REVIEW

Characterization of surgical cardiac tumors

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ABSTRACT

OBJECTIVE: The primary tumors of the heart are extremely rare. There are divided to benign, malignant and metastatic. Metastatic cardiac tumors are more common.

METHODS: The incidence in contemporary echocardiographic series is reported at a higher frequency of 0.15 %. 75 % of cardiac tumors are benign; approximately half of these are cardiac mommas. The malignant cardiac tumors are mostly histopathologically undifferentiated, followed by leiomyosarcomas and angio-sarcomas.

RESULTS: Cardiac tumors have a wide range of unique clinical presentation. Even the most benign and smallest tumor can lead to significant morbidity and mortality. The clinical presentations of the primary cardiac tumors are due to: blood flow obstruction, tumor embolization and constitutional symptoms. Clinical presentations can be varied and may resemble coronary disease, pericarditis, cardiomyopathy or valve malfunction. The recent technological advances in non-invasive imaging modalities such as echocardiography and cardiac magnetic resonance imaging is rapidly increases the early diagnosis and management approach.

CONCLUSION: In this review we aim to summarize the characterization of the most common cardiac tumors. Early recognition and treatment provided the best results (Tab. 2, Fig. 6, Ref. 66).

KEY WORDS: heart tumor, characterization, diagnosis, incidence.

Epidemiology

Both primary and metastatic cardiac tumors are rare clinical findings with an autopsy frequency ranging from 0.001 % to 0.030 % (1). The incidence in contemporary echocardiographic series is reported at a higher frequency of 0.15 % (2). Metastatic cardiac tumors are much more common (3) than primary lesion with bronchial carcinoma being the most frequent (4). Three-quarters of primary cardiac tumors are benign (Tab. 1); approximately half of these are cardiac myxomas, and the rest are lipomas, papillary fibroelastomas, and rhabdomyomas. In reported primary malignant primary cardiac tumors, those classified histopathologically as undifferentiated make up the bulk of these, followed by angiosarcomas and leiomyosarcomas (5). The limited incidence and difficulty of detecting cardiac tumors earlier during the initial course have traditionally provided knowledge about these rare clinical entities mostly based on case report collection (6). However, with recent technological advances in non-invasive imaging modalities such as echocardiography (7) and cardiac magnetic resonance imaging (8), and their frequent application, a rapid increase in clinical data on cardiac tumors has resulted (Fig. 1). These imaging modalities provide real-time heart images with high spatial and temporal resolution and an excellent tissue characterization of the tumor (9).

The earlier diagnosis of cardiac tumors before significant symptoms develop has led to an earlier referral pattern and management approach (10). In this review we aim to summarize the surgical characterization of the most common primary cardiac tumors.

General clinical features

Cardiac tumors have protean clinical presentations because of their potential to mimic other diseases (Tab. 2). Even the most be-

Tab. 1. Cardiac tumors by incidence, age at diagnosis, gender (ratio) and autopsy findings (note that some tumors are autopsy findings and they remain undiagnosed).

| Tumor Type          | Incidence (%) | Age (years) | Gender (ratio) | Autopsy (%) |
|---------------------|---------------|-------------|----------------|-------------|
| Benign tumors       |               |             |                |             |
| myxoma              | 45            | 30–60       | female 10      |             |
| papillary fibroelastoma | 15         | variable    | NP NA          |             |
| lipoma (hypertrophy)| 10            | adult       | NP 0           |             |
| hemangioma          | 3             | 30–40       | female 41      |             |
| fibroma             | 2             | children    | female 10      |             |
| rhabdomyoma         | <1            | children    | male 70        |             |
| atrioventricular nodal | <1       | 30–40       | female 100     |             |
| Malignant tumors    | 25            | 19          |                |             |
| sarcoma             | 20            | 18          |                |             |
| undifferentiated    | 24            | 30–50       | NP 9           |             |
| fibrous histiocytoma| 11–24         | children    | male 0         |             |
| rhabdomyosarcoma    | <1            | children    | male 15        |             |
| osteosarcoma        | 3–9           | variable    | male 0         |             |
| leiomyosarcoma      | 8–9           | variable    | NP 8           |             |
| angiosarcoma        | 37            | 30–50       | male 33        |             |
| lymphoma            | 2             | 35–40       | male 85        |             |

NA – no data, NP – no preference

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nign and smallest lesion can lead to significant morbidity and mortality depending on its location and which structures are involved. In addition to the size and location, friability, rate of growth and invasiveness influence the clinical consequences of cardiac tumors. In general the clinical presentation of primary cardiac tumors are mainly due to the classic triad of blood flow obstruction, tumor embolization, and constitutional symptoms either individually or in combination (11).

Blood flow obstruction through the heart represents the most common cause of acute presentation. The chamber involved and the size of the tumor factor into the character and severity of the symptoms. Clinical presentations can be varied and may resemble coronary disease, cardiomyopathy, pericarditis, or valve dysfunction. Large left atrial masses, typically myxomas, may present with left-sided obstructive symptoms resulting in dyspnea, orthopnea or pulmonary edema (12). Temporary valve orifice occlusion from a large mass can trigger syncopal episodes, hypotension, and even sudden death in some patients (13). Right atrial tumors may present with right-sided obstructive signs and symptoms such as hepatomegaly, ascites, or peripheral edema from venous hypertension. Large ventricular tumors, while not common, may simulate ventricular outflow tract obstruction or subvalvular stenosis (14). Tumor embolization, often seen in pedunculated tumors, may lead signs and symptoms of arterial occlusion such as stroke, retinal artery emboli, limb ischemia, or cerebral aneurysms (15, 16).

In about a third of patients, constitutional symptoms including fever, myalgias, chills, night sweats, weight loss, and fatigue accompany the presence of cardiac tumors (17). When constitutional symptoms are present it is not uncommon to see leukocytosis, elevated erythrocyte levels and sedimentation rate, hemolytic anemia, thrombocytopenia, and elevated C-reactive protein levels in the laboratory profiles. The non-specific nature of these

Tab. 2. Cardiac tumors by clinical manifestations, most frequent location, most frequent morphology and mobility.

| Tumor Type   | Clinical Manifestations | Location | Morphology | Mobility |
|--------------|-------------------------|----------|------------|----------|
| Benign tumors |                         |          |            |          |
| myxoma       | obstructive, embolic, constitutional | LA       | lobular, pedicle | M        |
| papillary fibroelastoma | embolic, sudden coronary occlusion | valves | smooth, pedicle | M        |
| lipoma (hypertrophy) | none, compression depending on size | any      | smooth     | NP       |
| hemangioma   | embolization, arrhythmias, SD | any      | lobular, broad base | M        |
| fibroma      | CHF, arrhythmias, chest pain | septum   | calcified, broad base | IM       |
| rhabdomyoma  | CHF, arrhythmias, cardiomegaly, SD | V        | smooth, broad base | IM       |
| atrioventricular nodal | asymptomatic, SD | AV node | smooth, cystic | IM       |
| Malignant tumors |                         |          |            |          |
| sarcoma      | fever, embolization | LA       | lobular, pedicle | M        |
| fibrous histiocytoma | dyspnea (A), arrhythmias (V) | LA | calcified, lobular | IM       |
| rhabdomyosarcoma | obstructive, arrhythmias | Any | lobular, broad base | IM       |
| osteosarcoma | dyspnea (A), arrhythmias (V) | LA | calcified, lobular | IM       |
| leiomyosarcoma | R CHF, arrhythmias, tamponade | LA | lobular, broad base | IM       |
| angiosarcoma | constitutional, chest pain, dyspnea | RA | lobular, broad base | IM       |
| lymphoma     | R CHF, dyspnea, Afib, tamponade | RA | lobular     | IM       |

A – atrial, AV – atrioventricular, CHF – congestive heart failure, IM – intra-myocardial, LA – left atrium, M – mobile, NP – no preference, RA – right atrium, SD – sudden death, V – ventricle
symptoms and laboratory abnormalities, which are thought to be from inflammatory mediators, not only delay the diagnosis of the tumor as they are often attributed to other clinical entities such as connective tissue disorders, endocarditis or other malignancies.

Certain clinical characteristics help differentiate between benign and malignant primary cardiac masses. Sarcomas constitute 99 % of primary malignant cardiac tumors, and generally occur after the fourth decade of life with no gender predilection (18). Multifocal involvement in the right atrium is common with sarcomas and clinical presentation spans refractory congestive heart failure, arrhythmias and myocardial ischemia from intramyocardial invasion, or hemopericardium (19). In contrast myxomas account for the bulk of benign tumors; they are frequently located in the left atrium and usually unifocal, may occur in younger patients, and have a higher female prevalence with a 3:1 ratio (20). Pericardial effusions and arrhythmias effusions are very rare among benign tumors.

**Characterization and diagnosis of cardiac masses**

Transthoracic echocardiography (TTE) is the primary modality for cardiac tumor detection and assessment. It provides a good to initial assessment of the tumor location, the structural involvement and its functional effect. However, echocardiography carries some limitations including the dependence on an adequate acoustic window, a suboptimal visualization of extracardiac extension, and a poor soft tissue characterization (21). Transesophageal echocardiography (TEE) provides improved image quality, but is more invasive, and carries a restricted field. TEE is as such very useful in the assessment of very small localized tumors and one important anatomical structures such as the aortic arch, the inferior vena cava, and the left ventricular apex cannot be assessed in their entirety (22). EKG-gated multislice computed tomography (CT) play an important role in the evaluation of cardiac masses (23). While MRI still remains superior to CT in the assessment of cardiac masses, current generation cardiac CT is beginning to rival MRI in resolution and tissue characterization for some cardiac masses. CT provides a superior resolution calcification and fat. However, use of iodinated contrast, effects of ionizing radiation, and the lower temporal resolution still limits its applicability for evaluation of cardiac masses. Cardiac MRI, therefore, is the modality of choice to evaluate both primary and secondary cardiac masses if echocardiographic images are inconclusive. Cardiac MRI is non-invasive, allows multiplanar imaging without field of view size restrictions and does not use ionizing radiation and has a lower risk of contrast induced nephrotoxicity (24). Cardiac MRI can assess the paracardiac space and great vessels thus circumventing the spatial restrictions of echocardiography. Additionally, MRI provides superior soft tissue evaluation than CT usually without the need of contrast agents (25).

**Neoplasm versus thrombus**

When a cardiac mass is diagnosed it is important to distinguish from an intracardiac thrombus since they can have a similar appearance but require vastly different treatments (26–28). Surgical intervention is required for a benign mass whilst thrombus can be managed with anticoagulation. Atrial thrombi are common in patients with atrial arrhythmias, especially in those with enlarged atria and have echocardiographic features similar to atrial myxomas (27). Delayed enhanced cardiac MRI or even coronary angiography can help differentiate between thrombi and cardiac tumors because the formers are avascular structures and therefore there is no contrast uptake and enhancement (28). In spite of this distinguishing feature, some reports have not found evidence of neovascularization in as much as 50 % of specimens despite the fact that postoperative pathohistological studies confirmed the diagnosis of heart tumor (29). Cardiac MRI provides significant additional information such as the presence of areas of necrosis, hemorrhage or calcification. The inversion time can also help distinguish thrombus from tumor or myocardium. In images with short inversion time thrombus appears brighter then tumor or myocardium and vice versa with longer inversion time. Furthermore myocardial scar, which is easily detectable on MRI, is a risk factors for thrombus formation (30, 31).

**Benign versus malignant**

MRI characteristics of a cardiac mass may significantly allow differentiation between benign and malignant cardiac tumors. The tumor signal heterogeneity to interrogate its borders and limits, the point of attachment, the multiplicity or lack-thereof of chamber involvement, tumor size, location, and extracardiac involvement are all feature that can help distinguish malignant from benign tumors. Cardiac magnetic resonance can ascertain the presence of cystic, necrotic, lipomatous, calcified and hemorrhagic components within a mass. Benign tumors are usually small, smooth with well-defined borders, without irregularities or infiltrations. They often have a thin pedicle, rarely involve the chamber wall, have minimal calcification or necrosis (32). Conversely, as a general rule, malignant cardiac tumors tend to be lobular, with ill-defined invasive borders, are usually broad-based, tend to be of large size, involve the chamber wall and have large and multiple foci of calcification and necrosis (33). A pericardial effusion in the setting of a cardiac mass should carry a high index of suspicion for malignancy until proven otherwise.

**Benign cardiac tumors**

**Myxoma**

Cardiac myxomas are the most common primary cardiac neoplasm in adults. Myxomas generally present between the fourth and the seventh decade and have a higher female prevalence. They are usually found in the atria (Fig. 2) being more common in the left atrium (75 %) than the right atrium (20 %) and rarely in the ventricles (Fig. 2) (34). Because of the wide variety of clinical manifestations myxomas, often come to clinical attention sooner. Only 10 % of the patients remain completely asymptomatic. Clinically, signs and symptoms are due to valvular obstruction which leads dyspnea, as well as hemolysis, hypotension, and syncopal episodes due to temporary obstruction of blood flow (Fig. 3). Myxomas can present with constitutional symptoms. Embolic phenomenon
ventricular valves (Fig. 4) or the vessel surface of the semilunar valves (40). The major morbidity associated with PFE is embolic phenomenon. Emboli to the cerebral, coronary or systemic circulations can lead to life-threatening condition (41). Although the tumor can embolize this is quite rare and most pathologic studies support thrombus on the tumor as the source of the embolic events associated with PFE (42).

**Fibroma**

Cardiac fibromas are rare benign tumors mostly diagnosed in children and infants, the majority of whom are younger than 1 year at presentation (1). They are fibrous, solitary, mass that frequently have central calcification typically located in the ventricular myocardium, often in the interventricular septum (43). Because they present with significant symptoms it is the most commonly resected cardiac neoplasm in children but can also regress spontaneously (44, 45).

**Rhabdomyoma**

Cardiac rhabdomyomas are the most common primary benign cardiac tumor in children (46). They are considered to represent fetal hamartomas and in about half of these tumors are associated with tuberous sclerosis (47, 48). Most of them are located in the ventricular myocardium and multiple site involvement being common may be observed with myxomas and manifest as cerebrovascular events such as transient ischemic attacks or strokes, and peripheral embolization (12). Anatomically, they are smooth, mobile, lobular masses often attached to the interatrial septum by a narrow pedicle. They are often, pedunculated but can also be sessile and have a broad base. Multifocal calcification invasion of adjacent structures is rare with myxomas (35).

**Lipoma**

Cardiac lipomas commonly arise from the epicardium but myocardial or endocardial origins have been reported. They are encapsulated tumors and most patients remain completely asymptomatic (36) although there are reports of significant hemodynamic compromise from these tumors (37). The most common cardiac finding that cardiac lipomas need to be differentiated from a cardiac lipoma is lipomatous hypertrophy of the interatrial septum. This entity is characterized by adipose-cell hyperplasia in the septum. With lipomatous hypertrophy, the septum usually exceeds 2 cm in transverse diameter and typically spares the fossa ovalis (38).

**Papillary fibroelastoma**

Papillary fibroelastomas (PFE) are endocardial tumors often discovered incidentally at the time of preoperative work-up or autopsy. They are the second most common primary cardiac tumor, are small (1 cm or less), pedunculated and are the most common valve tumor (1). Papillary fibroelastomas can occur in all age groups but there is a higher incidence in elderly patients generally those over 60 years old (39). While PFE can found on any valve surface they are typically attached to the atrial surface of the atrio-ventricular valves (Fig. 4) or the vessel surface of the semilunar valves (40). The major morbidity associated with PFE is embolic phenomenon. Emboli to the cerebral, coronary or systemic circulations can lead to life-threatening condition (41). Although the tumor can embolize this is quite rare and most pathologic studies support thrombus on the tumor as the source of the embolic events associated with PFE (42).

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common (Fig. 3). Diagnosis can be made during the prenatal period based on the unique findings of the presence of multiple masses of variable size on echocardiography. Cardiac rhabdomyomas can regress spontaneously but occasionally resection is necessary to avoid arrhythmias or left ventricular outflow tract obstruction.

Atrioventricular node tumor

The atrioventricular node (AV) tumor is a rare relatively small (2–6 mm in diameter) benign congenital mass located at the base of the atrial septum in the nodal area (49). It is often referred to as the cystic tumor of the AV node. It occurs in adults and is more prevalent in females (1). Because of their location they can induce life-threatening arrhythmias such as heart block and ventricular fibrillation.

Hemangioma

Hemangiomas account for approximately 2% of benign cardiac tumors (1). They affect all ages and may arise from any anatomical structure within the heart including the pericardium (34). Hemangiomas are very vascularized neoplasms that arise from proliferation of endothelial cells and are composed of capillaries and cavernous vascular channels (Fig. 5). Patients usually develop arrhythmias or signs of right heart failure (50).

Malignant cardiac tumors

Primary cardiac malignances are very uncommon and constitute only 25% of all cardiac tumors (51). Although rare, their diagnosis and clinical management remain a challenge (52). The majority of malignant tumors are sarcomas (53), tend to involve the right-sided chambers of the heart and frequently show extracardiac extension and involvement (54).
Angiosarcoma

Angiosarcomas are the most common primary malignant cardiac tumor and are more frequent in men. They often involve the right sided structures and about 80% occur in the right atrium. Angiosarcomas are aggressive tumor that invade adjacent structures and because of this are usually unresectable at the time of diagnosis (55). Local and distant metastasis is common feature at the time of diagnosis in most patients. This characteristic behavior results in non-specific signs and clinical symptoms (56). Morphologically, angiosarcomas are hemorrhagic masses with poorly defined borders and multiple calcified necrotic loci (57).

Osteosarcoma

Osteosarcomas are bulky, sessile masses generally attached to the wall of the left atrium as whereas metastatic osteosarcomas usually involve the right atrium. Patients generally experienced respiratory symptoms and heart failure due to atrial occupancy (58).

Leiomyosarcoma

Leiomyosarcomas are very rare and highly aggressive invasive tumors (59). These tumors are sessile masses with mucous appearance often located in the posterior wall of the left atrium. They tend to invade the pulmonary veins or the mitral valve and rarely present calcification loci. Patients frequently present with dyspnea, chest pain and non-productive cough. Other reported clinical symptoms include right heart failure, rhythm alterations, hemopericardium and sudden death (60).

Rhabdomyosarcoma

Cardiac rhabdomyosarcoma is the second most common primary sarcoma of the heart. They have a wide range of age presentation and most patients have nonspecific symptoms. Also they do not have any chamber predilection (5). They exhibit striated muscle features, can be bulky (> 10 cm in diameter) and are very invasive tumors with a tendency to extend to valve leaflets or pericardium (61). Rhabdomyosarcomas are multicentric in the majority of patients (62).

Lymphoma

Primary cardiac lymphomas are very rare and account for about 1% of primary cardiac tumors (63). However, the incidence of cardiac lymphomas is increasing due to the increasing incidence of immunosuppressed patients from transplantation and those with AIDS (64). They often arise in the right atrium and are very frequently associated to pericardial effusions (65), leading to the presentation of clinical symptoms such as right-sided heart obstruction, heart failure, cardiac tamponade, and atrial fibrillation (66). Lymphomas are nodular and firm without any necrotic foci which distinguishes them from sarcomas (Fig. 6).

Conclusions

Primary cardiac tumors are rare with metastatic being more common than primary lesions. About three-quarters of primary tumors are benign, with myxomas being the most common. Rhabdomyomas, fibromas, papillary fibroelastomas, lipomas, and hemangiomas round up the list of benign cardiac tumors. Myxomas often mimic other common diseases, and are prone to fragmentation and subsequent embolization. Papillary fibroelastomas present one of the highest risks of embolization. Rhabdomyomas, is the most common cardiac tumor of childhood, are often linked to tuberous sclerosis. Lipomas are usually asymptomatic and must be differentiated from lipomatous hypertrophy.

A quarter of primary cardiac tumors are malignant and the vast majority of these are sarcomas. Most primary malignant cardiac tumors show a predilection for right atrial involvement. Malignant primary cardiac tumors are aggressive, and usually fatal due to local invasion, intracavitary obstruction or metastatic disease. The incidence of primary cardiac lymphomas is increasing as in conjunction with acquired immunodeficiency syndromes.

Finally, cardiac tumors may mimic other common clinical entities as they often present with nonspecific symptoms. The detection of a pericardial effusion in the setting of a cardiac mass should always be considered as suspicious for malignancy until proved otherwise.

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