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Exploring the Clinical Spectrum, Diagnosis, and Outcomes of Cardiac Myxomas: A Comprehensive Retrospective Case Series

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ABSTRACT

Introduction and Background: Cardiac myxomas are rare tumors that present a complex clinical spectrum, leading to a challenging diagnosis. In this retrospective study, we explore the clinical manifestations, diagnostic complexities, and surgical outcomes of cardiac myxomas.

Methods: A retrospective analysis of 10 patients diagnosed with cardiac from 2018 to 2023 was conducted. Clinical records including age, gender, tumor dimensions, and symptoms were reviewed. Data were analyzed using descriptive statistics and SPSS V23.0.0 software.

Results: The median age of patients was 48.5 years, having a slight male predominance (60%). Cardiac symptoms were observed in 70% of the patients. These included dyspnea, palpitations, fatigue, syncope, and heart failure. Neurologic symptoms were present in 20%, while constitutional symptoms such as fever, weight loss, and fatigue affected 70% of patients. Myxomas were primarily located in the left atrium (70%), followed by the right atrium (20%) and left ventricle (10%). Echocardiography and histopathological evaluation confirmed diagnoses. All patients underwent successful surgical excision with no major complications.

Discussion: Our findings align with previous studies regarding age distribution and gender prevalence. Cardiac myxomas exhibit a diverse range of symptoms, making diagnosis challenging. Constitutional symptoms are frequently observed and may result from elevated interleukin-6 levels. Diagnostic tools such as echocardiography and histopathology play pivotal roles in confirming myxoma diagnoses. Surgical excision remains the gold standard treatment, ensuring positive outcomes.

Conclusion: Cardiac myxomas present with a myriad of clinical manifestations, necessitating a high index of suspicion for accurate diagnosis. This retrospective case series underscores the importance of prompt surgical

intervention following diagnosis, offering favorable outcomes and a resolution of symptoms. Further studies are needed to explore the underlying pathophysiological mechanisms of cardiac myxomas and their systemic effects.

INTRODUCTION

Cardiac masses are rare, accounting for only 0.2% of all tumors in humans, classified either as primary cardiac tumors, or secondary when metastatic from other parts of the body[1] with the latter being far more prevalent. The most common sources for a metastatic cardiac tumor tend to be a primary malignancy in the lungs, breast and skin i.e. melanoma. On the other hand, the most common primary cardiac tumor is a cardiac myxoma; a benign tumor originating from the endocardium,[1] with an incidence less than 1 per million per year.[2]

Cardiac myxomas were first described in 1952 by Goldberg et al after an unsuccessful attempt at resection of the intracardiac mass.[3] It is most frequently diagnosed in adults during the fourth decade of their lives[1,4] with a slightly higher predilection for the male sex in the ratio of 3:2.[5] Myxomas are categorized as either sporadic, accounting more than 90 percent of the cases and presenting mainly in middle-aged women;[6] or familial, which affects younger men with multiple tumors, potentially in different heart chambers.[7] The symptoms of cardiac myxoma can be varied and nonspecific, posing a diagnostic challenge requiring a high index of suspicion. The most common symptoms are shortness of breath, palpitations, fatigue and syncope.[1,2,5] In severe cases, it can lead to valvular regurgitation causing heart failure, or embolize to the cerebral circulation leading to stroke like symptoms.[1,2,8]

Most myxomas typically develop in the left atrium or on the surface of the mitral valve,[1-3,9,10] often causing constitutional symptoms such as weight loss and fatigue. Left atrial myxomas often present with dizziness, palpitations, chest pain and syncope. They are commonly detected as incidental findings on an echocardiogram.[3,9,10] Right atrial myxomas occur primarily in the interatrial septum and vena cava, usually without symptoms.[1,2,11] Lesions in either location can lead to obstructive and embolic complications. Ventricles are the rarest sites for myxomas,[12] and most of the diagnoses are made incidentally, as their presentation is usually insignificant without any particular symptoms.[12,13]

The diagnosis of cardiac myxoma consists of echocardiographic detection followed by histopathological confirmation on tissue biopsy. Treatment involves the surgical removal of the tumor.[1,2,9-12,14] The study presented in this article is a retrospective analysis of 10 patients with cardiac myxoma.

METHODS

Study Design:

A retrospective study was performed to assess cardiac myxoma cases identified at a tertiary care hospital between 2018 and 2023. The study exclusively examined cases with a confirmed diagnosis of cardiac myxoma, determined through histopathologic evaluation. Clinical records were reviewed to collect relevant information, including age, gender, date of diagnosis, dimensions of cardiac myxoma, and associated clinical manifestations. All these details are given in Table 1 and Table 2.

Statistical Analysis:

To assess the normal distribution of continuous variables, we employed the Shapiro-Wilk test which indicated a positively skewed data set, therefore we utilized descriptive statistics such as the median, interquartile range (IQR), and percentages to present the data accurately. Statistical analysis was conducted using IBM SPSS V23.0.0. This case series is written in accordance with PROCESS guidelines.[15]

RESULTS

A total of 10 diagnosed myxoma patients, comprising 6 males (60%) and 4 females (40%), were included in the study. The median age was 48.5 years, with an interquartile range of 18. The data exhibited a positive skewness, with a skewness of 1.25. Out of 10 patients included in the study, 5 (50%) exhibited cardiac symptoms including orthopnea, paroxysmal nocturnal dyspnea, lower extremity edema, palpitations, shortness of breath and exertional blackouts. Additionally, 3 patients (30%) were presented with neurological symptoms such as paraplegia, hemiparesis, dysarthria, headaches, vertigo, and dizziness. Systemic manifestations, including weight loss, fever, fatigue, nausea and generalized myalgias were reported by 7 patients (70%). Among them, 2 patients showed an elevated Erythrocyte Sedimentation Rate (ESR). Cutaneous symptoms were not observed in any of the patients. Patients had a variety of abnormalities during cardiac auscultation. One patient exhibited moderate aortic regurgitation (AR) murmur, another patient had a moderate mitral regurgitation (MR) murmur, and another patient displayed a moderate tricuspid regurgitation (TR) murmur. Additionally minor murmurs were observed in a separate patient. Furthermore, one patient displayed electrocardiogram (EKG) evidence of atrial fibrillation.

Table No. 1

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age (Sex):	35 F	25 M	50M	45F	60F	60F	46M	83M	47 M	50M
Murmurs:										
AR	–	–	–	–	–	–	–	+	–	+
MR	–	–	–	–	+	–	+	+	–	–
TR	+	–	–	–	–	–	–	+	+	–
PR	+	–	–	–	–	–	–	–	–	–
Echocardiography:										
Size of myxoma	–	–	–	3*3cm	4.1*5.1 cm	5.5cm*3.3cm	44mm*22 mm	25*28 mm		43*44 mm

Site of myxoma	L A	LV	RA	LA	LA	LA	LA	RA	LA	IAS
HFrEF	–	–	–	–	–	–	–	+	–	–
Dysfunctional RV	–	–	–	–	–	–	–	–	+	–
Pulmonary HTN	–	–	–	–	–	–	–	–	+	–
Clinical Manifestations										
Cardiac	+	–	–	–	+	+	–	+	+	–
Neurological	–	+	–	–	–	–	+	–	–	+
Systemic	+	+	+	+	+	+	–	–	–	+
ESR	–	+	–	–	–	+	–	–	–	–
EKG	–	–	+ (Atrial fibrillation)	–	–	–	–	–	–	–

Table No. 2

	1	2	3	4	5	6	7	8	9	10	Percentage (out of total patients) (%)
Cardiac symptoms											70
Palpitations	+				+	+		+			40
Dyspnea (Orthopnea, PND)	+			+	+			+	+		50
Lower extremity edema									+		10
Exertional syncope							+				10
Neurological symptoms											40
Paraplegia		+							+		20
Hemiparesis		+							+		20
Dysarthria		+									10
Headaches	+						+				20
Vertigo/Dizziness							+		+		20
Systemic symptoms											80
Fever			+					+			20
Weight loss	+		+							+	30
Nausea and fatigue	+			+	+	+				+	50

ESR elevation		+				+					20

All patients underwent echocardiography as part of their evaluation; however, the definitive diagnosis was established through histopathological examination. The echocardiogram results indicated specific findings in certain patients: one patient exhibited left ventricular systolic dysfunction with an EF of 35%, another patient had right ventricular dysfunction, while elevated pulmonary artery systolic pressures were observed in a separate patient. Among the patients included in the study, it was found that 2 patients (20%) had the myxoma located in the right atrium, while 7 patients (70%) exhibited the myxoma in the left atrium. Only 1 patient (10%) had the myxoma detected in the left ventricle. Furthermore, the size of the myxoma was determined for all patients. The recorded measurements ranged from 25 x 28mm (about 1.1 in) to 41 x 55mm (about 2.17 in).

DISCUSSION

Myxomas are notably common in individuals between their third and sixth decades of life[16] consistent with our study which reports a median age of 48.5. In certain studies, however, the ages have shown variability, spanning from 35-70 years (with mean ages of 68.7 years and 60 years). In our investigation, approximately 40% of the patient cohort comprises females, aligning with the demographic distribution observed in studies conducted by Angeli et al. and Gaisedrees et al.[17,18] Although gender contributes a significant determinant in the distribution and localization of myxomas within the heart, studies indicate that it does not exert a discernible influence on clinical outcomes and mortality rates.[17] All these details are mentioned in Table 1 and 2.

The precise origins of cardiac myxomas remain uncertain; nevertheless, there exists a consensus regarding their histopathological characteristics and the molecular elements implicated in tumor progression. Cardiac myxomas develop within the endocardium through the differentiation of multipotent mesenchymal cells.[19] Eosinophilic polygonal and spindle shaped cells are embedded in the sea of gelatinous matrix called ‘myxoid stroma’ that makes bulk of these tumors. In a literal sense the word ‘myxoid’ means related to ‘mucus’.[20] In histology, however, myxoid is used to refer to a tissue that contains a high amount of sugar.[21] Composing the stroma are glycosaminoglycans, mainly chondroitin-6-sulphate and hyaluronic acid.[20,22] Generally, considered benign, these tumors do have some malignant potential.[23] Existing literature attributes the rapid growth of these tumors to active angiogenesis and high microvascular density mediated by the autocrine secretion of vascular endothelial growth factor.[22]

The major symptoms associated with cardiac myxomas can be categorized into three primary groups: cardiac symptoms, neurological symptoms, and systemic symptoms.[24] The cardiac symptoms of a myxoma depend on its location, size and mobility inside the heart chambers.[14] Like a valvular ball valve action, it can obstruct the flow of blood and lead to a combination of exertional and obstructive symptoms.[25,26] The prevalent cardiac symptoms observed in our patient population were dyspnea, palpitations, fatigue, syncope, heart failure and lower

extremity edema. Notably patients have also been documented to present with cough, chest pain, and in some cases, myocardial infarction.[25,27] We found cardiac symptoms in 7 of our patients (70%). This finding is comparable with the rate reported by Garcia-Carretero et al. (40.9%) and the study conducted by Penede et al., which reported a cardiac symptom occurrence of 67% in a larger cohort comprising 112 patients.[24,25]

Neurological complications are also common, with patients presenting with hemiplegia, dysarthria, hemiparesis, abrupt retinal artery occlusion, and occasionally even vertigo and seizures.[16] These symptoms are a sequalae of cerebral infarction secondary to embolization.[1,22,28] Several factors have been proposed as potential indicators of future embolism. These include large tumor dimensions, increased left atrial diameter, morphological irregularities on the tumor surface, as well as the presence of atrial fibrillation.[29] Lee et al proposed that the mobility of a myxoma rather than its size, serves as a predictor for embolization.[16] Within our small cohort, neurologic symptoms were observed in 2 patients, corresponding to a prevalence rate of 20%. Comparable incidence rates have been reported in previous studies, including Pinede et al. (20.5%), Garcia Carretero et al. (13.6%), and Lee et al. (12%).

Constitutional symptoms, the third major class of symptoms, encompass an array of systemic manifestations from fatigue, weight loss and fever, and elevated inflammatory markers. Constitutional symptoms, as described above, were present in our study in 70% of patients. Increased levels of circulating interleukin-6 produced in the myxoid tissue mediated the plethora of constitutional symptoms.[30,31] Immunohistochemistry shows that myxoma cells are pluripotent cells having the potential to transform into endothelial cells and fibroblasts which are known to secrete IL-6. Interleukin-6 (IL-6), a crucial cytokine regulating immune and physiological responses, is mainly produced by monocytes and macrophages as; however, it is also produced by diverse cell lines including, T-cells, B-cells, hepatocytes, mesangial cells, and even tumor cells, underscoring its complex multifunctionality. Interleukin-6 is recognized as a versatile cytokine, actively participating in a multitude of essential pathways within the body. These encompass the synthesis of acute phase proteins like C-reactive proteins and hepcidin, the modulation of inflammatory processes and the regulation of immune responses. Interleukin-6 engages in a coordinated mechanism by binding with the IL-6 receptor and gp130, effectively eliciting an inflammatory cascade. This orchestrated response encompasses the synthesis of acute phase reactants, ultimately resulting in systemic manifestations such as fever.
This contributes to the systemic manifestations seen in cardiac myxoma.[32] Previous research studies demonstrated that elevated serum concentrations of interleukin-6 (IL-6) in myxoma patients were concomitant with systemic symptoms, suggesting that these manifestations were not merely coincidental superimposed pathologies: rather, there existed a direct connection between the two phenomena. Also, upon the successful resection of the tumor, these abnormalities resolved, further suggesting an increase in IL-6 levels and the constitutional effects associated with myxoma are intertwined.[32-34]

Patients typically exhibit a range of non-specific symptoms such as fever, fatigue, nausea, weight loss, myalgias, palpitations, headaches and dizziness which may lead to potential misinterpretation for other medical conditions.

The way a cardiac myxoma manifests clinically is primarily influenced by its specific location within the heart. The classic triad comprising hemodynamic obstruction, systemic manifestations, and embolic phenomena may or may not be evident.[35] Two-dimensional echocardiography is a valuable tool for identifying the location, size, shape, attachment and mobility of a myxoma.[7,35-37] However, CT and Cardiac MRI can also provide detailed information about tissue composition. This enables the characterization of hemorrhagic, fatty and solid tumors.[3,7,38,39] While echocardiography plays a crucial role in diagnosing cardiac myxoma, the definitive and most reliable test for its confirmation remains histopathological evaluation, considered the gold standard. According to a study conducted in Korea, among the 256 cases initially diagnosed as myxomas based on echocardiography, only 174 cases (65.7%) were subsequently confirmed to be true myxomas on histopathological examination. This finding suggests the potential for misdiagnosis of other cardiac pathologies as myxomas during initial imaging evaluation.[40,41]

The presence of concurrent medical conditions can pose challenges in accurate diagnosis. In addition, the clinical presentation of a myxoma itself displays clinical variability.[42] In our cohort, a patient had atrial fibrillation in addition to right atrial myxoma with constitutional symptoms like weight loss. On transthoracic echocardiography (TTE), it was difficult to accurately differentiate it from a thrombus since atrial fibrillation itself predisposes to thrombus formation. However, TEE in that patient showed a pedunculated mass in the right atrium attached to the interatrial septum as opposed to thrombus in a left atrial appendage raising our suspicion of a cardiac myxoma. Some patients also had moderate coexisting MR, AR and TR. We recognize that these murmurs might have been present as a sequela of the tumor causing obstruction or they might have been present due to primary valvular disorder. Nevertheless, during auscultation the conventional tumor plop was not easily discernible, and this led to a broader differential and delay in definitive treatment i.e., surgical resection. Another patient had right ventricular dysfunction, RA and RV dilation and peripheral edema in his legs. This patient had a left atrial myxoma but was initially treated as a right sided HF patient. The patient's myxoma was later discovered on a routine TTE.

Currently, two dimensional TTE is the first and most utilized imaging modality to detect myxomas. TTE accurately delineates essential parameters such as the precise location, dimensions, morphology, attachment, and mobility of cardiac myxomas, along with providing valuable insights into their hemodynamic features.[43] But certain drawbacks like suboptimal image quality of TTE, due to poor echogenicity, may impede detection in up to 5% of the patients.[38] Moreover, the exact location of the attachment point might not be discerned, especially in RA myxoma. These disadvantages of TTE are reduced by using TEE as it provides closer proximity to the tumor location and as a result, it allows for better visualization and attachment point identification.[42] Other modalities like CT scan, cardiac MRI and PET scan have also been used in various capacities. Surgical excision is the only definitive treatment and is highly effective. Upon diagnosis, prompt surgical excision is recommended to prevent systemic embolization and cardiovascular complications.[44] In our study cohort, all patients underwent surgical intervention, resulting in successful tumor excision, and during the follow-up period, no significant adverse events or complications were reported.

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