ORIGINAL ARTICLE

Atrial myxoma: 14 years experience

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ABSTRACT

Introduction: Cardiac tumors constitute only 0.2% of all tumors. Primary cardiac tumors occur infrequently with an incidence of 0.0017% to 0.19%, estimated on autopsies performed in non-selected populations. Left atrial myxomas are the most prevalent (75% to 80%) and right atrial are less common (10% to 18%). Surgical excision yields an excellent prognosis and recurrence rate of only 3% with a very low morbidity and mortality.

Objective: We aimed to review our experiences with this rare entity and highlight the various aspects of myxoma presentation, diagnosis and outcomes.

Methodology: A retrospective chart review done on patients underwent excision of myxoma with histo-pathological confirmation since January 1991 till December 2015. Standard surgical approach adopted was single atrial, augmented with Biatrial approach where needed.

Results: A total 42 cases were identified and 28 cases with complete data were included in the analysis. Mean age was 54.4 (±17.7) years, with female predominance (58% vs. 42%). Preoperative comorbidities included hypertension (39.2%), diabetes (28.5%), IHD, dyslipidemia, and COPD (10.7%) that were comparable among gender. The mean dimension of myxoma measured on echocardiography was 4.9x3.5x2.7 cm.

Sixty four percent had left sided and 35.7% had right sided myxoma. Most common symptom was dyspnea (71%), constitutional symptoms (39.3%) and stroke in (18%). Echo being the diagnostic modality of choice. Post-operative complications occurred in 6 patients and mortality occurred in 2 (7.2%). Mean post-operative follow up was 8.3 months and 10 years telephonic follow up completed in (32%) cases, with 2 late non-cardiac mortalities.

Conclusion: Our results showed that the prevalence of cardiac myxoma is comparable with global estimates. Female gender was predominant and age and right atrial myxoma was slightly higher in our sample compare to other published literature. Myxoma can be excised successfully with a low rate of morbidity, mortality and recurrence.

Key words: Atrial myxoma; Prevalence; Clinical characteristics; Morbidity; Mortality

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INTRODUCTION

Cardiac tumors constitute only 0.2% of all tumors found in humans.[1] Primary cardiac tumors arise from normal heart tissue and occur infrequently with an incidence of 0.0017% to 0.19% as shown by autopsies performed in non-selected populations.[2,3] Secondary tumors originating from other parts of the body are 20 to 40 times more frequent.[4] Three-quarters of cardiac tumors are benign, out of which approximately half are myxomas; the other half comprises of lipomas, rabdomyomas, fibroelastomas, and other rarer types.[3]

Mostly (85%) myxomas are located in the left atrium with the remaining 15% in the right atrium and ventricles.[5] Most left atrial myxomas are attached to the interatrial septum.[3] Valvular originations of such tumors are however, very rare.[6] Although they can occur at any stage of life, they occur more frequently between the ages of 30-60 years, with the reported average age being 50 years.[7] Female are three times more likely to develop this tumor and usually exhibit sporadic forms, while familial forms are more common in male patients with 10% familial transmitted in an autosomal dominant mode, occurring at a younger age. [8,9]

The classic triad of symptoms, of which at least one is present, comprises obstructive traits including dyspnea and syncope, constitutional symptoms such as fever and anorexia, and thromboembolic events.[9]

This study was conducted at Aga Khan University Hospital, Karachi, Pakistan and summarizes our 14 year experience of patients diagnosed with cardiac myxoma. The aim of the study was to analyze clinical presentation, diagnostic method and short term surgical outcomes in these patients.

METHODOLOGY

This is a retrospective study of all patients, who presented to our institute since January 1991, till December 2015 were scrutinized using AKUH Patient Care Online Inquiry and patients' medical records. All patients had echocardiographic findings of atrial myxoma confirmed on histopathology were included.

Outpatient and inpatient records were studied including age, gender, signs and symptoms on presentation, comorbids, NYHA class and pre-operative arrhythmias. A preoperative echocardiography finding on location, size, ejection fraction and mitral and tricuspid valve involvement was noted. Per-operative data was collected on approach taken, cardiopulmonary bypass, aortic cross clamp time and minimum temperature. Surgical notes were reviewed for the location of myxoma and any other significant finding.

Surgical technique

In all patients, after general anesthesia and insertion of standard invasive monitoring lines, a median sternotomy was performed and Cardiopulmonary bypass (CPB) with aortic and bicaval cannulation and moderate hypothermia was used. Myocardial protection was achieved by cold anterograde blood cardioplegia. The heart was manipulated after the aorta had been cross clamped to avoid tumor fragmentation and systemic embolization. The surgical approach for left atrial (LA) myxomas was right atrial, trans-septal and superior septal in most cases except 2 where bi-atrial approach was taken. Complete tumor resection was done with full thickness removal of the base and a cuff of normal surrounding interatrial septum to prevent recurrence. All four cardiac chambers were thoroughly examined grossly for additional myxomas. The surgically created defect was repaired with an autologous or bovine pericardial patch. Copious irrigation of the atria and ventricles with cold saline was done to eliminate any loose tumor fragments that might have been dislodged during removal of the tumor.

Post-operative data was collected on the duration of ventilator support, CICU stay, post-operative complications including but not limited to wound infection, pneumonia, acute kidney injury, pericardial effusion, arrhythmias and any thromboembolic event of new onset. Records were noted for any re-interventions and length of hospital stay. Length of follow-up, post-operative echo and histopathology findings were also taken into account. Follow-up out-patient and inpatient consultation notes were studied for any late complications, morbidity and mortality and telephone calls were made to all patients but only few could be reached.

RESULTS

A total 42 patients were diagnosed with myxoma, of which 14 patient files were missing; hence details of 28 patients were analyzed. All patients of cardiac myxoma underwent surgical resection at our institution during last 20-year period, except 3 patients, who were managed conservatively due to being high-risk in the presence of other comorbids. Female were predominant 16 (57.1%) vs. 12 (42.8%). Mean age was 54 ± 17 years, range (16-87). Most of patients 16 (57%) were presented a New York Heart Association (NYHA) class II, 7 (25%) were in class III and 2 (7.1%) patients presented in class IV (Table 1). Comorbidities included hypertension 11 (39%), diabetes mellitus 8 (28.6%), and dyslipidemia 3 (10.7%) (Table 1).

Table 1: Preoperative demographic and comorbidities of patients, n=28.

Variable	n (%)
Age in years (Mean ± SD)	54.4 ± 17.7
Male	12 (42%)
Female	16 (58%)
Comorbidities	
Diabetes Mellitus	7 (25.0)
Hypertension	10 (35.7)
Dyslipidemia	3 (10.7)
IHD	6 (21.4)
Cancer	3 (10.7)
Symptoms	**n (%)**
Dyspnea	20 (71.4)
Constitutional	11 (39.3)
Chest Pain	9 (32.1)
Dizziness	4 (14.3)
PND	3 (10.7)
Syncope	1 (3.6)
Palpitation	1 (3.6)

18 patients presented with obstructive symptoms, 4 with the duo of obstructive and constitutional symptoms and 5 had stroke as presenting symptom. The most common presenting symptom was dyspnea, occurring in 20 patients, followed by chest pain in 9 patients, 4 having dizziness and paroxysmal nocturnal dyspnea (PND). Other non-specific symptoms included cough 6 patients, fever 4, marked weight changes in 3 patients, vertigo in 2 patients, and abdominal discomfort in 2 patients. One patient had chronic hiccups and weight loss with factor VII deficiency and deranged coagulation profile. None of the patients had family history of myxoma (Table 1).

Trans thoracic or trans-esophageal pre-operative echo was the conclusive diagnostic investigation in all patients, augmented with CT chest and cardiac MRI in 2 patients. Echocardiography findings showed a mean ejection fraction (EF) of 53.9% ±14.9. Seven patients had normal A-V valve function, 9 had regurgitation in one valve, and 9 showed some degree of regurgitation in both A-V valves.

There were 16 (57%) left atrial (LA) myxomas, 10 (35.7%) right atrial (RA) myxomas and 2 arising from the mitral annulus. Of these, 19 arose from the inter-atrial septum, 2 each from the annulus of the mitral valve and the free right atrial wall (Table 2).

25 out of 28 patients underwent surgery soon after the diagnosis was made (Table II). All resected myxomas were sent for histopathological examination. Mean CPB time was 94.8 ± 29.8 mins and mean aortic cross clamp time (ACC) was 66.9 ± 22.5 mins. The mean minimum temperature recorded during surgery was 32.6°C. Associated procedures included CABG in 3 patients and MV replacement and repair in 1 patient each (Table2).

Table 2: Surgical procedure and morphology of myxoma

Surgical procedure	N
Isolated Myxoma Resection	20
Myxoma Resection+ CABG	3
Myxoma Resection+ MV repair	1
Myxoma Resection+ MV replacement	1
Site & Size	
Left Atrium	16
Right Atrium	10
Mitral Valve Annulus	2
Mean Myxoma Size (cm) (Length × Width × Breadth)	4.9 × 3.5 × 2.7

Histopathology confirmed the diagnosis of myxoma in all operated patients. The tumors ranged in size from 1 × 1 × 0.5 cm to 10 × 6.5 × 5.5 cm with a mean of 4.9 × 3.5 × 2.7 cm. Histological findings revealed loose myxoid stroma containing stellate and globular cells. Areas of hemorrhage with deposits of hemosiderin were seen and peripheral collagenization was occasionally noted. There was no evidence of pleomorphism or malignancy in this series.

The average length of hospital stay was 10 days (Table 3). The average ICU stay was 3 days after surgery, with a mean intubation time of 14 hours. Postoperative complications occurred in 6 patients, including pericardial effusion requiring drainage and AKI managed conservatively with IV fluids and medications. There was prolonged ICU stay of 74 hours and atrial fibrillation of new onset in 2 patients, and 2 early deaths (within 30 days of surgery) occurred. One patient being young but high risk preoperatively, on high inotropic support, went into fatal arrhythmia and could not be revived, while the second patient, who had associated pulmonary embolism and underwent resection of myxoma and pulmonary embolectomy, died of right heart failure.

Table 3: Intra and postoperative characteristics

Intra operative characteristics	Value
CPB time (min)	94 ± 29
ACC time (min)	66.9 ± 22.5
Minimum temperature	32^{0}C
Post-operative data	
Ventilator Support (hrs.) Median (IQR)	12 (10-17)
CICU stay (days)	2.5 (2.0-4.5)
Hospital stay (days) Median (IQR)	8 (7-107)
Complications	**n**
Pericardial Effusion	1
AKI	1
A-fibrillation	1
Prolonged CICU stay >72 hrs.	1
Mortality	2

llowed post-operatively with the average length of follow-up being 8.3 months. 9 patients underwent echocardiography at follow-up visits, whereas the rest were assessed by recurrence of symptoms. Telephonic calls were made to all patients, but only 9 could be reached. There were 2 late deaths (after 30 days of surgery), both from non-cardiac causes, one occurred secondary to porto-systemic encephalopathy secondary to hepato-renal syndrome and the other occurred in a patient due to brain metastases with hemorrhagic conversions not classified as myxoma on biopsy. The rest reported no recurrence or presence of any symptoms similar to pre-operative presentation (Table 3).

5 patients with left atrial myxomas diagnosed on echocardiography presented with neurologic symptoms. One patient had a posterior circulation ischemic stroke with a progressively decreasing score on the Glasgow Coma Scale (GCS). Another patient presented on his third episode of stroke after recovering from the past two, imaging revealed a right middle cerebral artery infarct causing left sided hemi-paresis. The third presented with left sided facial weakness with MRl showing an acute infarct in the right temporoparietal lobe and an old infarct in the bi-ventricular region, both cerebrovascular infarcts possibly due to embolization from myxoma. He also had bronchiectasis and dilated cardiomyopathy with severe LV dysfunction, hence was termed high-risk and planned for conservative management. Another patient presented with right hemiplegia along with aphasia, urinary incontinence and decreased vision in the left eye. A 36 years old male presented with bilateral posterior cerebral infarct secondary to atrial myxoma. He was in a vegetative condition with sluggish pupils and very low GCS, unresponsive to pain. Therefore, surgery was not performed.

A 65 year old patient with Thalassemia Minor, Factor VII deficiency and documented prior MI presented with the unique complaint of hiccups along with weight loss, dyspnea and chest pain. Lab workup showed deranged PT/INR and severe factor 7 deficiencies. Chest CT and TEE revealed a right atrial myxoma, which was successfully resected, and the patient discharged in stable condition with normal coagulation profile and factor VII levels, at 24 hours and one month post-operatively.

A 38 year old female with hypothyroidism presented with dyspnea. TEE revealed a mass in the left atrium. During resection, however, the mass was identified to be cystic, as it burst open during resection, leaking serous fluid, reported as cystic variant of atrial myxoma. Consequently, it was suctioned from the left atrium followed by thorough washout and the patient successfully discharged with no complications thereafter.

DISCUSSION

Cardiac myxoma is a neoplasm of mesenchymal origin that is usually located in the atria and occurs only on the endocardial surface. Its incidence is low as 0.0017% to 0.19% in non-selected populations.[3] Most of (65%) of patients in our series had left atrial and 35% had right atrial myxomas in contrast to previously described incident of 85% left atrial and 15% right atrial and ventricles.[5] however, an Indian study reported somewhat comparable rates of 72% left atrial and 22% of right atrial myxomas. Valvular origins have a reported incidence of only 1.5%,[6] and in our series there were 2 patients had myxoma of mitral valve annulus origin, one requiring mitral valve replacement and the other just repair after resection. None of our patients had a bi-atrial myxoma.

Female predominance with female to male ratio of 3:1 has been reported other studies (Table I),[2,10] and by Khan MS et al, as 1.44:1.[11] Our study, although consistent with the female predominance, revealed a lower female to male ratio of 1.2:1. The patients in our study had a mean age of 54 years, which was slightly higher than the 50 years of other studies conducted in the west; however it was even higher than a national study reporting the mean age as 33 years.[12.]

In our series 78% of the patients presented with

obstructive signs and symptoms, consistent with previous data reporting 54-95% patients having a similar presentation.[10, 13] The most common presenting symptom was dyspnea, present in 71% of patients, corresponding to the results by two earlier studies in the region.[11,12] Although constitutional symptoms like fever, weight loss and fatigue were presented in 54% of our patients, they were seen in conjunction with obstructive symptoms. Only 3 patients presented solely with constitutional symptoms - a relatively uncommon, but documented finding in other studies.[13] One patient had a peculiar presentation of hiccups along with dyspnea, found to have thalassemia minor and factor VII deficiency with a deranged coagulation profile. 2 of our patients complained of vertigo and 2 of abdominal pain at presentation, which were among the uncommon presentations previously documented.[13]

In our study, 18% patients presented with stroke, chiefly having nausea, headache, numbness, vomiting and seizures along with paraplegia or paresis, relatively lower rate as compared to 30-40% in western studies[14] and a regional study reporting rates of 37%.[15] None of our patients presented asymptomatically as in other studies.[2.] A majority (64%) of our patients presented in NYHA class II, which was consistent with other studies.[11,12]

Echocardiography is the screening and diagnostic method of choice. It is accurate, reliable, noninvasive, and it does not entail any risk of tumor fragmentation and embolization unlike cardiac catheterization.[2.] Echocardiography should be able to characterize the mass by morphologic shape and appearance, site of attachment, margins, and presence or absence of associated valvular and other abnormalities.[16] All patients with myxoma at our institute underwent transthoracic echocardiography pre-operatively while transesophageal echo was also performed in 11 patients. Transesophageal echo has a sensitivity of 100% as compared to 95% with transthoracic echo.[17] However, discrimination between primary cardiac tumors, such as myxoma, and other cardiac masses remain challenging, with atrial thrombi being the most common differential diagnosis of myxoma.[18,19.] Cardiac myxoma requires surgical intervention whereas thrombus formation may be completely resolved with appropriate timely anticoagulation therapy. Furthermore, the use of anticoagulation may potentially be harmful with increased risk of peripheral embolization in the presence of a cardiac tumor.[20] One patient in our study, presenting with dyspnea and weight loss, underwent echocardiography which revealed an echogenic mass of undetermined nature in the right atrium. Consequently, coronary angiography was performed, which diagnosed the mass as right atrial myxoma.

The role of angiography is limited to the preoperative diagnosis of concomitant coronary artery disease in patients, who were 40 years or more and currently has no role in establishing diagnosis of atrial myxoma[21,22] or neovascularization in myxoma. Other potential diagnostic methods include CT[23] and MRI.[24] Their advantage over echocardiography is that they provide sectional views of mediastinal, pulmonary and thoracic structures and are more accurate in assessing tumor attachment, endocardial site localization along with myocardial disease process and tumor stalk presence and size.[24] Only 2 patients in our study underwent CT and cardiac MRI along with echocardiography.

Histological diagnosis is based on the presence of typical myxoma cells in a mucopolysaccaride rich matrix.[25] All our diagnoses of surgically resected myxomas were histologically confirmed upon the identification of typical features.

The treatment of choice for myxomas is surgical resection. Current practices allow for safe procedures and the long-term prognosis is excellent, with a mid-term survival similar to that of the general population.[10,21,25,26] However, previous studies have reported an operative mortality of 3-4%[27] and major postoperative complications such as stroke,[27] cardiac tamponade,[28] transient supraventricular arrhythmias,[10] and respiratory failure.[29] In this series 6 patients developed postoperative complications, being pericardial effusion, AKI, prolong ICU stay and arrhythmias.

Two patients died during admission, one male patient aged 39, presented to us with right leg swelling and weight loss and was diagnosed with pulmonary embolism and pulmonary hypertension. TEE showed extremely enlarged right atrium and ventricle with decreased function, and echogenic mass most likely myxoma in the right atrium along with severe tricuspid regurgitation. A consented high risk myxoma resection from right atrial wall and tricuspid valve was done with pulmonary artery embolectomy, shifted to the ICU on very high inotropic support, developed sudden fatal arrhythmias on 1st post-operative day and could not be revived.

Another 55 year old male, known case of diabetes, hypertension, ischemic heart disease and pulmonary

tuberculosis was admitted with TEE showing a myxoma in the right atrium associated with moderate tricuspid and severe mitral regurgitation, and acute left ventricular failure. Angiography was performed which revealed coronary artery disease. He underwent resection of myxoma along with coronary artery bypass grafting and mitral valve replacement, however, on the 10th post-operative day; he developed cardiac arrest and could not be revived.

Recurrence is considered rare, occurring in only 1% to 5% of patients, and can be attributed to incomplete excision of the tumor, growth from a second focus, or intracardiac involvement by the tumor base.[25] Incidence of recurrence in sporadically-occurring myxomas is 10 times lower than familial forms.[30] When tumor location does not permit wide resection, laser photocoagulation is habitually performed in an area of 1 cm around the tumor peduncle. Both procedures are aimed at eliminating residual tumor cell groups that are capable of generating new proliferation.[25] We report no recurrence in any of our patients however, our short follow-up length was a due limitation.

The results should be interpreted with some limitations. This was a retrospective review that usually faces missing records and variables. Also of note is that such single centered estimates cannot be applied to other populations. Long term follow up was done on telephone that may have introduced a recall bias.

CONCLUSION

Our results indicate that surgery should be performed promptly after the diagnosis is made to avoid potential complications such as embolization or intra-cardiac obstruction. In our study, almost all patients underwent surgery soon after diagnosis, except a few who were managed conservatively due to the presence of multiple, significant co-morbids making them very high-risk patients. Overall prognosis after surgical resection was excellent.

Conflict of interest: None declared by the authors

Authors' contribution:

AH, HARK: Conduction of study work, literature search, manuscript writing

MT: Concept, manuscript editing

SH: Manuscript review, statistical analysis review

HU, SHF, SBH: Manuscript review

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