RESEARCH ARTICLE

Cardiac myxoma: Clinical and pathological features of a rare benign primary heart neoplasm among Tuzla Canton patients

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Objective: To investigate the clinical and pathological features of a rare benign primary cardiac tumour.

Methods: A retrospective analysis was conducted on 13 patients diagnosed with cardiac myxoma (CM) over a six-year period. Patient data including demographics, clinical presentation, imaging, laboratory, echocardiographic, histopathological characteristics, surgical intervention details, and postoperative outcomes were reviewed.

Results: The mean age of patients included in the study was 57,69±13,47 (range 29 to 80 years), with a female predominance. The most common location of the tumour was left atrium (69.2%), followed by the right atrium (23.1%) and the left ventricle (7.7%). The most common clinical presentation included a combination of dyspnea, angina, fatigue and palpitations (76.9%). Followed by a syncope (15.4%), while one patient was asymptomatic. There was significant association with left ventricular location of CM and the presence of arrhythmia (p=0.004). Besides usually observed histological findings, glandular structures with mucin forming glands were present in 30.8% of cases and calcifications in 15.4%. All patients underwent surgical resection with favorable short-term outcomes.

Conclusion: Cardiac myxoma is a rare but clinically significant neoplasm requiring prompt diagnosis and surgical management. Echocardiography remains essential for detection, and histopathology reveals a spectrum of features. Despite the study's small sample size, findings highlight the importance of early recognition and support the need for larger multicentric studies to better define its prevalence and behavior.

Keywords: echocardiography, myxoma, neoplasm, outcome, pathology

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Introduction

While metastases to the heart from other primary cancers are generally rare, they are up to 30 times more common finding compared to primary cardiac tumours [1]. Although cardiac myxomas (CM) represent the most common primary cardiac tumours encountered in clinical practice, their incidence in the general population is very low and varies from 0.0017% and 0.03% in autopsy series [2, 3]. Recent Spanish study estimated a higher incidence of 2.1 per million adjusted to the European population [4].

Cardiac myxomas are benign neoplasms of uncertain origin and histopathogenesis characterized by gelatinous consistency, typically arising within the atria [5]. They present a complex clinical challenge due to diverse clinical manifestations and potential for life-threatening complications [6].

Timely recognition and management are vital [7] requiring a high level of suspicion in order to make a timely diagnosis [8], since surgical removal of the tumour should be carried out without delay following diagnosis to avoid the risk of unexpected death, particularly in individuals experiencing hemodynamic instability [9].

Considering the rarity of primary cardiac tumours, we aimed to investigate clinical and pathological characteristics of this rare neoplasm over a six-year period in one of the most populous cantons in our country.

Methods

Patients and study design

This retrospective study included 13 patients diagnosed with cardiac myxoma who were admitted to the Cardiology Department between January 1, 2018 and December 31, 2024.

Comprehensive clinical data, including demographic information, medical history, presenting symptoms, diagnostic and laboratory findings, and clinical outcomes, were extracted from electronic medical records.

Inclusion criteria for the study were patients older than 18 years of age diagnosed with primary cardiac myxoma based on histopathological examination of excised specimens.

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Methods

Echocardiography served as the primary imaging modality for initial diagnosis, providing information on tumour size, location, mobility, and associated hemodynamic effects. Cardiac MRI was performed in one patient, later confirmed to have superficial thrombotic masses, who underwent imaging at another institution at his own request for a second opinion and further clarification of the differential diagnosis.

All patients underwent surgical resection of the cardiac myxoma. The surgical approach, including the use of cardiopulmonary bypass and surgical techniques employed for tumour excision, was tailored to individual patient characteristics and tumour characteristics. Intraoperative findings, including tumour size, location and attachment site were documented.

All tumour specimens were fixed in 10% buffered formalin, paraffin-embedded, processed and stained with Hematoxylin & Eosin.

In cases where morphology alone was insufficient, immunohistochemistry with a basic panel of antibodies (calretinin, S100, CD31, CD34, keratin and alpha SMA) was applied to confirm the diagnosis of cardiac myxoma.

Histopathological examination of excised specimens provided a detailed characterization of tumour histology and observation of investigated parameters: the presence of the smooth muscle cells within the myxoid stroma; glandular structures with mucin forming glands; haemorrhage, inflammatory cells; calcification; superficial thrombi; ossification and thymic rests. All above-mentioned histologic criteria were evaluated as absent; mild; moderate and pronounced.

All patients were followed according to the same postoperative protocol. The surveillance schedule included clinical examination, electrocardiogram, and transthoracic echocardiography performed at 1 month, 3 months and 6 months after surgery, followed by a repeat evaluation at 12 months. Thereafter, patients underwent regular annual clinical and echocardiographic follow-up. In this cohort, the total follow-up duration ranged from 6 months to several years (up to 5-6 years in patients operated in 2019).

Statistical analysis

The continuous numerical values were expressed by mean and standard deviation. The Spearman correlation coefficient was used to analyze the association between numerical data. The category variables were expressed in percentages and compared by exact Fisher test with Yates correction for small samples. Values of $p<0.05$ were considered statistically significant. IBM Statistics SPSS version 25.0 package was used for all calculations.

Ethical statement

The study was approved by the local ethics committee (Approval Date: September 18, 2025; Approval Number: 02-09/2-172-3/25.)

Results

Patients and tumour characteristics

Patient mean age was 57,69±13,47 (range 29 to 80 years). Out of 13 patients, 9 (69.2%) were women and 4 (30.8%) were men. Male patients were younger (mean age 51.50±15.08 years) compared to female patients (mean age 60.44±12.62 years), although without statistical significance (p=0.28).

The mean maximal diameter of the tumour was 4.51±1.72 cm (range from 2.2 to 8.0 cm). There was no significant difference in size of tumours located in left and right atrium (left: 4.51±1.94 cm, right: 4.73±1.55 cm, p=0.92).

Male patients had larger tumour diameter (5.40±1.81 cm) compared to females (4.12±1.63 cm), and patients younger than 50 (mean size 6.30±2.40 cm) had larger tumours compared to patients aged 50 and older (4.19±1.49 cm), but without statistical significance in both case (p=0.23; p=0.11, respectively).

The most common location of the tumour was left atrium (69.2%), followed by the right atrium with 23.1% and the left ventricle in one case (7.7%). Tumours located in left and right atrium were attached to the interatrial septum, mostly pedunculated. Only one patient had the tumour fixed to the free wall of the right atrium. In case of left ventricular localization, tumour mass was free in the ventricle.

There was no statistically significant difference in tumour localization between male and female patients (p=0.27).

Patients with left atrial myxoma were younger (mean age 54.22±13.79) compared to patients with tumours in other localizations, reaching the limit values of p=0.05.

One patient (7.7%) was asymptomatic and the diagnosis of myxoma was made on casual echocardiography. Two patients (15.4%) presented with a syncope, while others (76.9%) showed a combination of dyspnea, angina, fatigue and palpitations. One of the patients that presented with syncope, had neurologic symptoms by stroke type (ischemic cerebrovascular insult) which happened during vision screening.

There was no significant correlation between tumour size and type of symptoms (p=0.15).

All patients had normal values of ejection fraction ranging from 55 to 70%. Only one patient showed signs of arrhythmia on an electrocardiogram (ECG), while others had sinus rhythm. Tumours located in left ventricle showed an association with the presence of arrhythmia (p=0.004). However, this finding is based on a single patient and should be considered anecdotal and not generalizable.

Main comorbidities included hypertension (53.8%), mitral valve insufficiency (7.7%) or both (15.4%). Three patients (23.1%) had no comorbidities.

Laboratory findings showed abnormalities in the values of C reactive protein (CRP) and the presence of anemia. The majority of patients (92.3%) had increased values of CRP preoperatively. Although we noticed normal CRP preoperative values only in asymptomatic patient, and the

highest in patients with multiple symptoms, such as dyspnea, angina, fatigue and palpitations, there was no significant association between these variables (p=0.39).

There was no significant association between tumour size and presence of arrhythmia on ECG, nor with preoperative values of CRP (p=0.74; p=0.99, respectively).

Anemia was present in five (38.5%) patients. Patients with anemia had tumours located only in left atrium, but there was no significant association between tumour location and the presence of anemia (p=0.16).

According to available follow-up data at the end of February 2025, none of the patients experienced a recurrence of the disease nor lethal outcome.

Histologic characteristics of cardiac myxomas

Regarding the investigated histologic characteristics, we observed usual presented findings, such as inflammatory cells in majority of tumours (69.2%), mostly mild lymphocytic inflammatory infiltrate, haemorrhage with hemosiderin deposits in 92.3% of cases, ranging from mild to pronounced, and smooth muscle cells within the myxoid stroma (46.15%). Glandular structures with mucin forming glands were present in 30.8% of cases and calcifications in 15.4%. We found no osseous metaplasia nor thymic remnants in the tumour.

All histologic characteristics of examined tumours are summarized in Table 1.

The most representative histologic and immunohistochemical findings are presented in Figure 1 and Figure 2, respectively.

We compared all the histologic characteristics with tumour size and location, but we did not observe any statistical significance. We noted that tumours with haemorrhage, presence of calcification, superficial thrombi and inflammation were larger than those without these characteristics, but without statistical significance (p>0.05)

Discussions

Even though cardiac myxoma is uncommon, if not properly and promptly treated, it can result in significant morbidity and mortality [10].

A recent meta-analysis showed that echocardiography can diagnose up to 98% of cardiac myxoma cases, making it the only required modality for diagnosis [3].

Table 1. Histologic characteristics of examined tumours.

N (%)	Smooth muscle	Glandular structures	Haemorrhage	Inflammation	Calcification	Superficial thrombi
Absent	7 (53.8)	9 (69.2)	1 (7.7)	3 (23.1)	11 (84.6)	12 (92.3)
Mild	5 (38.5)	4 (30.8)	5 (38.5)	7 (53.8)	-	1 (7.7)
Moderate	1 (7.7)	-	6 (46.1)	3 (23.1)	2 (15.4)	-
Pronounced	-	-	1 (7.7)	-	-	-
Total	13 (100.0)	13 (100.0)	13 (100.0)	13 (100.0)	13 (100.0)	13 (100.0)

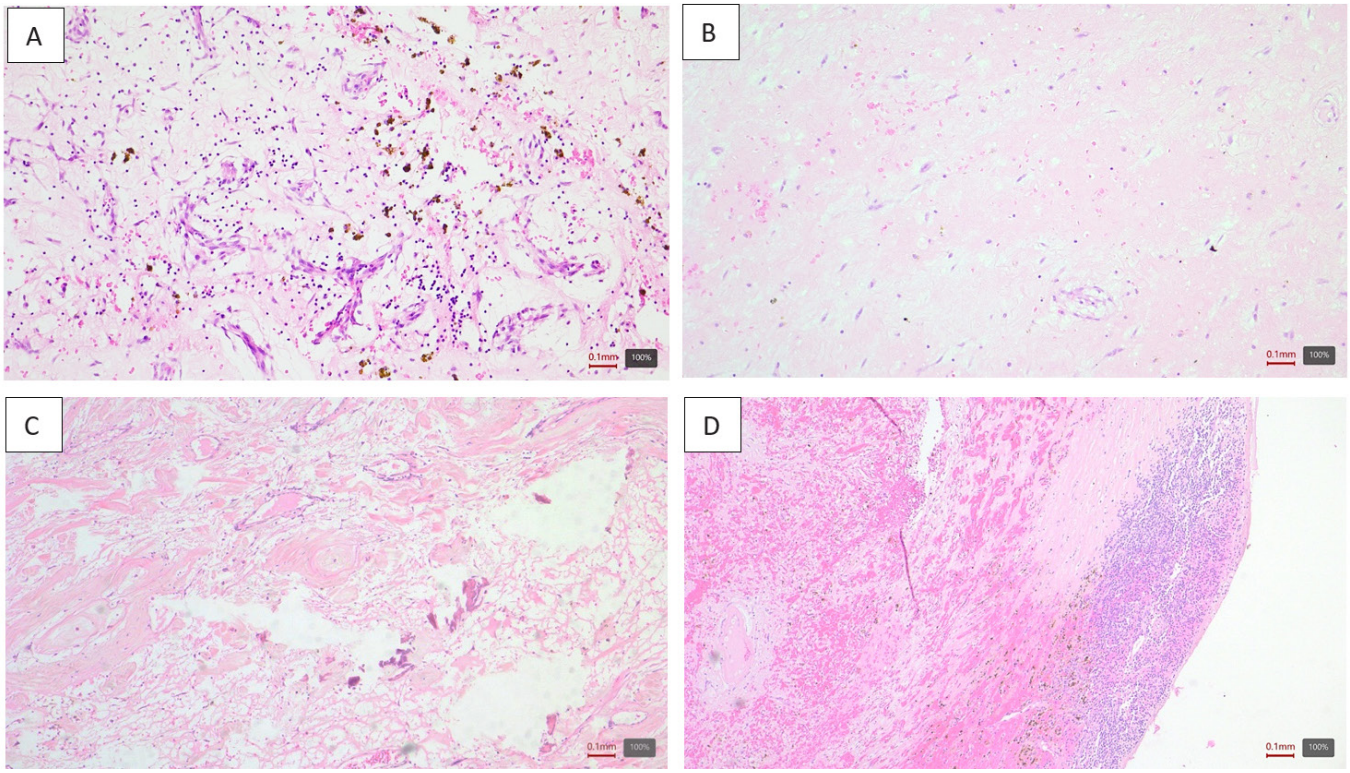

Fig. 1. Morphologic characteristics of examined cardiac myxomas: A: Haemorrhage with haemosiderin deposits within tumour tissue (HE, x100); B: Characteristic myxoid stroma (HE, x100); C: Myxoid and hyaline stromal material (HE, x100); D: Mild lymphocytic infiltrate throughout tumour tissue (HE, x100).

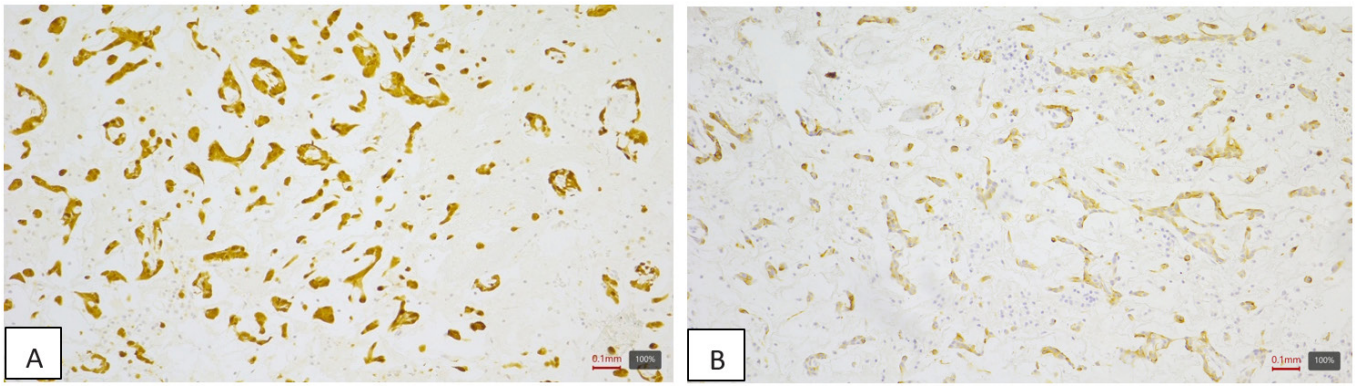

Fig. 2. A: Calretinin positivity (x 100) and B: CK7 positivity of tumour cells (x100).

In our study, all cases of CM were diagnosed by echocardiography, which served to determine tumour size, morphology, extension, site of attachment, pedunculated characteristics and hemodynamic manifestations.

Cardiac myxomas are more common in females, and are usually diagnosed between ages of 40 and 60, mostly around the age of 50 [3]. The age of our patients varied widely (from 29 to 80 years) but most were older than 50, with a mean age of 57.69±13.47 which is consistent with results in the literature [11, 12].

Meta-analysis of Oktaviono et al. showed that among 7156 patients, the left atrium is the most common location of CM, followed by the right atrium [3]. Cardiac myxomas in left ventricle are very rare, with only 2-3% of cases [13]. Although on small sample size, our data are in concordance with these findings.

In most cases, clinical manifestations of CM are nonspecific, which increases the time to a definitive diagnosis, leaving the possibility for the development of complications. One of the most common symptoms reported in the literature is dyspnea, followed by cardiovascular or hemodynamic symptoms such as palpitation, heart failure, and syncope [3, 14]. The majority of tumours presented in the left and right atrium, among patients in our study, were pedunculated. Pedunculated tumours may move through the atrioventricular valve at systole with a "wrecking ball" effect and cause valve obstruction, syncope and even sudden death [15].

Cardiac myxoma symptoms depend on the tumour size, location, mobility, invasiveness, and friability [16]. We noted that only patients with free left ventricular tumour had embolic complications that presented as cerebral ischemic events. Also, the same patient had arrythmia on ECG, due to atrial fibrillation, confirming the significant association between location in left ventricle and presence of arrhythmia, although due to the small sample size, these results should be interpreted with caution. Other studies found that myxoma of the left ventricle causes a variety of cardiac symptoms besides arrhythmia and embolic events, including syncope, dyspnoea, or hemodynamic compromise [17,18]. According to reports, women with cardiac myxoma experience more constitutional symptoms than men do, and for unclear reasons, the tumour primarily affects the right side of the heart. Malaise, anorexia, fever, arthralgia, and weight loss are among the symptoms, which frequently resemble connective tissue illnesses [19]. We also found that right atrial tumours are more common in women, usually with fatigue.

Elevated erythrocyte sedimentation rate (ESR), C reactive protein, interleukin-6 (IL6) and serum gamma globulin levels can be found in patients with CM, but have limited specificity [20, 21]. We also found majority of the patients with elevated CRP levels before the surgery. It can be explained by releasing cytokines by the tumour, especially IL6, which might be more sensitive in predicting inflammatory status than CRP [8].

The presentation of cardiac myxoma can be highly variable and may resemble a wide spectrum of neoplastic and non-neoplastic intracardiac masses. Because of this morphologic variability, the differential diagnosis must incorporate a combined pathohistological, imaging-based and clinical assessment [22].

Cardiac myxomas are tumours of uncertain origin and histopathogenesis. The main hypothesis suggests an origin from multipotent mesenchymal cells [5]. Diagnostic criteria of CM comprise neoplastic (lepidic) cells within the amorphous myxoid stroma [8]. Besides classic histologic characteristics necessary for the diagnosis of CM, we observed some rarely reported components, such as glandular structures, which represent entrapped foregut rests [5], and calcification.

Glandular differentiation in cardiac myxoma is considered an uncommon finding and has been described in only a small portion of reported cases, usually below 5%. Histologically, these glandular areas, may resemble gastrointestinal-type epithelium, with acini lined by columnar or goblet-like cells capable of producing mucin. Because of this resemblance, glandular elements in a cardiac tumour can easily mimic metastatic adenocarcinoma, and their identification requires careful correlation with clinical, radiologic and immunohistochemical features. Glandular structures are positive for pan-cytokeratin, CK7, CAM5.2, EMA, and carcinoembryonic antigen (CEA) while negative for CK20 and CDX2 [23, 24].

Calcifications are variably present in CM, in about 20% of cases. Some studies suggest that calcifications are more

frequently observed in right atrial myxomas, compared with other locations [22, 25]. We found calcifications in two cases of CM, both located in left atrium.

The presence of calcification in cardiac myxoma is primarily of diagnostic rather than prognostic relevance. Heavily calcified tumours may produce acoustic shadowing on transthoracic echocardiography, making it difficult to delineate the mass and potentially mimicking other calcified cardiac lesions, such as organized thrombi, sarcomas or metastatic tumour. In cases of pronounced tumour calcification, cardiac magnetic resonance is useful for additional information. Although calcifications are more frequently associated with long-standing tumours, current evidence does not suggest a significant impact on clinical outcomes [25].

Histologically, myxomas are characterized by a hypocellular myxoid matrix rich in proteoglycans, within which scattered polygonal, stellate, or spindle-shaped mesenchymal cells are embedded, typically without significant cytologic atypia or mitotic activity. This distinguishes myxoma from malignant cardiac tumours, such as myxofibrosarcoma, angiosarcoma, or epithelioid hemangioendothelioma, which demonstrate significant atypia, infiltrative borders, high mitotic index, and areas of necrosis [22]. Conversely, non-neoplastic entities such as thrombi lack stromal architecture entirely, consisting predominantly of fibrin and coagulated blood elements without viable tumour cells. Although organized thrombi may mimic myxoid tissue grossly, histologically they remain completely distinct. Lipomas and lipomatous hypertrophy of the interatrial septum also differ fundamentally, containing mature adipocytes rather than myxoid matrix, whereas fibromas exhibit dense collagenous stroma with sharply demarcated borders and no myxoid component [26].

Immunohistochemically, cardiac myxoma demonstrates characteristic profile that supports its origin from multipotent mesenchymal cells. The most consistently positive marker is calretinin, which shows strong, diffuse cytoplasmic and nuclear staining and is considered one of the most reliable markers for CM [27]. In addition, myxoma cells frequently show S100 positivity, while vascular components within the lesion may express CD31 and CD34, although the positivity of these markers is variable [28].

Imaging characteristics are one of the key components to differentiate CM from other cardiac masses. On echocardiography, typical cardiac myxomas appear as heterogeneous masses, arising from the interatrial septum, often pedunculated and variably mobile [8].

On MRI, myxomas usually appear iso- to hypointense on T1-weighted images, hyperintense on T2-weighted sequences owing to their myxoid content, and demonstrate heterogeneous post-contrast enhancement due to secondary changes, such as haemorrhage, cystic degeneration, or calcifications [29, 30]. Atrial thrombi, in contrast, are commonly located in the left atrial appendage, lack a stalk, and characteristically show no or minimal contrast enhancement, reflecting avascularity. Papillary fibroelastomas are usually small, highly mobile, frond-like valvular lesions whose homogeneous MR signal and valvular attachment distinguish them from septal myxomas. Lipomas demonstrate consistent fat signal (hyperintense on T1, signal suppression on fat-sat sequences), while fibromas appear as homogeneously low-signal masses with intense late gadolinium enhancement due to dense collagen. Malignant cardiac tumours or metastases tend to exhibit infiltrative margins, extracardiac extension, tissue heterogeneity, and often pericardial effusion or concomitant masses in other cardiac chambers [26].

Clinically, classic CM manifests through a triad of intracardiac obstruction, embolic events, and constitutional symptoms such as fever, malaise, or elevated inflammatory markers. In contrast, thrombus usually lacks systemic inflammatory manifestations. Papillary fibroelastomas are frequently asymptomatic, presenting mainly through embolic complications rather than obstructive physiology. Lipomas and fibromas tend to cause arrhythmias or conduction abnormalities when intramural, whereas malignant tumours may present with rapidly progressive heart failure, chest pain, signs of pericardial involvement, or symptoms related to the primary malignancy in the case of metastases [22, 31].

In our study, all patients underwent surgical resection as the primary treatment modality, and during the follow-up period, no recurrences were observed, indicating successful outcomes following surgical intervention. These findings align with previous literature reporting favourable outcomes following surgical resection of cardiac myxomas [32].

By reviewing the available literature, only a few studies published in our country [33] presented clinical characteristics of cardiac myxoma in multiple patients.

While this study provides valuable insights into the clinical and histological characteristics of cardiac myxoma, several limitations should be acknowledged. The main limitations of this study are the small sample size and the retrospective design, which restricts the ability to draw statistically significant conclusions and limits generalizability. Therefore, any statistically significant associations observed in this study should be interpreted cautiously, as the limited sample size may reduce the statistical power to detect true difference.

Conclusion

In conclusion, cardiac myxoma is a rare but clinically important benign heart tumour, most commonly located in the left atrium.

This study highlighted its varied clinical presentations, including dyspnoea, palpitations, and syncope, as well as its histological diversity. Echocardiography proved essential for diagnosis, and surgical resection led to favourable short-term outcomes with no recurrences observed.

Despite the small sample size, these findings emphasize the need for timely diagnosis and management, as well as

further multicentric research to better understand this neoplasm's prevalence and behaviour.

Authors' contributions

JS (Data curation, Investigation, Writing – original draft); NČ (Writing – original draft, Conceptualization, Methodology); EH (Validation, Writing – review & editing, Supervision), ES (Formal Analysis, Visualization, Investigation).

Conflict of interest

None to declare.

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