An Unusual Presentation of Cardiac Myxoma; a Case Report and Review of Literature

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Abbreviations

MR: Mitral Regurgitation; CHF: Congestive Heart Failure; DM II: Diabetes Mellitus Type 2; HTN: Hypertension; COPD: Chornic Obstructive Pulmonary Disease; TTE: Transthoracic Echocardiography; TEE: Transesophageal Echocardiography; EF : Ejection Fraction; DD: Diastolic Dysfunction; IABP : Intra-Aortic Balloon Pump; MV: Mitral Valve; OR: Operative Room; IAS: Inter-Atrial Septum; POD: Pos-Operative Day; NYHA: New York Heart Association Classification; LA : Left Atrium; RCA: Right Coronary Artery; CABG: Coronary Artery Bypass Graft; AF: Atrial Fibrillation; TTE : Trans-Thoracic Echocardiography; TEE: Trans-Esophageal Echocardiography; CT: Computed Tomography; MRI : Magnetic Resonance Imaging; F-FDG PET: F-Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET)

Introduction

First recognition of cardiac tumor is attributed to Columbus earlier in 1559 [1]. Though cardiac tumors can be primary or metastatic, later group is more common. The occurrence of metastatic cardiac tumors has been reported a 100-fold more commonly than primary lesions [2]. Roughly, three quarters of cardiac tumors are benign and remainders are malignant; half of benign cardiac tumors are myxomas [1, 3]. Although Cardiac Myxomas (CM) are benign tumors but they are a major cause of patient morbidity and mortality, due to impairment of cardiac dynamics and their thromboembolic potential [3,4].

Cardiac myxomas are slowly proliferating neoplasms of uncertain histogenesis with heterogeneous histomorphology and variable and sometimes clinically quite malignant pathological manifestations. Majority of cardiac myxoma occur sporadically while a relatively small proportion of diagnosed cases develop as a part of Carney complex syndrome with established familial pattern of inheritance [5].

Myxomas occur in all age groups and in both sexes, but more often occur in women between the third and sixth decades of life [3].

Myxomas can be polypoid, round or oval. They are gelatinous with a smooth or lobulated surface and usually are whitish,

yellowish, or brown in colour. The mobility of tumor depends upon the extent of attachment to the inter-atrial septum and the length of the stalk [1]. Although cardiac myxomas are benign, they have the potential to cause serious complications, including embolic events and partial or complete obstruction of intracardiac blood flow and catastrophic haemodynamic instability [4].

Cardiac myxomas are most commonly found in the left atrium (75%), followed by the right atrium (20%), right ventricle (3%–4%), and left ventricle (3%–4%) [8]. Most atrial myxomas, whether left or right, arise from the atrial septum, usually from the region of the limbus of fossa ovalis. About 10% have other sites of origin, particularly posterior wall, anterior wall and the appendages (in order of frequency) [1]. heart valves are extremely rare locations for this tumor to originate, either as the primary site or the site of recurrence [9,10]. When it occurs, it involves both leaflets with the same frequency and usually originates from the atrial side [9]. Few reports reported multiple and multifocal cardiac myxomas. When there are multiple, multifocal masses, especially in ventricular chambers, one should consider Carney complex, which has an autosomal-dominant inheritance pattern [8]. Familial myxomas mainly affect young people and the female predominance is not as marked [3].

Clinical manifestations among studies widely variable depending on the size of the tumor, location, and its mobility. Commonly reported manifestations include SOB, recurrent pulmonary edema, syncope, fever, weight loss, arthralgias and pulmonary or systemic embolism. However, it has been rarely reported for cardiac myxoma to present with severe MR preoperatively. Here we will present a case of left atrial myxoma presented with a decompensated CHF due to severe MR because of chordae rupture which has been also rarely reported as a cause of preoperative MR in cardiac myxoma.

Case Presentation

A 65-year-old female morbidly obese with a body mass index of 55 Kg/m² known case of DMII since 20 years on insulin, HTN, bronchial asthma and COPD since 10 years and iatrogenic Cushing syndrome on cortisone therapy since 1 year. Unfortunately,

she did not respond to the initial regimen of bronchial asthma and the doses have been escalated till oral prednisolone was introduced 10 months ago. Although her symptoms did not resolve completely, but the patient and her family did not seek a second medical opinion. 3 months ago, she started to develop worsening of her shortness of breath on exertion together with orthopnea and paroxysmal dyspnea. She presented to emergency department with severe respiratory distress and severe hypoxia and hemodynamic instability. Her physical examination was remarkable for hypotension, pulmonary edema and typical Cushinoid features. Bed side TTE revealed a big left atrial mass

filling almost the left atrium and prolapsing in-and-out in the left ventricle through mitral valve with severe mitral regurgitation. The mass was found attached to inter-atrial septum. TEE confirmed the diagnosis of big mass originating from interatrial septum freely mobile in and out through the mitral valve with severe MR, EF 55%, DDII (Figure 1). After insertion of IABP, the patient was intubated and shifted to cardiac critical care where inotropic support started. The decision was urgent surgery for tumor excision and MV surgery. The patient was taken urgently to cathlab to review her Coronary angiography and was found unremarkable, then the patient shifted urgently to OR.

Figure 1A & 1B: Echocardiographic image showing huge mass protruding into the LV from LA with severe MR

Operative details

Routine median sternotomy was done and cardiopulmonary bypass was established. We gained our access through right atrium and we incised the IAS at the fossa ovalis. A part of the IAS was excised where the base of the mass attached to and whole mass (10x5x3cm) was taken out as a one piece to prevent recurrence. It was found polypoid in nature and prolapsing into the left ventricle through the mitral valve and attached to

lateral papillary muscle and its chordate (Figure 2). Evaluation of the mitral valve revealed chordae were ruptured in A2, A3 and P2 with a ruptured part between A2 and A3. MV replacement (with both anterior and posterior native leaflet and chordal preservation) was done with a mechanical prosthesis (SJ # 29) with interrupted mattress Ethibond 2/0 sutures. Closure of the IAS was done using autologous pericardium patch. The patient was weaned-off smoothly from bypass and intraoperative TEE revealed well-seated valve prosthesis with no residual tumour parts without any complications.

Post-Operative course

The patient had an unremarkable ICU course except for late extubation and she was discharged home in her 15th POD after chest physiotherapy and routine physical training for walking and muscle strengthening.

The report of histopathology confirms the diagnosis of huge benign cardiac myxoma with no evidence of malignancy or atypical mitosis (Figure 3).

With frequent follow up she showed improvement in NYHA class from IV preoperatively to NYHA II two months post operatively with no recurrence so far.

Figure 2: The excised tumor in one piece with part of IAS and part of ruptured chordate at the other end

Figure 3: Histopathology slide showing the myxoma tissue composed of round, polygonal or stellate cells in loose myxoid matrix

Discussion

Primary tumors of heart and pericardium are rare with an incidence ranging from 0.001 to 0.03% [6, 7]. 75% of primary cardiac tumors are benign; approximately half of these are cardiac myxomas, and the rest are lipomas, papillary fibroelastomas, and rhabdomyomas.

Left atrial myxomas produce symptoms when they reach a weight of about 70gms, right atrial myxomas grow to approximately twice this size before becoming symptomatic. Tumors vary in size, ranging from 1–15cms in diameter [1]. Previous case reports have attempted to estimate the growth rate of myxoma, which has been highly variable. The rate of growth ranges from no growth in 15 years to 1.36 cm/month [8]. Our patients' symptoms became more evident to bring her to ER department with decompensated CHF after 10 months from initial presentation.

Early diagnosis is pivotal and surgical resection should be done promptly after diagnosis given the myriad complications that may occur with delay [8]. Unfortunately, related symptoms are often nonspecific and mimic many cardiovascular diseases, limiting early diagnosis [11, 12]. Clinical manifestations vary among studies widely variable depending on the size of the tumor, location, and its mobility. They range from causing no symptoms to causing high morbidity and mortality [8]. In about 10-20% cases, myxomas are discovered as an incidental finding and a high index of clinical suspicion is important for its early and correct diagnosis. [1, 12,13].

The classic presentation of left atrial myxomas comprises a triad of symptoms ("myxoma triad"), which includes embolic and obstructive phenomena and constitutional symptoms. Obstructive symptoms including dyspnea, recurrent pulmonary edema and syncope, are reported to be the most common presentation among the triad [3, 12, 14-16]. Unlike left atrial myxomas, Embolic events are considered the most frequent manifestation of valvular myxomas, followed by obstructive symptoms and less likely to present with constitutional manifestations [9, 17].

Rarely, LA myxoma coincides with or even manifests with MR as for our patient [18]. However, when a large tumor mass grows from the atrial septum into the left ventricle, it can compromise MV competence even if that is not obvious preoperatively [19-22]. MR can be a consequence of ventricular and annular dilatation, direct leaflet damage or rarely due to rupture of Chordae Tendineae as a result of the mechanical damage of the tumor [19,23]. Since 1970, only 4 cases were reported in literature regarding left atrial myxoma presenting with preoperative severe MR as a result of chordae tendineae rupture [24-27].

Our patient was admitted as a case of acute decompensated CHF due to severe MR after 10 months of her initial presentation. She had been misdiagnosed with uncontrolled asthma with cortisone therapy on base of that wrong diagnosis and we believe her initial presentation was obstructive in nature but not severe enough to cause significant symptoms. The tumor was found to be polypoid prolapsing into the left ventricle causes severe MR due to chorda rupture. This is in agreement to the believe that polypoid tumors more frequently prolapse into the ventricle through the mitral or tricuspid valve and this could result in destruction of valve apparatus [1,2].

Embolic manifestations are the most severe due to their morbidity and mortality [3]. Myxoma can cause an embolism by way of the tumor emboli or thromboemboli that are released from or formed on the surface of the tumor [28]. Previous reports have estimated that the risk of embolism associated with cardiac myxoma ranged from 30 to 40 %, and that >50 % of embolic events affected the central nervous system and retinal arteries [29]. Right-sided myxomas has lower incidence to embolize as compared to left-sided myxoma [30]. He et al think that tumor location, macroscopic appearance, mean platelet volume, and high platelet count are strong risk factors for embolic events in patients with cardiac myxomas. Elbardissi, et al. have suggested that patients with small tumors, minimal symptoms, and no evidence of MR have a high risk of embolism [29]. Shimizu K, et al. concluded that infected cardiac myxoma has an extremely high incidence of systemic embolization [31]. Tomas Francisco et al has concluded that villous myxomas have high tendency to embolize compared to that with a smooth surface and they highlighted the importance of the echocardiogram in describing the morphologic characteristics of these tumors [3]. Jong-Won Ha and associates reported a more frequent occurrence of systemic embolism in polypoid tumours as compared to round [1]. Two studies have suggested male gender is also considered a predictor for embolization [14,15]. Coronary artery embolization is an extremely rare and potentially lethal complication of atrial myxomas and it should be considered in patients with no cardiac risk factors. One case has been reported with an embolization to RCA and underwent CABG [32].

Constitutional symptoms including fever, weight loss, arthralgias, and Raynaud's phenomenon are observed in 50% of patients with cardiac myxomas [1]. These symptoms are thought to be as a result of production of IL-6 when it reaches a certain threshold [33]. This is supported by the postoperative regression of clinical and immunologic features that accompanies

normalization of IL-6 serum levels [33]. A few studies have found that the size of the tumor directly correlates with the amount of circulating IL-6 [33,34].

ECG findings may be nonspecific in 20% to 40% of patients. The most common ECG finding is left atrial hypertrophy (35%), followed by repolarization disorders (21%), conduction disorders (24%), and rhythm disorders (9%). AF and atrial flutter are rare in left atrial myxoma [35].

Echocardiography is widely available and applicable and most commonly used as the imaging technique of choice. It can delineate multiple cardiac structures and characteristics of a mass such as its mobility, attachment and potential hemodynamic consequences [36, 38]. TTE is approximately 95% sensitive for the detection of cardiac myxomas, and TEE approaches 100% sensitivity [13]. Operation for left atrial myxoma can be undertaken solely on the basis of echocardiographic findings [39].

On echocardiogram, a myxoma presents as a heterogeneous mobile mass with one of the two basic appearances, either polypoid or papillary. Polypoid myxomas are larger with a smooth surface and a rough core including lucencies and cystic areas due to hemorrhage and necrosis. Papillary myxomas tend to be smaller and have a stretched appearance with multiple villi [37]. TEE is commonly used when a valvular lesion is suspected, may also become necessary to better characterize a cardiac tumor in terms of size, morphology, attachment site, extension and hemodynamic affects [38]. The use of 3-dimensional (3-D) echocardiography is the newest approach in the assessment of intracardiac masses. Three-dimensional echocardiography allows for a volumetric assessment of a mass over a linear measurement as it is obtained with 2-dimensional imaging. With the cropping techniques available with 3D, various aspects of the mass can be better visualized including point of attachment, homogeneity, vascularity, and calcification [38].

However, echocardiography provides limited assessment of soft-tissue characteristics and extracardiac structures and may be limited by poor acoustic windows, particularly in obese patients and those with chronic lung disease. For these reasons, cardiac CT and MRI are often utilized synergistically with echocardiography in the evaluation and management of cardiac masses [40].

Cardiac CT is a fast imaging technique with Electrocardiographic (ECG) gating that provides high quality images with superior

spatial resolution. Electrocardiographic gating minimizes motion-related artifacts and allows a more precise delineation of the lesion margins. Compared to other cardiac imaging modalities, CT is optimal for the evaluation of calcified masses, the global assessment of the chest and lung tissue and corresponding vascular structures, and the exclusion of obstructive coronary artery disease or masses which involve the coronary arteries. Cardiac CT is also useful to detect metastases in suspected malignancies especially when coupled F-FDG PET. The ability of F-FDG PET/CT to detect the increased metabolism of glucose may help distinguish malignancy from a benign neoplasm. For example, primary malignant cardiac tumors and metastatic tumors show significantly higher glucose uptake as quantified by F-FDG PET/CT Standardized Uptake Value (SUV) than primary benign cardiac tumors. On cardiac CT, approximately two-thirds of myxomas are ovoid with a smooth or lobular shape, with the remainder villous in appearance. When visualized on non-contrast CT, they typically appear hypodense, consistent with blood, and may demonstrate calcifications more often in the right atrial location. On contrast-enhanced cardiac CT, myxomas appear as intracavitary filling defects with heterogeneous contrast enhancement, though the intensity may be variable depending on their chronicity and whether necrosis or hemorrhage is present. Significant disadvantages with CT include radiation exposure, a small risk of contrast-induced nephropathy, and lower soft tissue and temporal resolutions as compared with magnetic resonance imaging, and may be inconclusive because of multiple artifacts in case of intra-cardiac mechanical prosthesis [40,41].

Cardiac MRI is often the preferred imaging modality for cardiac masses because of its superior soft-tissue characterization, high temporal resolution, multiplanar imaging capabilities, and unrestricted field of view. Since MRI does not require the use of ionizing radiation, it is the modality of choice, along with echocardiography, for pediatric patients with cardiac masses. However, cardiac MRI is dependent on patient cooperation to obtain quality images and is specifically contraindicated in patients with claustrophobia and implanted magnetic devices. At times, MRI may also be limited for evaluating small mobile masses (e.g. papillary fibroelastoma or valvular vegetations) due to limitations in spatial resolution and typically does not provide detailed assessment of the coronary arteries in cases where the assessment of coronary artery disease prior to surgery is an important clinical question [40]. MRI features of cardiac myxoma and cardiac thrombus are demonstrated in Table 1.

Table 1: Cardiac myxoma versus cardiac thrombus features in cardiac MRI(30)		
Cardiac MRI features differentiating myxoma from thrombus		
Features	Myxoma	Thrombus
Location	Left atrium commonly a fossa ovalis	Left atrium commonly a left atrial appendage or left ventricle in association with infarct
Attachement	Narrow often pedunculated	Broad based
Mobility	Very mobile	Less mobile
Function impact	Prolapse of the lesion through atrioventricular valve	Left ventricular functional impairment common: prolapse through the valve is not evident

T1 signal	Heterogeneous intermediate T1 signal	Homogenous hypointense T1 signal*
T2 signal	Heterogeneous hyperintense T2 signal	Homogenous hypointense T2 signal*
Gadolinium enhancement	Heterogeneous pattern of enhancement common	Enhancement extremely uncommon unless very organized with high level of fibrous tissue
Inversion time on late Gadolinium sequences	200-300 ms	550-650 ms
* Thrombus signal return is dependent on whether the thrombus is acute, subacute or chronic. Signal characteristics described in the table are those demonstrated by chronic thrombus		

Since the ages and the symptoms of patients who have left atrial myxomas and coronary artery disease are similar, coronary angiography should be performed in older patients who are at risk for coronary artery disease [42,39].

The diagnosis of an atrial myxoma warrants an urgent resection due to the risk of embolization, cardiovascular complications and sudden death [8,38, 43]. Fortunately, benign cardiac myxomas are totally treatable tumors and surgery is usually curative with a low operative risk and an excellent short- and long-term prognosis [13,43-45]. However, if left untreated, the medium and long-term prognosis is fatal [46].

Bahnsen and Newman (1953) reported the earliest surgical approaches to myxomas by removing a myxoma from the right atrium via right anterior thoracotomy using a short period of caval obstruction at normothermia [1]. Craford (1955) successfully excised a myxoma from left atrium using cardiopulmonary bypass [1]. In 1944, biatrial approach has been introduced by Kabbani SS, et al. and accepted widely as it allows for the inspection of the four cardiac chambers, limits manipulation of the mass, and facilitates the complete excision of the tumor [1,39]. Left atrial access alone does not enable complete heart inspection, requires significant tumor manipulation in the event of a large mass, and may not permit radical resection. Similarly, a right atriotomy with septal incision may not accommodate removal of a large tumor mass without fragmentation [19].

Potential complications associated with the biatrial approach include supraventricular arrhythmias, conduction disturbances, and postoperative left-to-right shunting. The superior septal approach can in most cases provide good exposure of the left atrium and the mitral valve, but it has a possible adverse effect on sinus node function, due to its extensive horizontal right atrial incision [19].

The recurrence rate of myxoma has been reported to range from 1% to 5% [8]. Previous studies involving > 20 years of follow-up have indicated that the sporadic form of cardiac myxoma seldom recurs. Although the mechanism responsible for the recurrence remains unclear, younger men, patients with multiple lesions, and those with family history of myxoma are more susceptible to develop recurrence [11,47]. Previous studies showed that the recurrence might be due to the following reasons: inadequate resection, or multifocal pattern behavior of a benign myxoma, either in the same or in a different location as the primary tumor. Familial disposition may also play a role in recurrent development. The abnormal DNA ploidy pattern

of myxoma patients showed a high recurrence [48]. Still the relationship between local intracardiac recurrence and the adequacy of surgical resection is quite controversial [29].

Since late recurrence, although rare, has been reported, long-term clinical and echocardiographic follow-up is recommended [39]. There are no guidelines on the frequency and duration of monitoring [8]. However, Bjessmo and Ivert recommended surveillance echocardiography to be limited after uncomplicated resection. Given the potential for catastrophic morbidity and mortality of untreated myxoma, it would be most prudent to continue yearly surveillance indefinitely [8]. Though the majority of atrial myxomas are sporadic, it is imperative that first-degree relatives of patients with documented myxomas undergo screening for occult myxomas [13].

In genetic analysis novel frame shift mutation was detected in exon 2 in a heterozygous fashion in the causative gene of CNC, protein kinase A regulatory subunit 1 alpha (PRKAR1A). This genetic mutation is thought to cause haplo-insufficiency of PRKAR1A resulting in tumorigenesis and its detection can assist with myxoma prognosis [49].

Conclusion

The obtained results and review of literature indicated the feasibility and safety of cardiac myxoma surgery with significant improvement of echocardiographic data and functional outcome and minimal cardiac and non-cardiac morbidity. Early accurate diagnosis and prompt surgical management of cardiac myxomas is mandatory for better outcome.

We think from our point of view that our case is unique and rare because of three reasons: 1-its presentation with "severe mitral regurgitation", 2-its false misleading diagnosis from the start as a case of "bronchial asthma" since long time, 3-its presentation with "big size" 10x5x3cm.

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