Heart Neoplasms in Children: Retrospective Analysis

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Abstract

Background: The advancement of noninvasive imaging methods has resulted in the increase in diagnosis of heart neoplasms. However, the literature has few studies involving primary cardiac neoplasms in children.

Objective: To retrospectively review cases of primary heart neoplasms in children, considering the initial clinical manifestations, diagnostic tests used, surgical indication, histopathological types and immediate postoperative course.

Methods: The retrospective study was based on the assessment of medical records from 1983 to 2011. Only cases that were referred for surgical treatment during that period were included. Age at admission, prenatal diagnosis, family history, initial symptoms and the results of performed tests were assessed. Moreover, the date and indication of the surgery, intraoperative findings, the result of the histopathological analysis, as well as the immediate postoperative complications were recorded.

Results: Of the 18 patients studied, the most frequent clinical manifestations were dyspnea and heart murmur (7 and 6 patients, respectively); the most often used adjunct diagnostic method was echocardiography (18 patients); cavitary obstruction or ventricular inflow or outflow tract obstruction was the main indication for surgery (12 cases); the most common histological profile was rhabdomyoma (7 patients) and most patients showed good clinical outcome.

Conclusion: In this study, imaging diagnosis was basically attained through echocardiography, with good correlation with intraoperative findings. Histopathological findings were consistent with the literature, with rhabdomyoma being the most common neoplasm in children. The evolution after surgical treatment was favorable in most cases. (Arq Bras Cardiol. 2013;100(2):120-126)

Keywords: Heart Neoplasms / surgery; Retrospective Studies; Echocardiography.

Introduction

Heart neoplasms can be primary or metastatic and were first described in the XVI century[1]. However, the first excision of a heart tumor was performed in 1936, when Beck resected a teratoma covering the pericardial and ventricular layers[1]. In 1955, Crafoord performed the first resection of heart tumor with the assistance of cardiopulmonary bypass (CPB), and this has been the most widely used method since then[1].

Primary heart neoplasms are rare, with an estimated incidence between 0.0017% and 0.19%[2]. Nevertheless, there has been a considerable increase in the number of heart neoplasms diagnosed in the last fifteen years, especially with the advancement of noninvasive imaging methods[3]. During the fetal period, the diagnosis has been reported in around 0.14%[4]. Benign neoplasms usually predominate, accounting for more than 90% of tumors in pediatric patients[1]. Rhabdomyomas are the most common type of heart neoplasm during the fetal and childhood periods, accounting for over 60% of all pediatric primary heart tumors, and their association with tuberous sclerosis has been well established, with a reported incidence between 60% and 80% of cases[4].

The literature contains few studies involving case series of primary cardiac tumors in children[1] and most publications are case reports. The purpose of this study was to retrospectively evaluate cases of primary heart neoplasms in children, thus reviewing initial clinical manifestations, tests used for diagnosis, surgical indication, histopathological types and immediate postoperative evolution.

Methods

The present study included patients diagnosed with primary heart neoplasms in children aged up to 18 years, treated by team of Pediatric Cardiology and Pediatric Cardiac Surgery, Instituto do Coração, Hospital das Clínicas of the Medical School of the University of Sao Paulo. The retrospective study was based on the assessment of medical records from 1983 to 2011. We included only cases that had surgical indication during this period. Therefore, patients with small tumors, with no clinical implications and no relevant anatomic location, not causing obstructive phenomena and which, therefore, were referred to clinical follow-up only (e.g., some rhabdomyomas), were not included in this study.

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Age at admission, prenatal diagnosis, family history, initial symptoms and the results of examinations (echocardiography, magnetic resonance imaging, computed tomography and / or cardiac catheterization) were assessed. The date and the indication of surgery, intraoperative findings, the results of the histopathological examination, as well as the immediate postoperative complications were also recorded. The results are shown descriptively, aiming to establish an association between preoperative diagnostic observations, intraoperative findings, and histopathological analysis.

In general, the CPB was performed with cannulation of the aorta, two cavas and aortic clamping; myocardial protection was achieved with St. Thomas solution (2 mL of St. Thomas solution for every 100 mL of blood, with 20 mL/kg being infused at first; 1 mL per 100 mL blood, 10 mL/kg for the second infusion, for children up to 40 kg. For all other patients, 1 mL for each 100 mL of blood, 10 mL/kg) and the access used was a median sternotomy.

Results

Between January 1983 and December 2011, 18 patients diagnosed with primary heart neoplasms were referred for surgical treatment, considering local characteristics and / or associated clinical manifestations. The patients' age at the time of admission ranged from one day to 12 years and 4 months, with a median of 18 days, and 78% of patients were aged 5 months or younger. Of the 18 patients, 9 were females. Individual data are shown in Table 1.

Regarding the surgical procedures, total resection, partial resection and tumor biopsy respectively were performed in 8, 8 and 2 cases. As associated procedures, lung biopsy in a patient, tricuspid valvuloplasty in one, mitral valve repair in another, and ligation of the ductus arteriosus associated with atrioseptoplasty in 2 patients were also performed.

The clinical manifestations were: dyspnea, heart murmur, enlarged cardiac silhouette, arrhythmia, and cyanosis, in respectively 7, 6, 3, 3 and 2 patients. In 9 patients, the exteriorization was made by one to three of these manifestations. In 8 patients, the echocardiography results raised the suspicion, with an intrauterine (fetal) diagnosis in 5.

Imaging diagnosis was achieved in 18 patients by echocardiography (Figures 1, 2, 3 and 4), and in 6 there was complementation by CT scan or MRI. In 2 patients, it was necessary to perform cardiac catheterization to achieve the diagnosis. Coronary artery involvement was detected in 3 patients, namely the anterior descending artery in 2 cases, one later diagnosed as rhabdomyoma and another as fibroma, and diagonal artery in another case, later diagnosed as leiomyoma.

As for the number of tumors, multiple tumors were observed in 5 patients, all subsequently diagnosed as rhabdomyomas, and single tumor in the others, with concordance with intraoperative findings in 15 cases. Regarding location, the right and left ventricles were the most affected ones (13 cases). Two patients had tumors located in the left atrium and two in the right atriaum, one with tumor adherence to the ascending aorta, and the other with simultaneous involvement of the right ventricle. In one patient, the tumor was identified beside the ascending aorta only (Table 2).

Cavitary obstruction or ventricular inflow or outflow tract was the reason for surgical indication in 12 cases. Two others had an obstructive phenomenon associated with pericardial effusion as indication. One patient had pericardial effusion and compression of the inferior vena cava; another had arrhythmia associated with coronary involvement.

The age at surgery ranged from 5 days to 12 years and 4 months, with a median of 18 days, and 78% of patients were 7 months or younger. The time between diagnosis and surgery ranged from hours to 109 days, with a median of 14 days.

The tumors were further characterized from the histopathological point of view as rhabdomyoma, fibroma, teratoma, myxoma, and leiomyoma (respectively 7, 5, 3, 2 and 1 case), as shown in Figures 1, 2, 3 and 4. The most common location was ventricular and there was no association between tumor type and the affected side. The location was atrial in 2 patients with myxomas and 2 others with teratomas. In two teratoma cases, tumor adherence to the ascending aorta was observed.

Relevant complications in the immediate postoperative period were complete atrioventricular block in 3 patients, difficult-to-control systemic hypertension in one, and low output syndrome in 3 others: one of them had seizures and another had a fatal outcome (fibroma, submitted to total resection). The second death occurred in the operating room due to heart failure and it was not possible to remove the CPB (patient with rhabdomyoma, submitted to partial resection). Sixteen patients were discharged from the hospital, 8 of them without any complications in the postoperative period.

Discussion

Changes in clinical practice and imaging method advancements have contributed to the increased number of cases of primary heart neoplasms diagnosed in children. In this study we observed the importance of a differential diagnosis of heart neoplasms in pediatric patients with often nonspecific cardiac symptoms. The imaging diagnostic method employed was basically echocardiography, with good correlation with intraoperative findings. Histopathological findings were consistent with the literature, with rhabdomyoma presenting as the most common tumor in children. The evolution after surgical treatment was favorable in most cases.

In recent years, noninvasive imaging techniques have been used to replace angiography for the diagnosis of heart neoplasms, with echocardiography, computed tomography and magnetic resonance imaging being the methods of choice. Several studies have shown that, since the introduction of two-dimensional echocardiography, there has been a significant improvement in early diagnosis. This is also related to the fact that more experienced professionals have been trained to perform the echocardiographic examination in the prenatal period and in children. Magnetic resonance imaging has been requested to supplement the echocardiographic findings, such as the differentiation between rhabdomyoma and fibroma (foci of calcification and/or cystic degeneration favoring the fibroma)[2,3]. Currently, angiography is seldom used, being indicated in cases where there is suspicion of coronary involvement or when there is doubt about the diagnosis through other noninvasive imaging methods[5].

Table 1 – Elapsed time between patient admission and surgical treatment

Patient	Sex	Weight (kg)	Height (cm)	Age at admission	Age at surgery	Elapsed time*
1	M	2.72	46.5	14 d	15 d	1 d
2	M	3.05	49	8 d	9 d	1 d
3	M	3.36	52	1 d	12 d	12 d
4	M	3.84	52	10 d	26 d	16 d
5	F	2.3	47	1 d	5 d	5 d
6	M	3.14	52	1 d	23 d	23 d
7	M	9.7	73	150 d	210 d	60 d
8	F	5.33	59	90 d	114 d	24 d
9	F	2.4	48	1 d	20 d	20 d
10	F	5.82	63	11 d	120 d	109 d
11	F	3.35	51	22 d	27 d	5 d
12	M	4.78	56	90 d	90 d	0
13	F	28	128	10 yr	10.08 d	30 d
14	F	23.5	122	8.91 yr	9 yr	25 d
15	M	25	120	5.567 yr	5.586 yr	7 d
16	M	6.65	59	147 d	147 d	15 d
17	F	42	150	12.326 yr	12.326 yr	1 d
18	F	3.5	48	4 d	17 d	13 d

d: day(s); yr: year(s).

Rhabdomyomas can be single, but in general are multinodular, being located, in most cases, within the ventricles. The echocardiogram usually shows multiple intramural masses, with intracavitary extensions[2,6,7].

Fibromas present as single tumors and their preferential location in the ventricular septum. Calcifications in its central portion are pathognomonic of fibromas, reflecting the scarce blood supply to the tumor[2,4,6].

Myxomas are usually single, pedunculated and attached to the fossa ovalis, with location in the left atrium in 90% of cases. This location and this kind of adherence are suggestive of the diagnosis[2,4,6].

Teratomas have a cystic aspect and are multilobulated, being commonly found in the pericardium or attached to the great vessels[6].

The prenatal diagnosis of heart neoplasms has been estimated at around 0.14% of gestations[6]. The most frequently found intrauterine alterations are: cardiac arrhythmia, polyhydramnios, presence of single or multiple mass, pericardial effusion, cardiomegaly, intrauterine growth retardation and fetal hydrops. The rhabdomyoma is the most common type of heart neoplasm identified at intrauterine diagnosis, being, in most cases, a routine obstetric ultrasound finding. It is important to emphasize that the diagnosis of fetal rhabdomyoma is more commonly attained after the 20th week of gestation, appearing as multiple intracardiac masses or manifesting as arrhythmias[4,7].

In the series by Padalino et al[6], 38% of the heart neoplasms were diagnosed in the prenatal period. Beghetti et al[3] reported 56 patients with heart neoplasms demonstrated by echocardiography, of which 12 had an intrauterine diagnosis. In our study, fetal diagnosis was attained in 5 patients, with 4 of them later confirmed as rhabdomyomas and one as fibroma.

The signs and symptoms of heart neoplasms depend on their location and size. Tumors can manifest as symptoms of cardiac flow obstruction, myocardial failure, arrhythmias, pericardial effusion, embolism or sudden death[2,6,8].

In rhabdomyomas, the manifestations of tuberous sclerosis help to clarify the diagnosis[9,10]. Cardiac rhythm disorders, including Wolff-Parkinson-White syndrome, are typical manifestations of rhabdomyomas[9]. Arrhythmias are observed in 16% to 47% of cases of rhabdomyoma[4]. According to Fenoglio et al[11], 78% of children with rhabdomyomas that are symptomatic and untreated died before the end of the first year of life. In fetal life, the manifestations are arrhythmias, heart failure, hydrops and stillbirth. In this study, the manifestations of rhabdomyoma cases were heart murmur, cyanosis, dyspnea and arrhythmia.

Myxomas usually manifest as cardiac flow obstruction and embolic processes. The release of emboli occurs in 40% of patients and is responsible for definitive or transient cerebrovascular accidents. Arthralgia, weight loss and night sweats are other symptoms that can be observed. Laboratory alterations such as normochromic anemia, elevated erythrocyte sedimentation rate, C-reactive protein and globulin levels, and thrombocytopenia, may occur in myxomas[2]. In our review, the initial clinical manifestations of myxomas were cardiomegaly, dyspnea and arrhythmia.

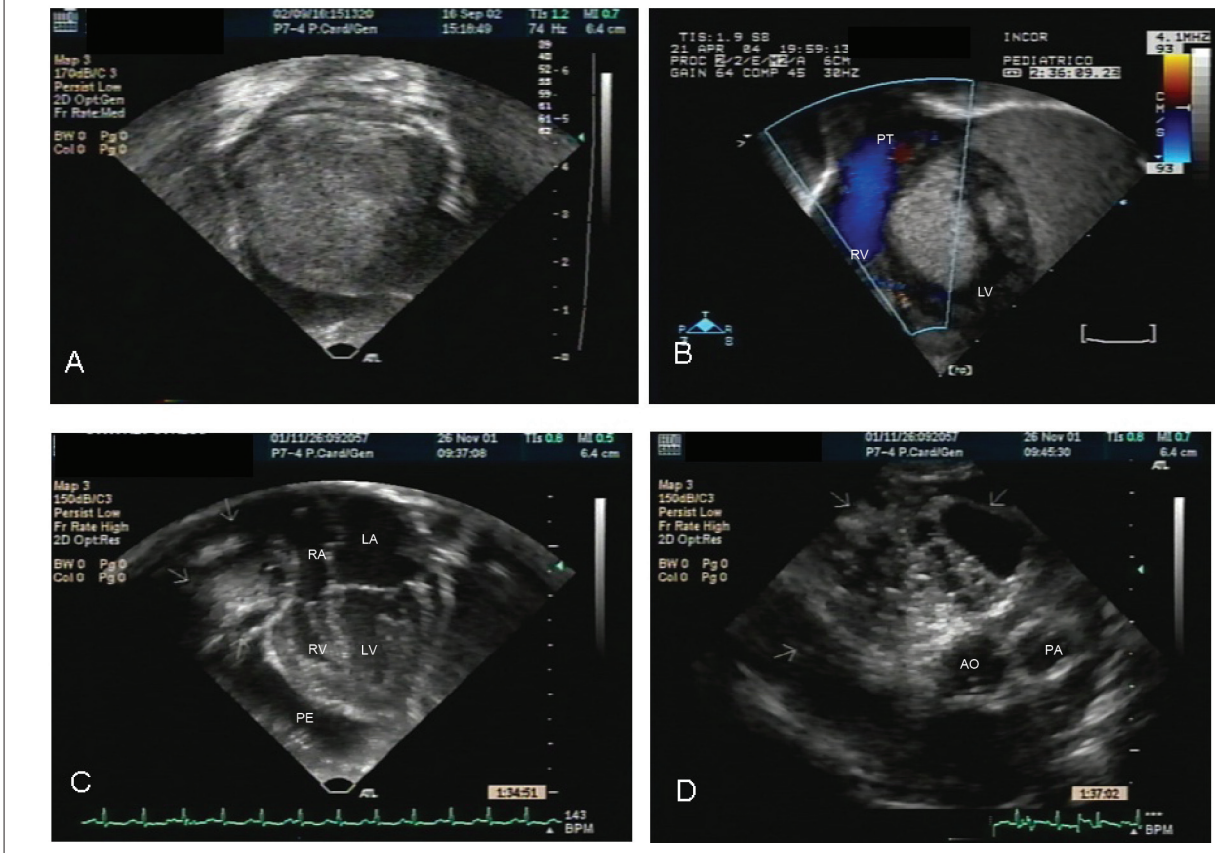

Figure 1 – 1a – *Echocardiographic image showing the left ventricle (LV) with its cavity nearly filled by the tumor mass (arrows), measuring 3 x 2 cm, later identified as a fibroma. This patient (case #9) was 3 hours old, asymptomatic, with a fetal diagnosis of heart tumor and pericardial effusion. Surgical treatment was based on tumor biopsy and pericardial drainage due to tumor extension, which showed no cleavage plane.* **1b** – *Echocardiogram in parasternal view, of neoplasm (arrows) affecting the left ventricle (LV), with free outflow tract. The neoplasm was classified as a rhabdomyoma after pathological analysis (case #6). PT: pulmonary trunk, RV: right ventricle, LV: left ventricle.* **1c** –*Echocardiogram in four-chamber view showing neoplasm (immature cystic teratoma - arrows) compressing the right atrium (case #11). RA: right atrium, LA: left atrium, RV: right ventricle, LV: left ventricle, PE: pericardial effusion.* **1d** – *Echocardiogram in parasternal view of immature cystic teratoma (arrows) in the region adjacent to the great vessels (case #11). AO: aorta, PA: pulmonary artery.*

Teratomas are rare primary heart neoplasms. Typically, they are located at the base of the great vessels, accounting for signs of extrinsic compression of these vessels[12]. We observed the presence of dyspnea, heart murmur, cardiomegaly and cyanosis as pre-diagnosis symptoms in cases of teratoma in our study. There was adherence to the ascending aorta in 2 of 3 cases of teratoma.

Indications for the surgical treatment of neoplasms include intractable arrhythmia, significant obstruction of ventricular inflow or outflow tracts, or evidence of embolization. In the absence of these symptoms, surgical intervention has been contraindicated or postponed.

In rhabdomyomas, the natural history is a favorable one. Several studies have reported spontaneous tumor regression with full resolution in more than 80% of cases during childhood[1,4].

In fibromas, however, the spontaneous regression is rare, and surgical treatment is recommended. The subtotal resection of larger tumors can be performed to prevent further loss of myocardial mass[4]. In the case of evolution to myocardial failure or impairment of a large cardiac area, with the impossibility of complete tumor removal, heart transplantation should be considered[4]. Conservative treatment in asymptomatic patients is controversial for this tumor type. Studies have shown the occurrence of sudden death due to arrhythmia in patients with fibromas[3].

The complete surgical excision of the teratoma is generally curative, without the need for cardiopulmonary bypass in most cases[6]. However, tumor recurrence or malignization has been reported[4].

Myxomas should be removed with a portion of adjacent cardiac tissue, due to the possibility of recurrence. According to Uzun et al[4], there was recurrence in 5% of cases in which incomplete tumor resection was performed. In cases where the resection was complete, survival was 100% after 16 years of postoperative follow-up[6].

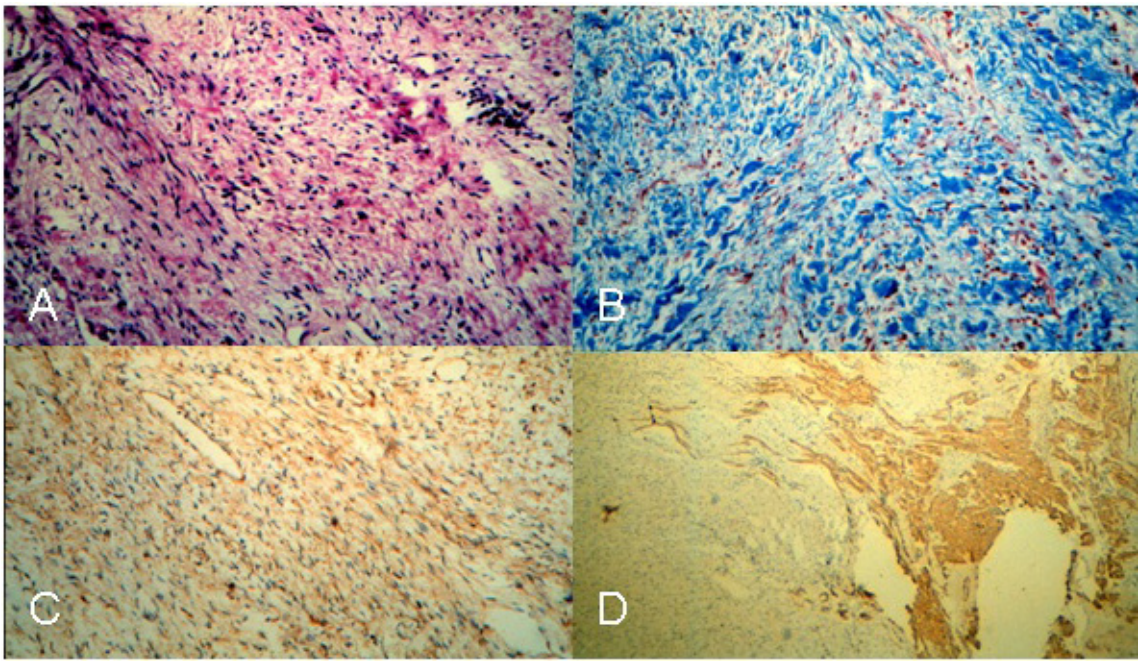

Figure 2 – *Photomicrographs of a cardiac fibroma (case #8).* **In A**, *the spindle cell pattern can be observed.* **In 2B**, *dense stromal fibrosis can be observed.* **In 2C**, *tumor cells are marked by vimentin, and* **in 2D** *they are negative for muscle actin. The asterisk shows positive cardiac muscle cells in the periphery. Stains: A - hematoxylin-eosin; B - Trichrome Masson, C - immunohistochemical staining for vimentin, D – Actin-marked.*

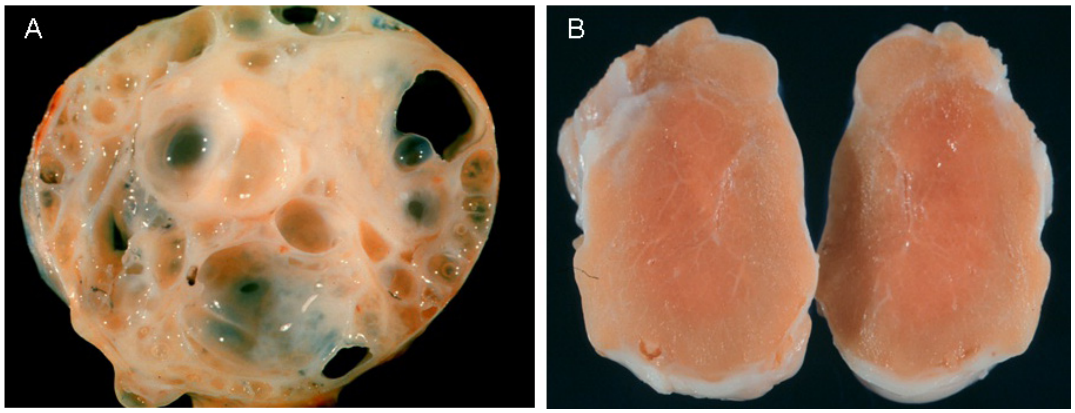

Figure 3 – 3A: *Macroscopic aspect of an adult teratoma, showing numerous cysts with delicate walls (case #12).* **3B**: *Macroscopic view of the cut surface of a rhabdomyoma. Whitish fibrous thickening are seen externally (case #4).*

Macroscopically, rhabdomyomas are usually multiple, disclosing a whitish nodular image, almost always involving the ventricles. Microscopically, they appear as large ovoid vacuolated cells, loaded with glycogen. The spider cells (Figure 4) are typical rhabdomyoma cells. The fibroma has as microscopic characteristic the proliferation of fibroblasts interspersed with collagen and elastic fibers. They are solid, with whitish lesions and have myocardial tissue around them. Myxomas are usually pedunculated and gelatinous, with a predilection for the fossa ovalis region in the left atrium. Microscopically, they are uniform, small and polygonal cells, with eosinophilic cytoplasm, myxoid matrix rich in polysaccharides and irregular nucleus. Teratomas are pale cystic masses, lobulated, filled with fluid and contain multiple immature tissues (epithelium, pancreas, skeletal muscle). They are encapsulated, single and adhered, in most cases, to the great vessels or located between the aorta and superior vena cava[11,13,14].

This study is limited by its retrospective nature and by the fact that it does not assess the late evolution of children submitted to surgery.

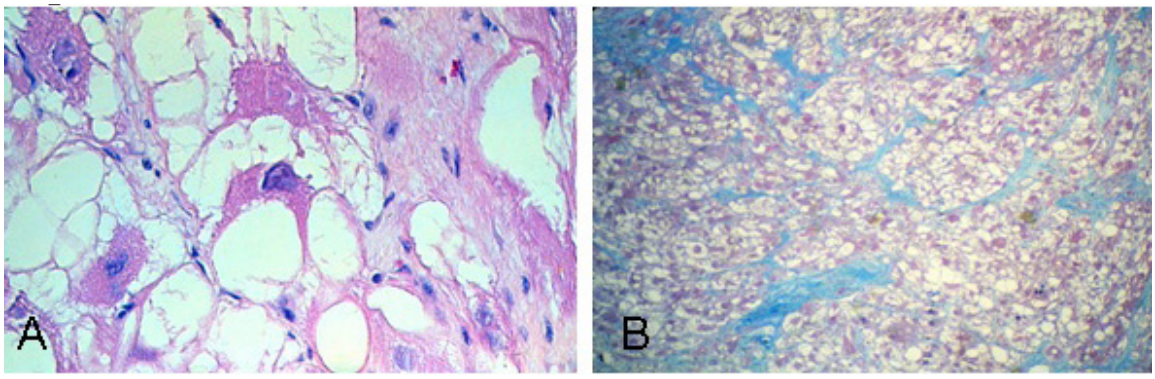

Figure 4 – *Photomicrographs of a rhabdomyoma (case # 3). In* **4A**, *the characteristic cells are observed, the so-called "spider cells" with delicate cytoplasmic projections and extensive vacuolization. In* **4B**, *cell blocks are separated by fibrous connective tissue (blue). Stains: A - hematoxylin-eosin; B - Masson Trichrome.*

Table 2 – Data on the pathological analysis, size and location of the resected heart neoplasms

Patient	Neoplasm	Size (cm)	Location
1	Rhabdomyoma	2.5x1.8x1.0 / 1.2x1.0x0.8	LV
2	Rhabdomyoma	1.1x0.8x0.4	LV
3	Rhabdomyoma	0.7 and 0.7	RV and LV
4	Rhabdomyoma	3.0x2.0x2.0	RV
5	Rhabdomyoma	2.3x1.5x1.3	LV
6	Rhabdomyoma	4.0x2.0x1.0	LV
7	Fibroma	5.0x5.0x1.0	RV
8	Fibroma	5.5 in diameter	RV
9	Fibroma	1.4x0.5x0.2	LV
10	Immature cystic teratoma	5.5x3.7x3.7	Pedunculated at ascending AO
11	Immature cystic teratoma	4.0x3.0x2.0	Adhered to RA
12	Immature cystic teratoma	4.3x4.0x3.5	Pedunculated between the ascending AO and SVC
13	Leiomyoma	NR	LV
14	Myxoma	7 in diameter	LA
15	Fibroma	4x3.5x2.5	LV
16	Fibroma	6x6x1.5	LV
17	Myxoma	8x5	LA
18	Rhabdomyoma	3x2.5	RV

RA: right atrium, LA: left atrium, RV: right ventricle, LV: left ventricle, SVC: superior vena cava, AO: aorta, NR: not reported.

Conclusions

Primary heart neoplasms are important diagnoses that must be recalled in pediatric patients. In this study, the diagnostic imaging with echocardiography basically showed good correlation with the intraoperative findings. Histopathological findings were consistent with the literature, with rhabdomyoma being the most common tumor in children. The evolution after surgical treatment was favorable in most cases.

Author contributions

Conception and design of the research: Penha JG, Zorzanelli L, Jatene MB; Acquisition of data: Penha JG, Zorzanelli L, Aiello VD, Caneo LF, Riso AA, Tanamati C, Jatene MB; Analysis and interpretation of the data: Penha JG, Zorzanelli L, Carvalho VO, Caneo LF, Riso AA, Tanamati C, Atik E, Jatene MB; Writing of the manuscript: Penha JG, Zorzanelli L, Barbosa-Lopes AA, Carvalho VO; Critical revision of the manuscript for intellectual content: Penha JG, Barbosa-Lopes AA, Aiello VD, Carvalho VO, Atik E, Jatene MB.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Study Association

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