CASE PRESENTATION

A 55 year old (67kg, 167 cm) male with a history of progressive shortness of breath presents for resection of cardiac tumor and possible mitral valve replacement.

1. What percentage of primary cardiac tumors are benign and what percentage of tumors are malignant?
2. What percentage of cardiac tumors are primary cardiac and what percentage are malignant extensions of other primary sources?
3. Where are cardiac tumors most commonly located – right atrium, left atrium, right or left ventricle?

The cardiac tumor was initially discovered during workup for a TIA 5 months ago at which time he presented with right-sided weakness which resolved. A TTE at the time revealed a lobulated mass in the left atrium extending from the interatrial septum and resulting in obstruction to mitral inflow. A CT was performed that revealed an intracavitary lesion but did not show any extracardiac disease. Now he presents with symptoms of worsening shortness of breath and dypsnea on exertion.

4. Does CT and MRI imaging confer an advantage over TTE or TEE?
5. What is the differential diagnosis of an intracardiac mass?
6. What are common primary cardiac tumors?
7. What are the most common primary benign cardiac tumors? Most common primary cardiac malignant tumors?

8. What are common presenting signs and symptoms of primary cardiac tumors?

His other past medical history includes hypertension, hyperlipidemia and gout. His medications include metoprolol, allopurinol, norvasc and atorvastatin. His blood pressure is 142/75, heart rate 65, SpO2 99%, and laboratory values include a Hgb of 14.5 g/dL, creatinine of 0.8, and platelets of 235 X 10^9/L. You begin to consider intraoperative monitoring.

9. How do you differentiate and distinguish an intracardiac mass using transesophageal echocardiography?

The patient undergoes a standard induction with fentanyl, versed and vecuronium. A 20g right radial arterial line is inserted into his right radial artery. An 8.5 French introducer is inserted with ultrasound guidance in his right internal jugular artery. Initial central venous pressures range between 8-10 mmHg. A Transesophageal echocardiography (TEE) probe is inserted without difficulty into his esophagus and a TEE examination is initiated.

10. What does a TEE examination entail for an intracavitary lesion? What findings are important for surgical management?

His TEE findings are as follows: normal left ventricular function, trileaflet aortic valve, no aortic insufficiency or stenosis, normal right ventricular function, mild tricuspid regurgitation, normal right atrium. An approximately 1X3 cm lobulated mass that extends via a stalk from the interatrial septum. The mass is resulting in obstruction of ventricular inflow and interacts with both the anterior and posterior mitral valve leaflets. No pericardial effusion is noted.
11. In what way can primary cardiac tumors result in valvular pathology and/or congestive heart failure?

After prep, drape and sternotomy, the patient is centrally canulated and placed on CPB. A right atriotomy is performed and upon direct inspection an approximately 1.2 X 3.1 cm circumscribed mass is removed from the left atrium. It extends from a stalk that adheres to the interatrial septum. Inspection of the mitral valvular leaflets reveals that the mass has resulted in mechanical damage to the mitral valve leaflets requiring a mitral valve repair.

12. What are the common surgical approaches to tumor resection?

Upon discontinuation of CPB with a native rhythm and an epinephrine infusion of 0.03 mcg/kg/min, the heparin is reversed and after bleeding has been controlled, the chest is closed and the patient is transported to the ICU with an ETT in place, sedation and monitors. After 4 hours while in the ICU, the patient is extubated and on POD #1, the patient is transported out of the ICU and then discharged from the hospital on POD #4.

13. What is the patient prognosis after surgical resection? Is there a difference in prognosis of patients with benign or malignant lesions?

14. What is the risk of recurrence?

**DISCUSSION**

**INCIDENCE**

The first successful resection of a primary cardiac tumor was performed by Crafoord in 1954. [1] The incidence of primary cardiac tumors is rare – ranging between 0.01-0.3%. [2,3]. Of primary cardiac tumors, about 75% are benign and 25% are malignant. Of the benign tumors, the most common are myxomas. Other primary benign cardiac tumors include
papillary fibroelastomas, rhabdomyoma, fibromas, lipomas, hemangiomas, and paragangliomas. Of the malignant primary cardiac tumors, 75% are sarcomas [3,4,5]. The incidence of cardiac tumors is increasing over the years most likely due to the increase in the use of echocardiography as a diagnostic modality and because patients more promptly presenting when having symptoms. [3] Cardiac myxomas most commonly arise from the left atrial septum. [6]

SIGNS AND SYMPTOMS

Patients can be asymptomatic but can also present with shortness of breath, dyspnea on exertion, congestive heart failure, hemodynamic compromise, peripheral or central emboli. The symptoms in this patient population mimic those of patients with cardiovascular disease. This is not surprising as many intracavitary lesions cause valvular changes due to mechanical interference. [3,7,8,9]. In addition, patients can also present with cardiac tamponade [3,8,10]. Myocardial lesions can result in alterations in the cardiac conduction system leading to arrhythmias and can also lead, in certain instances, to ventricular tachycardia if located within the ventricle. [3,7].

Patients with myxomas in general can present with three main patterns of symptoms– hemodynamic compromise, embolisms and constitutional manifestations [3]. Most commonly, myxomas result in mitral valve obstruction causing dyspnea and orthopnea secondary to pulmonary edema and/or heart failure. [11,12]. Right-sided myxomas result in corresponding right heart failure symptoms. [11,12] According to Kamiya and colleagues, when evaluating characteristics such as surface, size, and weight of the myxoma, only surface correlated with patient symptoms [3]. In addition, the degree of mobility, extent of attachment and the length of the stalk also were associated with hemodynamic compromise and embolic phenomenon [3]. 30-40% of patients present with symptoms of embolic load. This is the second most common presentation, second to hemodynamic compromise. [11,13]. Emboli to the CNS are most common, however, emboli to the coronary arteries, kidneys, spleen, extremities and pulmonary arteries can also occur. [7]. Constitutional
symptoms occur in 30% of patients. [14,15]. Although some evidence exists in implicating IL-6 in constitutional symptoms (fever, malaise, arthralgia and weight loss), it is largely unknown why these symptoms occur. [3]

Patients with myxomas are generally divided into two groups. The first group of patients consists of the more common types of myxomas and presentations. The majority present as single lesions (94%) and the risk of recurrence in the order of 1-2% [16,17,18]. The second group consists of about 7% of the myxomas that present. The myxoma type in this patient population portrays atypical biological behavior [16,17,18]. For example, there is multicentricity present (48%), location in a chamber other than the left atrium (38%) and a higher recurrence rate after surgical resection (12-22%) [16,17,18]. Patients also present at a younger age (mean age 28 years) and often with unusual conditions such as Carney complex [16,17,18]. In addition, there is a male preponderance and a genetic predisposition in this group [16,17,18].

Carney complex is a recently described entity that includes complex and familial myxomas as an autosomal dominant syndrome [3]. This complex is also associated with cutaneous and mammary myxomas, spotty skin pigmentation, endocrine over-activity, psammomatous melantoci schwannoma, primary pigmented nodular adrenal disease and testicular neoplasms [17].

DIFFERENTIAL DIAGNOSIS OF CARIAC MASSES

Generalities

To piece together the diagnosis of a cardiac mass, one must begin by identifying the location. Is the mass endocardial, intracavitary, myocardial, or epicardial/pericardial? What is the main chamber or main structure(s) involved? In general, benign tumors are more commonly found on the left side of the heart whereas malignant tumors are more often found on the right-sided structures. Next, evaluate the morphology of the lesion including its radiologic and
echocardiographic features, associated imaging findings, patient demographics, and pertinent clinical information. Ultimately, if you see a mass in the heart, it is most likely a metastasis from a primary located in another region of the body.

Left Atrial Masses

The two most common lesions to be confused in the left atrium are myxoma and thrombus. This distinction is important because the treatment for each is different. To distinguish between the two, one needs to not only evaluate the echocardiographic appearance but also use data from associated findings. The typical location of a thrombus in the left atrium is in the appendage (statistically thrombus more commonly occurs in the RA and RAA). [19] Thrombus is associated with patients who have underlying cardiac disease including atrial fibrillation, atrial dilation, mitral valve disease, dyskinesia or aneurysm [19,20,21,22] Myxomas commonly have a stalk (75% of the time) and attach to the septum. Patients with myxomas frequently have no underlying cardiac disease. [19] The myxoma classic clinical triad includes obstructive cardiac symptoms, embolic phenomena, and constitutional symptoms, although not all findings are always present.[11,14,15] The echocardiographic findings of a myxoma include a mass located behind but separate from the anterior mitral valve leaflet that prolapses into the ventricle during diastole. [23] Myxoma lesions manifest as spherical masses attached to the endocardial surface with an occasional internal hypoechoic areas, speckled echogenic foci, and frond like surface projections. [22] The echocardiographic features of a thrombus include a laminated appearance, irregular or lobulated border, microcavitations, and absence of a pedicle. [24]

Other left atrial tumors deserve consideration. Some malignant sarcomas (MFH, leiomyosarcoma, fibrosarcoma, and myxosarcoma) commonly involve the left atrium. Sarcomas, as opposed to myxomas, exhibit aggressive features including mural invasion, extension into the pulmonary veins and pericardium, broad-based attachment to nonseptal locations, and pericardial effusion. [22,25,26]
Valvular Masses
The differential diagnosis of a mass on a valve includes papillary fibroelastoma (the most common tumor on a valve), vegetation, thrombus, giant Lambl's excrescence, fibroma, and myxoma. [22,27,28,29] A myxoma can usually be distinguished from a fibroelastoma by its location. Myxomas may prolapse through a valve but are uncommonly attached to it. Fibromas are generally highly refractive ovoid masses that usually occur in children and young adults and typically involve the left ventricle, right ventricle and intra-ventricular septum. [29] Vegetations and thrombus can often be differentiated from tumor by clinical information, blood cultures, and lab tests. [30]

Differentiating a fibroelastoma from a lambl's excrescence can be challenging. They are thought to share a common pathogenesis. [31] In 90% of affected hearts, lambl's excrescences are multiple, small, and spread over a wider area than a fibroelastoma. [31] Lambl's excrescences tend to involve the atrial aspects of the AV valves, often at the line of coaptation and usually do not occur on the arterial side of the semilunar valves as opposed to fibroelastomas. [31] In contrast, fibroelastomas are more frequently found on the mid portion of the valve away from the contact surface. Fibroelastomas are rarely multiple. [31] Microscopically lambl’s excrescences have a central core of fibrous tissue and show a layered arrangement of collagen suggesting a staggered growth. [31] Fibroelastomas exhibit an avascular papilloma lined by single layer of endothelial cells. The core of the tumor is formed by fibrous connective tissue with scattered smooth muscle cells within the papillary projections. [29] On echocardiography, the distinction between a fibroelastoma and lambl's excrescence is primarily size, with the fibroelastoma being the largest. [29] In “zoom” mode a characteristic stippled edge, with a shimmer at the tumor-blood interface can be seen and the finger-like projections (referred to as “sea anemone” appearance) can be distinguished. [29]

Lipoma versus Lipomatous Hypertrophy of the Intra-Atrial Septum (IAS)
A lipoma is a true neoplasm. [32] It has a capsule and although it is usually asymptomatic, intracavitary lesions can obstruct blood flow and when they involve the conduction system, can result in arrhythmias. [33] The most frequent locations are the left ventricle and right atrium. [5] Echocardiography imaging reveals a homogeneously echogenic, nonmobile mass. [34] In contrast, lipomatous hypertrophy of the intra-atrial septum is a non-neoplastic accumulation of fat cells. [32] It has no capsule and spares the fossa ovalis area. [19] Associated with advancing age, obesity, and male sex, it is controversial whether this lesion can result in supraventricular arrhythmias. [19,32,35] There are microscopic differences between these two lesions. [32]

**Malignant Lesions**

Malignant lesions are often difficult to differentiate microscopically or macroscopically. Angiosarcomas tend to infiltrate the right atrium with an intracavitary mass which extends through the myocardium, along the epicardial surface with diffuse pericardial involvement. [36,37] Undifferentiated or unclassified sarcomas and rhabdomyosarcomas arise anywhere in the myocardium, extend into the cardiac chamber as a polypoid mass or multiple masses, invade the pericardium, and tend to involve the valves. [32,37,38] Primary cardiac lymphoma is more likely on the right side of the heart, although it can involve any chamber, commonly can be multifocal (like the sarcomas), and tends to extend into pericardium. [32,37,38] Lymphoma is less likely to demonstrate necrosis, involve the valves, or extend into the heart chambers when compared with sarcomas. [32,37,38] Ultimately all primary cardiac malignant lesions are associated with poor prognoses compared with primary cardiac benign lesions.

**Primary versus secondary cardiac neoplasms**

Secondary lesions are 30-40 fold more frequent than primary neoplasms of the heart. [39] This distinction is made on clinical grounds in almost every case since nearly all cardiac metastases manifest in patients with known primary
malignancies and are frequently associated with widespread systemic disease [19]. In metastatic cardiac involvement, symptoms usually affect the pericardium and can result in pericardial effusions, tamponade and/or constrictive pericarditis. Primary cardiac tumors can metastasize to other organs. Most frequently sarcomas metastasize to the lungs, brain, and bones. [40] The most common malignancies to metastasize to the heart are lung and breast cancers followed by lymphoma and leukemia. [32,41] Secondary metastasis to the heart most commonly targets the pericardium and epicardium although myocardium can be involved through direct tumor extension (i.e., renal cell carcinomas).

**TABLE OF CARDIAC TUMORS/CHARACTERISTICS OF CARDIAC TUMORS – see attached table**

**TEE EXAMINATION**

The intraoperative TEE examination of a patient with suspected or confirmed cardiac mass should begin with a comprehensive examination as described by Shanewise et al.[42] In addition, examination should focus on the identification of any mass that is present. The description of the mass should include chamber/valve of origination, associated valvular/chamber disturbances, presence or absence of a stalk including length, presence or absence of calcification, size, shape, mobility, extent of attachment as well as presence/absence of an effusion and/or extension beyond the myocardium. After excision, in addition to a comprehensive examination, the examination should describe the degree of resection, evaluate for any defects (ASDs, VSDs) as an atrial septal patch is sometimes necessary for myxomas that attach to the interatrial septum. [43]

Specific echocardiographic findings of each tumor are listed in Table 1.
**SURGICAL APPROACH**

The surgical approach involves institution of cardiopulmonary bypass and one of three approaches. The three approaches described are as follows: 1) a biatriotomy, 2) a right atriotomy, and 3) a left atriotomy. Although a biatriotomy and a right atriotomy are generally preferred the absolute accurate approach is still unclear. The main issue involves recurrence. [3] Although experience has dictated low/no recurrence rates with a right atriotomy, some authors still suggest a biatriotomy in order to surgically examine all four chambers. [44,45] The attachment of the tumor is generally resected widely. Because cardiac tumors present to many different chambers, the surgical approach of cardiac tumors may vary according to the location of the tumor. [46] For example, those located in the right ventricle can be approached through the tricuspid valve. Those in the left ventricle can be excised via a transaortic approach. [46] Generally, all visible tumor and surrounding tissue is shaved or resected with a cuff of normal tissue. [3] This may result in valve replacement/repair. Malignant tumors are difficult to resect due to invasion and tumor extension. [3]

**OUTCOMES**

The recurrence rate for myxomas is currently described in the context of the clinical type of myxoma present. The currently described risk of recurrence is 1% for sporadic myxomas. Complex myxomas carry a recurrence rate of about 20% and the familial cardiac myxomas recur at a rate of approximately 10%. [3] With respect to benign tumors that were not myxomas, the recurrence rate is low and the prognosis is good even the setting of incomplete resection. [3]

Outcomes for malignant tumors is generally worse than that of primary cardiac tumors and have been associated with poorer prognosis rates. [7]
| BENIGN TUMORS | 2nd most common benign tumor. Most common valvular tumor. Incidence: 0.0002-0.02% [47]. Men = women (Grebenc 2000). Predisposition to development: reaction to hemodynamic stress, iatrogenic trauma, radiation, infection, acquired or congenital heart disease [48]. | Chest pain, TIA, stroke, dyspnea, or sudden death due to obstruction of coronary ostia or embolization [49]. | Small (<1.5cm) mobile, pedunculated, homogenous valvular or endocardial mass which flutters or prolapses w/ cardiac motion. Valvular function usually unaffected [29]. In “zoom” mode on echo tumor has a characteristic stippled edge, with shimmer or vibration at the tumor-blood interface [29]. | Avascular papilloma lined by single layer of endothelial cells. Core of tumor formed by fibrous connective tissue with scattered smooth muscle cells [7]. | Gelatinous masses with multiple papillary fronds producing characteristic “sea anemone” appearance. Found mainly on the aortic or mitral valves, usually away from the valvular free edges [7]. | Recurrence after resection hasn’t been reported [49]). Most often arise from valve endocardium but can arise anywhere in the heart and occasionally in multiples. On AV valves, usually project into atrial side. On semilunar valves, project equally into atrial and ventricular side [19]. |
| **Rhabdomyoma** | **Represent up to 90% of the cardiac tumors in children. Usually discovered at age < 1yr [7]. 90% with multiple tumors. Nearly equal frequency in the RV and LV [19]. Approx. 50% of patients with rhabdomyomas have tuberous sclerosis [7]. Prevalence of these lesions in this population decreases with increasing age because of spontaneous tumor regression [7].** | **Most asymptomatic and discovered at prenatal US. However, affected children may be detected in utero because of nonimmune fetal hydrops, fetal death, and tachyarrhythmias [50,51].** | **Solid, hyperechoic masses usually located in the ventricular myocardium or ventricular septum and potentially protruding into and deforming the cardiac chambers [22,52].** | **Enlarged, vacuolated cells with sparse cytoplasm. “Spider cells” are typical and characterized by centrally located nucleus with radial extensions to the cell periphery [7].** | **Firm, white, well-circumscribed, lobulated nodules that occur in any location in the heart but most common in ventricles. They are myocardial (intramural) lesions [7].** | **Because majority of these regress spontaneously, surgery not routinely required unless life-threatening symptoms (LVOT obstruction or refractory arrhythmias) [50,51]. Although benign, their multiplicity, poor encapsulation and deep myocardial location make surgical resection difficult [5]. Poor prognosis due to malignant recurrent tachyarrhythmias (even with AICDs in place) [5].** |

| **Fibroma** | **Typically affects children. 33% are <1yr old at presentation. 2nd most common cardiac tumor in children but the pediatric cardiac tumor most commonly resected [7]. Increased risk of cardiac fibroma in patients w/ Gorlin syndrome (multiple basal cell carcinomas of the skin, mandible lesions, rib and vertebral anomalies) [32,53].** | **Some asymptomatic. Otherwise symptoms can include chest pain, dyspnea, conduction abnormalities (including sudden death from malignant ventricular arrhythmias) and CHF [54].** | **Echogenic mass that may display heterogeneity. Central tumor calcifications occasionally identified. Affected myocardium is usually hypokinetic [22,32].** | **In infants: cellular, fibroblast-rich tumors w/ little collagen. In adults: tumors composed mainly of collagen. Numerous elastic fibers, identifiable w/ special stains, found in >50% cases (Burke 1996). Fibrous tissue of varying cellularity replaces cardiac muscle [5].** | **Round, bulging, well-circumscribed. Located within ventricular myocardium, often extending into or even obliterating chamber lumen. Always a single tumor. Size 2-10cm [32].** | **Surgical outcome less favorable in patients w/ large tumors, those presenting with heart failure or recurrent arrhythmias as infants [55] Post surgical resection recurrence rare [56].** |
| Hemangioma | Vascular tumor that affects mostly adults, but occasionally children [5]. Accounts for about 5-10% of benign cardiac tumors [32]. May occur at any site in the heart or pericardium. May be mainly intramural or intracavitary [32,57]. | Most asymptomatic and discovered incidentally [32]. Symptomatic patients most commonly present with dyspnea on exertion but may also have chest pain, heart failure, arrhythmias, pericarditis, pericardial effusion, syncope, or sudden death [57,58,59]. | Hyperechoic lesions [7]. | Intramural hemangiomas are often poorly circumscribed, spongy tumors that appear hemorrhagic or congested. Endocardial-based hemangiomas are well-circumscribed, soft masses [32,57]. | Can occur in the setting of Kasabach-Merritt syndrome: multiple systemic hemangiomas associated with recurrent thrombocytopenia and consumptive coagulopathy [58]. |
| Lipoma | Very rare. Typically found in adults but can affect all ages [33,36,60]. LV and RA most frequent locations [5]. Usually a single lesion but multiple lipomas have been reported [32,33,34]. | Usually asymptomatic but intracavitary lesions can obstruct blood flow or involve conduction system resulting in arrhythmias and CHF [33,34,60]. | Echogenic, nonmobile mass [33,34]. | Mature adipocytes. Capsule usually present [7]. | Circumscribed, spherical or elliptical masses of homogenous yellow fat [32,33,34]. |
| Paragangioma | Very rare. Arise from intrinsic cardiac paraganglial (chromaffin) cells. Most reported in adults 18-85yrs (Jebara 1992). Up to 20% have associated paragangliomas in other locations and approx 5% of patients will have osseous metastases [61,62] | Majority are catecholamine-producing tumors and patients present with hypertension, headache, palpitations, and flushing (typical symptoms of a pheochromocytoma) [61,63] | Echogenic mass, poorly encapsulated, often infiltrates surrounding structures [62] | Made of nests of paraganglial cells classically described as “zellballen” [32]. | Most located on epicardial surface of the base of the heart in the roof of the LA. Less commonly found in the atrial cavity, IAS, and rarely the ventricles [32,61]Their extreme vascularity makes for a characteristic MRI appearance [64]. |
## MALIGNANT TUMORS

| Sarcoma | 2nd most common primary cardiac tumor. Most common primary malignant cardiac tumor [2] Affects adults (extremely rare in children) with mean age at presentation 41yrs [5,32] Metastasis are found in 65-90% at diagnosis [32,36] Most frequent location is the right heart. Most common type is angiosarcoma (37% of cases) followed by unclassified or undifferentiated sarcoma (24%) [2,32]. | Dyspnea is most common complaint. Characteristic clinical presentation is progressive, unrelenting CHF, cardiomegaly, chest pain, fever, hemopericardium, arrhythmias or sudden death [25,32] The rapid onset of SVC or IVC obstruction is also common [5]. | Spherical masses attached to endocardial surface, broad-based, non septal attachment [22] | Cardiac sarcomas usually poorly differentiated and precise histologic classification is difficult [5]. | Varied features. Majority are large, invasive masses at diagnosis and range from endocardial-based lesions (similar to myxoma) to large, infiltrative tumors. Cut sections are usually firm and heterogenous [32]. | Majority of angiosarcomas occur in the RA. Other cell types more commonly affect the LA (MFH, osteosarcoma, leiomyosarcoma), an important differentiating feature [2,32,36]. Rhabdomyosarcoma rises de novo – not from malignant degeneration of a rhabdomyoma [7]. Primary cardiac sarcomas most commonly metastasize to lungs [32]. |
### Lymphoma

Typically non-Hodgkins [32]. 16-28% of patients with disseminated lymphoma have cardiac involvement, but primary cardiac lymphoma rare. Seen with greater frequency in immunocompromised patients, particularly AIDS [65,66]. Mean age at presentation 60 yrs. Slight male predominance [38].

Unresponsive, rapidly progressive heart failure, arrhythmias, chest pain, cardiac tamponade, and SVC syndrome. Most primary cardiac lymphomas are either diagnosed at autopsy or fatal soon after diagnosis [32,38].

Hypoechoic myocardial masses in the RA or RV with associated pericardial effusion [65,66].

Multiple firm, white nodular masses. Homogeneous appearance. Contiguous invasion of pericardium is typical [32].

Most often affected areas are the RA followed by RV, LV, LA, IAS, and IVS. More than one chamber involved in over 75% of cases [32].

### References:


41. Roberts WC. Primary and secondary neoplasms of the heart. Am J Cardiol 1997; 80:671-682.