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Original Article

Surgical Treatment of Atrial Myxomas: Outstanding Outcome of a Treacherous Tumor

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ABSTRACT

Background: Primary cardiac tumors are quite rare and mostly benign in nature. Most of the benign heart tumors are myxomas. These might present with a wide range of symptoms from being completely asymptomatic to having life-threatening complications like stroke, heart failure, or even sudden death. This study summarizes our 6-year clinical experience with surgical resection of cardiac tumors at Chittagong Medical College and Hospital, Chattogram, Bangladesh.

Methods: Twenty patients who underwent surgical excision of primary intracardiac myxoma between February 2014 and February 2020 were included in the study. Seventeen (85%) of them were female and 3 (15%) were male. Mean age was 43.4 ± 14.1 years. The tumors were located in the left atrium in 19 patients and in 1 patient it was in

RÉSUMÉ

Introduction : Les tumeurs cardiaques primitives sont assez rares et pour la plupart bénignes par nature. La plupart des tumeurs cardiaques bénignes sont des myxomes, qui pourraient se manifester sous diverses formes allant de l'absence complète de symptômes à des complications mettant la vie en danger telles que les accidents vasculaires cérébraux, l'insuffisance cardiaque, voire la mort subite. La présente étude résume les six années d'expérience clinique en résection chirurgicale de tumeurs cardiaques au Chittagong Medical College and Hospital, Chattogram, Bangladesh.

Méthodes : Vingt patients qui avaient subi une excision chirurgicale d'un myxome intracardiaque primitif entre février 2014 et février 2020 ont fait partie de l'étude. Dix-sept (85 %) étaient des femmes, et trois

Tumors of the heart are rare. Cardiac tumors might be primary or metastatic. Primary cardiac tumors are uncommon with an incidence ranging from 0.0017% to 0.02%.[1] Secondary cardiac tumors are 20-30 times more frequent than the primary cardiac tumors. The patients with malignant cardiac tumors (secondary or primary) rarely reach surgeons' tables because of their aggressive behaviour, fatal outcome, and multiple associated comorbidities. More than 80% of primary cardiac tumors are benign. Atrial myxoma is by far the most common type of primary cardiac tumor in adults with an excellent survival rate after surgery. They are predominantly found on the left side, especially in the left atrium.[2] In pediatric patients, the incidence of cardiac fibroma is high. Sarcomas are the most common type of primary malignant cardiac tumor; undifferentiated sarcoma and angiosarcoma are the most common subtypes.[3,4] Cardiac metastases predominantly originate from lung and breast cancer. Melanomas have the highest propensity for cardiac metastases.[5] Over the years, the number of patients who present with cardiac metastases has increased because of improved ability to detect malignant diseases with better imaging techniques.[6]

Cardiac myxomas are commonly diagnosed between the fourth and the sixth decades of life and are associated with excellent survival after surgical treatment.[7] In contrast, primary malignant cardiac tumors affect mostly younger patients[4] and these tumors are associated with dismal prognosis and survival, despite extensive multimodal therapy.[8,9] Median survival is 3-12 months for sarcomas, up to 5 years for lymphomas, and 6 months for cardiac metastases.[7] In general, the clinical course of malignant cardiac tumors is

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Ethics Statement: The research reported has adhered to the relevant ethical guidelines.

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the right atrium. The most common attachment site was the interatrial septum. Most of the patients presented with dyspnea. Preoperative diagnosis was established using transthoracic echocardiography with colour Doppler. Surgery for all patients was via median sternotomy.

Results: All 20 patients survived the surgery. Mean tumor dimension was 4.6 ± 3.5 cm in the longest diameter. Solid tumors were detected in 13 patients (65%) whereas papillary myxomas were found in 7 patients (35%). On follow-up of these 20 patients, there was no perioperative death. One patient presented with recurrence 28 months after the surgery.

Conclusions: Although cardiac myxomas carry the risk of serious systemic and cardiac symptoms, prompt surgical excision gives excellent outcome.

(15 %), des hommes. L'âge moyen était de 43,4 ± 14,1 ans. Dix-neuf patients avaient une tumeur située dans l'atrium gauche, et un patient avait une tumeur située dans l'atrium droit. Le site de fixation le plus fréquent était le septum interauriculaire. La plupart des patients accusaient une dyspnée. Le diagnostic préopératoire était établi par échocardiographie Doppler couleur transthoracique. Tous les patients opérés ont subi une sternotomie médiane.

Résultats : Les 20 patients ont survécu à l'intervention chirurgicale. La dimension moyenne de la tumeur était de 4,6 ± 3,5 cm dans le plus grand diamètre. Treize (65 %) patients avaient des tumeurs solides, et sept (35 %) patients, des myxomes papillaires. Aucun décès périopératoire n'a été observé durant le suivi de ces 20 patients. Un patient a eu une récidive 28 mois après l'intervention chirurgicale.

Conclusions : Bien que les myxomes cardiaques comportent un risque de symptômes systémiques et cardiaques sérieux, l'excision chirurgicale rapide apporte d'excellents résultats.

characterized by aggressive growth and fatal outcome.[9,10] The clinical features of cardiac tumors depend on the size and site of the tumor.[11] Cardiac tumors might be clinically silent or might cause various nonspecific symptoms such as dyspnea, angina pectoris, cerebral or peripheral embolisms, and arrhythmias. Systemic manifestations in the form of weight loss, fever, and arthralgia might also occur which, may mimic endocarditis.[12-14] Because of the likelihood of embolization, sudden cardiac death, and hemodynamic compromise, immediate surgical treatment is indicated.[5,15,16] In this article, we report our 6-year experience of surgical treatment of atrial myxomas at Chittagong Medical College and Hospital, Chattogram, Bangladesh. Our aim was to examine clinical and surgical data, including postoperative outcome and complications of the patients, who underwent cardiac tumor surgery.

Methods

The study was carried out in the department of Cardiac Surgery, Chittagong Medical College and Hospital on the patients who received surgery between February 2014 and February 2020. This retrospective observational study was conducted on 20 patients, who had undergone surgery for suspected cardiac tumor during that period. Preoperative diagnosis was mainly established using transthoracic echocardiography (TTE). Echocardiography is an excellent diagnostic tool and defines the site, size, shape, and relations of the mass with intracardiac components (Fig. 1). Preoperative coronary angiography was performed in 15 of these patients, who had history of chest pain, significant electrocardiogram changes and were aged older than 40 years. Twelve of them had normal coronary angiogram whereas 3 had nonsignificant coronary artery disease not warranting any coronary intervention.

Surgical procedure

All the operations were performed via median sternotomy. The tumor was excised using cardiopulmonary bypass, with aortic and bicaval cannulation and mild hypothermia. Myocardial protection was achieved with cold blood cardioplegic solution. Injection dexamethasone (5 mg) was given intravenously to all patients just before application of cross-clamp and was continued thrice daily until the features of anaphylaxis or neurologic complications were excluded postoperatively in the intensive care unit. Care was taken not to manipulate the tumor before the cross-clamp had been applied on the aorta. Complete removal of the tumor mass and its attachment site was the basic principle of excision. Figure 2 portrays the steps of surgical removal of an atrial myxoma from the left atrium. Excision of myxomas was approached using left atriotomy in 16 patients; the biatrial approach was used in 3 patients and right atrial approach was used in 1 patient. Extreme care was taken to take out the tumor as a single piece and not to allow spillage of tumor fragments inside the left atrium, openings of the pulmonary veins, or the left ventricle. After removal of the tumor the cardiac cavity was thoroughly irrigated with cold normal saline and simultaneous sucked out using a wall sucker to remove any tiny tumor fraction if released accidentally. The use of cardiotomy sucker or vents was minimal to avoid sucking up of tumor fragment or any substance released during tumor handling. After excision of the tumor the adjacent parts and the margins were carefully burnt using electrocautery. In 7 cases, where tumors were attached with a wide base to the interatrial septum, the affected areas of the interatrial septum were also excised along with the tumor. These iatrogenic defects were directly sutured in 3 patients and were closed with fresh autologous pericardial patch in 4 patients. The mean extracorporeal circulation time was 45.8 ± 5.6 minutes and the mean cross-clamp time was 25.8 ± 2.9 minutes (Table 1).

Statistical analysis

All data were analyzed and are presented as continuous and categorical variables. Continuous variables are described as mean ± SD and categorical variables are presented as absolute numbers along with the percentages.

Results

A total of 20 patients underwent surgical excision of cardiac tumors. The mean age was 43.4 ± 14.1 years. The disease had a strong female dominance in our series; 17

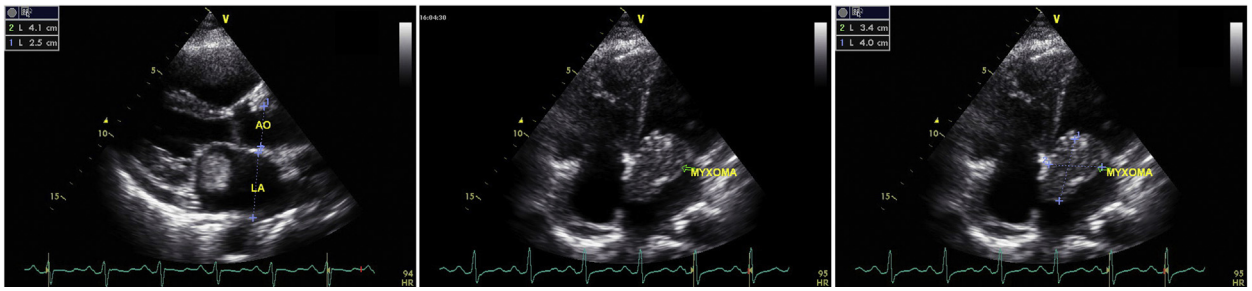

Figure 1. Echocardiographic findings of a left atrial myxoma. AO, aorta; LA, left atrium; V, ventricle.

patients (85%) of 20 were female. The baseline characteristics of the patients are summarized in Tables 2 and 3. All of the patients were symptomatic. The most frequently observed symptoms were cardiac such as dyspnea, palpitation, and features of heart failure. A few patients presented with fever, weight loss, and fatigue. The preoperative comorbidities included diabetes mellitus in 11 patients, chronic obstructive pulmonary disease in 8, history of cerebral embolic stroke in 2, transient ischemic attack in 1, peripheral thromboembolism in 1, hypothyroidism in 2, arterial hypertension in 7, noncritical ischemic heart disease in 2, and atrial fibrillation in 3 patients.

In 19 patients (95%; n = 20) the myxoma originated from the left atrium. In 17 patients (85%) cardiac myxomas were attached with the interatrial septum whereas in 2 patients (10%) those were attached with the left atrial free wall. One patient (5%) in our series had the myxoma located in the right atrium. No tumor had originated from the left or right ventricle in our series. No tumor was attached to the mitral valve. In 6 patients the tumors were prolapsing through the mitral valve and in 3 patients, the posterior leaflet of the mitral valve was prolapsed.

On the basis of their gross external features, tumors were divided into solid (Fig. 3) or papillary (Fig. 4). The solid tumors appeared firm with a smooth regular surface. Papillary myxomas were irregular, with myxomatous exterior, and more friable. Solid tumors were detected in 13 patients (65%) and papillary myxomas were found in 7 patients (35%) in our series.

The mean tumor dimension was 4.6 ± 3.5 cm in the largest diameter. The largest tumor in our series had a length of 9.3 cm (Fig. 5). It is really amazing that human life is sustainable with such a huge mass inside the heart! Histopathologic examination was done in all cases. All tumors were benign myxomas. This was confirmed by histopathology that contained a myxoid stroma. Polygonal cells with scant eosinophilic cytoplasm were scattered throughout the myxoid matrix. The cells were arranged singly and in small loose clusters, but lacking mitotic figure. A few scattered foamy macrophages along with scattered lymphocytes and delicate blood vessels were also present (Fig. 6).

Mean intensive care unit and postoperative hospital stay were 2.3 ± 1.5 and 7.4 ± 2.5 days, respectively. All patients in our series survived the surgery and were discharged from the hospital in good health. Two patients (10%) suffered from low-output cardiac syndrome postoperatively. Two patients (10%) had transient atrial fibrillation. One patient (5%) experienced transient acute renal failure postoperatively, but had a smooth recovery within a week (Table 4). No further thromboembolic event or cerebrovascular stroke was observed.

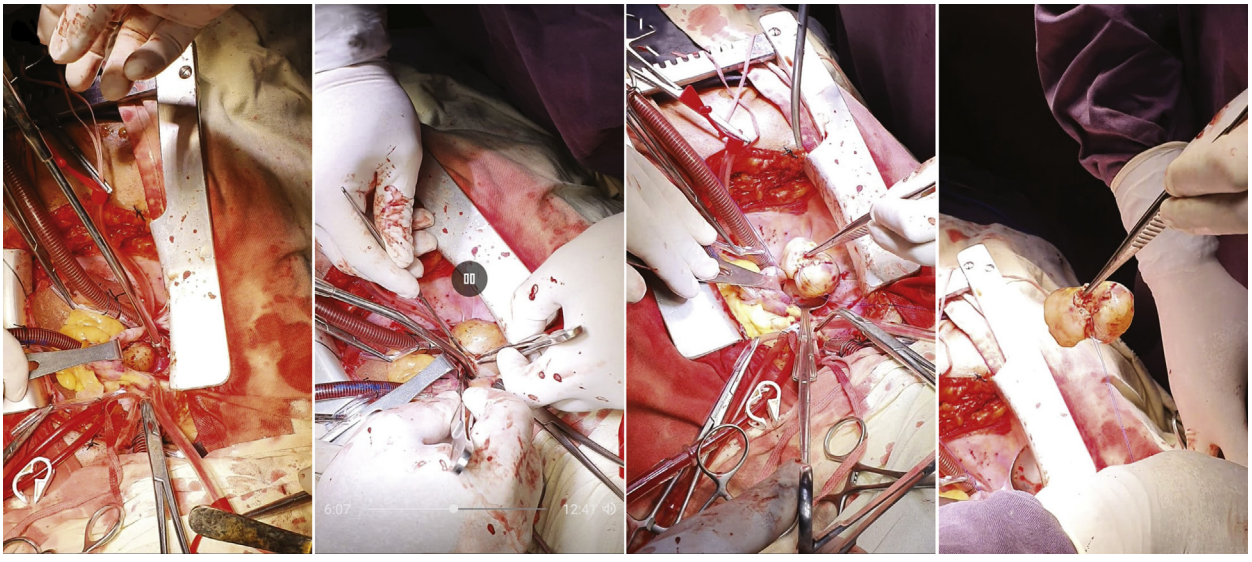

Figure 2. Surgical removal of an atrial myxoma from the left atrium.

Table 1. Demographic characteristics and comorbidities of the patients

Characteristics and comorbidities	Value
Number of patients	20
Age: Mean ± SD, years	43.4 ± 14.1
Male:female ratio	3:17
History of stroke, n (%)	2 (10)
History of TIA, n (%)	1 (5)
Peripheral thromboembolism, n (%)	1 (5)
Atrial fibrillation, n (%)	3 (15)

TIA, transient ischemic attack.

One patient (5%) showed a recurrence of tumor 28 months after the initial surgery. This 45-year-old female patient was operated in 2017 and returned to our emergency department in early 2020 with severe heart failure. Echocardiographic examination revealed recurrent atrial myxoma occupying the left atrium. The patient was admitted and was being prepared for surgery. With diuretics and other supportive therapy her failure improved. However, with the onset of COVID-19 crisis, the patient refused reoperation and decided to leave the hospital. No further information is available to date.

Among the 20 patients, 15 (75%) patients were in New York Heart Association (NYHA) class I whereas 5 (25%) were in NYHA class II and 1 patient in NYHA class III at 1 month after surgery. All patients were followed-up in the Cardiac Surgery outpatient department for 6 months. Then they were referred to the cardiologists for further follow-up. Echocardiographic examination was recommended on an annual basis.

Discussion

Although primary cardiac neoplasms are very rare, metastatic tumors within the heart have been found in up to 20% of autopsies after cancer deaths.[17] Very few patients receive surgery for cardiac tumors, either primary or metastatic. In our patient population, 20 patients underwent such surgery in a period of 6 years. Echocardiography was our main diagnostic tool, which aided in determining tumor size, location, and relation with other intracardiac structures. In terms of suspected malignancy, magnetic resonance imaging or computed tomography can be used to improve the diagnostic accuracy. Computed tomography scan was done in 1 patient in our study because of suspected malignancy.

Myxoma is the most common variety of benign cardiac tumor. In our study, all patients had cardiac myxomas and we did not encounter any patient of other variety of benign, malignant, or secondary cardiac tumors. Myxoma has a favourable prognosis after surgery.[18] Myxomas commonly occur in the middle-aged and elderly population[19] and the prevalence is higher in women.[20] Cardiac myxoma rarely occurs in young patients and only 0.4% of the reported patients were younger than 10 years old. Young patients with cardiac myxomas are often in a syndromic context known as Carney complex. This was first described as "the syndrome of myxomas, spotty pigmentation and endocrine over activity" by Carney in 1985 at the Mayo Clinic[21] and has been reported to be associated with germline mutation PRKAR1A.[22]

Table 2. Preoperative functional status of the patients

Variable	Value
New York Heart Association class	
I	3 (15)
II	9 (45)
III	7 (35)
IV	1 (5)
Left ventricular ejection fraction on echocardiography	
> 55%	14 (70)
45%-55%	3 (15)
30%-45%	3 (15)

Data are presented as n (%).

Table 3. Intraoperative data

Intraoperative characteristic	Value
Surgery time, min	198 ± 23
Cardiopulmonary bypass time, min	45.8 ± 5.6
Cross-clamp time, min	25.8 ± 2.9
Tumor diameter, cm	4.6 ± 3.5

The clinical features and manifestations are often nonspecific and related with the location, size, and mobility of tumors. There are 3 main patterns of clinical presentation of myxomas: cardiac symptoms (dyspnea, syncope, palpitations, arrhythmia, congestive heart failure, and sudden death); systemic embolization (embolism in the peripheral arteries and transient ischemic attack or cerebral vascular accident), and constitutional manifestations (fever, malaise, weight loss, arthralgia, and fatigue). In our series, most of the patients presented with cardiac symptoms. Cardiac consequences might be intermittent. Of all patients with myxoma, 20%-25% have neurological complications. Systemic embolism is not related to the size of myxomas, but it depends on friability and mobility of the tumor.[23,24] Temporary or permanent neurological defects might arise when the friable tumor tissue embolizes into systemic circulation. Fever, malaise, and weight loss might be because of the possible elaboration of the cytokine interleukin-6.[25] The locations of myxoma are 75% in the left atrium, 23% in the right atrium, and only 2% in the ventricles.[26-28] The most common site of attachment is the fossa ovalis. Our study also revealed similar findings. Other rare arising sites are the heart valves.[29,30] Multiple locations are present in 50% of familial forms.[31]

The surgical approach (incision, cannulation for cardiopulmonary bypass, and concomitant procedures) depended on the location and size of the tumor. The use of cardioplegia, as well as cooling the patients during cardiopulmonary bypass was according to the surgeon's preferences and did not seem to have an effect on the outcome. We excised the tumors completely with an acceptable safety margin. Because of the high incidence of myxomas and their abundance in the left atrium with the stalk in the interatrial septum, the left atrial approach was typically used. In our series, no patient needed concomitant mitral valve repair or replacement. In general, when the tumor adheres with the valves, attempts should always be made to preserve the valvular structure.

Our department was established on March 29, 2009. The first atrial myxoma patient received surgery on February 5, 2014. Thereafter 20 patients received surgery within next 6

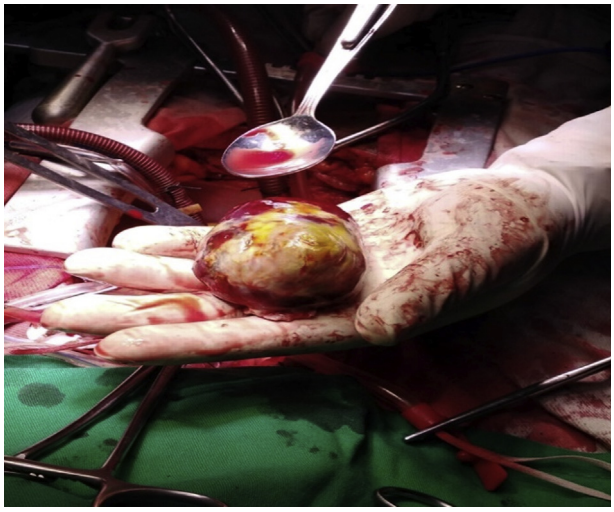

Figure 3. A large solid atrial myxoma placed on the palm of the surgeon just after removal from the left atrium.

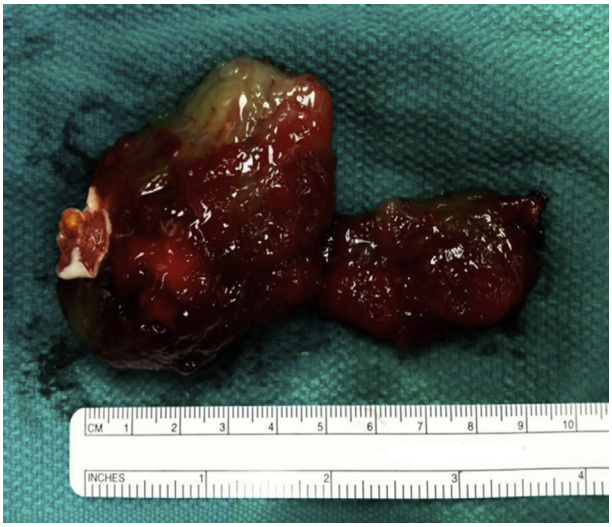

Figure 5. A huge atrial myxoma approximately 9.3 cm in the longest diameter, the biggest in our series.

years. This department is the first and the biggest public sector cardiac surgery centre in the region. Because of their risky movements and frail health conditions, the myxoma patients seem to be discouraged in going to centres far away from home. They appear to represent in a disproportionately higher number when a new public cardiac surgical centre like ours is established in a barren territory.

Since the first excision of an atrial myxoma performed by Swedish cardiovascular surgeon Clarence Crafoord in 1954,[32] resection of benign cardiac tumors has gradually become a routine procedure with favourable prognosis. Elbardissi et al.[1] reported that the recurrence rate of myxoma after resection was 13%, but was much more common with familial myxomas than with sporadic tumors (22% vs 3%). Local recurrence of myxoma is very rare but might be related to incomplete resection, multicentricity, origin in a location other than the left atrium, familial tumors, or part of a disease complex like Carney complex.[21] Only 1 patient (5%) in our series had recurrence. None of our patients presented with Carney complex or history of familial atrial myxoma.

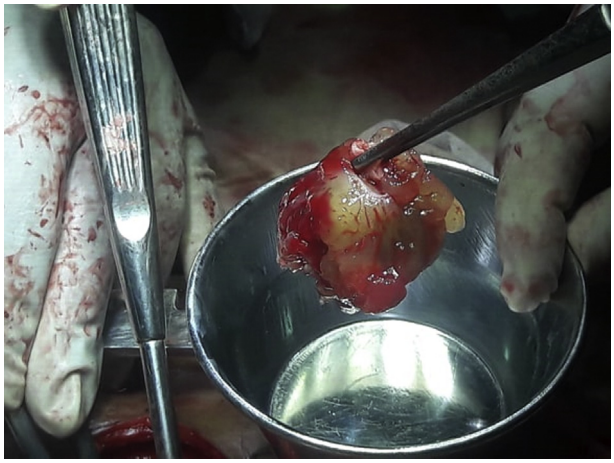

Figure 4. A resected papillary type atrial myxoma.

Follow-up after surgical excision of myxoma involved medical history, physical examination, TTE, and transesophageal echocardiography. TTE has nearly 95% sensitivity for detecting cardiac myxomas whereas transesophageal echocardiography has 100% sensitivity.[33,34] Computed tomography scan and magnetic resonance imaging might also be helpful to detect recurrence. Familial cardiac myxoma affects the patient's treatment, follow-up protocol, and requires family screening with TTE.

The limitations of this study include the small number of cases, long study period, and also that the follow-up beyond 6 months was not done by us. For a single-centre study of a rare tumor like atrial myxoma, this is not unusual. The long-term follow-up is done by our cardiologist colleagues. We are in regular contact with them. They quickly contact us with any unusual findings during follow-up.

In conclusion, atrial myxoma is the only type of cardiac tumor that reaches cardiac surgeons' operating tables in a significant number. Although these tumors carry the risk of serious systemic and cardiac symptoms, on-time surgical removal gives excellent results with a low recurrence rate. The male:female ratio was 3:17 in our series. These tumors might grow huge often without producing significant symptoms. It is really amazing that patients can survive with a huge mass of even 9.3 cm length inside the heart, and might return to normal life after surgical intervention. The poor myxoma patients seem to represent in disproportionately higher numbers when a new public cardiac surgical centre is established in a barren territory. Recurrence is rare if proper surgical principles are applied during surgery. Regular long-term follow-up after surgery with medical history, physical examination, and echocardiography is recommended for all patients with cardiac myxoma.

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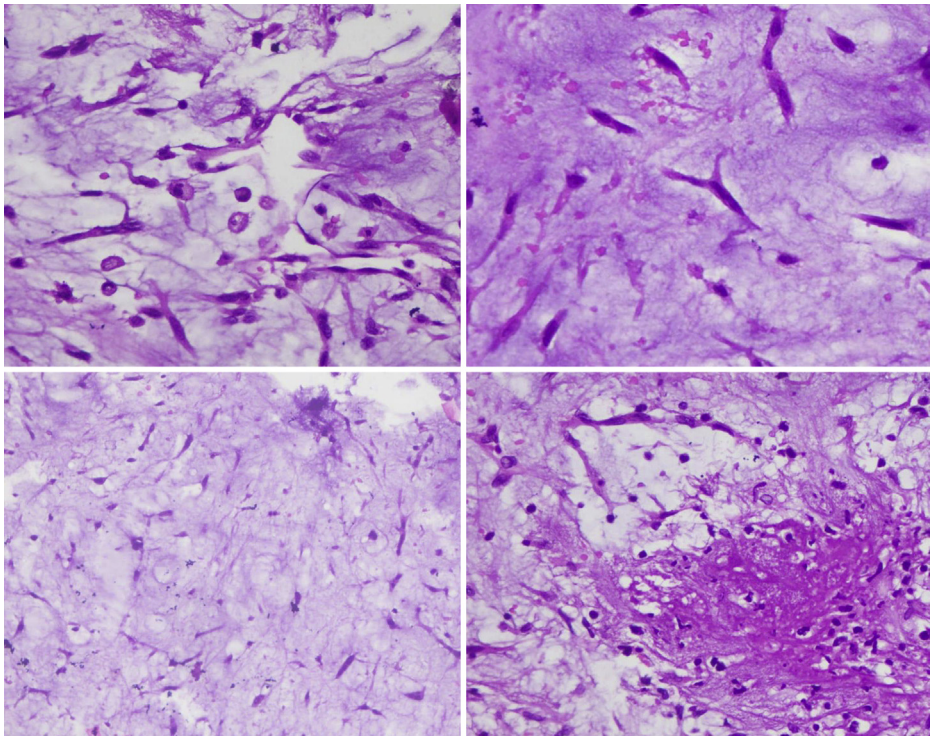

Figure 6. Histopathologic slides showing atrial myxoma. Polygonal cells with scant eosinophilic cytoplasm are scattered throughout the myxoid matrix. The cells are arranged singly and in small loose clusters, but lacking mitotic figure. A few scattered foamy macrophages along with scattered lymphocytes and delicate blood vessels are also present.

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Table 4. Postoperative outcomes

Variable	Value
Mean ICU stay, days	2.3 ± 1.5
Mean hospital stay after surgery, days	7.4 ± 2.5
Postoperative adverse events, patient n (%)	
Atrial arrhythmia (transient)	2 (10%)
Low output cardiac syndrome	2 (10%)
Acute renal failure	1 (5%)

ICU, intensive care unit.

Disclosures

The authors have no conflicts of interest to disclose.

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