NOWOTWORY Journal of Oncology • 2002 • volume 52
Number 2 • 118–122

Clinical profile and outcome of patients with cardiac myxomas treated surgically. A 20-year experience with long-term follow-up

Marek Jemielity, Bartłomiej Perek, Sławomir Katarzyński, Marcin Misterski, Wojciech Dyszkiewicz

Introduction. Primary neoplasms of the heart are very rare, benign cardiac myxomas being the most common. The aim of this study was to present the clinical profile and long-term outcome of patients (pts) who underwent surgical resection of cardiac myxoma.
Material and methods. Between 1981 and 2000, 21 pts (12 female and 9 male), mean age 43.9 ± 14.5 years (range:21-74 yrs) underwent surgery for cardiac myxoma. Before surgery we performed physical examination, ECG, chest X-ray, echocardiography (M + 2D) and coronary artery angiography (in patients over 40 years of age). All pts were operated by median sternotomy in moderate hypothermia (26-28°C) with the use of cardiopulmonary bypass. At the end of the follow up clinical examination and echocardiography (M + 2D) were performed.
Results. Before operation 19 pts (90.5%) presented with cardiac signs related to mitral orifice obstruction. Six of them (28.6%) were NYHA class II, 8 (38.1%) - class III and 5 (23.8%) - class IV. Events of embolism occurred in 6 pts (28.6%). Ten pts (47.6%) had nonspecific systemic or constitutional symptoms, including permanent fever and significant weight loss. Two pts (9.5%) were asymptomatic, diagnosis being established accidentally. In all cases definite diagnosis was made by echocardiography. The myxomas were located in the left atrium in 18 pts (85.7%), in the right atrium in 2 pts (9.6%) and in the right ventricle in one pt (4.7%). One pt (4.7%) died in hospital because of low cardiac output syndrome and, eventually, multiorgan failure. The mean follow up of 5.4 ± 4.0 years (range: 3 mos - 20 yrs) was completed by all pts. Two pts died during follow up for noncardiac-related reasons. The cumulative survival rate calculated from the Kaplan-Meier curve was 85.2% after 5 years. No tumor recurrences were observed. At the end of follow up all pts were in NYHA class I or II.
Conclusions. Most preoperative symptoms of heart myxomas are related to mitral valve obstruction. The final diagnosis can be made by echocardiography. Surgical resection is a safe and curative therapy with a low risk of recurrence.

Przebieg kliniczny i wyniki leczenia chirurgicznego u chorych ze śluzakami serca – 20 lat doświadczeń

Wstęp. Pierwotne nowotwory serca należą do rzadkości. Pośród nich łagodne śluzaki są najczęstszymi pierwotnymi guza serca. Celem pracy było przedstawienie charakterystyki klinicznej i ocena odległych wyników leczenia chorych operowanych z powodu śluzaków serca.
Chorzy i metoda. Od 1981 r. do 2000 r. operowano 21 chorych (12 kobiet i 9 mężczyzn), w wieku od 21 do 74 lat (średnio 43,9±14,5 lat). Przed operacją chorych poddano badaniu fizykalnemu, wykonano badanie EKG, zdjęcie radiologiczne klatki piersiowej, echokardiografię (M + 2D) i koronografię (u chorych powyżej 40 lat). Wszystkich operowano ze sternotomii pośrodkowej w umiarkowanej hipotermii (26-28°C), z użyciem krążenia pozaustrojowego. Podczas ostatniej obserwacji odległej oceniano stan kliniczny i ponownie wykonano echokardiografię (M + 2D).
Wyniki. Przed operacją u 19 chorych (90,5%) stwierdzano objawy typowe dla zwężenia lewego ujścia żylnego. Sześciu spośród nich (28,6%) znajdowało się w II klasie wydolności według Nowojorskiego Towarzystwa Kardiologicznego (NYKA), 8 chorych (38,1%) w klasie III i 5 (23,8%) w klasie IV. Epizody zatorowe przed operacją obserwowano u 6 chorych (28,6%). Dziesięciu chorych (47,6%) prezentowało niespecyficzne objawy ogólne, w tym przewlekłe gorączki i znaczną utratę masy ciała. Dwóch chorych (9,5%) było bezobjawowych przed operacją. We wszystkich przypadkach ostateczne rozpoznanie stawiano na podstawie badania echokardiograficznego. Śluzaki lokalizowano w lewym przedsionku u 18 chorych (85,7%), w prawym przedsionku u 2 (9,6%) i w prawej komorze u 1 (4,7%). Jeden chory (4,7%) zmarł w szpitalu z powodu zespołu niskiego rzutu

Department of Cardiac Surgery
Institute of Cardiology, Karol Marcinkowski
University of Medical Sciences in Poznan

serca. Wszyscy chorzy znaleźli się w obserwacji odległej, która wyniosła 5,4±4,0 lat (od 3 miesięcy do 20 lat). Dwóch chorych zmarło w okresie obserwacji odległej z przyczyn nie kardiologicznych. Prawdopodobieństwo przeżycia po 5 latach od zabiegu, wyliczone z krzywej Kaplan-Meier'a, wyniosło 85,2%. Nie zanotowano nawrotów guza. Podczas ostatniej obserwacji odległej wszyscy chorzy znaleźli się w I lub II klasie wg NYHA.
Wnioski. Objawy zwężenia lewego ujścia żylnego dominują w obrazie klinicznym u chorych ze śluzakami serca. Ostateczne rozpoznanie stawia się na podstawie echokardiografii. Zabieg chirurgiczny jest bezpieczny, obarczony niewielkim ryzykiem wznowy i zapewnia wyleczenie.

Key words: cardiac myxoma, clinical presentation, surgery
Słowa kluczowe: śluzaki serca, objawy kliniczne, leczenie chirurgiczne

Introduction

Primary heart tumors are very rare and account for less than 0.1% of all neoplasms [1]. Approximately 75% of them are benign [2]. Cardiac myxoma is the most common lesion and accounts for more than 80% of primary benign cardiac tumors [2, 3]. Other, extremely rare tumours are: rhabdomyoma, fibroma, lipoma and benign teratoma. Before the development and introduction of angiocardiography and echocardiography heart neoplasms were diagnosed mainly post mortem. Myxomas may resemble many cardiovascular or systemic diseases, and can be found in any of the cardiac chambers, although a majority arises from the septum of the left atrium [4]. Nowadays most cases of myxomas (even small one) can be detected in living patients utilizing noninvasive techniques [5]. Surgical resection is a method of choice, considered to be complete and curative therapy [6]. The first successful removal of cardiac myxoma was performed by Crafoord in 1954 (7). Since then a variety of approaches have been developed, including an isolated left or right atriotomy, right atriotomy with transseptal incision and biatrial technique [8, 9].

The aim of this study was to present our experiences gathered over a 20-year period. We report the clinical profiles and long-term outcomes of patients who had undergone surgical resection of cardiac myxomas.

Material and methods

Patients

Between 1981 and 2000, 21 patients (12 female and 9 male) underwent cardiac myxoma resection at the Cardiac Surgery Department of The Karol Marcinkowski University of Medical Sciences in Poznan, Poland. Patient age ranged from 21 to 74 years (mean: 43.9 ± 14.6 years).

Preoperative examination

Before surgery historical review and physical examination were performed and clinical status according to NYHA functional classification was assessed. Chest X-ray (postero-anterior and side projections), ECG, cross sectional echocardiography and coronary artery angiography (in patients over 40 years of age) were carried out. In echocardiography the size of tumor and the following parameters were assessed: aortic root diameter (Ao), left ventricle end-diastolic dimension (LVED), left atrium dimension (LA), right ventricle dimension (RV), ventricular septum dimension (IVS), left ventricle posterior wall dimension (LVPW).

Operation

In each patient documentation of atrial myxoma prompted urgent operative intervention. All patients were operated with the use of routine cardiopulmonary bypass (CPB). After median sternotomy CPB was installed with aortic and bicaval venous cannulation. During insertion of venous cannulas care was taken to minimize manipulation of the heart to avoid tumor embolization. Moderate systemic hypothermia (26° to 28°C) was employed. Topical cooling with cold saline and continuous antegrade infusion of hyperkalemic crystalloid cardioplegia (St.Thomas II formula) were used to induce and maintain cardiac arrest. After the aorta was cross-clamped, right atriotomy was performed and the right atrium and ventricle were explored. If the myxoma was located in the left atrium, interatrial septum was cut down. Tumors attached to the interatrial septum were resected with the pedicle and a full-thickness portion of the adjacent interatrial septum (en bloc resection). The surgically created atrial septal defect was closed primarily in 18 patients and with a pericardial patch in one. Tumors arising from free atrial and ventricular wall were excised with the rim of at least 5 mm of the endocardium and myocardium. The mitral valve was checked for valvular damages or incompetence caused by annular dilatation secondary to the myxoma. All resected tumors were examined histologically.

Follow up examination

At the end of follow up the clinical examination and echocardiography (M + 2D) were performed. NYHA functional class was reassessed. In transthoracic echocardiography the heart was inspected for tumor recurrence and the same parameters as before operation were measured again.

Data management

All continuous variables are expressed as mean ±standard deviation. Differences between continuous variables (pre- vs. postoperative Ao, LVED, LA, RV, IVS, LVPW) were evaluated by t test, between categorical variable (pre- vs. postoperative NYHA) by chi-square or Fisher exact test. A probability value of $p < 0.05$ was considered significant. The cumulative survival rate was calculated using the Kaplan-Meier method. Statistica 5.0 for Windows was used for statistical analyses.

Results

Preoperative clinical profile

Before operation, 19 patients (90.5%) presented with cardiac signs. Among them, the most common progressive congestive cardiac failure (varied from easy fatigue to dyspnea at rest) was present in 14 cases (66.7%), palpitations in 7 (33.3%) and acute heart failure with pulmonary edema in 2 (9.5%). Six of them (28.6%) were

found in functional NYHA class II, 8 (38.1%) in class III and 5 (23.8%) in class IV (Figure 1). One patient with a right atrial myxoma had peripheral edema. Events of embolism occurred in 6 patients (28.6%). Embolic locations were the central nervous system (4 patients) and the upper or lower extremities (2 patients). Ten patients (47.6%) had nonspecific systemic or constitutional symptoms, including permanent fever (in 7 cases) and significant weight loss (over 10 kg within the last 6 months prior to diagnosis and surgery) (in 8 cases). Two patients (9.5%) were asymptomatic and diagnosis was established accidentally. In routine chest X-ray radiographic evidence of left atrium enlargement were observed.

In our group the time interval between the clinical symptoms onset and the final diagnosis varied between 3 and 166 months.

Electrocardiographic findings included left atrial hypertrophy (6 patients), nonspecific ST-segment abnormalities (5 patients) and premature atrial beats (2 patients). All patients were in normal sinus rhythm. Chest radiograms were abnormal in 12 patients (57.1%). Pulmonary edema (2 cases), interstitial markings or chronic congestive heart failure signs (7 cases) and left atrial enlargement (9 cases) were observed. In all cases the definite diagnosis was made by transthoracic or transesophageal (after 1995) echocardiography. The tumor was located in the left atrium in 18 patients (85.7%), in the right atrium in two patients (9.6%) and in the right ventricle in one (4.7%). The size of tumor calculated from 2-dimensional echocardiograms varied between 3.5 x 3 cm to the 8.1x 3.5 cm. Coronary arteriography did not show any significant changes, therefore no patient required additional bypass surgery.

Operative findings

During operation cardiac myxomas were at the localization indicated by preoperative echocardiography. The tumors found in the left atrium were attached to the interatrial septum in 17 and to the posterior wall in 1 patient. In one case the large, pedunculed tumor arising from the atrial septum, prolapsed to the left ventricle through mitral valve. Although the valve was obstructed prior to surgery, the mitral valvular apparatus was intact and after tumor resection the valve was neither incompetent nor stenotic. In the right atrium two myxomas arose from the septum. Right ventricular myxoma was attached to the free wall 2 cm below the tricuspid valve. The size of tumor assessed intraoperatively varied from 3 cm to 7 cm. The mean weight of the tumors was 32 ± 5 g (ranged from 14 to 95 g). The majority of them were pedunculated with a short stalk (<1 cm) (n=16, 76.2%), white the others were sessile-based. The myxoma with smooth surface was noted in 15 patients (71.4%) and with villous or papillary one in the others (28.6%). The friable villous-surface cardiac myxomas had a tendency to fragment easily, so special attention was paid to remove them as the entire tumors. All the patients had the tumor removed completely and all excisional margins showed no microscopic evidence of tumor. Histological examination revealed myxoma in all the cases, with microscopic calcifications in 33.3% (7 patients). The characteristic myxoma cells containing pink eosinophilic cytoplasm and ovoid nucleus were embedded in amorphous myxoid matrix. In 16 patients (76.2%) these cells surrounded numerous vessels.

In-hospital results

In our series there was one in-hospital death (4.8%). A 52-year old male patient died three days after surgery, because of low cardiac output syndrome and, eventually, multiorgan failure. He had pulmonary edema at admission to hospital. Very soon he developed cardiogenic shock. He had to be intubated prior to operation due to respiratory failure. Surgical intervention was performed urgently. His mitral valve was occluded by the huge tumor (as described above). Soon after operation an intraaortic balloon pump was employed, but the patient did not manage to recover and died three days later. Nobody required reoperation in the early postoperative period.

Postoperative organ complications occurred in five patients (23.8%). Two of the patients had atrial fibrillation treated with antiarhythmic drugs. The other two had evidence of significant pleural effusion, which was successfully evacuated by pleural puncture. One patient developed pneumonia and was referred to pulmonary disease department, where he stayed three weeks and then was discharged from hospital in a good overall condition. We observed neither organ (neurologic, renal etc.) nor surgical complications.

The mean in-hospital stay was 10.2 ± 3.3 days (range: 6 -14 days). All patients were discharged from hospital in stable condition.

Follow-up examination

The follow up ranging between 3 months and 20 years (mean 5.4 ± 4.0 years) was complete. During follow up two non cardiac-related deaths occurred. One 78-year old female patient died 18 years after surgery, because of breast cancer. The other, a 56 year old man with coexisting malignant colon tumor, died 15 months after surgery. The cumulative survival rate calculated from the Kaplan-Meier curve was 85.2% after 5 years (Figure 2). During follow up, three patients required cardiac-related hospitalization. In one case sick sinus syndrome was diagnosed four years after tumor resection and the patient underwent uneventful permanent pacemaker implantation. The others had rhythm disturbances (atrial fibrillation), but treated medically.

At the end of follow up, all patients were in functional NYHA classes I or II (Figure 1).

Up to now no echocardiographic evidence of the tumor recurrence has been noted. The dimensions of the cardiac chambers did not change as compared to the preoperative state (Table I).

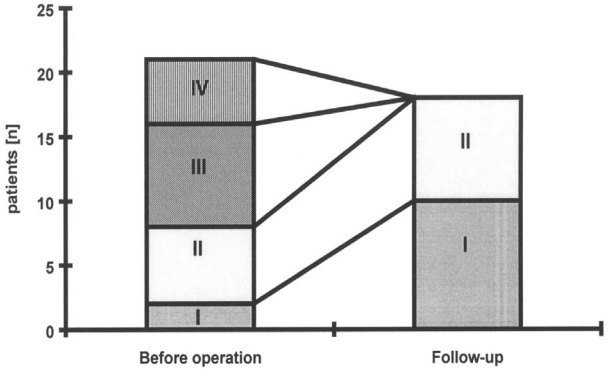

Figure 1. NYHA functional class before operation and at the end of follow up

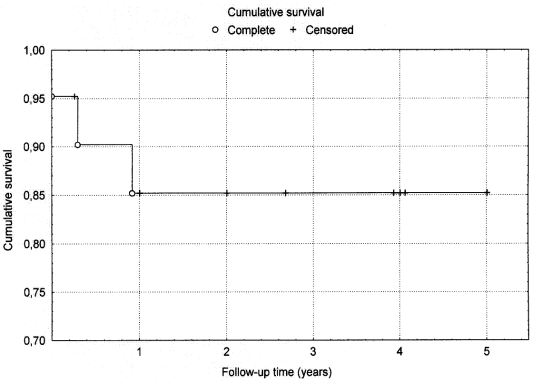

Figure 2. Cumulative survival rate calculated using Kaplan-Meier curve 5 years after tumor resection

Table I. Echocardiographic parameters prior to surgery and at the end of follow up

	before operation	end of follow up	*p* value
Ao [mm]	29.7±2.3	30.1±2.7	0.54*
LVED [mm]	47.1±6.4	47.5±5.1	0.81*
LA [mm]	45.8±9.1	44.4±7.5	0.42*
RV [mm]	24.9±4.9	24.9±3.5	0.95*
IVS [mm]	10.7±1.3	10.7±1.2	0.84*
LVPW [mm]	10.6±1.2	10.3±1.3	0.63*

* ns (no statistically significant difference)
Ao - aorttic root diameter, LVED - left ventricle end-diastolic dimension, LA - left atrium dimension, RV - right ventricle dimension, IVS - ventricular septum dimension, LVPW - left ventricle posterior wall dimension

Discussion

Although the clinical manifestation of cardiac myxomas are not typical, some authors outline three following main patterns of presentation: cardiac, embolic and systemic [1, 4]. Cardiac symptoms (dyspnea, dizziness, progressive congestive heart failure and palpitation) associated with mitral valve obstruction are the most frequent [8, 9, 10]. The floating tumors render blood flow from the pulmonary veins to the left atrium difficult and moving in the diastole in the direction of the mitral valve cause syncope, acute pulmonary edema and even sudden cardiac death [4]. The gelatinous and fragile tumors are sources of embolic material, therefore both permanent or transient embolic complications (to central nervous system, coronary arteries, extremities and kidney) are observed in around 20-30% [8, 9]. In one recent report 80% of the myxoma cases were admitted to hospital with stroke or transient ischemic attacks [23]. The third pattern comprises constitutional symptoms and signs of generalized illness like fatigue, muscle weakness, loss of body mass, permanent fever and arthralgia [1, 4]. This is probably caused by proinflammatory interleukin-6 produced and secreted by some myxoma cells [11]. In our series, cardiac symptoms of mital valve obstruction dominated and were presented by all symptomatic patients. More than two-thirds of thromboembolic complications affected the central nervous system, thus proving earlier observations [8, 12].

Approximately 70% to 80% are found in left atrium, 10% to 20% are in the right atrium, and less than 10% are in both atria or either ventricle [4, 8, 9]. Atrial myxomas usually arise from the interatrial septum in the area of fossa ovalis, but they can also be found at the free wall of the atrium [8, 13]. In our series only one tumor was attached to the free atrial wall, that is less than observed by the others [19]. In rare instances they may have multiple foci and can involve mitral valvular tissue [12, 14].

Among examinations routine ECG and chest X-ray, as nonspecific, are unlikely to suggest the diagnosis of myxoma [1]. ECG findings are: nonspecific ST changes, left atrial hypertrophy or premature atrial complexes [4, 8]. It is estimated that at least one-third of the patients had normal ECG [4]. The results of earlier reports were thus confirmed. We did not find any ECG changes in more than 50% of patients and the most common findings were signs of left atrial hypertrophy and ST changes. On chest X-rays of some patients nonspecific cardiomegaly (including left atrial enlargement) could be seen, as in our two asymptomatic patients, and intensified pulmonary vascularity was observed [4]. In rare instances pulmonary edema secondary to severe mitral valve obstruction is noted. Calcifications making the tumor visible and pleural effusion are unusual [1, 8]. Echocardiographic examination is usually the method of choice and in more than 95% of cases definite diagnosis is possible [5, 8]. It allows to determine localization and size even of small tumors, the site of attachment and presence of any myxoma prolapse [9, 12]. An introduction of transesophageal echocardiography increased the sensitivity of this diagnostic tool. In our group cross sectional echocardiography allowed to establish the final diagnosis in all cases, to localize adequately the tumor site and to calculate the approximate size. The hemodynamic examination is recommended when tumors are atypically located especially inside the ventricles or there are some others diagnostic doubts. During cardiac catheterization, measurements of pulmonary artery pressure are enabled [8]. Moreover, coronary arteriography is recommended in all patients aged over 40 years undergoing cardiac procedures. Computer tomography and magnetic resonance are also very helpful [4]. Some authors reported incidental diagnosis made during

cardiac surgery for mitral stenosis, but it was before the introduction of transesophageal which is echocardiography useful in some difficult cases [1, 10].

In general, patients benefit from surgical correction, which is considered to be curative treatment [1, 10]. Likewise in our group, most patients in reviewed studies were found in functional NYHA classes I and II after operation [1, 8]. The most frequent postoperative complications are arrhythmias, including supraventricular rhythm disturbances or atrial fibrillation [1, 4, 12]. In our series atrial fibrillation occurred in two patients in the early postoperative period and in two other patients during follow up. Exceptional permanent cardiac pacemaker implantation is necessary [1, 4]. During follow-up thromboembolic events, mainly related to atrial fibrillation are reported [9, 12].

The rate of cardiac myxoma recurrence is 4% to 5% [8, 15]. It usually happens within 5 years after the operation [16]. It can be a result of inadequate resection, especially in patients with multifocal familial myxomas, or intraoperative implantation or transformation from benign to malignant lesion [1, 8]. In order to avoid it we inspected heart chambers very carefully and special attention was paid not to manipulate the heart and the tumor during the operation. Moreover, none of our patients had familial myxoma, which may partially explain no cases of recurrence. Also, histological type can influence the recurrence rate [4]. Pinede et al. observed the recurrences only in patients with active and poorly differentiated forms. They distinguished active with a dense myxoma cells from *inactive* with a sparse, sometimes calcified, cell infiltrate and *normally differentiated* with numerous rudimentary or well-formed vessels surrounded successively by cells then by condensed matrix from *poorly differentiated* with many isolated, dispersed cells or lepidic cells gathered in short chains throughout the matrix [4]. In our group of patients the majority of myxomas were normally differentiated and inactive - characterized by a very low probability of recurrence. Some authors suggested that although cardiac myxomas were usually considered benign, yet they might have an intrinsic malignant potential (documented recurrences, multicentricity and distant metastases) [17]. It has been proposed recently that recurrent tumors represent an intrinsically more aggressive subgroup that produced high levels of IL-6 [18].

Conclusions

Basing on 20 years of experience we can conclude that a majority of preoperative symptoms of heart myxomas are related to mitral valve obstruction. The final diagnosis can be made by cross sectional echocardiography. Surgical resection is a safe and curative therapy with a low recurrence risk.

Marek Jemielity M.D., Ph.D.
Department of Cardiac Surgery, Institute of Cardiology
Karol Marcinkowski University of Medical Sciences
Dluga 1/2, 61-848 Poznan, Poland
e-mail: mjemility@poland.com

References

1. Dein JR, Frist WH, Stinson EB et al. Primary cardiac neoplasms. Early and late results of surgical treatment in 42 patients. *J Thorac Cardiovasc Surg* 1987; 93: 502-511.
2. Blondeau P. Primary cardiac tumors. French studies of 533 cases. *Thorac Cardiovasc Surg* 1990; 38: 192-195.
3. Centofanti P, Di Rosa E, Deorsola L et al. Primary cardiac tumors: early and late results of surgical treatment in 91 patients. *Ann Thorac Surg* 1999; 68: 1236-1241.
4. Pinede L, Duhaut P, Loire R. Clinical presentation of left atrial cardiac myxoma. A series of 112 consecutive cases. *Medicine* (Baltimore) 2001; 80: 159-172.
5. Mugge A, Daniel WG, Haverich A et al. Diagnosis of noninfective cardiac mass lesions by two-dimensional echocardiography. Comparison of the transthoracic and transesophageal approaches. *Circulation* 1991; 83: 70-78.
6. Larsson S, Lepore V, Kennergren C. Atrial myxoma: Results of 25 year's experience and review of the literature. *Surgery* 1989; 105: 695--698.
7. Chitwood WR Jr. Clarence Crafoord and the first successful resection of a cardiac myxoma. *Ann Thorac Surg* 1992; 54: 997-998.
8. Jones DR, Warden HE, Murray GF et al. Biatrial approach to cardiac myxomas: A 30-year clinical experience. *Ann Thorac Surg* 1995; 59: 851--856.
9. Bjessmo S, Ivert T. Cardiac myxoma: 40 years' experience in 63 patients. *Ann Thorac Surg* 1997; 63: 697-700.
10. Gawdzinski MP, Sypula S. The long term results of treatment of heart myxomas with special attention to very rare myxoma of the right ventricle. J Cardiovasc *Surg* (Torino) 1996; 37: 121-129.
11. Jourdan M, Bataile R, Sequin J et al. Constitutive production of interleukin-6 and immunologic features in cardiac myxomas. *Arthrithis Reum* 1990; 33: 398-402.
12. Ugurlu B, Oto O, Okutan H et al. Stroke and myxoma. *Asian Cardiovasc Thorac Ann* 2000; 8: 130-133.
13. Tsukamoto S, Shiono M, Orime Y et al. Surgical treatment of 22 cardiac myxomas: A review. *Ann Thorac Cardiovasc Surg* 1999; 5: 146-149.
14. Castells S, Ferrans V, Octavio De Toledo MC et al. Cardiac myxomas: surgical treatment, long-term results, and recurrence. *J Cardiovasc Surg* 1993; 34: 49-53.
15. Actis Dato GM, de Benedictis M, Actis Dato A Jr et al. Long-term follow--up of cardiac myxomas (7 - 31 years). *J Cardiovasc Surg* 1993; 34: 141-143.
16. Gray IR, Williams WG. Recurring cardiac myxoma. *Br Heart J* 1985; 53: 645-649.
17. Shinfield A, Katsumata T, Westaby S. Recurrent cardiac myxoma: seeding or multifocal disease. *Ann Thorac Surg* 1998; 66: 285-288.
18. Mendoza CE, Rosado MF, Pacheco P. Interleukin-6 production and recurrent cardiac myxoma. *J Thorac Cardiovacs Surg* 2001; 121: 395-396.

Paper received: 9 September 2001
Accepted: 22 January 2002