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Cardiac myxomas: Short- and long-term follow-up

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Abstract

Background: *Cardiac myxomas are the most frequently encountered benign intracardiac tumors, that, if left untreated, are inexorably progressive and potentially fatal. Patients with cardiac myxoma can be treated only by surgical removal. This study summarizes our experience over 22 years with these tumors.*

Methods: *Fifty seven patients (M/F: 14/43, age: 57.9 ± 14.6 years) with cardiac myxomas underwent surgical resection at our institution. There were 82.4% left atrial myxomas, 14.0% right atrial myxomas, 3.6% biatrial myxomas. The duration of symptoms prior to surgery ranged from 6 to 1,373 days (median 96 days). The surgical approach comprised complete wide excision. The diagnostic methods, incidence of thromboembolic complications, valve degeneration, surgical repair techniques, recurrence and re-operation were reviewed and the Kaplan-Meier survival curve was calculated.*

Results: *There were no in-hospital deaths. Hospital stay amounted to a mean of 13.7 ± 6.9 days. Late follow-up was available for 54 (94.7%) patients for a median 7.5 years after surgery (23 days to 21.4 years). Fifty two patients are alive, while five patients had died after a mean interval of 6.3 years. Cause of death was cardiac in 40% of the patients (n = 2) and non-cardiac in the other 60% (n = 3).*

Conclusions: *Surgical excision of cardiac myxoma carries a low operative risk and gives excellent short-term and long-term results. Surgical excision of the tumor appears to be curative, with few recurrences at long-term follow-up. After diagnosis, surgery should be performed urgently, in order to prevent complications such as embolic events or obstruction of the mitral orifice. Follow-up examination, including echocardiography, should be performed regularly.*(Cardiol J 2009; 16, 5: 447–454)

Key words: atrial myxoma, cardiac tumors, cardiac surgery

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Introduction

Cardiac myxomas can occur at any age, with two peaks in the third and sixth decade of life, most frequently observed in women [1–6]. They arise from the endocardial tissue. Between 75 and 83% of cardiac myxomas are located in the left atrium, 10–18% are located in the right atrium where they often show a predilection area close to the oval fossa. Morphologically they commonly present with a pedicle 1–2 cm long determining the mobility of the tumor. Tumor prolapse through the mitral or tricuspid valve can lead to destruction of the valve or the annulus [7].

Myxomas are less frequently seen in the ventricles, there again showing a preference for the right side [1, 2, 4, 5, 8, 9]. More than 95% of atrial myxomas appear solitary, but a multifocal intracardiac growth is possible [5, 9, 10]. Most of these myxomas show a pedicle. Solid tumors are ovoid-round, elastic and smooth, whereas papillary tumors are lobulated and gelatinous and are more likely to embolize to the cerebral and other peripheral vessels [2, 3, 5, 7, 11]. The average size is about 5–6 cm with an average weight of 46 g. The rate of growth is not exactly known [7, 12, 13].

Relating to histology they show a stroma containing few cells but plenty of mucopolysaccharides, often with peripheral hemorrhage and necrosis. On rare occasions, calcifications can be seen [3, 5]. In the past, immunohistochemical and histological studies classified benign cardiac myxomas as real neoplasms that develop from embryonic pluripotent mesenchymal stem cells. These undifferentiated cells can transform and proliferate into tumor cells [5, 14]. An explanation for the preferential tumor localisation at the oval fossa is based on the thesis that the interatrial septum is the last structure developing from fetal mesenchyma, containing the most immature tissue.

The histogenesis of cardiac myxomas has been a subject of controversy. Although they are histologically classified as benign, they show biologically malignant symptoms. In up to one quarter of operated patients. local recurrence can be seen, sometimes associated with sporadic locally invasive growth [15].

Often, the first manifestation of intracardiac tumors is embolization into cerebral and peripheral vessels. A tumor-associated embolization can be detected in 30–60% of patients with a localisation of the myxoma in the left heart. Sometimes histopathology of an embolus can lead to diagnosis of a primary heart tumor [2, 4, 5, 16–19].

Embolizations can be caused by blood clots adherent to the tumor or tumor fragments. Fragments from the right heart can cause inflammation of the pleura with consecutive pleural effusion, pulmonary hypertension or pulmonary embolism [4, 5, 18, 20]. Fragments from the left heart can cause emboli in almost any organ, but are most frequently seen in the brain, kidneys, lower extremities or the aorto-iliacal region [2, 21, 22]. Especially neurological symptoms are frequently seen in young patients, i.e. transient ischemic attack, stroke, spinal or retinal infarction [22, 23]. Another dramatic appearance is the embolization into the coronary arteries [2]. Multiple organic emboli can include many organs; differential diagnosis must include systemic vascular diseases and bacterial endocarditis, especially in the absence of typical symptoms of obstruction or common tumor symptoms [11].

Methods

All patients undergoing cardiac myxoma excision at the Department of Cardiothoracic and Vascular Surgery, Johannes Gutenberg-University, Mainz, Germany, from January 1985 to December 2008 were identified from a retrospective chart review. This study includes preoperative, short- and long-term follow-up data. Telephone interviews by standard questionnaire with all living patients were taken, with the patients' general practitioner or specialist consulted for long-term follow up data.

The study was approved by the local bioethical committee and all patients gave their informed consent.

For descriptive presentation of the results, nominal variables were evaluated as absolute and percentage figures, quantitative and ordinal variables were presented as mean, median, minimum and maximum. Relations between categorical variables were investigated with contingency tables and χ^2 test. Post-operative survival was determined by Kaplan-Meier procedure. All tests were used for descriptive data analyses. A p-value < 0.05 was considered statistically significant.

Results

Eighty nine patients with primary or secondary heart tumor were operated in the Department of Cardiothoracic and Vascular Surgery at Johannes Gutenberg-University, Mainz, Germany, between January 1985 and December 2008. Figure 1 shows the fragmentation of the histological subtypes of all cardiac tumors. In our study, we focus on the patients with cardiac myxomas (n = 57) (Table 1).

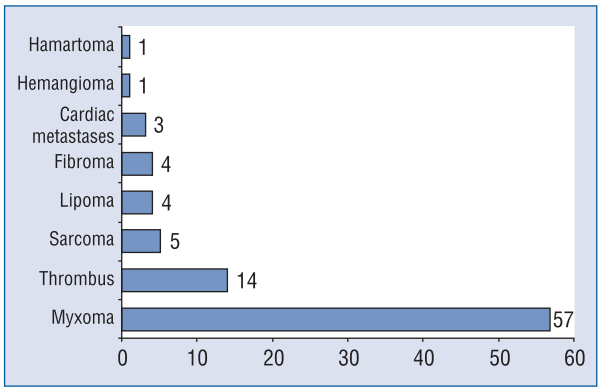

Figure 1. The fragmentation of the histological subtypes of all cardiac tumors (n = 89).

Table 1. Clinical characteristics of the study population.

Patients	57
Age at operation	57.9 ± 14 years
Sex (males/females)	14/43
Duration of symptoms prior to surgery	6–1,373 days (median 96 days)
Coronary angiography	35
Coronary surgery	5
Operation electively	44
Operation urgent	9
Operation emergency	4

For cardiac strength and congestive heart failure (CHF) the New York Heart Association (NYHA) classification was used. Twenty seven (47%) patients were NYHA I, 18 (32%) patients NYHA II, 10 (17.5%) patients NYHA III, and two (3.5%) patients NYHA IV.

In 27 patients (47.5%) their specific symptoms did not change their quality of life; 20 patients (35%) felt a reduction of quality of life; and 10 patients (17.5%) complained of a substantial loss of quality of life, even their ability to handle everyday life.

Electrocardiography was performed in every patient; 34 patients (59.6%) showed a sinus rhythm, seven (12.3%) patients each showed multiple atrial and ventricular extra systoles, 16 patients (28.1%) showed continuous arrhythmia.

In 19 (82.6%) of 23 arrhythmic patients, the myxoma was located in the left atrium, in two patients (8.7%) it was located in the left and right atrium, and in two patients (8.7%) it was located in the right atrium.

Coronary angiography was performed in 35 patients (61.4%) and five cases of coronary artery disease needing surgery were detected. Transthoracic echocardiography was employed in 57 patients, in all cases (100%) the estimated diagnosis could be verified. In this investigation 47 (82.4%) of the tumors were located in the left atrium, eight (14.0%) in the right atrium and in two (3.6%) the tumor was located both in the left and right atrium. Additionally to these findings, a tumor prolapse into the adjoining cavity of the heart could be observed in 12 cases (21.0%). In addition, a disturbance of intracardiac blood flow was observed in six patients (10.5%), a mitral valve disturbance in two patients (3.5%), and anterior wall hypokinesis in one patient (1.7%). Additionally, computerized tomography (CT scan) and also magnetic resonance imaging (MRI) of the thorax were carried out in four cases each. These additional diagnostic imaging techniques confirmed the findings of the echocardiography. In one patient the pre-operative diagnosis was confirmed by biopsy of a myxoma located in the right atrium.

The surgical excision of the tumors was performed through median sternotomy with cardiopulmonary bypass in cardioplegic arrest. The mean stay in intensive care unit was 3.4 days (minimum: 1 day, maximum: 13 days).

Forty four (77.2%) cases of tumor excision were operated electively, nine (15.8%) cases were classified as urgent, and four (7.0%) cases were classified as emergency due to life-threatening symptoms.

In 55 (96.5%) patients, a complete tumor excision was performed, two (3.5%) patients required a second look resection for complete wide excision. A right atrial and transseptal surgical approach was used for tumor location in the left atrium, a right atriotomy only for tumor location in the right atrium. Additionally, five patients required a coronary artery bypass grafting operation (two single, and three triple).

Intraoperatively, in one patient the tumor was broadly based including the whole atrial septum and the upper wall of the left atrium. The upper wall was reconstructed with an autologous pericardial patch, the intraatrial septum with a Dacron patch.

One patient showed a right atrial myxoma with a transseptal growth into the left atrium. A complete wide excision was accomplished; the septum was repaired with a Dacron patch.

A local recurrence of a left atrial myxoma occurred one year after primary operation and included the left atrial upper wall, the atrial septum, and both mitral valve leaflets.

During a second look operation, a complete wide excision was performed including the whole atrial septum, left atrial upper wall and both mitral valve leaflets. The mitral valve was replaced with a mechanical valve. For reconstruction of the left atrial upper wall a free pericardial patch was used, for the atrial septum a Dacron patch was used, and for reconstruction of right atrial geometry an autologous pericardial patch was used.

Intraoperative complications were caused by prolonged bleeding from the left atrial upper wall in one patient, and prolonged cardiopulmonary bypass caused by arrhythmia in four patients (atrial fibrillation n = 1, atrio-ventricular block n = 3). No other complications were seen.

In the early post-operative phase there were no deaths. Early complications occurred from first post-operative day up to the tenth postoperative day (mean: 2.4 days). Twenty six patients (46%) showed no complications. The most common complication was continuous arrhythmia with atrial fibrillation. Ten of 34 patients who had shown sinus rhythm prior to operation presented with arrhythmia post-operatively. Ten of 23 patients who had shown arrhythmia prior to operation presented with a sinus rhythm post-operatively.

Further post-operative complications comprised one case each of pericardial effusion, stroke, myocardial infarction, pulmonary embolism, and two cases of unilateral pleural effusion. One patient developed a myocardial infarction on the first post-operative day with bilateral pleural effusion, consecutive continuous arrhythmia and subileus. Another patient had to undergo re-thoracotomy because of retrosternal bleeding.

The smallest tumor size was 1.5 × 1.7 × 0.5 cm, the largest 10.5 × 8.0 × 6.0 cm. The average size was 5–6 cm in diameter. The mean volume was 57.7 cm^3 (minimum: 1.2 cm^3, maximum: 504 cm^3, median: 134.0 cm^3). In our group of patients, in 47 cases (82.4%) the myxomas were located in the left atrium, in eight (14%) cases they were located in the right atrium, in two (3.6%) cases tumor growth was seen in both the left and the right atrium. Correct tumor localisation could be determined pre-operatively in 41 cases (71.9%), being the left atrium in all cases. In the others the pre-operative determination of tumor localisation was incorrect.

The outer appearance was ovoid-round with a firm and smooth surface in 28 (49.1%) cases. Twenty six (45.6%) myxomas were lobulated or polyploid-villous and gelatinous. Three (5.3%) tumors could not be classified. Thirteen myxomas were described as pedunculated. There was no significant difference between ovoid-round and polyploid-villous myxomas concerning embolic events or symptoms caused by hemodynamic disorders respectively.

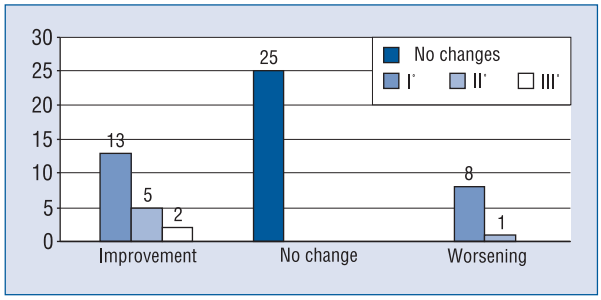

Figure 2. Post-operative changes in New York Heart Association classification (n = 54).

We have complete follow-up of 54 (94.7%) out of 57 patients. The mean follow-up time was 7.5 years (minimum: 23 days, maximum: 21.4 years). Five patients (9.3%) died after an average of 6.3 post-operative years (minimum: 2 months, maximum: 16.6 years, median: 8.7 years). According to Kaplan-Meier, the mean survival was 15.5 years with a maximum follow-up time of 17.4 years.

Two patients died of CHF, one patient died from pulmonary metastases of breast cancer, and one patient died from pneumonia. One other patient died from chronic alcoholism. In none of the patients was a post-mortem examination performed for exclusion of local tumor recurrence.

During follow-up, 13 patients (25.9%) improved by 1 step in NYHA classification, five patients (9.1%) by 2 steps, and two patients (3.6%) improved by 3 steps. Within NYHA I and II there was no post-operative improvement of cardiac output in 25 (45.2%) patients. Eight patients (14.4%) worsened by 1 NYHA step, whereas one patient (1.8%) worsened by 2 steps (Fig. 2).

Almost all patients were seen for regular echocardiography at least once a year. With the exception of one case there was no post-operative recurrence of disease. During follow-up, 11 patients received antiarrhythmic medication, two patients underwent sinus ablation, and in one case a pacemaker had to be implanted.

Eleven years after surgery, one patient had a stroke due to continuous arrhythmia.

Discussion

From a pathologic-anatomic point of view one distinguishes primarily benign, primarily malignant

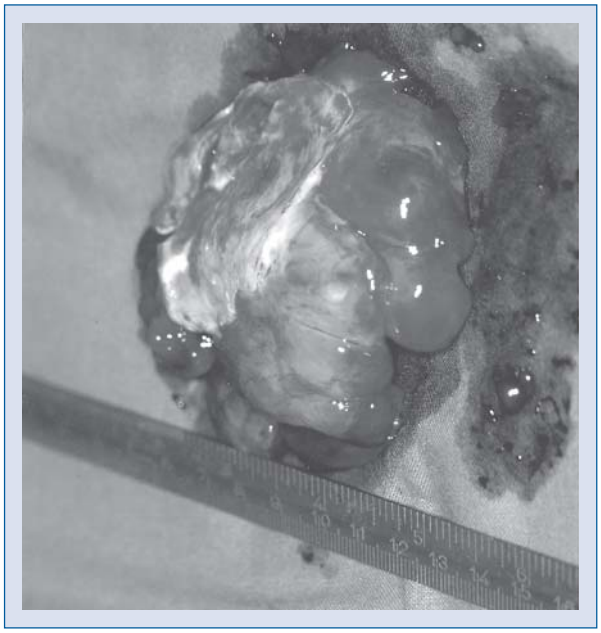

Figure 3. Myxoma.

and secondarily malignant heart tumors. From 75% to 80% of all heart tumors in adults are primarily benign. Despite the fact that from a pathologic--anatomic point of view only half of all benign heart neoplasms are myxomas [1, 3, 4, 16, 24, 25], in most surgical series, as well as in our study, myxomas are actually the most common benign primary heart tumors. One assumes that other benign tumors cause less cardiac symptoms, and are therefore less frequently discovered [24, 25]. In accordance with the literature we found myxomas more often in females [6]. Most patients were aged over 50 years, the average being 58.

The macroscopic structure of myxomas is ovoid-round with a firm and smooth surface or lobulated respectively polypoid-villous and gelatinous. The latter are more likely to cause embolic events [2, 3, 5, 7, 11]. In our study 28 myxomas (49.1%) showed a soft and lobulated surface, 26 myxomas (45.6%) were firm-elastic and smooth. The average size was 5–6 cm in diameter, as in previous studies (Fig. 3) [12, 13]. Most of the tumors are located in the left atrium at the interatrial septum close to the oval fossa, being attached to a 1–2 cm pedicle determining the motility of the tumor. The second most common location of myxomas is the right atrium [1, 2, 4, 5, 8–10, 16, 24–26]. In our study, tumor location was the left atrium in 47 (82.4%) cases of myxoma, in eight cases (14.0%) tumor location was the right atrium, and in two (3.6%) cases, tumor location was both the left and the right atrium.

Patients often present with a classic triad of symptoms: heart failure due to obstruction, stroke due to embolism, and constitutional, rheumatologic symptoms thought to be due to tumor secretion of cytokines and interleukin-6. A pedunculated tumor can result in obstruction of the mitral orifice, inlet or outlet obstruction, or compression of a ventricle and ensuing CHF, syncopes, or shock. Myxomas obstructing the left atrium can lead to pulmonary-venous congestion or incompetence or stenosis of the cardiac valves [4, 5, 19, 27–29].

The size, morphology and consistency (such as length of the pedicle of the tumors) influence the severity of clinical symptoms [7, 17].

Atrial fibrillation is the most common arrhythmia seen with cardiac tumors. In accordance with our results, it can be observed in 15% of patients with left atrial myxoma [10, 11]. Arrhythmia can be due to tumor infiltration into the conduction system [10].

Myxomas are often diagnosed after an incident of cerebral, coronary or peripheral embolism. From 30% to 60% of the patients with myxoma localisation in the left heart show systemic embolization [2, 4, 5, 16–19]. In our study 28.6% of the patients had a history of cerebral embolism, two patients had a history of pulmonary embolism. Polypoid-villous (papillary) myxomas had a more frequent history of embolization than myxomas with a smooth surface [5, 7]. One possible explanation is that papillary myxomas are more liable to fragmentation, erosion and embolism. Moreover, predilection for thrombus growth is given on a rough surface. In this respect, our study did not show any statistically significant differences.

Patients often present with common symptoms like loss of weight, fatigue, night sweat, fever and rheumatologic symptoms like arthralgia and morning stiffness [2, 5]. Some authors saw a correlation between tumor size and frequency of common symptoms [7, 30]. Our data did not show any statistically significant correlation.

For primary diagnosis, echocardiography is of great importance. One can identify size, motility and localisation of cardiac tumors. Additionally, hemodynamic effects can be seen by doppler-ultrasonography [28]. In all of our patients cardiac myxomas were diagnosed by echocardiography. Corresponding to Dein et al. [24] and Miralles et al. [25] information from echocardiography suffices as an indication for operation, and is a non-invasive, inexpensive investigation for follow-up.

CT-scan and MRI detect heart tumors larger than 0.5–1 cm in diameter. The advantage of these methods is complete imaging of the surrounding

anatomical structures [31, 32]. In our study, CT-scan or MRI was performed on eight patients with uncertain results in echocardiography.

Coronary angiography is not mandatory in primary heart tumor patients, but it is recommended in patients aged over 40 with risk factors for coronary heart disease [5, 11, 17, 18]. In our study coronary angiography was performed in 35 patients (61.4%); five patients (5.2%) had hemodynamically relevant stenoses and underwent surgical myocardial revascularisation.

In some cases the diagnostic method was CT--scan-guided fine-needle-aspiration or transvenous catheter-biopsy [18, 33]. With uncertain results concerning malignant heart tumors, a histopathological investigation of CT-guided aspiration of pleural effusion can be performed.

Since Craaford [34] performed the first operation on a patient with left atrial myxoma in 1954, operative techniques have developed, including minimally invasive surgery [19, 26, 35]. An endoscopic approach can be an alternative to the standard median sternotomy. First choice treatment today is wide excision under cadiopulmonary bypass. All cardiac myxomas in our study were operated in this way. The operation should be completed swiftly after diagnosis to prevent thrombo-embolic events [2, 36]. The mean time between diagnosis and surgery in our patients was 4.3 days.

The standard surgical approach is via median sternotomy. In special circumstances anterolateral thoracotomy or port access can be used instead [2, 4, 5, 16, 17, 19, 24–26, 35, 37, 38]. In our study, median sternotomy was used exclusively.

The individual surgical technique depends on tumor size, localisation and extension. Surgical approach to left atrial tumors can be gained by right--atrial and transseptal incision, biatrial incision or directly by left atrial incision [2, 11, 16, 20, 24–26, 29, 35, 37, 39]. In our study left atrial access was always realized by right-atrial incision followed by transseptal incision. In cases of right atrial myxomas, only right atrial incision was performed. Some authors demand a careful inspection of every cardiac cavity [16, 39]. For this reason, right atrial incision followed by transseptal approach is recommended for left atrial tumors.

For surgical therapy of cardiac myxomas, tumor excision has to be realized with a tumor free safety margin to prevent recurrence of disease. Left atrial myxomas located at the septum require a wide excision, followed by direct closure of the septum or, preferably, with a pericardium, Goretex (PTFE) or Dacron patch [2, 17].

In the current study 47 (82.5%) patients underwent septum surgery; direct closure of the septum could only be performed in ten (17.5%) patients.

Under difficult anatomical circumstances, caused by localisation and size of the tumor, standard excision can be impossible. A case report by Scheld et al. [40] described the excision of the heart followed by auto-transplantation for successful resection of a left atrial myxoma. Despite this, a complete excision of benign tumors can be impossible in some cases. In one patient, surgical excision of the tumor was incomplete due to tumor extension; local recurrence of disease, including affection of the upper wall and the septum of the left atrium as well as both mitral valve leaflets was seen one year after primary surgery. Second look surgery including wide excision of all those structures was performed; reconstruction of the left atrium by pericardial and Dacron--patches followed as well as mechanical mitral valve replacement.

Common post-operative complications in the literature are: effusion of the pericardium and the pleura, osteomyelitis of the sternum, pneumonia, maladaption of circulation after reconstruction, and arrhythmia [27, 38, 41]. Bateman et al. [41] describe atrial fibrillation as the most common arrhythmia, followed by atrial flutter. Some cases of bradycardiac arrhythmias and consecutive pacemaker implantations are described [38]. Twenty three (40%) patients in our group developed arrhythmia post--operatively.

Very good early post-operative results in our study correspond to those of excision of cardiac myxoma in the literature. The surgical mortality is given as 1 to 4.3% [2, 4, 9, 11, 13, 16, 17, 37]. In our study we had intraoperative deaths.

The long-term prognosis after cardiac myxoma surgery is excellent, so long as there is no irreversible secondary damage, i.e. tumor-infiltration of cardiac valve or embolic events. If surgery is performed at an early stage, a cure of the disease without disabilities is possible [1, 2, 13, 17, 39, 41]. In our study's long-term follow-up, mean survival time was 8.35 years. Two cases of death were most likely due to CHF in old age. Further information was not documented.

Several authors mention recurrence of disease in myxoma patients [2, 9, 17, 42, 43]. McCarthy et al. [9] divided cardiac myxomas into three categories of clinical appearance, and defined their risk of recurrence. The most common subtype is the sporadic myxoma, the average patient is older than 50 years, the tumor is usually unilocular, and the estimated risk of recurrence is less than 1%.

The next subtype is defined as a complex myxoma; these tumors are associated with dermatosis, dermal myxomas, myxoid fibroadenomas of the breast, Cushing's disease, pituitary adenoma, and rarely seen testicular tumors. In these cases, the risk of recurrence is about 20%.

Finally, there is a so-called hereditary cardiac myxoma. Most of these patients are young and have a positive family history. These myxomas show traits similar to complex myxomas. Risk of recurrence is about 10%. To lower the rate of recurrence, some authors demand wide excision of atrial myxomas including the pedunculated base as well as the attachment insertion in the atrial septum [2, 13].

Conclusions

1. Nowadays surgical excision of cardiac myxomas on cardiopulmonary bypass is both a state-of-the-art and low risk procedure.
2. After diagnosis, surgery should be performed quickly, in order to prevent complications such as embolic events or obstruction of the mitral orifice.
3. Follow-up examination including echocardiography should be performed regularly.

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The first two authors listed contributed equally to this article.

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