

91 TUMORS OF THE HEART AND GREAT VESSELS

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CARDIAC TUMORS

According to Hoch-Ligeti and colleagues,¹ the first human primary cardiac tumor was reported by Columbus in 1559, and cardiac myxoma was first described by King in 1845. Since then, a large variety of benign and malignant primary cardiac tumors has been reported.

INCIDENCE, EPIDEMIOLOGY, AND ETIOLOGY Primary cardiac tumors are rare. In autopsy series, their incidence varies between 0.0017 and 0.28%.² Among 533 cases of primary tumors and cysts of the heart and pericardium reviewed at the Armed Forces Institute of Pathology, 60% were benign tumors, 17% were cysts, and 23% were malignant tumors.² (Table 91.1). Among benign tumors, myxomas are by far the most common (about 40%). Myxomas affect both sexes about equally and occur in all age groups but more often between the fourth and sixth decades.² Although usually sporadic, they can occasionally be familial and multiple.

The primary malignant cardiac tumors are usually sarcomas; angiosarcomas are the most common, followed by rhabdomyosarcoma. Malignant tumors affect predominantly the right side of the heart, in contrast to benign tumors, which are common on the left side.^{3,4} Cardiac tumors can also occur in children and infants, the most common ones being rhabdomyoma and rhabdomyosarcoma.^{2,5}

With the exception of asbestos for pericardial mesothelioma, the etiology of cardiac tumors is largely unknown.¹ Hereditary factors play a role in a few cases of cardiac myxoma. Particles resembling Coxsackie B4 virus have been detected in a human cardiac myxoma by electron microscopy and immunofluorescence, but viral cultures were unsuccessful.⁶ Rhabdomyoma can occur in patients with tuberous sclerosis, and neurofibroma can occur in patients with Von Recklinghausen's disease.¹ Whereas hepatic angiosarcomas have been reported after exposure to arsenic, vinyl chloride, and thorium dioxide, no such causative factors have been described for cardiac angiosarcomas.⁷

CLINICAL FEATURES **Benign Primary Cardiac Tumors.** *Myxomas.* About 75% of myxomas occur in the left atrium, but they can also arise in any other cardiac chamber.^{2,5} These tumors occur exclusively on the endocardial surface.⁸ In patients with myxoma, a typical clinical triad—systemic symptoms, embolic episodes, and signs of valvular or intracavitary dysfunction—has been described.⁵ Presenting symptoms are protean and include dyspnea on exertion, paroxysmal nocturnal dyspnea, fever, weight loss, dizziness, syncope, hemoptysis, and Raynaud's phenomenon. Arrhythmias and sudden death can occur.² Physical signs include various murmurs, often mitral systolic or diastolic, which typically vary with respiration or body position. A characteristic “tumor plop” can be heard following the second heart sound.⁵ It can be confused with a third heart sound or the opening snap of the mitral valve and is thought to be secondary to tension on the tumor stalk during diastolic prolapse of left atrial myxomas into the left ventricle or by the tumor striking the myocardium.⁵ Associated conditions may include clubbing, fibroadenomas of the breast, lentiginous skin lesions, and multiple blue nevi,^{1,5} as well as pituitary adenomas and testicular Sertoli's cell tumors.⁹

Laboratory studies can reveal anemia (possibly hemolytic) or erythrocytosis, leukocytosis, thrombocytopenia, increased serum immunoglobulin levels, elevated sedimentation rate, and cross-reactive proteins. High serum levels of interleukin-6 have been reported, which could explain some of the systemic manifestations of the disease; however, these levels return to normal after surgical resection.⁵

The diagnosis, as for any cardiac tumor, is based on a high index of suspicion. Chest radiographs can reveal cardiomegaly or calcifica-

tions within the tumor. More definitive imaging techniques include two-dimensional echocardiography, either transthoracic (TTE), which is useful as a screening method, or transesophageal (TEE), which is more invasive but allows much better visualization of the tumor. While both TTE and TEE are equally effective in detecting cardiac tumors, TEE is superior to TTE in assessing localization and extracardiac spread of tumors.¹⁰ Computed tomography (CT) with intravenous contrast, particularly gated and ultrafast CT, is another excellent imaging modality. While cardiac tumors are often diagnosed by echocardiography or CT, magnetic resonance imaging (MRI) is superior to other noninvasive imaging modalities in several respects. Of the imaging techniques, MRI provides the highest quality tumor localization, morphologic differentiation between tumor and surrounding tissues, and demonstration of the effects on adjacent tissue.¹¹ Radionuclide scanning methods using technetium, gallium, or thallium isotopes have been reported as well.⁴ All these imaging techniques can accurately show the tumor and often obviate the need for catheterization and angiography with their potential risk of tumor embolization.^{4,5}

Histologically, these soft gelatinous tumors are thought to arise from the subendocardial mesenchyme and contain polygonal to stellate myxoma cells (“lepidic cells”), often around vascular channels in an eosinophilic matrix, with various areas of hemorrhage.² The cells are positive for factor VIII and can also express neuron-specific enolase an S-100 protein.⁵

Treatment is surgical, with complete excision of the tumor and its base.⁵ Close follow-up is necessary, since recurrence is possible.¹²

Other Benign Tumors. Papillary fibroelastomas arise usually from the valvular endocardium, most commonly the aortic valve.^{2,13} They resemble a “sea anemone,”² being composed of papillary fronds similar to normal chordae tendinae. They can be asymptomatic or produce anginal symptoms (by obstruction of coronary ostia) as well as embolic phenomena with transient ischemic attacks or stroke.^{2,14,15} TEE is a sensitive technique that can detect such tumors, even when transthoracic echocardiography is unrevealing.¹⁴ Several authorities have recommended that papillary fibroelastomas be removed surgi-

Table 91.1. Type and Frequency of Primary Cardiac Tumors*

<i>Benign tumors (N=319, 59.8%)</i>	
Myxoma	24.4%
Lipoma	8.4%
Papillary fibroelastoma	7.9%
Rhabdomyoma	6.8%
Fibroma	3.2%
Hemangioma	2.8%
Teratoma	2.6%
Mesothelioma of the A-V node	2.3%
Granular cell tumor	< 1.0%
Neurofibroma	< 1.0%
Lymphangioma	< 1.0%
<i>Cysts (N=89, 16.7%)</i>	
Pericardial cyst	15.4%
Bronchogenic cyst	1.3%
<i>Malignant tumors (N=125, 23.5%)</i>	
Angiosarcoma	7.3%
Rhabdomyosarcoma	4.9%
Mesothelioma	3.6%
Fibrosarcoma	2.6%
Lymphoma	1.3%
Extraskelatal osteosarcoma	< 1.0%
Neurogenic sarcoma	< 1.0%
Malignant teratoma	< 1.0%
Thymoma	< 1.0%
Leiomyosarcoma	< 1.0%
Liposarcoma	< 1.0%
Synovial sarcoma	< 1.0%

*From 533 cases reviewed by the Armed Forces Institute of Pathology.²

cally, even if asymptomatic, given the risk of embolic complications from fibroelastomas.^{15,16}

Rhabdomyomas, the most common primary heart tumors in infants, occur almost exclusively in children and are often multiple. They are associated with tuberous sclerosis in one-third of patients.² Rhabdomyomas tend to regress spontaneously, and surgical excision is usually necessary only in the presence of outflow tract obstruction.^{17,18} Lipomas are, in fact, less common than lipomatous hypertrophy of the atrial septum and can occur anywhere in the heart, like hemangiomas. Fibromas frequently arise from the interventricular septum. Hamartomas of mature cardiac myocytes are very rare.⁸ Pericardial cysts are most common in the right costophrenic angle, and bronchogenic cysts can be found in the myocardium.²

Malignant Primary Cardiac Tumors. Angiosarcomas represent the most common malignant tumors. In contrast to myxomas, they are most often seen in the right atrium. The peak age is between 20 and 50 years, with a two- to three-fold male predominance.² Like myxomas, they present with a variety of symptoms, including palpitations, dyspnea, and chest pain (pleuritic and/or pericardial). Most commonly, however, primary cardiac tumors present with signs and symptoms related to congestive heart failure or thromboembolism.³ The electrocardiogram may be normal or may reveal nonspecific findings such as ST/T changes, arrhythmias or conduction defects. In 10% of patients, the presenting symptoms are systemic, with fever, weight loss, and malaise, without cardiac symptoms. These tumors can spread locally to the pleura or mediastinum. Metastases are common (64% of cases),⁷ affecting the lung, liver, bone, adrenals, central nervous system, and lymph nodes.^{1,2}

The tumors are composed of malignant cells forming vascular channels. Immunoperoxidase stain for factor VIII is positive.¹ The term hemangiopericytoma is reserved for rare cases where more solid areas are seen.² The relationship between cardiac angiosarcomas and Kaposi's sarcoma deserves further study. Cardiac involvement has been described in patients with both the African form of Kaposi's sarcoma and that seen in AIDS patients.¹ Whether such involvement can occur without skin lesions is uncertain.

Complete surgical resection of cardiac angiosarcomas is usually impossible. Orthotopic heart transplantation in patients with cardiac angiosarcomas has been described in two small case series. The first such case series, from Spain, described the experience with cardiac transplantation in two patients with angiosarcoma of the right atrium, but without evidence of metastases.¹⁹ Total removal of the tumor was accomplished, but the patients died 8 and 9 months after transplantation, respectively, of multiple brain metastases. A second series of patients with primary cardiac tumors who underwent orthotopic heart transplantation was reported from Columbia Presbyterian Medical Center (New York, NY). Of the 4 patients with primary cardiac sarcomas, 2 were alive and tumor free at 16 and 6 months after transplantation, respectively. One other patient was alive with diffuse metastatic disease at 38 months, and the fourth died suddenly at 2.6 months after the operation.²⁰

In other cases, resection has been possible using cardiopulmonary bypass,^{21,22} followed by various combinations of radiotherapy and chemotherapy based on doxorubicin. A few patients thus treated have survived to 3 years.^{21,22} Regardless of treatment strategy, survival for patients with primary cardiac sarcomas remains poor, with a mean survival of 16.5 months after diagnosis according to a recent report.²³

Rhabdomyosarcomas are seen in all age groups, but more commonly in adults. The male:female ratio is about equal, and they arise in any cardiac chamber. They are multiple in 60% of the cases. The prognosis is also poor, with a survival of less than a year. Fibrosarcomas and malignant fibrous histiocytomas also arise in any portion of the heart. Primary cardiac lymphomas and extraskeletal osteosarcomas are exceptional, as well as the other malignant tumors listed in Table 91-1.

Metastatic Tumors to the Heart. It should be kept in mind that cardiac metastases are far more frequent than primary neoplasms by a factor of 20 to 40-fold.² Some tumors have a high propensity for cardiac or pericardial metastases. According to statistics from 3,877

autopsies of cancer patients compiled by the Armed Forces Institute of Pathology,² the frequency of cardiac metastases was, in decreasing order: leukemias (46%), melanoma (37%), thyroid cancer (30%), lung cancer (28%), sarcomas (26%), esophageal cancer (23%), renal cell cancer (22%), lymphomas (22%), and breast cancer (21%). Almost any cancer, however, can metastasize to the heart. We found a high frequency of cardiac metastasis and/or invasion in patients with malignant pleural mesothelioma.²⁴ In 19 autopsies, cardiac invasion was found 14 (74%), with more than half involving the pericardium and more than one-quarter the myocardium.²⁵

TUMORS OF THE GREAT VESSELS

Primary tumors involving the aorta, pulmonary artery, and vena cavae are rare, appearing in the literature mainly as case reports or in small retrospective case series.²⁶⁻²⁸ As is the case with primary cardiac tumors, risk factors for the development of tumors of the great vessels remain poorly defined. Prior radiation exposure has been postulated as a possible causative factor.²⁹ Plastic polymers, such as Dacron, have been linked to aortic tumors in animal studies. Nonetheless, aortic tumors arising around a Dacron graft in humans, while reported, are extremely rare.³⁰ The mode of presentation of tumors of the great vessels typically involves thromboembolic events or an obstructive syndrome.²⁶ MRI and TEE are useful in differentiating tumors of the great vessels from intraluminal thrombus, mediastinal lymphadenopathy, or adjacent lung tumors.²⁸

Benign tumors reportedly found in the aorta include endothelial papillary fibroelastomas arising in the aortic sinuses. These tumors may present with emboli to the brain and heart or by intermittent prolapse into a coronary artery.³¹ Intra-aortic myxomas have also been detected after the patient presents with recurrent arterial emboli.²⁷

Malignant tumors of the aorta and pulmonary artery are often aggressive, poorly differentiated sarcomas arising from intimal cells and showing myofibroblastic differentiation ("intimal type"). More rarely, they are identified as angiosarcomas or leiomyosarcomas.²⁶ Other tumor types, such as malignant hemangioendothelioma, schwannoma and fibrous histiocytoma, have also been reported to arise in the great vessels.³²⁻³⁴ Sarcomas of the inferior vena cava, in contrast to those of the aorta and pulmonary artery, tend to be well-differentiated leiomyosarcomas. Malignant tumors of the great vessels are frequently confined to the lumen on diagnosis.

Sarcomas of the pulmonary artery present at a mean age of 41 years, while sarcomas of the aorta present at a mean of 62 years. In a review of 60 cases,³⁵ the median age was 52 years, and the male:female ratio was 1:2. The median duration of symptoms was 10 months. The clinical picture was suggestive of pulmonary embolism, with dyspnea (70%), chest pain (48%), cough (34%), hemoptysis (30%), and syncope (25%). Metastases to lungs were common (67%), as were lymph node metastases (20%). The cornerstone of therapy for the tumors of the great vessels is complete surgical excision. The use of various grafts has been advocated.³⁶ Postoperative radiation therapy and chemotherapy, often with an anthracycline-based regimen, are also employed.^{26,32} Regression of pulmonary metastases has been observed after a combination of etoposide, vincristine, ifosfamide, and doxorubicin.³⁶ The average survival is 10 months.^{36,37} According to Burke and Virmani, however, mean survival after diagnosis for sarcomas of the pulmonary artery was 23 months, as opposed to 5 months for aortic sarcomas.²⁶ Of those patients with pulmonary artery sarcomas who underwent surgical resection, actuarial 3- and 5-year survival after resection was 69%. Completeness of resection correlated with increased survival, while tumor size and grade did not.³²

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