Cardiac Neoplasms
Radiologic-Pathologic Correlation

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KEYWORDS

• Cardiac neoplasms • Cardiac tumors • Radiologic-pathologic correlation • Computed tomography • Magnetic resonance imaging

KEY POINTS

- Primary cardiac neoplasms are rare, and their clinical presentation may mimic more common non-neoplastic cardiac diseases.
- The varied imaging appearances of primary cardiac neoplasms can be explained by their underlying pathology.
- Primary considerations for the imaging diagnosis of primary cardiac neoplasms are location, tissue characterization, and clinical features such as age and associated syndromes.

INTRODUCTION

Cardiac neoplasms are a diagnostic challenge on many levels. They are rare, their clinical presentation may mimic other much more common cardiac diseases, and they are at an uncommon intersection of oncologic and cardiac imaging. Despite these obstacles, it is often possible to arrive at a favored diagnosis using advanced imaging techniques and knowledge of the pathologic basis of cardiac neoplasms. As with imaging tumors elsewhere in the thorax, a foundation in the pathology of cardiac neoplasms explains an entire spectrum of imaging appearances. Furthermore, knowledge of cardiac tumors ranging from imaging appearances to epidemiology informs the diagnostic approach to these lesions and ultimately their management. This work will explore the imaging approach to cardiac neoplasms with emphasis on the most common, clinically significant tumors and the relationship between their pathology and imaging manifestations.

An epidemiologic context is the first step to arriving at a clinically relevant diagnosis or a short differential diagnosis. Primary cardiac neoplasms are rare in both autopsy series and clinical practice, with metastatic disease being 40 to 100 times more common. This difference between the incidence of primary tumors and metastatic disease may be inconsistent with the clinical experience of cardiac imagers who frequently evaluate cardiac neoplasms. However, it should be noted that most epidemiologic data are derived from autopsy series or large clinical databases in which cardiac spread may be detected in the larger context of metastatic disease but not undergo further diagnostic evaluation.

Primary cardiac neoplasms occur at an incidence of 30 per 100,000 people per year.[1,2] Approximately 80% of primary cardiac tumors are benign. The World Health Organization has classified neoplasms of the heart into either benign tumors and tumorlike lesions such as myxoma,

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malignant lesions such as angiosarcoma, and pericardial tumors such as solitary fibrous tumors.[3] In patients older than 16 years, the most common primary cardiac neoplasms are myxomas, lipomatous tumors, and papillary fibroelastomas. In patients younger than 16 years, the most common tumors are rhabdomyomas, teratomas, fibromas, and myxomas.[1]

The most common presenting symptom of a cardiac tumor is dyspnea, but the manifestations of a neoplasm will depend on the location of the lesion and size. Even benign cardiac tumors may cause obstruction of blood flow, decreased cardiac output, arrhythmia, or heart failure, which can be fatal.[2,4] In addition, systemic manifestations such as fatigue, anorexia, and fever may also be seen.[2]

MYXOMA

Clinical Considerations

Cardiac myxoma is the most common benign primary cardiac neoplasm, accounting for up to 80% of all cases,[5] but only represent 10% of benign primary cardiac tumors in children.[1] Approximately 3% to 10% of cardiac myxomas are associated with Carney complex,[6] an autosomal dominant disorder characterized by pigmented lesions of the skin and mucosae, cardiac myxomas, cutaneous tumors, and multiple other endocrine and nonendocrine neoplasms. In this disorder, pituitary neoplasms lead to acromegaly and adrenocortical tumors lead to Cushing syndrome.[7] In this disorder, cardiac myxomas are responsible for 50% of the related mortality and are often found in multiple locations, in younger patients, and have a higher risk of recurrence.[6,7]

Symptoms are variable and include shortness of breath and chest pain as well as constitutional symptoms such as fever and weight loss.[5,8] Embolism may be a presenting sign of a myxoma in up to 30% of patients.[6] Myxomas within the left heart have been shown to present earlier with worse shortness of breath when compared with right heart tumors.[8]

Although they can be located in any chamber, most myxomas are located within the left atrium and originate at the interatrial septum. These lesions may have an irregular border, a pedunculated morphology, and be mobile.[5,9] The size of the tumor is related to the degree of mobility and the potential that the lesion can obstruct the atrioventricular valve.[5]

Pathologic Features

At gross inspection, most myxomas are soft, gelatinous, or friable lesions, ranging from 2 to 11 cm in size.[10] The contour of the tumor is most often lobular and smooth but can be villiform in appearance, which is thought to be associated to thromboembolism.[6,10]

Histologically, myxomas demonstrate myxoma cells in a myxoid stroma with possible calcification and hemorrhage. These lesions may demonstrate heterotopic elements such as bone, glands, and giant cells. In addition, the use of the immunohistochemical test of PRKAR1A, a cAMP-dependent protein kinase type 1α regulatory subunit, can be used as a screening tool to evaluate for Carney complex in the setting of myxomas.[6]

Imaging Features

Transthoracic echocardiography is the initial imaging modality of choice for the evaluation of cardiac myxomas, although findings are nonspecific. On echocardiography, a myxoma may be heterogenous or homogeneous and may have calcification.[5] Although computed tomography (CT) is not the preferred method to characterize the tumor, typical findings on a contrast-enhanced CT include a spherical or ovoid mass that is lower in attenuation than surrounding myocardium.[10] Characteristic features of a myxoma on MR imaging is T2-weighted hyperintensity, hypoperfusion on first-pass perfusion following the administration of intravenous gadolinium, and a heterogeneous appearance on delayed enhancement when compared with the myocardium (**Figs. 1** and **2**).[5,9] Gradient echo imaging may demonstrate susceptibility artifact due to hemosiderin. Parametric techniques can also be applied to characterize the mass with T1 mapping demonstrating T1 times between 1285 and 1356 msec and T2 mapping demonstrating T2 times between 76 and 270 msec at 1.5 T.[5]

Management

Surgical resection is the treatment of choice and is associated with excellent outcomes. In one series of 95 patients, there was only a single recurrence over 5 years following excision.[11] Patients are regularly followed with transthoracic echocardiography 1 year following excision and then at 5 years.[6]

RHABDOMYOMA

Clinical Considerations

Rhabdomyoma is the most common primary cardiac tumor of infancy and childhood representing 60% of pediatric primary cardiac neoplasms.[12] These lesions are most often diagnosed during the first year of life or prenatally.[13] Cardiac

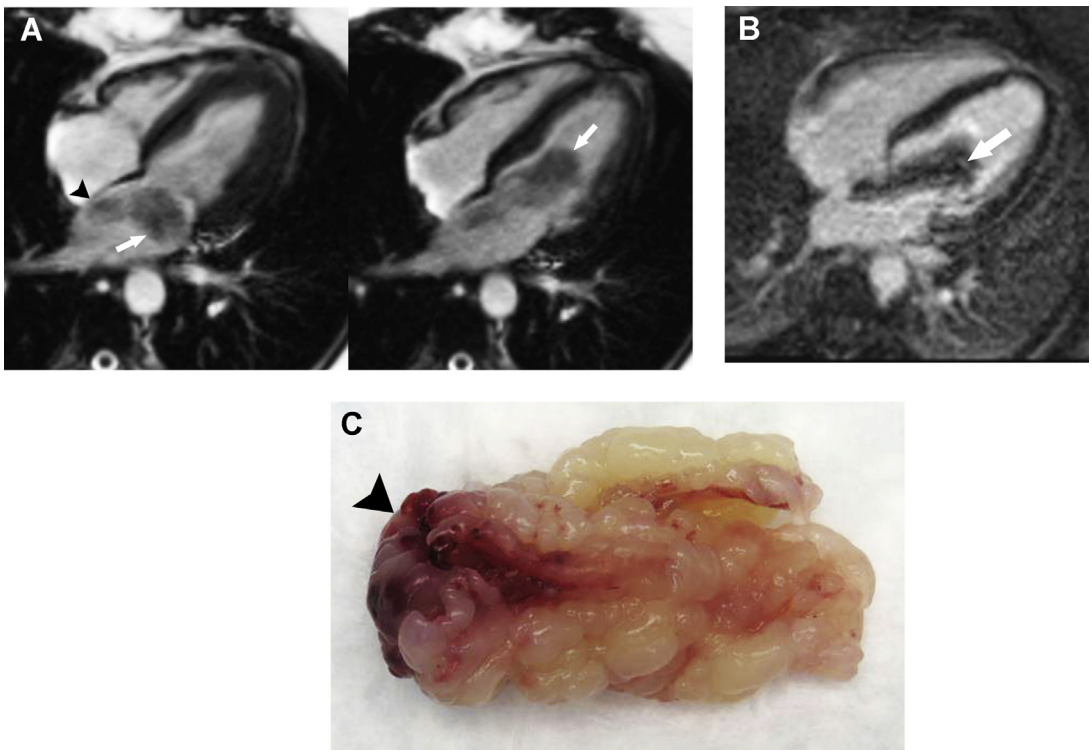

Fig. 1. A 35-year-old man with cardiac myxoma. (*A*) Axial SSFP MR composite image shows a mass (*arrow*) in the left atrium with stalklike attachment (*arrowhead*) to the interatrial septum. Note the prolapse of the mass across the mitral valve plane between systole (*left*) and diastole (*right*), characteristic of myxoma. (*B*) Axial late gadolinium enhancement MR image shows small foci of internal enhancement, a useful differentiating feature from thrombus. (*C*) Gross specimen shows the cut stalk (*arrowhead*) and a smooth polypoid mass. SSFP, steady-state free precession.

rhabdomyomas are associated with tuberous sclerosis in 30% to 50% of cases but also occur sporadically and rarely in association with congenital heart disease.[13,14] Tuberous sclerosis is characterized by cortical tubers and subependymal nodules within the brain, multiple retinal hamartomas, adenoma sebaceum of the skin, and periungual fibromas.[14] Rhabdomyomas may precede other sequelae of tuberous sclerosis such as skin abnormalities and neuroimaging findings by months or years.[12] Symptoms of cardiac rhabdomyomas vary and are based on the size and location of the tumor. They may be asymptomatic or result in congestive heart failure from obstruction. Arrhythmias have also been reported.[15]

Rhabdomyomas are most commonly located within the ventricles attached to the myocardium but are less commonly located in the atrioventricular groove.[9,12] They are multiple in 60% of cases, typically in the setting of tuberous sclerosis.[12]

Pathologic Features

At gross inspection, rhabdomyomas are lobulated masses with a glistening cut surface. Sporadic tumors tend to be larger in size than those associated with tuberous sclerosis.[13] At histology, these neoplasms tend to have large cells in relation to the myocardium with abundant glycogen. "Spider cells" are present in all tumors that have a centrally located mass of granular cytoplasm with elongated projection of myofibrils extending peripherally from the nucleus to the cell membrane.[13,16] These lesions demonstrate positive immunohistochemical staining for desmin, actin, and myoglobin.[13]

Imaging Features

On transthoracic echocardiography, rhabdomyomas are uniformly hyperechoic in appearance (**Fig. 3**).[12] On contrast-enhanced CT, they are most often hypodense masses with little contrast enhancement.[17] On MR imaging, these tumors are homogenous in appearance, isointense to slightly hyperintense to myocardium on T1-weighted imaging, mildly hyperintense in relation to the myocardium on T2-weighted imaging, hypoenhancing on first pass perfusion, and isointense

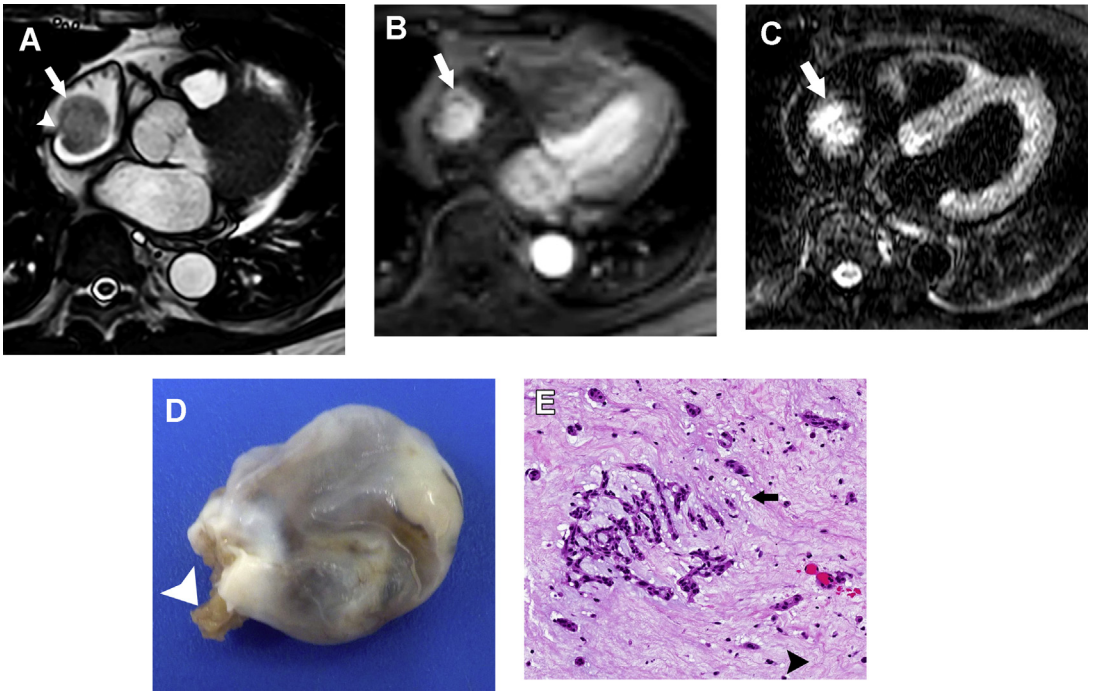

Fig. 2. A 62-year-old man with cardiac myxoma. (*A*) Axial steady-state free precession MR image shows a mass (*arrow*) in the right atrium with stalklike attachment (*arrowhead*) to the wall of the atrium. (*B*) Axial T2-weighted MR image shows significant hyperintensity of the mass (*arrow*), attributed to the myxoid component of these tumors. (*C*) Axial perfusion MR image in the early arterial phase shows diffuse enhancement of the mass (*arrow*), excluding thrombus as a diagnostic consideration. (*D*) Gross specimen shows the cut stalk of the mass (*arrowhead*) and a variegated white and gray tan external surface. (*E*) Photomicrograph (original magnification, 40x; hematoxylin-eosin stain) shows spindle cells without atypia (*arrowhead*) and paucicellular myxoid material (*arrow*).

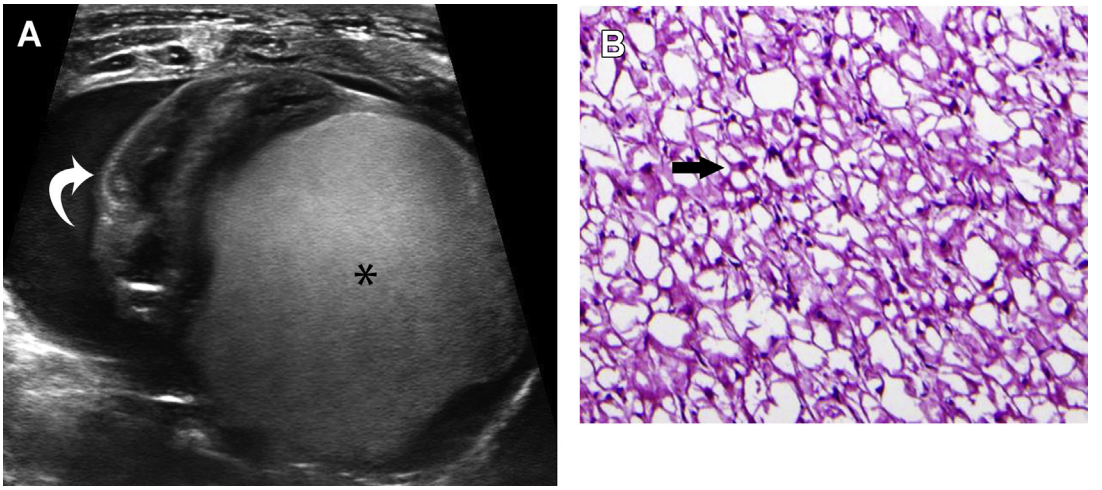

Fig. 3. Neonate with cardiac rhabdomyoma. (*A*) Transthoracic echocardiographic image shows a homogeneously hyperechoic mass (*asterisk*) displacing the heart to the right (*curved arrow*). (*B*) Photomicrograph (original magnification, 40x; hematoxylin-eosin stain) shows large vacuolated cells with centrally placed nucleus and myofibrils radiating to the cell membrane, "spider cells" (*arrow*).

to myocardium on myocardial delayed enhancement.[9,12]

Management

Most rhabdomyomas spontaneously regress.[18] When there is outflow obstruction leading to heart failure or arrhythmias, surgical resection may be performed. In addition, everolimus, a mammalian target of rapamycin inhibitor, may be used as therapy.[12]

FIBROMA

Clinical Considerations

Cardiac fibroma is the second most common primary cardiac neoplasm of infancy and childhood after rhabdomyoma.[13] Although cases do occur in adults, greater than 80% of cardiac fibromas are in children.[19] These tumors occur more frequently in nevoid basal cell carcinoma (Gorlin) syndrome, a phakomatosis characterized by multiple basal cell carcinomas; odontogenic cysts; ocular pathology such as congenital cataracts, microphthalmia, and coloboma of the iris; and other tumors such as medulloblastoma. Two percentage of patients younger than 45 years with basal cell carcinomas have this syndrome.[20]

Patients with cardiac fibromas may be asymptomatic but may also present with arrhythmias, congestive heart failure, and sudden death believed to be secondary to distortion of the conducting system of the heart rather than infiltration.[19] The most common locations of a cardiac fibroma are the left ventricular free wall, interventricular septum, and right ventricular free wall.[21]

Pathologic Features

At gross inspection, cardiac fibromas tend to be solitary well-demarcated white tumors ranging from 3 to 8 cm in diameter. Cut surfaces are either white, gray, or tan (**Fig. 4**). At histology, the tumor contains prominent spindle-shaped fibroblasts with a collagen matrix.[19] The collagen matrix increases with age and the amount of cellularity decreases with age.[22] Cells express alpha smooth muscle actin and do not express desmin, CD 34, or S100 protein.[19] Calcification is seen but this is more likely in older patients.[22]

Imaging Features

Chest radiographs may show calcification in cardiac fibromas.[21] Transthoracic echocardiography is successful in identification of the mass and demonstrates mixed echogenicity. On contrast-enhanced CT, fibromas tend to enhance either homogenously or heterogeneously.[21] On MR imaging, the lesion may have a thin rim of myocardium with a heterogeneous signal intensity on both T1- and T2-weighted images. Following the administration of intravenous gadolinium, the mass demonstrates avid hyperenhancement on delayed imaging with or without decreased enhancement centrally.[9]

Management

Surgical resection is the treatment of choice for cardiac fibromas with excellent early and late-term outcomes. If a tumor is difficult to resect due to location, subtotal resection has also been shown to result in excellent long-term survival.[23]

HEMANGIOMA

Clinical Considerations

Hemangiomas account for 5% to 10% of all benign cardiac neoplasms and can occur in any age group.[24] Although patients are often asymptomatic, the most common symptom is dyspnea on exertion.[25] Rarely patients may develop Kasabach-Merritt syndrome manifesting as recurrent thrombocytopenia and consumptive coagulopathy.[24] These tumors can occur in any chamber of the heart but are most common in the ventricles.[4]

Pathologic Features

At gross inspection, hemangiomas are red and hemorrhagic.[26] On histology, there are 3 variants capillary, cavernous, and arteriovenous. The lesions are composed of a dilated mixture of mature vessels supported by fibrous connective tissue.[24]

Imaging Features

Transthoracic echocardiography of a hemangioma reveals a solid vascular mass.[12] On contrast-enhanced CT, hemangiomas are heterogeneous masses that may contain calcifications and avidly enhance.[17] On MR imaging, hemangiomas are heterogeneous and hyperintense to myocardium on T2-weighted imaging[4] and isointense to hypointense to myocardium on T1-weighted imaging (**Fig. 5**).[25] They enhance on first pass perfusion but may have variable enhancement on myocardial delayed imaging.[9] Differentiation of hemangiomas from other vascular tumors, even malignant neoplasms such as angiosarcoma, can be difficult on MR imaging.[12]

Management

Surgery remains the treatment of choice; however, the complication rate is higher than other neoplasms given the vascularity of hemangiomas.

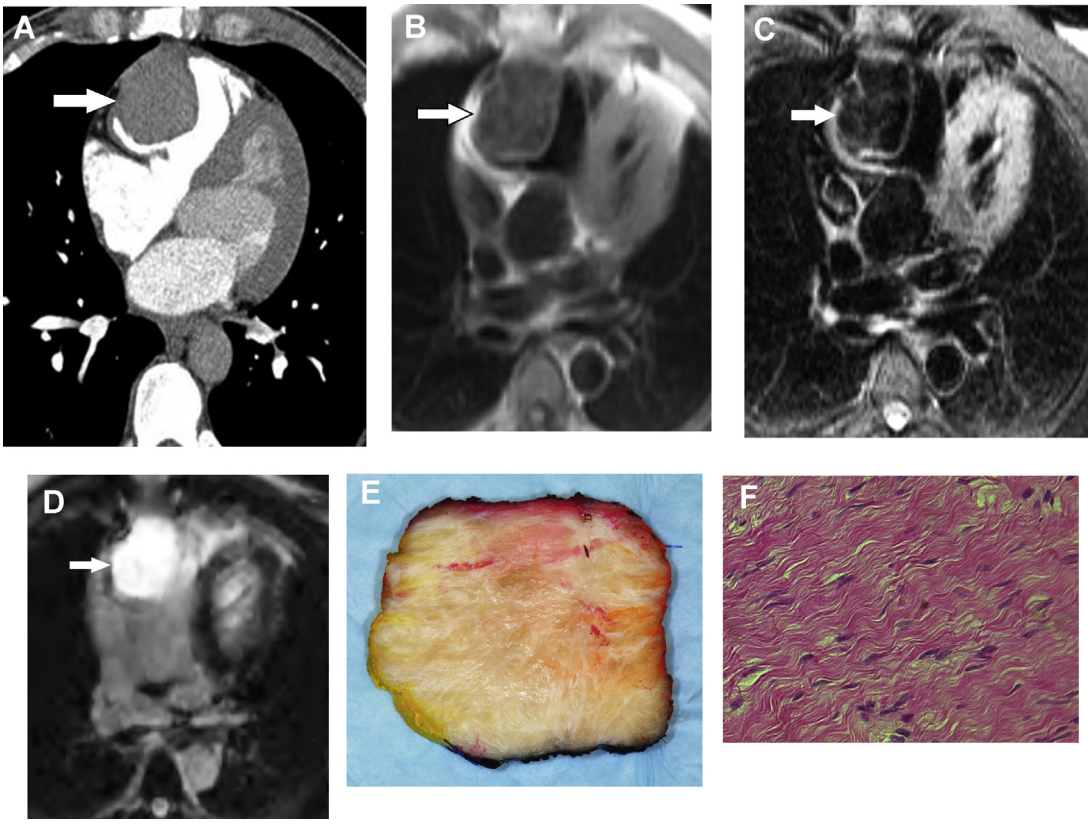

Fig. 4. A 45-year-old man with cardiac fibroma. (*A*) Contrast-enhanced axial CT image shows a smooth, well-circumscribed right ventricular mass (*arrow*) without pericardial effusion or evidence of local invasion. (*B*) Axial T1-weighted MR image shows the mass (*arrow*) to be uniform and slightly hypointense relative to skeletal muscle. (*C*) Axial T2-weighted MR image shows uniform hypointensity of the mass (*arrow*) without cystic components. (*D*) Axial late gadolinium enhancement MR image shows intense, diffuse enhancement (*arrow*) of the mass suggesting fibrotic tissue. (*E*) Sectioned gross specimen shows a homogeneous, whirled, white, solid cut surface. (*F*) Photomicrograph (original magnification, 40x; hematoxylin-eosin stain) shows multiple bland fibroblasts with normal appearing nuclei and no evidence of mitosis.

Preoperative coil embolization can be considered to reduce complications.[24]

ANGIOSARCOMA

Clinical Considerations

Cardiac angiosarcomas are the most common primary cardiac malignancy in adults with specific differentiation, accounting for 40% of cardiac sarcomas. Patients are usually younger than 65 years, peaking in the fourth to fifth decade, with a slight male preponderance of 1.3:1.[27]

Cardiac angiosarcomas occur almost exclusively in the right atrium near the atrioventricular sulcus (80%–90% of cases). Symptoms generally result from obstruction, tumor emboli, or local invasion into the myocardium and atrial free wall. A common presentation includes chest tightness, dizziness, dyspnea, and symptoms related to congestive right heart failure. Nonspecific symptoms such as weight loss, malaise, anemia, and fatigue may also coexist. Pericardial effusion, which is diagnosed in 56% of patients, can manifest as cardiac tamponade and occurs more frequently in cardiac angiosarcomas than with other types of cardiac sarcoma due to the propensity for pericardial involvement. An insidious onset of arrythmia is frequently described in the young and often indicates myocardial invasion.[28]

These tumors are prone to local and distant metastases with the lung being the most common site. Additional areas reported include the liver, mediastinal lymph nodes, bone, adrenal glands, and spleen. Patients undergoing surgical resection interestingly demonstrate a propensity for brain metastases, thought to be due to intravascular dissemination at tumor resection and manipulation.[29]

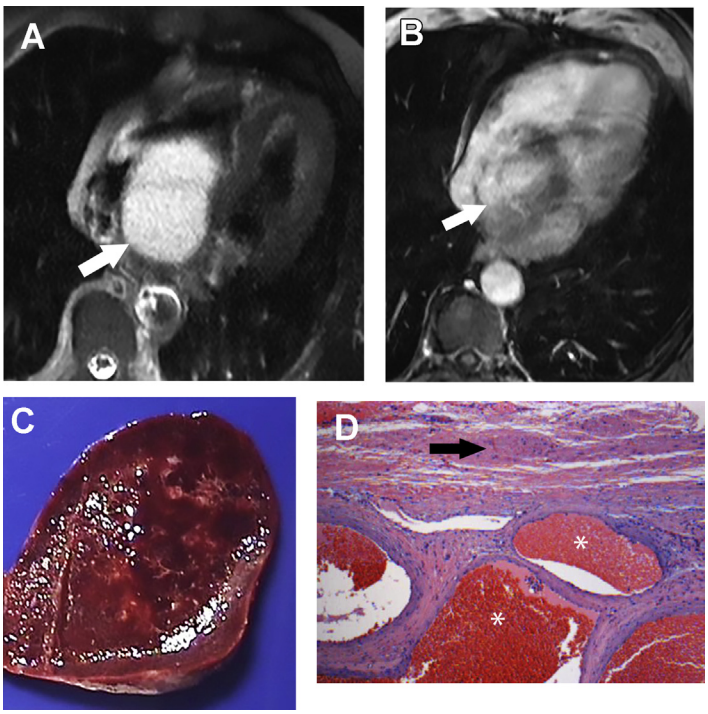

Fig. 5. A 71-year-old man with cardiac hemangioma. (*A*) Axial T2-weighted MR image shows a homogeneously hyperintense intracardiac mass (*arrow*) displacing the adjacent cardiac chambers. (*B*) Axial postcontrast T1-weighted MR image shows heterogeneous internal enhancement. (*C*) Sectioned gross specimen shows an encapsulated mass with red-tan, spongy fibrous tissue and maroon-red fluid. (*D*) Photomicrograph (original magnification, 40x; hematoxylin-eosin stain) shows dilated vascular channels (*asterisk*) and overlying myocardium (*arrow*).

Pathologic Features

Cardiac angiosarcomas occur in the right atrium 80% to 90% of the time. At surgical resection, the mass typically projects into the cardiac chambers with permeative growth into the myocardium and local invasion of the pericardium, vena cava, tricuspid valve, and even the coronary arteries. Gross pathology reveals a large lobulated mass that is dark red and brown in color, reflecting its hemorrhagic and necrotic components. If pericardial invasion is present, a thickened rind of gray-black tissue is observed that is inseparable from the remainder of the tumor.[30]

Histologically, the predominant feature is multiple endothelial-lined vascular channels with branching anastomoses and sinusoids. Interspersed are densely packed populations of anaplastic spindle cells that resemble those of Kaposi sarcoma. The epithelioid variant, which is most common in the heart, is characterized by round cells with abundant cytoplasm and frequent mitoses. Immunohistochemistry can be used as an adjunct when evaluating these tumors. Staining is variable and heterogeneous, dependent on the dominant histologic pattern. Staining for CD31 is positive in more than 90% of cases but is nonspecific for cardiac angiosarcomas. Expressivity of BNH9, a monoclonal antibody against blood group–related H and Y antigens, is the most specific marker.[31]

Imaging Features

The presentation of dyspnea and congestive heart failure typically prompts evaluation with echocardiography or coronary angiography. The sensitivity of transesophageal echocardiography for the detection of cardiac masses is 75% to 97%.[30,32] Information about tumor location, shape, size, attachment, and mobility are provided by this modality. CT, MR imaging, and fluorodeoxyglucose (FDG) PET/CT usually provide further mass characterization and metastatic evaluation.

Two morphologic types have been described on imaging. The first is that of a discrete low-attenuating mass, 6 cm in average size, with irregular boarders and a broad attachment to the myocardium, most commonly arising from the right atrial free wall (**Fig. 6**).[33,34] Cavitations may decompress and freely communicate with the cardiac chambers, spilling tumor elements into the systemic circulation. Calcifications may also be present. The extent of myocardial invasion, mass effect on the cardiac chambers, and involvement of the great vessel are also pertinent findings. The second morphologic type is a diffusely infiltrative mass inseparable from the pericardium. A

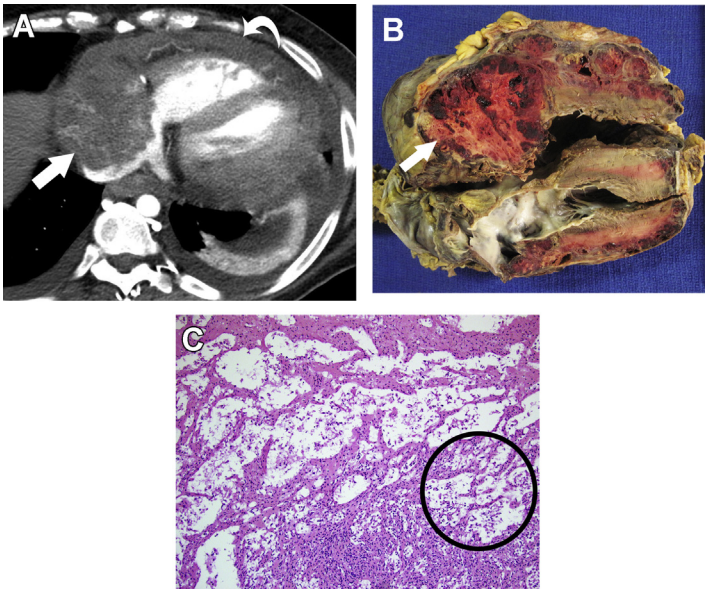

Fig. 6. A 25-year-old man with cardiac angiosarcoma. (*A*) Contrast-enhanced axial CT image shows an aggressive mass (*arrow*) centered in the right atrium with internal vascular enhancement. A pericardial effusion is present (*curved arrow*). (*B*) Sectioned gross specimen shows the mass (*arrow*) with internal dilated vessels. (*C*) Photomicrograph (original magnification, 40x; hematoxylin-eosin stain) shows a proliferation of vascular interconnected spaces (*circle*) and malignant spindle and epithelioid cells.

complex, mixed density pericardial effusion is invariably present, frequently with hemorrhagic and necrotic tumor debris. Pericardiocentesis yields a bloody aspirate that may contain malignant cells.[35]

Tumor location, tissue composition, and local invasion are often shown to better advantage on cardiac MR imaging (CMR) compared with other modalities with an additional benefit of differentiating between neoplasm and tumor mimics (such as thrombus). CMR classically demonstrates an aggressive hypervascular mass with intense heterogeneous enhancement. Intralesional flow voids, related to large tumoral vessels, are well displayed on spin echo sequences. In addition, CMR patterns can differ between the 2 morphologic subtypes. The first pattern is characterized by a heterogeneous "cauliflower"-shaped mass that is hyperintense on both T1-and T2-weighted images that indicate hemorrhagic and necrotic content. The second morphology of diffuse pericardial infiltration appears as pericardial thickening and effusion with linear contrast material occupying vascular channels, producing a "sunray" appearance on the postcontrast sequences.[33] The 2 imaging patterns may coexist in the same patient.

Management

The prognosis for cardiac angiosarcoma is poor, due to its rarity, resistance to chemoradiotherapy, and early metastasis, which is found in 56% to 89% of cases at presentation.[36] A recent retrospective study of 68 patients reports a median overall survival of 13 months for the entire cohort, which is shorter than that of other sarcoma subtypes. However, of those presenting with metastatic disease, the median overall survival dropped to 6 months.[27] The treatment remains controversial and is most often multidisciplinary. Surgical debulking or total resection is the mainstay, particularly in the setting of localized disease. A postsurgical survival of 1 to 60 months, with a median overall survival of 11 to 14 months, has been reported in 2 separate reviews.[27,37] In contrast, a 1-year survival of 10% is shown in patients with medical therapy alone.[38]

Surgical outcomes are further optimized with neoadjuvant chemotherapy, which uses a doxorubicin-/ifosfamide-based regimen. This regimen has been shown to extend median overall survival to 15.5 months from 12 months.[32] Most cases, however, are nonsurgical; thus, treatment depends largely on cytotoxic chemotherapy, such as anthracycline, ifosfamide, and taxanes. A recent trend combines cytotoxic and targeted drug therapies, with the latter focusing on vascular endothelial growth factor A and tyrosine kinase. For example, a trial using pazopanib combination therapy reports a median overall survival of nearly 10 months.[39]

OTHER SARCOMAS

Clinical Considerations

Most of the primary malignant cardiac tumors are sarcomas, accounting for greater than 90% of

cases. Undifferentiated high-grade pleomorphic sarcoma (UHGPS), rhabdomyosarcoma (RS), osteosarcoma (OS), and leiomyosarcoma (LS) are discussed further. The most common of these tumors is UHGPS, previously known as malignant fibrous histiocytoma. UHGPS has a slight female predominance with a mean age of 47 years with a wide age range. RS, on the other hand, is the most common primary cardiac malignancy of childhood. A slight male predilection has been reported, and unlike other sarcomas, no chamber preference is observed. As such, clinical presentation varies. LS and OS account for less than 20% of sarcomas and typically occur in the left atrium.[40]

Presenting symptoms among cardiac sarcomas are nonspecific and include chest pain, palpitations, and embolic phenomena. Patients may also present with syncope, pneumonia, fever, arrhythmias, peripheral edema, and sudden death. Because UHGPS has a left atrial predilection, symptoms related to pulmonary congestion, mitral stenosis, and pulmonary vein obstruction can be seen.

Pathologic Features

Cardiac sarcomas appear as large, aggressive, multifocal masses with a tendency to infiltrate multiple cardiac chambers, although generally with a left heart predilection. On gross inspection, sarcomas are described as soft, lobulated, gelatinous masses containing necrotic areas. Histologically, UHGPS is composed of undifferentiated spindle cells with frequent mitotic activity and nuclear pleomorphism, sharing histologic features with intimal sarcomas of the aorta and pulmonary artery. It often has storiform architecture with variable degrees of collagenized stroma.

Imaging Features

Primary cardiac sarcomas are generally aggressive, heterogeneous masses that have a broad-based attachment with internal necrosis and cavitations. Violation of tissues planes is typical with associated pericardial effusions and lymphadenopathy. At CMR, these tumors exhibit heterogeneous high signal on T2-weighted imaging and low-to-intermediate signal on T1-weighted imaging with a variegated pattern of enhancement.

Location is usually the most helpful feature in suggesting a tissue diagnosis. For example, UHGPS, OS, and LS typically arise from the posterior wall of the left atrium in contradistinction to a septal origin of cardiac myxoma and a right heart location of angiosarcoma.[41] Certain mass characteristics, when present, can provide further delineation. If dense, amorphous calcifications of osteoid matrix deposition are present, OS is favored. If there is invasion of the pulmonary veins or mitral valve in a slightly younger adult patient, a diagnosis of LS can be suggested. RS presents as multiple masses always involving the myocardium with extracardiac extension common, tending to be nodular in growth rather than sheetlike.[33]

Management

Outcomes are generally grim for cardiac sarcomas, even when detected early and aggressive therapy is used. For UHGPS, a median overall survival of 15 months (range of 11–18 months) is reported in patients following tumor surgical resection[42] but drops to 5 months in nonoperable cases. The role of chemotherapy and/or radiation therapy is controversial. Combination therapy with ifosfamide, doxorubicin, cyclophosphamide, and paclitaxel can be used with varying degrees of response. Cardiac transplantation, however, does not provide significant survival benefit.[43]

CARDIAC LYMPHOMA

Clinical Considerations

Primary cardiac lymphoma (PCL) is a rare extranodal lymphoma accounting for 1% to 1.5% of all primary cardiac tumors, with the majority involving the right heart. PCLs are aggressive and are usually of the non-Hodgkin type. A typical patient is an immunocompetent male adult (2:1 male to female ratio) in his 6th to 7th decade of life. The mean age is 60 years with a range of 12 to 86 years.[44] Certain subtypes occur more commonly in the immunocompromised. Post-transplant lymphoproliferative disorder, a B-cell proliferation related to Epstein-Barr virus infection, may develop mostly in lung and cardiac transplant recipients. Primary effusion lymphoma (PEL) uniquely affects patients with human immunodeficiency virus, which is associated with human herpesvirus-8 (HHV-8)/Kaposi sarcoma–associated herpesvirus.

Symptoms are variable, with dyspnea, congestive heart failure, constitutional complaints, and chest pain being the most common clinical symptoms. The anatomic location produces specific clinical syndromes. For example, right atrial lymphoma may obstruct venous inflow and cause superior vena cava syndrome, which is seen in 5% to 8% of cases.[44] Alternatively, tumor infiltration may induce arrhythmia or cause coronary artery obstruction, the latter resulting in angina. Tumor embolism and pericardial effusion with or without tamponade are also typical. Diagnosis can be made from pericardial fluid analysis, although

direct endomyocardial biopsy is commonly performed.

Pathologic Features

At gross inspection, PCLs are gray-white coalescing masses with a "fish flesh" consistency, most commonly in the right heart.[44] Most of the PCLs are of B-cell lineage and in 80% of cases are of the diffuse large B-cell lymphoma (DLBCL) type.[45] DLBCL demonstrates a uniform population of lymphoid cells on histology that express markers such as CD19, CD20, CD22, CD79a, or PAX-5, which establish a B-cell lineage. Classic type DLBCL is most commonly observed. Chronic inflammation-associated DLBCL and PEL variants are described, the former occurring in association with valve replacements and the latter occurring in association with HHV-8 infection in the immunocompromised. Burkitt lymphoma and follicular lymphoma comprise the remainder of B-cell subtypes.[46] Differentiation can be made by expressivity of CD5, CD23, and BcL-2 antigens, which are present in follicular subtype and further corroborated by c-myc gene translocations seen in Burkitt lymphoma.[44]

Imaging Features

PCL commonly presents as a homogenously low-attenuating, hypoenhancing mass on contrast-enhanced CT, involving the right atrium or right ventricle in 92% of cases.[47] Necrosis and involvement of the cardiac valves are atypical and, if present, should invoke an alternative diagnosis such as angiosarcoma. Extension along the epicardial surface with encasement of the coronary arteries, aortic root, and great vessels is classic (**Fig. 7**).[33] There is often pericardial thickening and massive pericardial effusion, which can occasionally be the only imaging manifestation, particularly in the PEL subtype.[48] Stigmata of elevated right heart pressures are then assessed.

Similar to lymphoma elsewhere, PCL is highly metabolic. Although FDG PET/CT imaging is valuable in initial staging, it is usually used to monitor treatment response. Interpretation is occasionally made difficult by physiologic myocardial activity. A nodular pattern of intense radiotracer uptake (standardized uptake value >10) with a correlative mass on the CT images improves diagnostic and staging accuracy.[49]

Additional information can be obtained through CMR, specifically the assessment of tumor mobility and tumor point attachment, which is best shown on cine steady-state free precession (SSFP) imaging. SSFP also provides high-contrast resolution between tumor, myocardium, blood pool, and adjacent soft tissues. Tissue characterization is generally performed on conventional T1- and T2-weighted sequences. PCLs demonstrate signal characteristics of hypercellular tumors: hypointense on T1-weighted imaging and mildly hyperintense on T2-weighted imaging. The enhancement pattern of this tumor is variable, either homogeneous or heterogeneous. The value of postcontrast imaging is the differentiation between tumor and thrombus with thrombus demonstrating no central contrast uptake.

Management

Treatment is often multimodal and includes surgical, medical, and radiotherapeutic approaches. Considered a systemic disease, chemotherapy is the mainstay with a regimen historically including anthracycline-containing agents, doxorubicin, vincristine, and prednisone. Combination immunotherapy with rituximab can also be used. Surgery and radiation therapy are usually performed for symptom relief.

The prognosis for both primary and secondary PCL is generally poor with a median overall survival of 63 months, reported in a recent retrospective study.[47] This is in contrast to a median overall survival of 12 months previously reported.[50]

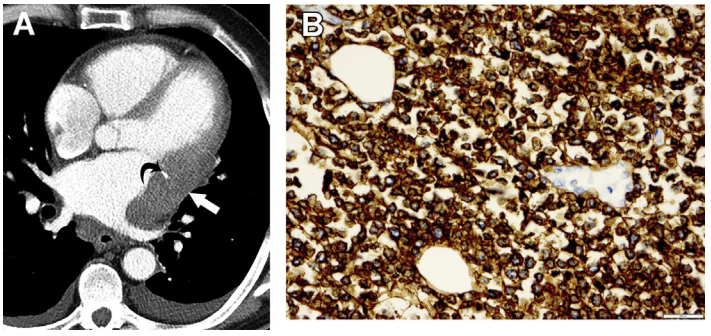

Fig. 7. A 69-year-old man with cardiac large B-cell lymphoma. (*A*) Contrast-enhanced axial CT image shows a mass (*arrow*) centered on the left atrioventricular groove, surrounding but not occluding the left circumflex coronary artery (*curved arrow*). (*B*) Photomicrograph (original magnification, 40x; CD20 stain) shows diffuse positive staining for B-cell marker CD20.

SUMMARY

When confronted with a cardiac mass, the most important imaging considerations are the location of the tumor, the possibility of metastatic disease, and the clinical presentation. When considering the differential diagnosis for primary malignant cardiac masses, location is usually the most helpful feature. Myxomas tend to be left sided, and their overall frequency skews left-sided heart masses as more frequently benign. Cardiac lymphoma and angiosarcoma, the most common primary cardiac malignancies are predominantly right sided. Necrosis, surface enhancement ("sun-ray" appearance), and valvular involvement favor angiosarcoma, whereas homogeneity and vascular encasement favor lymphoma. Other cardiac sarcomas tend to be left sided, specifically arising from the posterior wall of the left atrium.

The pathology of primary cardiac tumors explains their varied imaging features, including calcification in OS and T2 hyperintensity in myxoma. Integrating the imaging and pathologic features of cardiac tumors furthers our understanding of the spectrum of appearances of these tumors and improves the clinical imager's ability to confidently make a diagnosis.

DISCLOSURE

Author, Elsevier.

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