Clinicopathological Profile of Cardiac Myxomas in Bahraini Population

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Background: Cardiac tumors could be either primary (benign or malignant) or secondary. Myxomas are the most frequent benign cardiac neoplasms of the heart, usually affecting the ages between 30 and 70 years and are typically found in females.

Objective: To evaluate the clinicopathological manifestations of cardiac myxomas in the Bahraini population.

Design: A Retrospective Study.

Setting: Mohammed Bin Khalifa Cardiac Center, BDF-RMS Hospital, Bahrain.

Method: Twelve cases of cardiac myxoma patients were reviewed from 2005 to 2012. Personal characteristics and clinicopathological manifestations were documented.

Results: Twelve patients with cardiac myxoma tumors were included in the study. Seven (58%) patients were females; the age range was from 44 years to 70 years and the mean range was 57.6 years. In eight (67%) patients, the tumors were found in the left-atrium, in three (25%) patients in the right-atrium and in one (8%) patient in the right-ventricle. The most common presentation was chest pain, seven (58%), followed by neurological symptoms, five (42%) and shortness of breath, four (33.5%). Five (42%) patients had diabetes mellitus, four (33.3%) had dyslipidemia and two (17%) had hypertension.

Conclusion: Myxomas were the most common benign primary cardiac tumors in our institute, mostly arising from the left-atria. Five years of follow-up revealed no recurrence. Most patients presented with extra-cardiac manifestations and surgical intervention was the treatment of choice.

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Cardiac tumors could be primary (benign or malignant), arising from the heart or secondary/metastatic. The most frequent and most challenging benign tumors of the heart are cardiac myxomas; they usually arise from subendocardiac reserve or lepidic cells, which occasionally have divergent differentiation[1,2]. They could arise in any cardiac chamber, but usually arise from the left atrium in the fossa ovalis area. The next most common sites are the right atrium and both ventricles. Myxoma could be solid or macroscopic papillary in appearance[1-3]. Cardiac myxomas could present as strokes, peripheral or pulmonary embolism, with or without systemic symptoms.

The most commonly affected age is between 30 and 70 years and is mostly found in females. Patients with cardiac myxomas can have variable clinical symptoms and usually present with three clinical presentations: obstructive, emboli and/or systemic symptoms. Solid tumors commonly have obstructive symptoms and papillary tumors have embolic and systemic symptoms[1]. Histologically, myxomas have an acid-mucopolysaccharide-rich myxoid matrix stromal appearance, which shows polygonal cells containing eosinophilic cytoplasm[1].

The aim of this report is to evaluate the clinicopathological features of the cardiac tumors operated on in our institution.

METHOD

Twelve cases of cardiac myxoma were reviewed from January 2005 to December 2012. The following data were documented: patients' clinical parametrics, such as symptoms, comorbidities, biochemical and hematological data. The duration of the disease, history of cerebrovascular symptoms and personal history, such as smoking were documented. All cases were reviewed histologically by two pathologists to confirm the diagnosis of myxoma.

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RESULT

Twelve cases of cardiac myxomas were reviewed; seven (58%) patients were females. The age ranged from 44 years to 70 years; the mean age was 57.6 years. In eight (67%) patients, the tumor originated from the left atrium, three (25%) from the right atrium and one (8%) from the right ventricle.

Seven (58%) patients presented with chest pain. Five (42%) patients presented with neurological symptoms and four (33.5%) patients presented with shortness of breath. One patient presented with symptoms of myocardial infarction, and another patient had heart failure. Table 1 shows the clinicopathological profile of the 12 patients.

Seven (58.3%) patients had dyslipidemia, and these patients also had increased CK and CKMB levels. No other significant biochemical alterations were found. There was no family history of any cardiac tumors in any of the patients in this study.

All patients had a single tumor on the echocardiogram, and each was removed successfully by surgical intervention, see figures 1 and 2. All were examined microscopically and showed characteristic features consistent with a myxoma tumor, see figures 3 and 4. Five years follow-up revealed no recurrence.

Table 1: The Clinicopathological Profile of the Patients with Myxoma

Case No	Gender	Age	Presenting Complaint	Tumor Site
1	Female	50	Chest Pain, Shortness of Breath	Right Atrial Myxoma
2	Male	56	Shortness of Breath	Left Atrial Myxoma
3	Male	57	Chest Pain	Right Atrial Myxoma
4	Female	70	Chest Pain	Right Ventricular Myxoma
5	Female	64	Chest Pain, Cough and Vomiting	Left Atrial Myxoma
6	Female	57	Chest Pain, Left Upper Limb Weakness	Left Atrial Myxoma
7	Male	59	Left Upper and Lower Limbs Pain and Weakness	Left Atrial Myxoma
8	Male	52	Chest Pain, Left Sided Body Numbness	Left Atrial Myxoma
9	Female	63	Shortness of Breath	Left Atrial Myxoma
10	Male	59	Shortness of Breath	Right Atrial Myxoma
11	Female	54	Heart Failure, Previous Stroke	Left Atrial Myxoma
12	Female	44	Right Hemiplegia	Left Atrial Myxoma

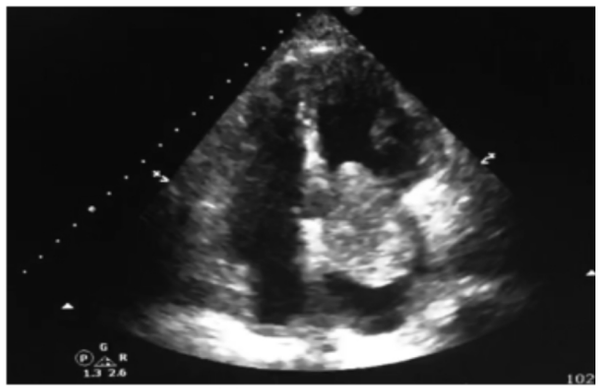

Figure 1: Echocardiogram Showing a Well-Circumscribed Myxoma within the Left-Atrium

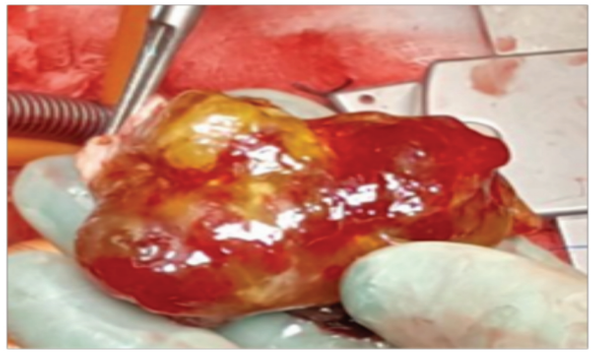

Figure 2: Gross Appearance of the Cardiac Myxoma

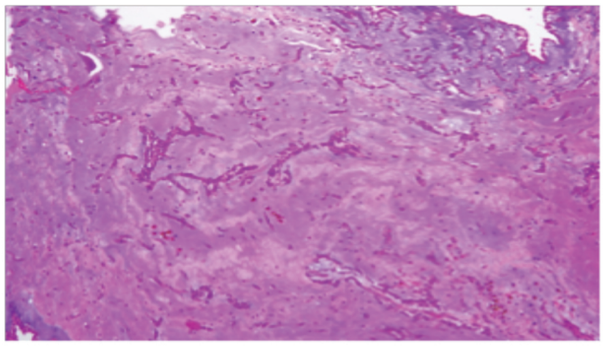

Figure 3: Low-Power View of Microscopic Appearance Showing a Myxoma Tumor, with Abundant Myxoid Stroma (H&E X20)

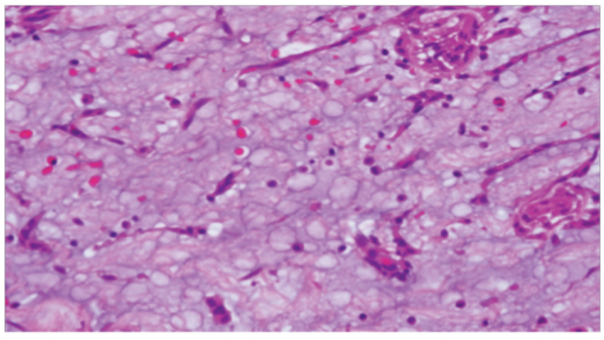

Figure 4: High-Power View of Microscopic Appearance Showing Round, Polygonal and Stellate Cells Arranged in Cords Seen in Abundant Myxoid Stroma (H&E X40)

DISCUSSION

Cardiac myxomas are the most common cardiac neoplasms[1]. The prevalence of primary cardiac tumors is very rare; the estimated incidence ranges from 0.001% to 0.03%[2-14]. The majority are benign and approximately half of all primary benign cardiac tumors are myxomas; others could be lipomas, papillary fibroelastomas and/or rhabdomyomas[3-7,15-16]. Undifferentiated sarcoma and angiosarcoma are the most common primary malignant tumors[4-5,10-12,16].

Cardiac myxomas typically arise from subendocardial reserve cells or multipotent mesenchymal cells, such as entrapped embryonic foregut cells, which may show some divergent differentiation, such as neural or glandular differentiation[3,12,15]. The majority of cardiac myxomas occur in middle-aged females and few in the elderly[1-2,17-18.] However, familial type myxomas occur in a younger age group, with male predominance; it could be seen in unusual locations and have a tendency to be multifocal, in one or more cardiac chambers, as well as having a gelatinous appearance with little fibrosis[2,10,17.] They have either static growth or occasionally show slow growth, ranging from 1.3mm/month to 6.9mm/month in diameter[19].

Complex myxomas or Carney syndromes occur in association with multiple neoplasias, such as thyroid, testicular, breast, neural systems and pigmented nodular adrenocortical disease and they are attributed to PRKAR1A genes[2,10,12]. Kontogiorgi et al have found aneuploidy DNA (diploid) content with 42.9% of cells in the DNA synthetic phase[6].

The Herpes Simplex Virus (HSV) infection has been considered as a predisposing factor in the pathogenesis of sporadic myxomas, and the presence of HSV-1 and/or HSV-2 DNA was detected in 35% of the sporadic myxomas[6,9].

The recurrence rate is 3% and it is associated with incomplete excision and multicentricity. The recurrence rate of the familial and complex types is 12% and 22%, respectively[5,6]. The malignant potential of cardiac myxomas is controversial and only a few cases of extra-cardiac metastasis of myxomas as well as metastatic chondrosarcomas resembling malignant cardiac myxomas have been described[6,11]. Our study did not reveal any recurrence and there was no familial inheritance.

Cardiac myxomas could arise from any cardiac chamber, but they have a special predilection for the left atrium. Approximately 75% of cardiac myxomas originate from the left atrium at the border of the fossa ovalis, while 20% originate from the right atrium and the rest arise from the ventricles[1-2,15]. In our study, eight (67%) cases originated from the left atrium, four (33%) from the right atrium and one (8%) originated from the right ventricle. Cardiac myxomas could also arise from the superior vena cava or the pulmonary veins[8].

Most cardiac myxomas present as a single lesion and only 5% would present as multiple lesions, such as polycentric myxoma; all patients had single lesions[15]. Two morphological types have been described: solid, which is non-mobile with regular round surface and papillary, which is asymmetrical, soft and pedunculated with an irregular shape and mobile surface[1,12,15]. The latter, due to irregular, friable and villous surface, frequently leads to thrombus formation or systemic embolisation[1,15]. The length of the stalk, the extent of the attachment to the heart and the amount of collagen in the tumor are the deciding factors in the mobility of the tumor[5,10]. Cardiac myxomas arising from the right-atrium typically have broad bases while those from the left-atrium are more likely to be calcified and might present with syncope[5,7].

In a study by Demir et al, inferior myocardial infarction was observed in 63.6% of cases, anterior infarction in 22.7% and posterior infarction in 9.1%[15]. Angiogram was normal in 23.8% cases and right-coronary artery embolization was noted in 47.6% cases[15]. It was proposed that the increased incidence of right-coronary artery embolization might have been due to the conductive position of the coronary ostium relative to the aortic blood flow[15].

The majority of the patients present with one or more of the classic cardiac triad: cardiac symptoms and signs resulting from obstruction, signs of systemic embolization or systemic constitutional symptoms, or a combination of these[3-4,20]. The presentation depends on the morphology, size, mobility and location of the cardiac myxoma[3,6]. The most common cardiac manifestations are shortness of breath and orthopnea from pulmonary venous hypertension or frank pulmonary edema, the former being the most common, followed by pre-syncope or syncope due to the ball-valve effect of the cardiac myxomas[1,3,4,6]. Patients with solid tumors are more likely to experience obstruction of the pulmonary or systemic venous drainage, mitral stenosis, shortness of breath, cardiac failure and arrhythmias[1,6,15]. Patients with papillary cardiac myxomas usually suffer from central or peripheral embolization symptoms, such as strokes, systemic/pulmonary embolisms and low hemoglobin due to tumor fragmentation and clot formation[1,9]. One-third of the patients present with neurological manifestations, such as aphasia, cerebrovascular attacks or transient ischemic attacks[1,3,20].

The extra-cardiac manifestations include primary pigmented nodular adrenocortical disease, skin lesions (melanotic schwannomas, lentigines and blue nevi), weight loss, arthralgia and fever, with abnormal laboratory findings, such as elevated sedimentation rates and protein abnormalities[3,15,20].

The clinical signs and laboratory findings are occasionally unpredictable[15]. The symptoms could resemble those of collagen vascular disease, rheumatic heart disease, disseminated malignant disease or infective endocarditits[4,10,13]. These symptoms resolve after tumor removal.

The presentation also depends on whether it is sporadic or familial. The right-sided cardiac myxoma in the younger age group with extra-cardiac manifestations is associated with the autosomal dominant familial type, also known as Complex Cardiac Myxomas[4].

The diagnosis of cardiac tumors has significantly improved following the rapid advances in cardiac imaging. Transthoracic echocardiogram (TTE) is usually the initial investigation for diagnosing cardiac myxoma, however, it has a lower specificity. Transoesophageal echocardiogram (TOE) is very sensitive, especially for the early cardiac myxoma[3,15-17]. It could identify the

location of the tumor, the number (single or multiple), the size, as well as tissue morphology and valvular abnormalities[6,12]. CT and MRI could be helpful in identifying the size and shape of the tumor[3,5,6]. Recently, MRI has become the modality of choice in differentiating left-cardiac myxoma from malignancies[6].

Cardiac myxoma has an acid mucopolysaccharide stroma with eosinophilic polygonal cells called myxoma/lepidic cells[4,12]. These cells could be found either individually or in clusters and might contain a single or multiple nuclei. Mitotic figures are not commonly seen[1]. Mallick et al described a rare glandular differentiation in their pediatric case[2].

The best curative modality is surgical excision; however, a conservative treatment could be used in high-operative-risk patients, asymptomatic patients and slow-growing tumors[15,17-18]. Because of the high risk of embolization, surgery should not be delayed in papillary myxomas[15]. Postoperative recovery is rapid, however, cardiac arrhythmias and atrioventricular conduction defects could be seen[3,20]. In our study, all patients were treated with surgical excision and all had an uneventful postoperative recovery.

Antithrombotic therapy is generally not recommended despite the high risk of embolization. Thrombolytic agents might increase hemorrhage and cause rupture of small fragments, leading to an even higher risk of embolization[5,15]. Long-term follow-up is recommended in familial myxomas. In Carney's syndrome, the prognosis is poor due to the malignant potential of the other extra-cardiac tumors[6].

CONCLUSION

Cardiac myxomas are very rare cardiac tumors that typically present with extra-cardiac manifestations, leading to significant morbidity and mortality. Echocardiography and MRI are vital in the diagnosis. Long-term follow-up is necessary for familial and young age groups due to the high-risk of recurrence. Since papillary myxomas are associated with a high-risk of embolization, surgery should not be delayed.

In our study, predominance of elderly females revealed a left-cardiac preference and no recurrence or familial inheritance were documented.

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