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Primary malignant cardiac tumors

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Approximately 10% of surgically resected heart tumors are malignant. Of these, over 90% are sarcomas, and the remainder lymphomas. Sarcomas of the heart may be of a variety of histologic types. Angiosarcomas are usually right-sided, typically in the atrium. Most other heart sarcomas arise in the left atrium and may be clinically mistaken for myxoma. Left atrial sarcomas are typically pleomorphic, and may have areas of osteosarcoma or chondrosarcoma.

Malignant tumors account for approximately 10% of primary cardiac neoplasms removed at surgery (Table 1). For the majority of patients with primary malignant heart tumors, the preoperative diagnosis is that of cardiac myxoma. In comparison to primary malignancies, cardiac myxomas are far more common, occur often in similar intracardiac locations, and may have similar imaging characteristics. Therefore, the surgical pathologist often provides the unsuspected diagnosis of cancer, which, in the heart, is generally an incurable condition.

Although metastases are the most common heart malignancy at autopsy, surgical resection for metastatic cardiac disease is relatively uncommon. In series of surgically resected cardiac tumors, 10% to 15% are metastases.[1,2] In contrast to epithelial malignancies, which are always metastatic if found in the heart, sarcomas that present as heart masses are usually primary in that location. However, the finding of a right-sided sarcoma that is not angiosarcoma should raise the suspicion of a metastasis from an occult or previously excised primary.

The vast majority of malignant cardiac tumors are sarcomas; rarely, lymphoma may present as a cardiac mass (Table 1). The classification of cardiac sarcoma follows that of soft tissue sarcomas. According to the WHO, cardiac sarcomas are classified as undifferentiated pleomorphic sarcomas (roughly synonymous with malignant fibrous histiocytoma, MFH), angiosarcomas, fibrosarcomas, synovial sarcomas, leiomyosarcomas, and rhabdomyosarcomas. There are several gray areas in this classification that are the subject of potential controversy. The spectrum of undifferentiated sarcomas includes epithelioid and pleomorphic, MFH-like sarcomas without clear distinction. There are sarcomas with "myofibroblastic" features with differentiation intermediate between MFH-like tumors and better-differentiated fibrosarcoma. In the heart, these have been variously termed myxoid MFH, fibromyxosarcoma, and myxofibrosarcoma, and often show a range of features from dedifferentiated to fibrosarcoma-like areas. In extracardiac sites, the term fibrosarcoma itself has fallen somewhat out of favor, and is being replaced by designations for specific soft tissue lesions such as fibromyxoid sarcoma, which is characterized by specific chromosomal translocations. The situation is complicated in the heart by the fact that myxoid change is common in a variety of benign and malignant conditions, and may be due in part to the intravascular location. The fairly recent description of a number of intracardiac inflammatory myofibroblastic tumors is another source of controversy in terminology, as it is now generally accepted that these are low-grade sarcomas, at least in other sites. Yet another variable in terminology is the use of the terms "osteosarcoma" and "chondrosarcoma"; if there is

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Table 1 Incidence of primary cardiac tumors excised surgically*

Tumor type	Percent of surgically excised cases
Benign	89
Myxoma	77
Other benign tumors	12
Malignant	11
Sarcoma	10
Varied, not angiosarcoma	6
Angiosarcoma	4
Primary lymphoma	1

*From six institutional series reported since 2000.[2,35-39]

any area of either type of differentiation, the sarcoma is often designated as such, despite the fact that there are usually extensive areas that are undifferentiated, or, in the case of chondrosarcoma, that show rhabdomyosarcomatous differentiation. Finally, the classification of "leiomyosarcoma" is not always uniform. Whereas most soft tissue experts do not require desmin positivity for the diagnosis, strict use of the term rests on "typical" histologic features and extensive smooth muscle actin positivity. There is some subjectivity in this area, which may account for a fairly wide range in incidence of cardiac leiomyosarcoma in published reports. To date, there is no evidence that histologic classification of sarcomas has any bearing on outcome or treatment.

There are few data that correlate cardiac sarcoma grades and outcome, because of the overall dismal prognosis of these tumors. However, grading as applied to soft tissue sarcomas is appropriate, and follows either the NCI (National Cancer Institute) system or the FNCLCC (Fédération Nationale des Centres de Lutte Contre le Cancer) system. In the latter, three scores (each graded 1-3) are added: one each for tumor differentiation, mitotic count, and tumor necrosis; the resulting total score determines grade 1, 2, or 3.[3]

The initial clinical symptoms that result from cardiac tumors are generally related to the size and site of the mass, and not the histologic type of tumor. In general, symptoms are caused either by obstruction of blood flow, which may result in heart failure or pulmonary hypertension; embolic phenomena; chest pain from ischemia or pericardial symptoms; systemic symptoms; or pericardial constriction due to effusions. Echocardiography is the simplest and one of the most sensitive tools for detection of cardiac masses, but additional information regarding tissue characteristics and extension of the tumor into adjacent structures may be obtained from MR and CT. Angiography is generally not performed, unless the patient may require concurrent coronary revascularization in addition to mass excision.[3]

Angiosarcoma

Cardiac angiosarcomas account for 36% of excised heart sarcomas (Table 2), and occur over a wide age range (36 months to 80 years) with a peak incidence in the fourth decade.[4] It occurs with equal frequency in men and women. It most often arises in the right atrium near the atrioventricular groove (80%), but has been reported in the other three chambers as well as in the pericardium. Left atrial involvement is unusual, although it has been reported.[5] The pericardium is often involved as extension from the atrium, and rarely may be the dominant site of tumor. Clinical features are related to the location, size, and extent of regional involvement, as well as to the presence or absence of metastases.[5] Most are initially silent. Because of frequent pericardial involvement, dyspnea is not an early symptom as is the case with other cardiac sarcomas. The most common presenting symptoms are chest pain, and symptoms related to right-sided heart failure, hemopericardium, and supraventricular arrhythmias. Sometimes, early pericardial involvement may lead to pericardial biopsy during emergency surgical cardiac decompression for tamponade or cardiac rupture. Familial angiosarcoma of the heart has been reported.[6]

Angiosarcomas usually form lobulated, variegated masses in the right atrial wall (Figure 1), protruding into the chamber. They range from 2.0 cm to several centimeters in diameter. The pericardium is frequently involved, and hence a hemorrhagic pericardial effusion is a frequent accompaniment.[7] Cardiac angiosarcomas are histologically similar to extracardiac angiosarcoma and are composed of malignant endothelial cells that form vascular channels or papillary structures. There may be areas of anaplastic or spindle cell appearance with poorly formed vascular channels that resemble leiomyosarcoma or fibrosarcoma, but large numbers of extravascular erythrocytes and the identification of vacuoles with red blood cells may help diagnosis. Immunohistochemical studies indicate that factor VIII-related antigen,

Table 2 Histologic types of 204 surgically removed cardiac sarcomas (from 15 series[1,2,4,7,35-45])

Sarcoma type	Frequency (% of cardiac sarcomas)	Typical cardiac location
Angiosarcoma	34	Right atrium, pericardium
Unclassified	20	*
Malignant fibrous histiocytoma	12.5	Left atrium
Leiomyosarcoma	9	Left atrium
Osteosarcoma and chondrosarcoma	6	Left atrium
Fibrosarcoma	5.5	*
Rhabdomyosarcoma	4	*
Myxosarcoma	4	Left atrium
Fibromyxosarcoma	2	Left atrium
Synovial sarcoma	2	Left atrium, pericardium
Liposarcoma	0.5	*
Malignant mesenchymoma	0.5	*
Malignant peripheral nerve sheath tumor	0.5	*

*Variable, or little data.