4-3-2009

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As submitted to: ***International Journal of Cardiology***

and later published as:

International Journal of Cardiology

Volume 133, Issue 2, 3 April 2009, Pages 152-156

DOI: 10.1016/j.ijcard.2008.11.103

Primary Cardiac Tumors

Review Article

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Keywords: cardiac tumors, primary cardiac tumors, myxomas, papillary fibroelastomas, sarcomas

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Word count - 2,946

Abstract

Primary cardiac tumors are a rare entity compared to tumors that metastasize to the heart. Patients with such tumors may be asymptomatic. Many cases are found incidentally during evaluation of an unrelated medical condition. It is important for the clinician to have a high index of suspicion when evaluating a patient presenting with signs and systemic symptoms concerning for possible malignancy, plus cardiac specific symptoms or complications. These can include new onset dyspnea, congestive heart failure, arrhythmias or murmurs varying with body positions. Imaging, particularly the use of cardiac echocardiography, remains the cornerstone of diagnosis, and may be combined with new imaging modalities of cardiac CT and MRI. The aim of this paper is to describe the epidemiology and pathophysiology of the various benign and malignant primary cardiac tumors.

Primary Cardiac Tumors

Primary cardiac tumors are a rare entity. They have an autopsy frequency of 0.001% – 0.28%. By contrast metastatic involvement of the heart is far more common, occurring in 1.5% - 21% of all autopsies performed on patients (1,2,3). Approximately three-quarters of primary heart tumors are benign with atrial myxomas comprising three-quarters of those. Of the 25% of primary cardiac tumors that are malignant, approximately three-

quarters are sarcomas (4). The aim of this paper is to describe the epidemiology, pathology, and pathophysiology of the various benign and malignant primary cardiac tumors.

Presentation

Primary cardiac tumors may be asymptomatic with up to 12% of cases found incidentally during evaluation of an unrelated medical condition (5). They often present in a subtle manner though dramatic presentations are sometimes encountered. In the case of malignant disease there may be direct invasion of the myocardium, causing arrhythmias or heart block, or pericardial effusion which may progress to life-threatening tamponade. They may also produce signs and symptoms of heart failure by causing progressive valvular regurgitation (6). Pulmonary venous hypertension secondary to physical obstruction of a cardiac chamber filling may result in dyspnea or frank pulmonary edema. Systemic emboli may occur to the brain or extremities. Constitutional symptoms, such as fevers and arthralgias, can sometimes be present (7). Interestingly, body position may influence the severity of symptoms due to the movement of tumor within the heart, and a characteristic early diastolic “tumor plop” may be heard on auscultation.

Benign Cardiac Tumors

Atrial Myxomas

Atrial myxomas are the most common primary cardiac tumors, comprising up to 50% of all primary cardiac tumors (figure 1) (8). Myxomas occur with increased frequency in the third to sixth decades of life (9). Up to 90% occur in the left atrium where they are

usually attached to the atrial septum, in or adjacent to the fossa ovalis (10). The remainder occur in the right atrium or, infrequently, in the ventricles. They are more common in women, with a 2:1 female preponderance. Patients can present with systemic embolization (cerebral or peripheral) or with symptoms due to obstruction of the mitral valve. They will often have constitutional symptoms such as anemia, fever, and weight loss. Additionally, the erythrocyte sedimentation rate is often increased (5).

"Syndrome myxoma" refers to one of several genetic disorders which should be suspected in patients younger than 40 years who present with multiple cardiac myxomas. These can include biatrial, ventricular and recurrent myxomas. These syndromes are typically associated with blue nevi, cutaneous lentiginosis, peripheral tumors and endocrine neoplasms. Myxoma syndromes include LAMB (**l**entigines, **a**trial myxomas, **m**ucocutaneous myxomas, and **b**lue nevi), NAME (**nevi**, **a**trial myxomas, **m**yxoid neurofibroma, and **e**phelides and Carney syndrome (atrial, cutaneous and mammary myxomas, lentigines, blue nevi, endocrine disorders and testicular tumours)
If diagnosed, all first degree relatives should be screened for the condition (11,12).

Structurally, most myxomas have a stalk, are gelatinous, and have a broad base. The surface may be friable or villous. There can be different consistencies within the myxoma, including areas that may be hemorrhagic or cystic (11,13).

The diagnosis of atrial myxoma by imaging requires prompt resection since there is a risk of embolization and sudden death. Surgical outcome is generally good, with a 20-year survival rate of 85%. However, there is a recurrence rate after resection of approximately 5%. Therefore careful, serial follow-up is required (7).

Papillary Fibroelastomas

Papillary fibroelastomas are rare, comprising less than 10% of all primary cardiac tumors examined at autopsy or post resection (figure 2a, figure 2b, figure 3) (14). They are the most common valvular tumor and the third most common primary cardiac tumor (after myxoma and fibroma). Papillary fibroelastomas have been referred to by various names, including myxofibroma, cardiac papilloma, papillary fibroma and giant Lambl's excrescences. Giant Lambl's excrescences are caused by wear-and tear of valves, commonly the aortic valve, and comprise a densely hyalinized central core lined by endocardial-type spindle cells. Papillary fibroelastomas occur predominantly in males with a mean age at the time of detection of 60 years. Although the natural history of these tumors is not fully known, lesions have been observed to develop over periods ranging from 6 months to 15 years (15,16). In 90% of cases these tumors are found on cardiac valves. Other sites include the coronary sinus os, right ventricular endocardium, the left ventricular septum, and the both the right and left outflow tracts. Lesions usually occur on left-sided cardiac valves, with approximately 36% involving the aortic valve and 29% affecting the mitral valve (17,18). In one case series (19), where lesions were identified pathologically from surgical specimens, tumors tended to occur in areas of endocardial

irritation, including degenerative aortic valve sclerosis, mitral valve prolapse, prior surgical repair of congenital ventriculoseptal defect, systolic anterior motion of mitral valve, and hypertrophic cardiomyopathy. Some lesions occur as congenital malformations, including a case of a 9-month-old child with a tricuspid valve tumor obstructing the right ventricular outflow tract, but most are acquired (20).

The majority of papillary fibroelastomas are solitary with multiple tumors seen in <10% of patients. Most lesions are less than 20mm in their largest diameter. They have been described pathologically as having the appearance of sea anemones, with multiple papillary fronds arising from a central stalk (15,21).

Papillary fibroelastomas are rarely cause valvular dysfunction. However, left-sided tumors can be associated with serious symptoms including angina, transient ischemic attacks and sudden death. While tumor embolization may be responsible for the central neurological events it is also possible that the tumors serve as a nidus for clot formation which may subsequently embolize (22,23).

Echocardiographically, the distinguishing feature between papillary fibroelastoma and a Lambl's excrescence is size, with fibroelastomas being larger. Myxomas can usually be distinguished from fibroelastomas based on location with the former usually attached to the atrial septum and the latter to a left sided valve (24).

The size of the lesion does not always correlate with the risk of developing serious morbidity and there may be no warning signs before a serious event. Surgical removal of lesions (in the absence of major surgical contraindications) may therefore be considered (25,26).

Rhabdomyomas

These lesions occur almost exclusively in children, in the majority before one year of age. They are the most common primary cardiac neoplasm in children. Rare cases have been reported in adults. These lesions are usually found on the ventricular walls or the atrioventricular valves (27). Microscopically lesions demonstrate striated muscle fibers with features typical of myocytes. Symptoms may result from arrhythmias or mechanical complications due to obstruction of blood flow in the heart. The majority of rhabdomyomas regress spontaneously (28).

Fibromas

Cardiac fibromas are the second most common pediatric cardiac tumors. They may also occur in adults. Fibromas usually arise in ventricular muscle. Histologically, they have features of fibroblasts and may give a false appearance of malignant myocardial infiltration due to encompassing areas of myocardium (28,29). Symptoms are due to conduction abnormalities, resulting in arrhythmias and sudden cardiac death, and mechanical obstruction of blood flow within the heart, which can lead to congestive heart failure. Unlike rhabdomyomas, fibromas do not regress on their own in children and often require resection (11).

Lipomas

Lipomas comprise a benign accumulation of adipocytes. They may occur anywhere in the heart and can occur in the pericardium, subendocardium, subepicardium, and intra-atrial septum. Tumor size ranges from a few centimeters to many kilograms. Symptoms, when they occur, are due to arrhythmias and conduction block or may be related to anginal pain due to compression of coronary arteries (30,31). These tumors tend to progressively enlarge and, when symptomatic, need to be excised.

Lipomatous septal hypertrophy

Lipomatous septal hypertrophy is due to increased growth of adipocytes within the atrial septum. They occur only in the interatrial septum. Found mainly among elderly and obese patients it is not a true cardiac tumor (32). The accumulation of fat in the septum may result in atrial arrhythmias or atrio-ventricular conduction abnormalities. In the absence of these effects these no treatment is required (33).

Malignant Cardiac Tumors

Sarcomas

Approximately 25% of primary cardiac tumors are malignant. The majority are sarcomas (Figure 4). Sarcomas have variable presentations, depending more on tumor location than pathological type. This makes early diagnosis difficult. Patients may present with

vague symptoms such as dyspnea, or more dramatically with pulmonary hemorrhage or even cardiovascular collapse.

Angiosarcomas

Angiosarcomas occur most frequently in the adult population and are more common in males. They have a propensity to occur on the right side of the heart, especially the right atrium (34,35). Lesions may be large, replacing the atrial wall and extending into the chamber, even occasionally completely filling it. They can invade the vena cava, tricuspid valve and pericardium. Mesenchymal in origin they are composed of malignant cells forming vascular channels. Microscopically, a sinusoidal pattern is often seen. There are two clinicopathological forms of angiosarcoma. In the first type tumor deposits involve the epicardium or pericardium, are usually small and asymptomatic, and are associated with skin lesions of or risk factors for Karposi's sarcoma. The second type involves large symptomatic lesions, occurring in the right atrium, which are not associated with Karpoi's sarcoma or its risk factors. Treatment with chemotherapy or radiation does not relieve symptoms as well as tumor resection, although survival data on surgically treated lesions in both types are rare (36).

Rhabdomyosarcomas

Rhabdomyosarcoma is the second most common primary sarcoma. These tumors occur equally in both sexes and are multicentric in up to 60% of patients. Patients often present with non-specific symptoms. They may occur in any cardiac chamber, are bulky and

invasive, grow rapidly, and often have invaded pericardium by the time of diagnosis (37). Surgical resection of small tumors is often attempted, but due to local and distant metastasis, and poor response to radiation and chemotherapy, prognosis is poor (38).

Leiomyosarcomas

Primary leiomyosarcomas of the heart are extremely rare and comprise less than 0.25% of all primary cardiac tumors. They are usually found in the left atrium and histologic demonstrates spindle-shaped cells. Presenting symptoms result from arrhythmias, including sudden death, and hemopericardium (39). Patients may also present with symptoms due to obstruction which may mimic pulmonary thromboembolism or mitral valve stenosis. These tumors are highly aggressive, spread systemically, have early local resurrence, and are locally invasive. Resection is mainly palliative. Extensive resection followed by chemotherapy may improve prognosis (39,40).

Imaging

Diagnosis of intracardiac tumors is often possible by transthoracic echocardiography (TTE), with a detection rate of 95.2%. In cases where there is doubt or image quality is not optimal, transesophageal echocardiography (TEE) may be attempted. (41). Both CT scanning and cardiac MRI produce high resolution images of the heart. Both can provide additional information regarding extent of tumor within the heart or into adjacent extracardiac structures, and may help in making histologic distinctions. Contrast

enhancement can be used to differentiate tumors from thrombi since thrombi do not usually show enhancement and fat-suppression techniques may further define tumors such as lipomas (42). Finally, these techniques provide good definition of lesions prior to any surgical interventions.

Conclusion

Primary cardiac tumors are rare with three-quarters being benign (mostly myxomas). The remaining 25% are malignant, mainly sarcomas. Diagnosis often requires a high index of suspicion as presentations can be variable. Signs and symptoms can include new onset dyspnea, congestive heart failure, arrhythmias or murmurs varying with body positions. Echocardiography remains the cornerstone of diagnosis but cardiac CT and MRI can often provide additional useful information. Surgical resection is the primary treatment modality, with radiotherapy and chemotherapy being largely palliative.

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Figure 1

Sixty-four year old man who presented with vague neurologic symptoms. Transthoracic echo revealed a left atrial mass at the junction of the atrial septum and anterior mitral leaflet prompting this transesophageal echocardiogram. Surgical resection demonstrated a myxoma.

Figure 2a

In-situ operative field view of left atrial appendage showing attached mass which was histologically diagnosed as papillary fibroelastoma.

Figure 2b

Histological preparation of papillary fibroelastoma showing avascular papillary structures lined with endothelial cells.

Figure 3

Intra-operative image of atrioventricular papillary fibroelastoma.

Figure 4

Thirty-five year old woman who presented with dyspnea. Transthoracic echocardiogram showed a large irregular left atrial mass prompting this transesophageal echocardiogram. Surgical resection demonstrated a myxofibrosarcoma.