

Surgical Treatment of Primary Cardiac Tumor Associated with Malignant Arrhythmias

Yongqiang Jin, Xiaomei Li, Rui Liu, Guoliang Chen, Xiaoya Zhang, Qingyu Wu

Heart Center, The First Hospital of Tsinghua University (Beijing Huaxin Hospital), Beijing, China

ABSTRACT

Objective: Pediatric primary cardiac tumor is an extremely rare disease. The tumor can extend into the conduction system and cause malignant arrhythmias. We retrospectively reviewed 6 consecutive cases of children with primary cardiac tumor that manifested as rhythm disturbance.

Methods: In our center, 6 children were enrolled from October 2009 to August 2016. Detailed operative data and follow-up information were comprehensively collected and statistically analyzed.

Results: The patients were ages 1 to 16 years and weighed 7.9 to 44.5 kg. Preoperative ventricular tachycardia was present in 3 patients, frequent ventricular ectopic beats in 1 patient, supraventricular tachycardia in 1 patient, and atrial flutter in 1 patient. All 6 patients underwent a complete tumor resection. The tumors were localized in the left ventricular free wall (3 patients), left ventricular outflow tract (1 patient), left atrium (1 patient), and right atrium (1 patient). One patient received 2 radiofrequency ablation procedures before tumor resection. Postoperative sick sinus syndrome occurred in 1 patient because the tumor infiltrated the sinoatrial node. Tumors from 2 patients were pathologically diagnosed as fibroma and 4 as rhabdomyoma. Reoperation of mitral valve repair was performed in 1 patient 1 year after tumor resection. The mean (\pm SD) follow-up time was 63.7 ± 31.4 months, and all children were well, with Ross functional classification I and no signs of recurrence or metastasis.

Conclusions: In conclusion, cardiac tumor is a rare but nonneglectable reason for arrhythmia, and surgical resection is the optimal procedure, with satisfactory results.

INTRODUCTION

Pediatric primary cardiac tumors are extremely rare, with estimated prevalence between 0.027% and 0.08% [Nadas 1968; Isaacs 2004]. Clinical manifestations are

Received December 5, 2019; received in revised form January 27, 2020; accepted January 30, 2020.

Correspondence: Qingyu Wu, Heart Center, The First Hospital of Tsinghua University (Beijing Huaxin Hospital), No. 6 Jiuxianqiao 1st Road, Chaoyang District, Beijing, 100016, China; 86-010-64308261 (e-mail: wuqingyu@mail.tsinghua.edu.cn).

variable, as the masses differ in terms of size, location, multifocality, and extent of invasion. Patients with tumor can be asymptomatic or present with outflow tract obstruction, congestive heart failure, arrhythmia, respiratory distress, pericardial effusion, syncope, and even sudden death [Xu 2017]. When tumors extend into the conduction system, they can cause arrhythmias. It has been reported that clinically significant arrhythmias (cardiac arrest, ventricular fibrillation, ventricular tachycardia, supraventricular tachycardia, etc.) occur in approximately one-quarter of pediatric tumors [Xu 2017]. Surgical resection of tumors is an effective option. In recent years, 6 consecutive pediatric patients with primary cardiac tumors and associated arrhythmias received total tumor resection surgery in our center. Herein, we describe our center's experience in treating these patients.

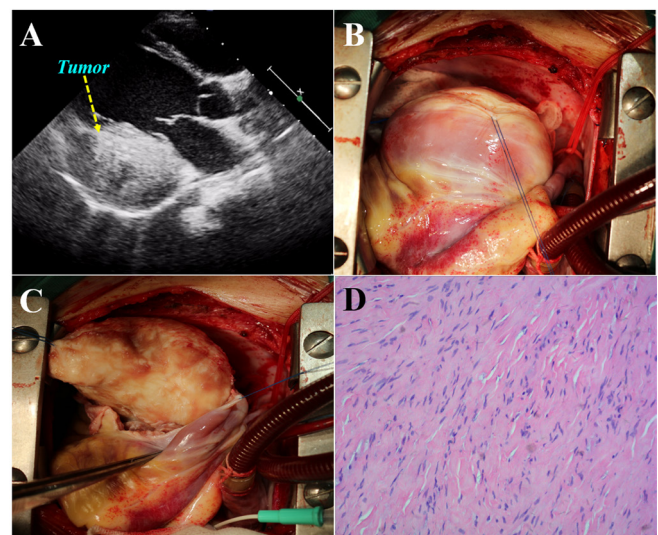


Figure 1. Echocardiography examination and operative and pathologic findings of a large left ventricle fibroma (patient 2, preoperative frequent ventricular ectopic beats). A, Echocardiography shows a well-defined hyperechoic mass with diameter $\sim 51 \times 58$ mm on the left ventricular posterior wall. B, Perioperatively, tumor was apparent on the left ventricular posterior wall. C, The surgeon sharply stripped and radically resected the tumor body. D, Pathologic results showed that tumor cells were arranged in fascicles; muscle tissue (dyed brown) and fibrous tissue (dyed red) were of mixed distribution (hematoxylin and eosin stain, 20×10).

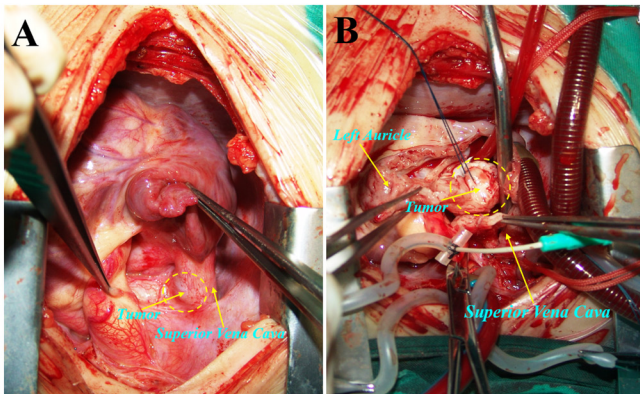


Figure 2. Perioperative findings of a pediatric rhabdomyoma infiltrating the sinoatrial node. The child was diagnosed with sick sinus syndrome postoperatively (patient 3, preoperative atrial flutter). A, The tumor was located in the right atrium and widely extended to the superior vena cava. B, The left atrium and superior vena cava were excised, and the tumor was sharply stripped and radically resected.

METHODS

All subjects' parents gave their written informed consent, and the study protocol was approved by the institute's committee on human research (in accordance with Declaration of Helsinki) and the ethics committee of our hospital. We retrospectively reviewed all 6 consecutive pediatric patients who presented to our institution from October 2009 to August 2016 with rhythm disturbances and were diagnosed as having cardiac tumor. Records were collected for all information including demographic characteristics, narrative history, electrocardiography (ECG), 24-h Holter monitors, electrophysiological examinations, echocardiography, chest x-ray, chest computed tomography (CT), cardiac magnetic resonance imaging (MRI), operative details, postoperative data, and pathologic diagnoses. Clinically significant arrhythmias were defined according to Miyake [2011]. After discharge, follow-up data were collected through clinical consultations and regular telephone interviews. Statistical analysis was performed with SPSS software (version 22.0, IBM Corp., Armonk, NY). Normal data are presented as mean \pm SD, and nonnormal data are presented as median and range.

RESULTS

General Data

A total of 6 consecutive patients were selected for the surgical series (2 males and 2 females; mean age at operation, 5.8 ± 5.5 years; median 4.7; range 1 to 16). Their main clinical presentations were all rhythm disturbances. Preoperative ECG and 24-h Holter monitor showed that ventricular tachycardia (VT) was present in 3 patients, frequent ventricular ectopic beats in 1 patient, supraventricular tachycardia (SVT) in 1 patient, and atrial flutter/atrial fibrillation (AF) in 1 patient. The masses were detected

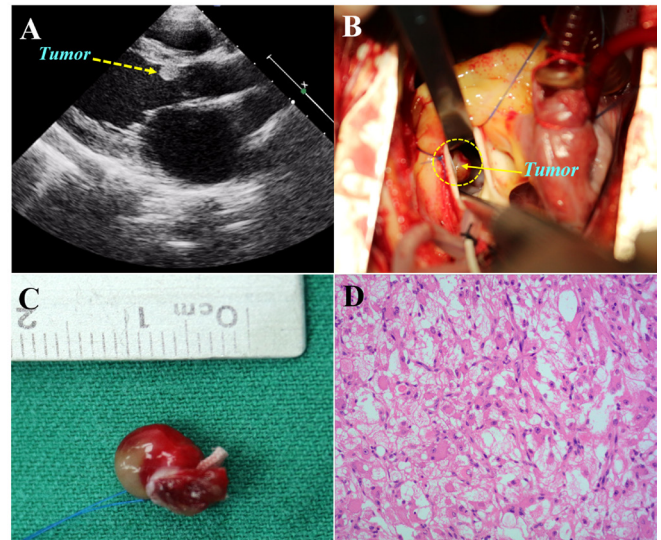


Figure 3. Echocardiography examination and operative and pathologic findings of a left ventricular outflow tract (LVOT) rhabdomyoma that caused refractory VT (patient 6, preoperative VT). A, Echocardiography showed a well-defined hyperechoic mass with diameter 6.7×5.0 mm at LVOT. B, The aorta was excised, and the tumor was exposed. C, The tumor was of extremely small size. D, Pathologic results show typical spider-like cells in the middle of rhabdomyoma cells (hematoxylin and eosin stain, 20×10).

by echocardiography (all 6 cases), CT (4 cases), and MRI (3 cases) for a complete diagnosis. The mass was localized in the left ventricular free wall (3 patients), left ventricular outflow tract (1 patient), left atrium (1 patient), and right atrium (1 patient). Details of patients' characteristics are shown in Table 1.

Operative Details

We followed the concept of radial excision of tumors whenever feasible; thus all 6 children underwent a complete resection. Surgery was performed through a median sternotomy under cardiopulmonary bypass (CPB) with bicaval and ascending aortic cannulation and moderate systemic hypothermia (30 to 32°C). Associated procedures included left ventricular patch reconstruction in a 7-year-old girl (patient 2), as the tumor had widely invaded the left ventricle (Figure 1). The mean CPB time was 80.0 ± 36.1 minutes (range 36 to 136). The mean aortic cross-clamping (ACC) time was 56.0 ± 38.3 minutes (range 10 to 121). The median mechanical ventilation was 10.8 ± 6.1 hours (range 6 to 22.6). The median intensive care unit length of stay was 2.2 ± 1.7 days (1 to 9). The sizes of masses were 5, 6, 10, 51, 35, and 59 mm. It was pathologically confirmed that 4 cases were rhabdomyoma and 2 cases were fibroma. Further operative details are shown in Table 2.

Early Outcome

All patients survived. There was no postoperative low cardiac output syndrome, pericardial and pleural effusion requiring drainage, multiple organ dysfunction syndrome, or thromboembolic event. One patient (patient 3) was diagnosed

Table 1. Detailed characteristics of enrolled patients

No.	Gender/ Age	Weight (kg)	Symptoms	X-ray (CTR)	ECG	24-hour-Holter monitors	Preoperative antiarrhythmic medications	Tumor size (mm)	Surgery
1	M/4y7m	19.9	Recurrent tachycardia	0.51	HR: 250 bpm, wide QRS complex tachy- cardia, atrial-ventricu- lar dissociation	Sinus rhythm, combined with frequent ventricular ectopic beats, sometimes double or multiple.	Amiodarone, Metoprolol	30×33×27	Complete excision
2	F/7y4m	23.6	Palpitation	0.61	HR:122 bpm, frequent ventricular ectopic beats	Ventricular ectopic beats ac- count for 53.9%, with 76321 beats in 24 hours.	Amiodarone, Metoprolol	51×35×59	Complete exci- sion + left ven- tricular patch reconstruction
3	F/1y2m	12	Recurrent tachycardia	0.56	Atrial flutter, atrial rate: 300 bpm, 2:1 conducted to ventricle	Total beats were 158 997 in 24 hours. HR was 49-220 bpm and the average was 110 bpm. Atrial flutter or atrial fibrilla- tion account for 99%.	Propranolol, Sotalol	15×19×19	Complete excision
4	M/1y	7.9	Recurrent tachycardia		HR:260-280 bpm, sus- tained supraventricular tachycardia	N/A	Amiodarone, Metoprolol, Propranolol, Sotalol	17×20×13	Complete excision
5	F/16y	44.5	Palpitation	0.40	HR: 158 bpm, par- oxysmal ventricular tachycardia	Total beats were 117 130 in 24 hours, with 388 polymorphic ventricular ectopic beats, 34 ventricular bigeminy, 95 non- sustained ventricular tachy- cardia. HR was 159-170 bmp when ventricular tachycardia.	Verapamil, Amiodarone, Metoprolol	32×23×21	Complete excision
6	F/4y9m	17.9	Recurrent tachycardia		HR: 136 bpm, ven- tricular tachycardia	N/A	Amiodarone, Metoprolol, RFA (twice)	6×5×10	Complete excision

CTR cardiac thoracic ratio, RFA radiofrequency ablation

with sick sinus syndrome (SSS) postoperatively, because the mass localized in the right atrium and infiltrated the sinoatrial node (Figure 2). The patient received oral sotalol (a nonselective β -blocker) without any obvious discomfort. The other 5 patients were discharged in good clinical condition.

Follow-Up

The mean duration of follow-up was 63.7 ± 31.4 months (range 26 to 112). Reoperation for mitral valve repair was performed in 1 patient with multiple masses (patient 4). In the initial operation, we found that the masses were close to the anterior mitral leaflet. Echocardiography early after surgery showed mild mitral valve regurgitation, but after 1 year, the patient had progressively severe mitral valve regurgitation. During follow-up, patient 3 felt no discomfort with medication therapy. The other 4 patients were all well, with Ross functional classification I, free from any adverse events, without taking any medication, and with no signs of recurrence or metastasis.

DISCUSSION

Pediatric primary cardiac tumor is an extremely rare heart disease. Neoplasms can grow anywhere within the cardiac chambers or in the myocardium. More than 90% of tumors are benign [Tzani 2017]. As tumors differ in term of size, location, multifocality, growth rate, and extent of invasion, clinical patterns vary greatly. Some children can remain asymptomatic until adulthood. Some may experience complications such as obstruction of outflow tracts, compression of coronary artery, thromboembolism, and refractory arrhythmias [Shi 2017]. With the emergence of new noninvasive imaging techniques such as echocardiography, CT, and MRI, earlier diagnoses and treatment of pediatric cardiac tumor have become available [Kwiatkowska 2017].

If tumor invades the conduction system, it might cause various rhythm disturbances, which is an important manifestation for pediatric patients. Miyake [2011] defined the clinically significant arrhythmias for pediatric patients as follows:

Table 2. Operative details and early postoperative results

No.	CPB (min)	ACC (min)	MV (h)	ICU (h)	Tumor location	No. of masses	Pathological diagnoses
1	36	30	8	21	LV	1	fibroma
2	136	121	12	39	LV	1	fibroma
3	106	72	6	117	RA	1	rhabdomyoma
4	78	53	22	89	LA, LV	3	rhabdomyoma
5	70	50	7	22.5	LV	1	rhabdomyoma
6	54	10	10	33	LVO	1	rhabdomyoma

CPB cardiopulmonary bypass, ACC aortic cross-clamping, MV mechanical ventilation, AO aorta; LV left ventricle, RA right atrium, LA left atrium, IAS interatrial septum, LVO left ventricular outflow

(1) sudden cardiac arrest with documented or suspected ventricular fibrillation, (2) ventricular tachycardia, (3) manifest pre-excitation, and (4) supraventricular tachycardia. They confirmed that when these arrhythmias are present, surgical resection of masses was strongly advocated. According to those definitions, all of our patients had clinically significant arrhythmias with surgery obviously indicated. Notably, our results demonstrated a close relationship between the location of masses and the episodes of arrhythmia. The reason may be that the masses encroach into the cardiac conduction system and interfere with electrical conduction to cause arrhythmia.

For the diagnoses of tumors, echocardiography has an obvious diagnostic value and can be the primary imaging method applied in children, because it can correctly show the location and size of tumors. Echocardiography is also very sensitive to hemodynamic changes and helps to determine the timing of surgery. All patients in our series received echocardiography to identify the location and size of tumors and sufficiently evaluate hemodynamic changes. In addition, CT and MRI are of significant importance in helping make a confirmed diagnosis and gain more information for surgery strategy.

For the timing of surgery, the multicenter European Congenital Heart Surgeons Association Study confirmed that surgery is advocated with symptoms, ECG abnormalities, or apparent echocardiographic impairment [Padalino 2012]. A study by Delmo [2016] suggested that the indications for surgery included hemodynamic disturbances, respiratory distress, severe arrhythmia, and significant embolization risk. A Chinese study indicated that the resection of tumors should be undertaken as soon as possible after masses are found [Wang 2016]. In our series, all 6 children had symptomatic arrhythmias and apparent indication for surgery.

The strategy we follow is radical excision of tumors whenever feasible. Refined and gentle manipulation is suggested so as not to cause tumor fragmentation and embolism. On the premise of not damaging adjacent tissue structures, the masses should be completely excised to avoid the regrowth of tumors. In this series, all 6 pediatric patients received total resection. The results showed that surgery effectively terminated arrhythmias in all 6 cases. During follow-up, all patients

had satisfactory outcomes. Our experience suggests that total resection is a safe and effective strategy for children with primary cardiac tumor and associated arrhythmias.

Our experience also indicates that for refractory and malignant arrhythmias, aggressive surgical intervention is the optimal option. Patient 6 received radiofrequency ablation (RFA) twice because of repeated episodes of VT; however, VT was still present. Echocardiography was rechecked, and a mass beneath the right coronary cusp was found (Figure 3). Although the mass was small in size, it was strongly correlated with the marked site in electrophysiological mapping. Finally, a total resection of the mass was performed (Figure 3). The patient's VT was completely eliminated in the postoperative period. Based on the experience of this case, indications are that arrhythmias resulting from the cardiac mass were refractory, and poor results are achieved with antiarrhythmic medication or RFA. For these patients, physicians should consider whether resection of a mass is indicated, regardless of tumor size.

In conclusion, pediatric primary cardiac tumor is a very rare disease. Some patients can manifest with symptomatic arrhythmias. Surgical resection of tumor is the optimal procedure to terminate arrhythmias, with satisfactory early and late results.

ACKNOWLEDGMENT

We thank all parents of the 6 children enrolled in this study.

REFERENCES

- Delmo Walter EM, Javier MF, Sander F, Hartmann B, Ekkernkamp A, Hetzer R. Primary cardiac tumors in infants and children: Surgical strategy and long-term outcome. *Ann Thorac Surg*. 2016; 102(6):2062-2069.
- Isaacs JH. Fetal and neonatal cardiac tumors. *Pediatr Cardiol*. 2004; 25:252-273.
- Kwiatkowska J, Wałdoch A, Meyer-Szary J, Potaż P, Grzybiak M. Cardiac tumors in children: A 20-year review of clinical presentation, diagnostics

and treatment. *Adv Clin Exp Med*. 2017; 26(2):319-326.

Miyake CY, Del Nido PJ, Alexander ME, et al. Cardiac tumors and associated arrhythmias in pediatric patients, with observations on surgical therapy for ventricular tachycardia. *J Am Coll Cardiol*. 2011; 58(18):1903-1909.

Nadas AS, Ellison RC. Cardiac tumors in infancy. *Am J Cardiol*. 1968; 21:363-366.

Padalino MA, Vida VL, Bocuzzo G, et al. Surgery for primary cardiac tumors in children: Early and late results in a multicenter European Congenital Heart Surgeons Association study. *Circulation*. 2012; 126(1):22-30.

Shi L, Wu L, Fang H, et al. Identification and clinical course of 166 pediatric cardiac tumors. *Eur J Pediatr*. 2017; 176(2):253-260.

Tzani A, Doulamis IP, Mylonas KS, Avgerinos DV, Nasioudis D. Cardiac tumors in pediatric patients: A systematic review. *World J Pediatr Congenit Heart Surg*. 2017; 8(5):624-632.

Wang ZF, Yin Q, Yang Y, et al. Clinical analysis of 48 cases of cardiac neoplasm. *Chinese Journal of Extracorporeal Circulation*. 2016; 14(4):226-228.

Xu Z, Wu Q, Li H, Zhang M. Surgical resection of giant left ventricular fibromas in children. *J Card Surg*. 2017; 32(10):662-664.