HEART TUMORS IN 33 FETUSES - REVIEW OF TWENTY-TWO YEARS OF THE SINGLE-CENTRE EXPERIENCE

Authors:
Katarzyna Więckowska¹, Katarzyna Piątek¹, Maria Respondek-Liberska²,³

¹. Medical University of Lodz, 5th Grade, Scientific Student’s Circle of Prenatal Cardiology
². Department of Diagnoses and Prevention Fetal Malformations, Medical University of Lodz, Poland
³. Department of Prenatal Cardiology, Polish Mother’s Memorial Hospital Research Institute, Lodz, Poland

Abstract
INTRODUCTION: Cardiac tumors (CT) have been diagnosed since the eighties of the last century. The three most commonly diagnosed types of CT are rhabdomyomas, teratomas and fibromas. Severe fetal disturbances, such as arrhythmias, fetal hydrops, ventricular obstructions, may be associated with the heart tumor.

AIM OF THE STUDY: To present the key role of the echocardiographic examination in the perinatal care and to present some demographic changes in this population of the youngest patients.

MATERIAL AND METHODS: From the Filemaker database of the Department for Diagnosis and Prevention of Congenital Malformations, Polish Mother’s Memorial Hospital & Medical University of Lodz, all cases with prenatal diagnoses of cardiac tumor in singleton pregnancy were compiled over a 22-year period (1993–2015). 33 cases of heart tumors in fetuses had 72 fetal echo examinations. The average number of cases per year was 1,5 (range 1 – 5). The retrospective analysis of the material was performed using the Statistica package. The analysis included the assessment of the cardiovascular condition defined by Cardiovascular Profile Score, location and number of tumors; age, past obstetric history, place of residence of the mother, type of delivery and neonatal follow-up.

RESULTS: The number of fetuses with cardiac tumor cases did not increase during this period. The maternal age was 28,1 years (± 5,2 years) and was decreasing over time. The primigravidae constituted 60% of examined population. The history of past miscarriages was observed in 26% of women. The majority of tumors were detected and diagnosed in the third trimester – at mean 29,6 hbd, but the diagnosis was made earlier in the past decades (regression analysis, p=0,042). The average duration of pregnancy was 36,6 hbd (range: 27–42 hbd). There was no statistical difference between decades in term on pregnancy duration.

The cardiac tumors were more frequent in the female fetuses (71,4% to 28,6%; X² test; p=0,006). The proportions between the groups of single and multiple tumors changed in last five years – currently the multiple tumors are more frequent (87,5%). The mortality in the group of single tumors was twice as high as in the group of multiple tumors. The percentage of cesarean sections between 1993 and 2005 was 67% and between 2006 and 2015 was 75% (p=0,63). The mortality of neonates with cardiac tumors declined over the period taken into account.

CONCLUSIONS: The perinatal care of the fetuses with cardiac tumors improved over last 20 years. The characteristics of analyzed population had shown that fetal CTs affected healthy, young mothers, more often primigravidae, more often female fetuses. The prevalence of CTs did not increase over time. The gestational age at the time of the diagnosis decreased, thus the period of fetal echo monitoring increased. However, the rate of cesarean sections also increased, which requires further studies and explanations.

Key words: prenatal cardiology, heart tumors single and multiple , ecology, rate of cesarean sections, CVPS

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DESCRIPTION:
Cardiac tumors, intracardiac masses located in a lumen or walls of the cardiac chambers, in their septa or in the pericardium and have been diagnosed during fetal life since the eighties of the last century. The defects are rare:

Corresponding author: Maria Respondek-Liberska, majkares@uni.lodz.pl
perinatal fetal heart tumors prevalence, managements or demographic data in this and previous decade? Do we know any relationship between occurrence of cardiac tumors and hazardous environmental pollutions or other risk factors?

**INTRODUCTION**

Cardiac tumors, intracardiac masses located in a lumen or walls of the cardiac chambers, in their septa or in the pericardium and have been diagnosed during fetal life since the eighties of the last century. The defects are rare: the National Polish Registry of Prenatal Cardiac Anomalies reports their prevalence of 1.2% among all fetuses diagnosed with fetal cardiac abnormalities in all prenatal cardiac centers.

In general, heart tumors are easy to detect in utero thanks to 2D ultrasound. The real-time three-dimensional echocardiography adds the visualization of continuity, curvature and exact location of tumor, as well as the assessment of dynamic changes of fetal cardiac size and wall motion, although the resolution of this technique is inferior to 2D imaging.

The diagnostic procedure may be extended to MRI scan.

Fetal cardiac tumors may cause hemodynamic compromise in fetus and later on and still there is lack of information about the cause of the problem.

The aim of this research was to answer the question: are there any changes in prenatal and perinatal fetal heart tumors prevalence, managements or demographic data in this and previous decade? Do we know any relationship between occurrence of cardiac tumors and hazardous environmental pollutions or other risk factors?

**MATERIAL & METHODS**

From the Filemaker and archival databases of the Department for Diagnosis and Prevention of Congenital Malformations of the Medical University and Department of Prenatal Cardiology at Polish Mother’s Memorial Hospital (same unit) all cases of prenatal diagnoses of cardiac tumors in singleton pregnancies were compiled over a 22-year period (1993–2015). Thirty three fetuses had a single or multiple heart tumor. Seventy two fetal echo examinations were performed in them.
The analysis included the assessment of the cardiovascular condition defined by Cardiovascular Profile Score, location and number of tumors; age, past obstetric history, place of residence of the mother, type of delivery and neonatal follow-up. The retrospective analysis of the material was performed using the Statistica 12 package.

At the same time the National Polish Registry of Prenatal Cardiac Anomalies was searched for the reports on characteristics and outcome in the overall population of fetal cardiac tumors in Poland between 2004 (the year of establishing of the Registry) and 2015.

RESULTS:
The average number of fetuses with heart tumors was 1,5 per year (range 0 – 5). The number of cases per year is presented in Figure 1. There was one startling peak of diagnosed fetuses in 2009 and it coincided with peak of sacrococcygeal teratomas diagnosed in our institution.

There was a large variability in tumors size. The average size of the tumors was 18,4x16,1x12 mm. The maximal diameters range
between 4 and 47 mm. One third of fetuses have a tumor placed in the right heart, one third in the left, remaining in both sides (Figure 2). The location of tumor did not play a key role in prognosing the neonatal survival. The maternal and fetal characteristics are presented in Table 1.

Pregnant women were most frequently referred for echocardiographic examination because of abnormal four-chamber views observed during obstetric ultrasonographic scans. If a cardiac tumor was suspected, fetal echocardiographic examination was performed to assess cardiac anatomy, number of tumors, their localization, and the hemodynamic status. The first observation of the tumor was made at 20 week of gestation (the latest at 40th week of gestation!).

The average age of the gravida was 28.1 years (± 5.2 years). Examined mothers of fetuses with cardiac tumors were healthy women < 30 years of age. Primigravidae accounted for a large part of the population: they constituted 60% of patients in the last six years (Fig. 3). 26% of patients had a bad obstetric history, but this percentage diminishes in years.

Regarding fetuses population, the majority of affected patients were female. These proportions changed from the past decade, when the boys were more often touched by cardiac tumors (χ² test, p=0.006; Fig 4).

In six out of 33 cases fetal heart tumor coexisted with congenital heart disease. They are listed in Table 2.

Multiple cardiac tumors were more frequent than the single ones which stems from the theory that the multiple rhabdomyomas are the most common type of CT. The mortality in the group of single tumors (rather more malignant fibromas or teratomas) was twice as high as in the group of multiple tumors (implicitly rhabdomyomas) – 38% to 19% (Fig. 5.)
The overall mortality in the analyzed population has dropped down to about 20% in late nineties of the twentieth century. We should therefore ask if this outcome may be better in future years. The mortality of fetus in the group of a bad cardiovascular condition (CVPS < 8) was more than eight times higher than in the group of good cardiovascular profile (CVPS ≥ or = 8), which was statistically proven with p=0.0002 (X² test, Fig. 6).

The prenatal diagnosis of fetal heart tumor in the last decade was made earlier during gestational age than it was being done in the past years and it was statistically proven (Fig. 7).

When the mothers’ place of residence was taken into account, the occurrence of cardiac tumors in certain parts of Poland, especially around the Kuiavian-Pomeranian voivodeship, was observable.

Therefore, the ecological situation of this region was checked, based on the data of the Inspection of Environmental Protection. According to the data from years 2007 and 2008 cardiac tumors were recorded in regions of high concentration of benzapirene and other polycyclic aromatic hydrocarbons (red on the map). Benzene can also be a suspect factor (Fig. 8).

The data below were obtained from the National Polish Registry of Prenatal Cardiac Anomalies data from years 2004-2015.

In the group of multiple tumors the average birth weight of a neonate was 3277 g (2050 g – 4080 g). 66.7% of children died within 10 minutes after the labor. The majority (53%) of alive neonates was discharged home, 33% were referred to the tertiary cardiac care center, 7% to the Intensive Care Units of these centers, there were no neonatal deaths recorded in this group. One third (33%) of neonates underwent a cardiosurgical procedure.

In the group of single tumors the average birth weight of a neonate was 2930 g (1000 g – 3950 g). The questionnaire concerning the labor was filled in 37.9% of cases. 54.5% of children died within 10 minutes after the labor. The follow-up of 27% of alive children is not known, 27% of neonates were discharged home, 18% were referred to the tertiary cardiac care center, 9% to the Intensive Care Units of these centers. 18% died in the neonatal period. Three neonates underwent a cardiosurgical procedure, one out of them died after the surgery.

DISCUSSION:

Fetal cardiac tumors are rare anomalies. Based on the National Polish Registry of Prenatal Cardiac Anomalies between 2004 ans 2015, 76 cases out of 7097 (1,07%) between 2004 and 2015 presented at different fetal cardiac centers with cardiac tumors of all types. 47 cases (61%) were multiple lesions. Average number of US examinations before the tumor was detected was 3.6, and the diagnosis was made at 28.6 weeks of gestation on average.

In National Polish Registry of Prenatal Cardiac Anomalies database only 34.2 % of parents sent a follow-up letter, so the final outcome is relative difficult to follow. In our unit and tertiary teaching hospital we had more data for analysis.

Types of fetal cardiac tumors

Rhabdomyomas

It is the most comon type of tumor (76% - 83%)\textsuperscript{5,6,7,8}. They usually are multiple (less often single), homogenous, well-circumscribed masses, variable in size and location\textsuperscript{5}. Normally, they do not cause cardiac compromise, but cases of obstructive or arrhythmogenic tumors are known.

These tumors are likely to appear at 20 weeks of gestational age and predominatingly disappear completely in infancy\textsuperscript{3,11}. According to Yinon et al.\textsuperscript{6} about 80% patients with rhabdomyosarcoma are alive and well at follow-up appointment in infancy. In about 12% of pregnancies the intrauterine or neonatal death was observed. They were associated with:

- fetal hydrops,
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- large size of the tumor (>20-40 mm),
- delivery before 31 weeks of gestation,
- fetal dysrhythmia, especially treatment-resistant SVT. 

Association with tuberous sclerosis

These tumors are commonly associated with Bourneville-Pringle disease, known also as tuberous sclerosis. This genetical disorder is inherited autosomally dominantly with high penetrance. It is caused by mutations in Hamartin.
(TSC-1) and Tuberin (TSC-2) genes. Located on 9q34 and 16p13 chromosomes. Hamartin and tuberin are responsible for tumors suppression. In Bourneville-Pringle disease nodules, especially hamartomas, are present in the skin, brain, kidneys and visceral organs. Cardiac tumors are usually rhabdomyomas. The spectrum of the disease is very wide. Some signs may be absent. In case series reported by Sciacca et al. about 30% of rhabdomyomas associated with TS were observed in fetal echocardiographic examination. In case of postnatal diagnosis, 50 to 80 percent of cases are associated with rhabdomyomas. The intracranial lesions are found in 40% of cases in the MRI examinations, what means that absence of brain tumors does not rule out tuberous sclerosis.

Recently, the tuberous sclerosis is achieved by molecular testing. The material is obtained during cordocentesis, chorionic villus sampling or amniocentesis. The early diagnosis should be conducted when the family history of epilepsy, chronic headaches or subtle skin lesions, such as nodules or cafe-au-lait spots, is positive. Genetic counselling is needed in all cases of fetal rhabdomyomas.

**Teratomas**

Teratoma is a cystic pericardial tumor. It may be attached to the aortic root or to the pulmonary artery. In the largest number of cases a teratoma is single, it consists multiple cysts. Moreover, pericardial effusion is associated with this kind of heart tumor. Although it is histologically benign, it may be life-threatening because it leads to heart’s compression and in consequence to fetal hydrops and intrauterine death.

Outcome of pregnancies known from literature differ. Ynon et al. recall three cases, none of them ends favourably. On the other hand, a multidisciplinary approach to this rare tumor may have superb effects. Tollens et al. present a management algorithm for cases diagnosed with teratoma in antenatal period. It bases on the presence of fetal hydrops and size of the tumor’s mass.

**Fibromas**

These rare tumors are usually single and they are difficult to distinguish from rhabdomyoma. Sometimes they degenerate centrally and form cysts. There is an

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Table 3: Echocardiographic findings and neonatal outcome in analysed population.
Heart tumors in 33 fetuses – Review of twenty-two years of the single-centre experience

association between fibromas and pericardial effusion. There are few articles reporting fetal diagnosis of cardiac fibroma\textsuperscript{18,19}.

CONCLUSIONS:

This report shows that fetal cardiac tumors occur in the population of healthy young mothers, expecting their first child. The risk factors are not easily detectable.

We have found that clinical condition and neonatal outcome is not different between neonates with single and multiple tumors, which is consistent with the analysis performed by Niewiadomska-Jarosik et al. (2010)\textsuperscript{20}. The tumors were located mostly in the left ventricle, but these observations were made on a small populations\textsuperscript{21}. When they are placed in the LVOT, they may induce a cardiovascular compromise in fetus.

Due to the fact that the prognosis of the outcome cannot be made only on the basis of the size\textsuperscript{22}, location or number of the tumors the cardiovascular condition of the fetus (CVPS) should be monitored subsequently to the time of labor.

The perinatal care has done a milestone – the diagnosis is made earlier which enables longer monitoring of the fetus in future years. The role of fetal echocardiography must be stressed. There is no monitoring of cardiac tumors without the prenatal cardiologist. The multidisciplinary approach including 2-D echocardiography, histology, genetics, and cardiac surgery is recommended\textsuperscript{23,24}.

In case of single tumor surgical procedures is likely to be performed in neonate. The multiple tumors have chance to dissapear in infancy, therefore the observation and early neurological care is recommended. Children with confirmed tuberous sclerosis may benefit the antiepileptic treatment introduced before the onset of clinical seizures, continued to the second year of age\textsuperscript{25}.

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References


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Katarzyna Piątek: data base analysis, literature search, work with manuscript
Maria Respondek-Liberska: concept of the research, final version

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