tracts, arrhythmias, and cardiac shock are the common manifestations.[12] Echocardiography may reveal a spherical or an oval mass with strong echogenic focus and a clear boundary.[13] The site, number, and ventricular outflow tract obstruction of fetal cardiac rhabdomyomas can be observed from the fetal apical four-chamber view.[14] Actually, about 30—50% of fetuses with cardiac rhabdomyomas are associated with

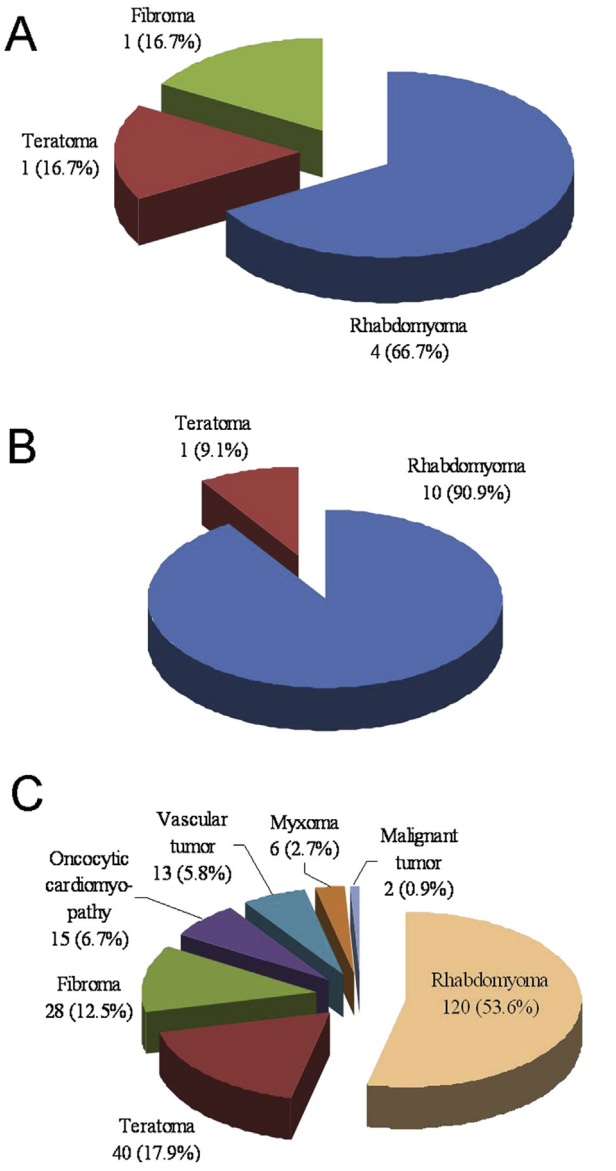

Figure 1 Incidences of primary cardiac tumors in (A) fetal,[6] (B) fetal,[4] and (C) fetoneonatal groups.[4]

cerebral tuberous sclerosis or sebaceous adenoma.[14] Yao et al[14] reported five cases of fetal cardiac rhabdomyomas, one of which had tuberous sclerosis. Gamzu et al[15] described that 39% of suspected cardiac rhabdomyomas *in utero* had tuberous sclerosis. Similarly, infants with a cardiac rhabdomyoma who survived postnatally were examined by magnetic resonance imaging at the age of 1 year or 2 years, and one of them was noted to have tuberous sclerosis. Most scholars think that cardiac rhabdomyomas are myocardial hamartomas instead of true tumors.[16] However, clonal cytogenetic abnormalities found in recurrent rhabdomyomas were suggestive of the true tumor nature of cardiac rhabdomyomas.[17] Histological studies of fetal cardiac rhabdomyomas revealed typical "spider cells" with positive immunoreactivities to periodic acid-Schiff, myoglobin, desmin,[18] actin, and myogenin.[19] Treatment strategies depend on fetal/neonatal conditions. Bader et al[19] reported 18 live births with prenatally diagnosed

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