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ORIGINAL ARTICLE

Primary Cardiac Tumours in Infancy and Youth in the Small Population: a Seven Year Review

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Summary

Introduction. Primary tumours of the heart are rare in fetuses, neonates and children; the incidence varies from 0.003% - 0.08% (4, 6, 9, 10) up to 0.2% in children referred for cardiac examination (3, 15). Rhabdomyoma is the most common cardiac tumour during fetal life (60-75%). Teratoma is less common (14 to 19%) with fibroma, myxoma, hemangioma also being described (3, 4, 6, 10, 16, and 18). Multiple rhabdomyomas are associated with tuberous sclerosis in up to 90-95% of cases (3, 4, 5, 6, 10, 12, and 16). No previous study was done on this topic in Latvia so our aim was to determine the incidence, the course and the outcome of primary cardiac tumours in children in our small population.

Aim of the study. The aim of our study was to determine the incidence of primary cardiac tumours in our paediatric population, to investigate the nature of the pathology, the course and the outcome of the disease in childhood in Latvia and to compare our results with data from the international literature.

Materials and methods. We reviewed retrospectively the clinical, echocardiographic, operative, histological and follow-up data on 17 cases of a primary heart tumours detected within the period of January 1, 2000 till December 31, 2006 in the Clinic for Pediatric Cardiology and Cardiac Surgery of the University Children's Hospital in Riga, Latvia.

Results. the incidence of primary heart tumours in the paediatric population in Latvia is 2.4+/-1.4 cases per year. 94% (16) of the primary cardiac tumours in children were benign and 6 %(1) malignant. Radical excision performed in all 7 cases of surgical treatment. Rhabdomyomas comprise 47% (n=8) of all the benign tumours with tuberous sclerosis present in 88% of the cases.

Conclusions. Most primary cardiac fetal tumours tend to appear in the third trimester of pregnancy, a normal early fetal scan might not rule out cardiac tumours. Relatively often (29% of the cases) the cardiac tumours were an incidental finding. The localization, number and visual appearance of the tumours in echocardiography was indicative of the type of tumour. 41% of the patients with primary cardiac tumours were in need of urgent surgical treatment. Almost all benign primary cardiac tumours were not the cause of death and with the exception of tuberous sclerosis there is good overall prognosis, in the case of malignant primary cardiac tumour the prognosis is poor.

Key words: primary cardiac tumour, echocardiography, congenital heart disease.

INTRODUCTION

Primary tumours of the heart are rare in fetuses, neonates and children. They are found in 1/10,000(0.01%) of routine autopsies of patients of all ages (10) and in 0.0017% of autopsies in the paediatric age group (6, 18). According to the literature, the incidence of primary heart tumours in infancy and childhood varies from 0.003% to 0.08% (4,6,9,10) with a reported incidence of up to 0.2% in children referred for examination for cardiac disease (4,15). The incidence of primary heart tumours in fetal echocardiography is 0.14% (9, 18)-0, 2 %(10). Most of the evidence in this article is based on case reports rather than large cohort studies. The frequency and type of cardiac tumours in children differ from those in adults. The majority of primary cardiac tumours in children are benign. Rhabdomyoma is the most common cardiac tumour during fetal life and childhood and accounts for 60-75%. Teratoma is less common (from 14 to 19%) with fibroma, myxoma, hemangioma also being described (3, 6, 10, 15, 16, and 18). Multiple rhabdomyomas are associated with tuberous sclerosis in up to 90-95% of cases but these tumours tend to regress with time (3, 5, 6, 10, 15, 16, and 18) although some authors (12) suggested rhabdomyomas could develop during childhood in tuberous sclerosis. Malignant primary cardiac tumours are extremely rare and are observed in 4-9% of cases with rhabdomyosarcoma as the leading malignancy.

During the past decade the number of cardiac masses detected in paediatric population has increased significantly because of the widespread use of non-invasive imaging techniques.

AIM OF THE STUDY

The aim of our study was to determine the incidence of primary cardiac tumours in our paediatric population, to investigate the nature of the pathology, the course and the outcome of the disease in childhood in Latvia and to compare our results with data from the international literature. There are no previous studies on this subject available in Latvia and we suspected a primary heart tumour is a relatively frequent pathology in our small population. The number of primary heart tumours cases in our study demonstrated unusual appearance in infancy which were unexpected to us, and which we felt were worthy of description.

MATERIALS AND METHODS

There were 2,294, 000 inhabitants in the year 2006 in Latvia, 18.9 % (433,566) of them children (17). The life births rated from 19 664 in year 2001 to 22 264 in year 2006 (17) and there are approximately 250 newly diagnosed congenital heart diseases in the paediatric population in Latvia annually. All children with a suspected heart anomaly and those with known cardiac pathology are treated and followed-up in our centre, the only paediatric cardiology clinic in our country.

It was a retrospective descriptive study; all the patients with primary heart tumours diagnosed within the time between January 1, 2000 until December 31, 2006 from the local database of the Clinics for Pediatric Cardiology and Cardiac Surgery of University Children's Hospital, Riga, Latvia were included in the study. Retrospective review of our database detected 18 cases, including four diagnosed prenatally, with a diagnosis of a primary heart tumour seen between January 1, 2000 until December 31, 2006 in our centre. In one prenatally diagnosed case (rhabdomyosarcoma) the pregnancy resulted in a stillbirth and this patient was excluded from further study.

The confidentiality of the patients included in the study was fully preserved and the design of the study in based under the existing legislation of our country.

The patients were analysed according to the localization of the tumour and its morphology on echocardiography and/or the histology of the tumour, the surgical therapy and the follow up. The demographic, clinical and diagnostic data were collected and analyzed. The data were obtained from the case histories and videotapes of the patients treated and followed-up in our centre. All the surgically resected masses and one case of prenatally diagnosed tumour, which resulted in a still birth were sent for histological examination. Postoperatively the patients were followed-up 9-72 months (medium 45+/-16, 8 months).

There was a total of 34,620 in-patient and out-patient echocardiograms (5942 of them fetal echocardiographies) performed in the time period from January 1, 2000 till December 31, 2006.

RESULTS

There were 17 cases of primary heart tumours diagnosed within the seven years of the research period, including three diagnosed prenatally between 24 and 36 (medium 27,3+/-3,5) weeks of gestation during routine fetal scan and been referred to the fetal cardiologist. Additional four cases were detected in the neonatal period, seven within the first year of life, at the age of 1 to 10 years in two cases and five at the age of 10 to17 years. From all 17 patients five of them were females (29%) and 12 (71%) were males.

There were 16 (94%) benign: Rhabdomyoma 8, Fibroma 2, Teratoma 1, Myxsoma 1, Lymfangioma1 and 3 unknown aetiology primary heart tumours and one (6 %) malignant: Mesotelioma.

Within the analyzed cases, the cardiac mass found posnatally by chance was in 5 cases (29%) and another five (29%) were found on echocardiography, having been referred because of a history of seizures and/or the diagnosis of the tuberous sclerosis. Eight patients (47%) had clinical symptoms of congestive heart failure or arrhythmia or abnormal chest x-ray, 6% (n=1) of patients were referred for cardiac examination due to abnormal findings on the chest x-ray performed as an out-patient, 24% (n=4) were referred for the cardiac examination due to a murmur of the heart and only 12% (n=2) were sent to the cardiologist due to symptoms such as cough, sweating, tachypnoe (patients 5 and 11 years old). In one case the manifestation of the tumour was cyanosis, respiratory distress and the signs of congestive heart failure in a newborn.

There are 3 unusual cases of the cardiac masses, all diagnosed prenatally, in the study group where the histology is unknown. We assume that they are benign nature because there are no hemodynamically relevant changes observed, the patients have no congestive heart failure and possible malignancy is not suspected clinically. All three patients were born in full term. In the first case the solid mass (7.5 x7.5 mm) obstructed the left ventricular outflow tract with maximum pressure gradient of 80 mmHg on continuous wave Doppler, but fortunately normal cardiac function on fetal echocardiogram at 30 weeks of gestation. The infant was asymptomatic postnatally even the cardiac mass remained the same size; the gradient subsequently had decreased until 16mm Hg at the age of four. In the second case the tumour was localized in the posterior wall of the right atrium and decreased in size significantly with the time. In the third patient a large firm tumour mass was found localized within the ventricular septum, but as it does not increase in size and is not obstructive, excision of the mass has been deferred. In case 2 and 3 the serum alpha-fetoprotein levels were controlled and they were elevated after the birth 844 and 44766 IU/ml respectively with a normal value up to 10 IU/ml, but decreased significantly to the normal values until the age of 6 months. As the nature of these three tumours is unknown the possibility of tuberous sclerosis was excluded by geneticist counselling and brain computed tomography.

Rhabdomyomas were diagnosed echocardiographically based on the characteristic findings and correlation with tuberous sclerosis. Rhabdomyomas comprise 50% (n=8) of all the benign tumors. There was tuberous sclerosis present in seven patients (88%) of the cases of rhabdomyomas. In one of them the patient deceased at the end of the operation due to acute cardiac insufficiency and critical dysfunction of the left ventricle after the extirpation of the tumour which was firmly connected to the posterior wall of the left ventricle. The indications for the surgery were severe compression of the left ventricle by the tumour. All the remaining patients with rhabdomyomas except the one who died at the end of surgery were followed-up for 3-84 months, there was no hemodynamically significant obstruction or resistant arrhythmias observed and therefore surgery was not indicated. There was one

death from an unrelated cause. There was a tendency for regression of the multiple rhabdomyomas but they are still detected echocardiographically in all the patients. The age of these patients at the end of the study (December 31.2006) ranged from 9 months – 15 years (medium 9, 4+/-6 years). These patients had mental retardation of variable degree, seizures, received anticonvulsive treatment and were followed-up by paediatric neurologists and psychiatrists. Most of the rhabdomyomas were observed to regress with a time in accordance with the literature (3, 4, 5, 6, 7, 10, and 11). Although none of the patients had complete regression of tumours. Only three of the patients from this group experienced congestive heart failure in neonatal period but none had serious arrhythmia and only one was in need of surgery. In the group of rhabdomyoma and all the benign primary cardiac tumours only one deaths due to the tumour occurred.

Over the time period there was an increasing rate of surgical intervention, which took place in 7(41%) cases, all the surgically treated cases are represented in Table 1. In 6 cases the operation was performed in our centre, but in one case abroad due to social reasons. Radical excision was performed in all cases of surgical treatment of primary heart tumour.

(Table 1).

In one case with a giant fibroma of the right ventricle the excellent surgical result was achieved by removing the mass following the principles of the Batista procedure to preserve the function of the left ventricle (19).

In one case from our operated patients group the heart tumour was found by chance as the patient was referred for follow up due to prenatally diagnosed muscular ventricular septal defect. The fetal echocardiogram was performed at 26 weeks of gestation and there were no signs of the cardiac mass at that time. At the age of three months the male infant presented asymptomatic but the echocardiogram showed typical appearance of myxoma in the right atrium, no ventricular septal defect was found. The nature of the tumour was confirmed after the mass was successfully removed by surgeon.

There was one malignant tumour detected. It was a malignant epitheloid mesothelioma which recurred 20 months following operation, the only case of recurrence of the tumour in our study. The patient has declined further palliative treatment.

In general the incidence of primary heart tumours in the paediatric age group was 0.049% in children referred for the cardiac examination with a prevalence of cardiac tumours in the paediatric population 3.92/100,000 in Latvia.

DISCUSSION

Primary heart tumours are a rare pathology in the paediatric age group (4, 6, 9, 10, and 15). The increase in the incidence of both neoplastic and nonneoplastic cardiac lesions detected annually has increased during the past two decades due to improved imaging techniques such as sonography, magnetic resonance and computed tomography. There are some limitations to our study. First of all, we have not examined entirely all paediatric patients with tuberous sclerosis in the country. Therefore the data about rhabdomyomas is not absolute. Secondly, the fact that specialized cardiac examination in the paediatric age group in our population is performed only in our centre explains the comparatively low incidence of primary cardiac tumours in the group of patients referred for the cardiac examination to a tertiary centre. The incidence of primary heart tumours in the paediatric population in Latvia is 2.4+/-1.4 cases per year or 0.049% in the children referred for cardiac examination. According to the international literature the incidence of the primary heart tumours in the paediatric age group varies from 0.003% to 0.08% (6,9,10,15) with a reported incidence up to 0.2% in children referred for the examination due to cardiac disease (4, 15) .

The possibility for antenatal diagnosis has improved during the past decade in our country. However, only three from seven neonatal cases were diagnosed in utero. Fetal cardiac tumours tend to appear between 20 and 30 weeks of gestation, therefore a second trimester fetal anomaly scan can not completely rule out a cardiac tumour (5, 8, 11, 13, and 14).

Absence of specific symptoms makes difficult to diagnose primary heart tumour early and sudden death could be the only presentation of the disease. Only 18% of our patients had signs of congestive heart failure clinically and/or there were parental complaints connected with clinical findings. There are no reported data of sudden death caused by primary heart tumour during this study period to our knowledge.

Although multiple rhabdomyoma was the most common primary cardiac tumour in the paediatric age group in Latvia, it constituted only 47% of all the primary heart tumours in paediatric age group whereas in the literature it accounts for up to 75% of the detected cardiac tumours in childhood (4, 6, 8, 9,10, 16). This discrepancy could be explained by the possible absence of existing cases among the neurological and psychiatric patients who are not yet diagnosed. There is a correlation between multiple cardiac rhabdomyomas and the diagnosis of tuberous sclerosis observed in 90-95% (1, 2, 3, 4, 5, 6, 10, 11), but in our study group 88 % of rhabdomyoma cases were associated with tuberous sclerosis. The second most common cardiac tumour was fibroma (12%), but it ranked first among the patients who underwent surgery for the heart tumour. We observed only a single case of each, teratoma, myxoma and lymphangioma, within the period covered by the study. In the case with a giant fibroma in the right ventricle the surgeon had preferred to use unique approach - principle that was proposed by R.Batista (1996) for critical patients with dilated cardiomyopathy - partial left ventriculectomy alternative to the heart transplantation (19). The case of myxoma at age of three months is extremely unusual as the myxoma it self is very rare in the paediatric age group. The myxoma is common cardiac mass in adults with female predominance and mostly located in the left atrium. In our case this all was opposite with no family history of myxomas. Only an accidental finding of muscular

ventricular septal defect on fetal echocardiogram at 26 weeks of gestation with subsequent follow up postnatally protected this infant from possible sudden death.

As previously described in literature, the malignant primary heart tumours in infancy are also very rare and carry a poor prognosis. Our study has demonstrated a dismal outcome in group of malignant primary heart tumour with tumour recurrence and multiple metastases 1 year 8 months after surgical tumour excision. The serum alpha-fetoprotein was used as the marker to predict the nature of the tumour in the group of clinically asymptomatic cardiac masses with unknown histology. However, the value of initial level of serum alpha-fetoprotein in judging the presence of possible immature or malignant elements is questionable. Two further elements can increase levels postnatally, specifically prematurity and the presence of tumour involving the germ cells. The presence perinatally of a tumour of the germ cells produces strongly elevated levels, albeit in most reported cases, the tumours either contained immature elements or malignant elements from the yolk sac (14). The serum alpha-fetoprotein decreases after an inverse logarithmic curve to approximately 100μg/L at 1 month of life, and then to a normal level at 1 year of age. It has been suggested that the rapidity of serum alpha-fetoprotein decrease is a more accurate prognostic factor than any isolated value (14).

CONCLUSIONS

Relatively often the primary cardiac tumour was an incidental finding. The localization, number and visual appearance of the tumour in echocardiography was indicative of the type of tumour and aided in planning management. Benign primary cardiac tumours were not the cause of death and with the exception of tuberous sclerosis there is good overall prognosis but every case is individual according to the localization, size and haemodynamic consequences. In the group of benign tumours congestive heart failure was observed only in one case following the successful operation, but 83% were free of congestive heart failure. The overall prognosis is good in this group.

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Table 1. Characteristics of the operated patients

Case	*Gender*	*Age at diagnosis*	*Presenting symptoms and reason for referral*	*Hystology, size, localization and characteristics of the tumour*	*Outcome*
1	Female	13 month	Systolic heart murmur and premature atrial contractions	*Fibroma* 75 x 55 x 30 mm, within the myocardium of the right ventricle anterior wall; firm, circumscribed, not encapsulated with calcification islands	Total tumour excision (using the Batista procedure principles); alive and doing well
2	Male	5 years	Heart failure and systolic heart murmur	*Fibroma* 47 x 66 mm; in the right ventricle, firmly connected with its anterior wall	Operated abroad; alive, heart failure
3	Male	3 month	Muscular ventricular septal defect on fetal echocardiography at 26 weeks of gestation	*Myxoma* 20 x 30mm, pedunculated, with a stalk attached to the right atrium lateral wall; thin capsule, polycystic	Total tumour excision; alive and doing well
4	Male	11 years	Heart failure and abnormal chest X-ray (massive pericardial effusion)	*Epytheloid malignant mesotelioma* 200 x 100 x 80mm, polycystic, dense, encapsulated, firmly connected to the epicardium of the right ventricle with extension to the right atrium, aorta and pulmonary artery	Tumour excision; alive; tumour recurrence
5	Female	11 years	Abnormal chest X-ray	*Lymfangioma* 50 x 25 x 30 mm; polycystic, tight to the left ventricle, left diphragma, firmly connected to the pericardium	Total tumour excision; alive and doing well
6	Male	1day	Heart failure, cyanosis and abnormal chest x-ray (cardio/thoracic ratio of 0.8)	*Rhabdomyoma* 45 x 30mm; subepicardial, dense, without capsule, connected to the posterior wall of the left ventricle	Tumour excision; deceased at the end of operation due to heart failure and deficient left ventricular volume
7	Female	14 days	Heart failure, systolic heart murmur	*Teratoma* (immature grade I) 30mm x 28mm x 20mm; intrapericardial, multicystic, connected to the ascending aorta, compresses the right atrium and superior vena cava	Total tumour excision; alive and doing well