
Cardiovascular Anatomy and Cardiac Malignancy

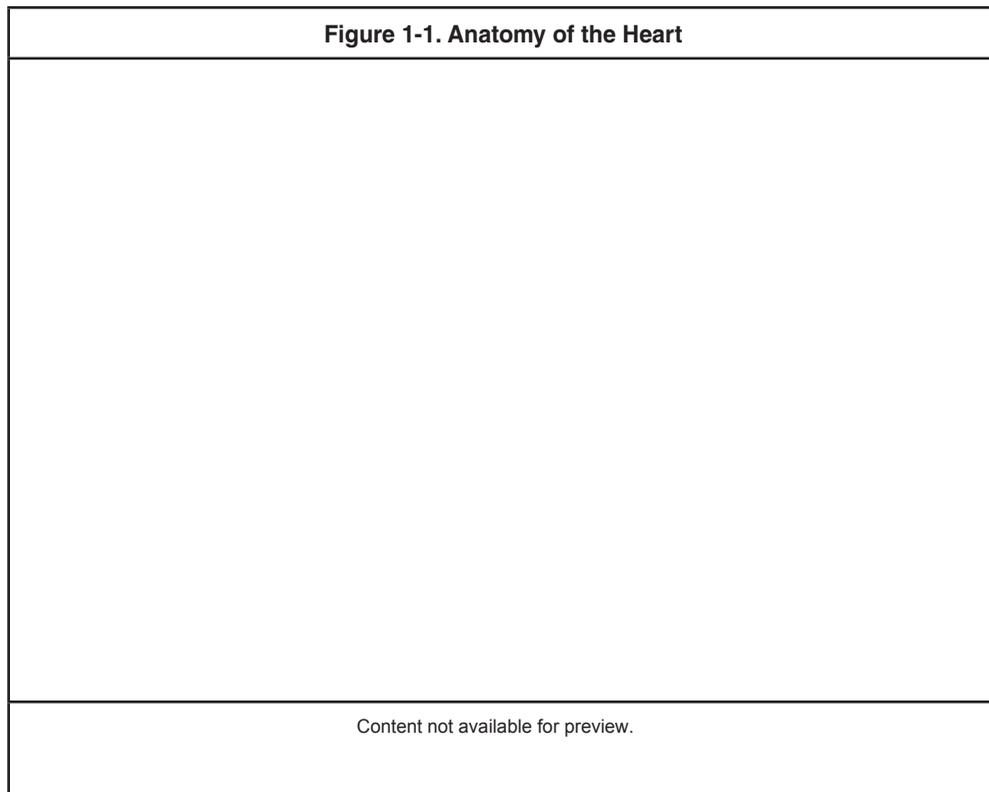
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Overview

This chapter will cover basic cardiac anatomy and tumors that are commonly found in the heart. The heart is divided into four chambers: left atrium, right atrium, left ventricle, and right ventricle. Different cardiac chambers have a propensity to have different cardiac masses or tumors. Cardiac tumors are rare entities: metastasis to the heart from another primary cancer is 30 times more likely (Bisel, Wróblewski, & La-Due, 1953). Malignancies that are commonly associated with metastasis to the heart include breast, lung, leukemia, sarcoma, and melanoma, although almost any cancer can metastasize to the heart (Hanfling, 1960). The incidence of primary cardiac tumors ranges from 0.3%–0.7% in most autopsy series, with 75% of these being benign (Yu, Liu, Wang, Hu, & Long, 2007). Clinical presentation and treatment of cardiac tumors frequently depend on the chamber location and malignant potential. If the tumor is malignant and not resected, 90% of patients are deceased within 9–12 months; even with resection, prognosis can be poor (Reardon, 2010).

Left Atrial Structures and Masses

The left atrium is a posterior chamber of the heart. The structures of the left atrium include the pulmonary veins, left atrial ridge, left atrial appendage, and fossa ovalis. Oxygenated blood enters the chamber through one of the four pulmonary veins and proceeds through the mitral valve with each cardiac cycle. Left atrial tumors can be benign or malignant. The benign tumors include myxoma, lipoma, papillary fibroelastoma, rhabdomyoma, fibroma, and teratoma. It is more common to have a benign tumor in the left atrium. If malignant, the most common histology of the left atrium is malignant fibrous histiocytoma, also known as pleomorphic sarcoma, and leiomyosarcoma (Glancy, Morales, & Roberts, 1968) (see Figure 1-1).



Myxomas: Common tumors of the left atrium include myxomas, which are mostly benign and account for up to half of the benign cardiac tumors. These usually are sporadic, left atrial, arising from the fossa ovalis, and solitary. They can, however, exist in any of the four cardiac chambers. Many are pedunculated with a 1–2 cm based attachment to the endocardial septum. Surgical resection is curative in 95% of the cases and has a low morbidity and mortality (Piazza et al., 2004). Rarely, benign myxomas are misdiagnosed and are actually malignant sarcomas or can have malignant transformation potential. Thus, the goal of excision is to remove the entire tumor and not leave remnants. About 5% of myxomas can be hereditary and present as part of the Carney syndrome consisting of myxomas, spotty pigmentation, and endocrine changes (Bireta et al., 2011) (see Figure 1-2).

Lipomas: These usually are benign tumors of adipose tissue that can be found in the subendocardium or subepicardium but also can be intramuscular. These tumors usually are well encapsulated.

Papillary fibroelastomas: These are small (less than 1 cm) benign tumors that protrude from a central stalk and usually are single and mobile. Most are located on the ventricular surface of the aortic valve, with the atrial side of the mitral valve being the second most common location. These usually can be distinguished from Lambl excrescences, as they are located on non-contact areas of the valve. Lambl excrescences are thin and elongated echoreflexive structures with undulating hypermobility seen on the atrial side of the mitral and tricuspid valves and the ventricular side of the aortic valve.

Figure 1-2. Left Atrial Tumor

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Paragangliomas: These are chromaffin tumors of the sympathetic nervous system and are fleshy tumors that can be found on the surface of the heart or the pericardium. The paragangliomas that grow into the anterior mediastinum arise from the parasympathetic chain and are relatively asymptomatic. Posterior paragangliomas arise from the sympathetic chain and can present with symptoms consistent with catecholamine response of the tumor. Some of these tumors present with severe malignant hypertension secondary to the release of catecholamines. They can be diagnosed by measuring the level of catecholamines in the urine and can be localized by computed tomography scan or metaiodobenzylguanidine scintigraphy (Lee et al., 2006). Patients should be treated with alpha and beta-blockade combination medication followed by surgery. These are highly vascular tumors and have a characteristic appearance on cardiac angiogram (see Figure 1-3).

Lymphoma: Lymphoma can present in any of the four chambers and is best treated with chemotherapy with occasional debulking of the tumor if hemodynamic compromise occurs.

Clinical Manifestations of Patients With Cardiac Tumors

Cardiac tumors can present as constitutional symptoms, intracardiac obstruction, embolic phenomena, arrhythmias, or cardiac tamponade (Butany, Leong, Carmichael, & Komeda, 2005; Butany, Nair, et al., 2005; Weinberg, Conces, & Waller, 1989). Constitutional symptoms may be vague but include fever, malaise, weight loss,

Figure 1-3. Paraganglioma

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night sweats, polymyositis, and cachexia (Debourdeau, Gligorov, Teixeira, Aletti, & Zammit, 2004). These symptoms are likely promoted by the release of inflammatory cytokines from the tumor, such as interleukin-6 and antimyocardial antibodies, and often normalize once the tumors are resected from the heart (Pinede, Duhaud, & Loire, 2001).

Diagnostic Evaluation

Common laboratory abnormalities include anemia, elevated erythrocyte sedimentation rate, C-reactive protein, thrombocytosis, and hyperglobulinemia. Left atrial tumors also have presented as arrhythmias such as atrial flutter or embolic phenomena that include transient ischemic attacks or stroke (Hayes, Liles, & Sorrell, 2003). If on the left side, the emboli also can result in myocardial infarction as the tumor emboli occlude the coronary arteries (Pinede et al., 2001). Unfortunately,

left-sided tumors also present with intracardiac obstruction of the mitral valve causing cardiogenic shock.

Assessment Findings

Normal heart sounds of the cardiac cycle include a first heart sound (S_1) caused by the closing of the mitral and tricuspid valves. Mitral valve closure usually occurs slightly before tricuspid valve closure. S_2 , the second heart sound, is caused by closure of the aortic and pulmonic valves, with the aortic valve closure occurring slightly earlier than the pulmonic valve closure. A patient with a left atrial tumor that is large enough to obstruct the mitral valve may have a loud, widely split S_1 because of late closure of the mitral valve. This also is seen with mitral stenosis and preexcitation. A presystolic crescendo murmur may be present if the tumor obstructs the mitral valve orifice. A tumor plop may be heard early in diastole after the opening snap as the tumor protrudes through the mitral valve.

Treatment and Prognosis

Current treatment of malignant left atrial tumors includes neoadjuvant chemotherapy and resection of the tumor followed by postoperative chemotherapy. Left atrial tumors remain a surgical challenge because of the posterior location of the tumor in the chest. Cardiac autotransplantation is a relatively new technique for the removal of left atrial cardiac masses and is advocated especially for malignant left atrial tumors, as survival is very dependent on obtaining a negative margin (Hoffmeier, Schmid, & Scheld, 2004; Mery, Reardon, Haas, Lazar, & Hindenburg, 2003; Reardon, DeFelice, Sheinbaum, & Baldwin, 1999; Reardon, Malaisrie, et al., 2006; Reardon, Walkes, & Benjamin, 2006). This technique involves complete excision of the heart, ex vivo tumor removal with cardiac reconstruction, and cardiac reimplantation (Reardon, 2010; Reardon, Walkes, DeFelice, & Wojciechowski, 2006). Besides routine postoperative complications, bradycardia may result because the vagal innervations to the heart have been interrupted. The most common histology of malignant tumors of the heart is sarcoma. The majority of patients with malignant left atrial tumors die from metastatic disease rather than local recurrence. Complete resection with new techniques such as autotransplantation has improved the chance of obtaining negative surgical margins with a median survival of 36 months. Median survival of patients undergoing standard resection is 11 months versus 22 months with cardiac autotransplantation (Bakaeen et al., 2003; Blackmon et al., 2008; Murphy et al., 1990; Putnam et al., 1991; Reardon, Malaisrie, et al., 2006).

Postoperative Management

The role of neoadjuvant and postoperative chemotherapy for cardiac sarcoma is unclear. Several drug combinations are routinely used in the treatment of sarcoma, including doxorubicin and ifosfamide, gemcitabine and docetaxel, and dacarbazine. The Sarcoma Meta-Analysis Collaboration (1997) concluded that doxorubicin-based chemotherapy improved time to local recurrence and overall recurrence-free survival with a trend toward improved survival in patients with sarcoma. Pervaiz et al. (2008) also found that the addition of ifosfamide improved the efficacy of the regimen. However, this has not been evaluated in patients with sarcoma of the heart.

Left Ventricular Structures and Masses

The left ventricle receives blood through the inlet of the mitral valve. Blood then moves toward the apex, which contains fine trabeculations. Blood is then pumped with ventricular contraction toward the left ventricular outlet tract and out to the aorta through the aortic valve. Left ventricular tumors can present as left ventricular congestive heart failure (including symptoms of dyspnea, edema, and chest pain) and as deadly arrhythmias such as ventricular tachycardia, which cause sudden cardiac death (Ottaviani, Maturri, Rossi, & Jones, 2003; Schrepfer et al., 2003). Left ventricular tumors have presented with arrhythmias such as heart block if they invade the atrioventricular (AV) node. Common tumors of the left ventricle are similar to tumors of the left atrium, with sarcoma being a prominent malignant tumor. However, some unique tumors of the left ventricle include rhabdomyoma and fibroma. Treatment also is similar to that for left atrial tumors, with resection and chemotherapy as the mainstay of treatment. Chemotherapy regimens are similar to those for left atrial sarcoma. Ventricular tumors may be excised via three main techniques: through the atrioventricular valve, through the transaortic valve, and via ventricular incisions.

Rhabdomyomas: These are the most common tumors found in children and infants and are frequently found in the ventricles. They usually are multiple and are associated with tuberous sclerosis. They can produce arrhythmias such as ventricular tachycardia. Most are just observed, as they tend to regress with age. Resection is only considered for incessant, uncontrollable, life-threatening arrhythmias.

Fibromas: These are benign connective tissue tumors described as firm and circumscribed but unencapsulated and usually are found in children. They typically are intramural and almost exclusively originate in the left ventricle. Tumor calcification can frequently be seen on chest x-ray. Gorlin syndrome is a genetic condition that has been identified with cardiac fibromas, multiple basal cell carcinomas, keratocystic odontogenic (jaw) tumors, and skeletal abnormalities.

Right Atrial Structures and Masses

The right atrium consists of the inferior vena cava and superior vena cava, which receives deoxygenated blood from the systemic venous system. It also receives blood from the coronary sinus. The Eustachian valve is at the border of the inferior vena cava and helps form a fenestrated network termed the *Chiari network*. The anterolateral portion of the right atrium is made of pectinate muscle and appendage. The smooth and rough portion of the right atrium is separated by a muscle ridge called the *crista terminalis*. Blood flows through the right atrium and through the tricuspid valve. Right atrial tumors tend to be more malignant than left-sided tumors, with the most common histology being angiosarcoma. Right atrial tumors also may be the result of extension of infradiaphragmatic tumors such as renal cell carcinoma, hepatocellular tumors, or uterine tumors (see Figure 1-4).

Clinical Manifestations

Right atrial and right ventricular tumors can present with embolic phenomena. If the tumor is on the right side, the emboli usually result in a pulmonary embolism, which if left untreated can result in cor pulmonale (right-sided heart failure). If the tumor

Figure 1-4. Right Atrial Tumor

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is large enough, pulmonary hypertension can occur, causing hypoxia, clubbing, and polycythemia. Right heart failure may occur, which manifests as dyspnea, increased abdominal girth, and peripheral edema. Heart failure symptoms usually present later in the disease as compared to left-sided tumors (Esaki et al., 1998). On physical examination, a diastolic (period of ventricular filling) rumble that varies with inspiration may be the result of tricuspid valve obstruction. P₂, the closure of the pulmonic valve, may also be delayed.

Treatment

Complete and early resection of right atrial tumors is needed because of the aggressive nature of these tumors and the resulting symptoms and complications. Surgery may involve extensive resection including removal of a majority of the right atrium, transection of the right coronary artery with bypass graft placement, and resection of up to one-third of the right ventricle. Treatment of right atrial sarcoma involves a combination of neoadjuvant chemotherapy and surgical excision, with most of these patients dying of metastatic disease. Surgical resection resulted in survival when disease-free margins were obtained at excision (median survival 27 months versus 4 months), achieving a significantly higher overall five-year survival rate than those with positive surgical margins (Reardon, 2010; Vaporciyan & Reardon, 2010). Systemic therapy is important and is similar to regimens discussed for left-sided tumors. (See the Postoperative

Management section of left atrial tumors for common systemic chemotherapy agents.) Some unique tumors of the right atrium include lipomatous hypertrophy of the interatrial septum and angiosarcoma.

Lipomatous hypertrophy of the interatrial septum: This is a benign mass composed of adipose tissue that collects at the atrial septum and protrudes into the right atrium. It appears on imaging as a barbell shape of the septum sparing the fossa ovalis. It usually does not create symptoms and is incidentally found on routine transthoracic echocardiography. No treatment besides observation is necessary.

Angiosarcoma: Angiosarcoma is the most common malignant tumor of the right heart. Treatment and management includes resection with aggressive chemotherapy, as previously discussed (see Figure 1-5).

Right Ventricular Structures and Masses

The right ventricle receives blood through the tricuspid valve, and, similar to the left ventricle, consists of three sections. The inlet region contains the tricuspid valve apparatus. The apical region is highly trabeculated. Blood then flows with contraction into the right ventricular outflow tract and through the pulmonic valve into the pulmonary artery and on toward the lungs. Tumors of the right ventricle are similar to tumors of the right atrium and should be treated as such. A unique tumor of the right ventricle is leukemia, which has been predominantly noted in right ventricular wall lesions. This

Figure 1-5. Right Atrial Synovial Sarcoma

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tumor regresses with chemotherapy. Many varied regimens exist for leukemia depending on the type and classification. Treatment agents include but are not limited to doxorubicin, vincristine, prednisone, and tyrosine kinase inhibitors.

Pericardium

The pericardium is the sac that surrounds the heart and has both a visceral and parietal layer. The most common tumor of the pericardium is mesothelioma (Fine, 1968). Presenting symptoms may include pericarditis or pericardial hemorrhagic effusion. This tumor can extend into the conduction pathways, primarily the AV node, which can cause complete heart block and sudden cardiac death (Strauss, Asinger, & Hodges, 1988). The prognosis for patients with mesothelioma is poor.

Metastatic Tumors to the Heart

Almost any tumor can metastasize to the heart to almost any chamber, but lung cancer is the most common metastatic tumor to the heart. Other common cancers include breast cancer, lymphoma, leukemia, and melanoma. Infradiaphragmatic tumors can extend through the inferior vena cava into the heart, usually from malignant renal or hepatic tumors (Hanfling, 1960).

Diagnosis of Cardiac Tumors

The primary modalities of choice for diagnosing cardiac tumors include transthoracic echocardiography, transesophageal echocardiography, myocardial magnetic resonance imaging (MRI), and computed tomography angiography (CTA) (Leja, Shah, & Reardon, 2011).

Transthoracic echocardiography: This is an initial noninvasive screening tool for assessing gross cardiac structure and function. However, it is not very sensitive for cardiac tumors because it can often miss structures in the posterior of the atrium and ventricles. The tumor has similar visual characteristics to myocardium and can be missed. This is a good tool for assessing pericardial effusion (fluid around the heart), which is associated with cardiac tumors.

Transesophageal echocardiography: This often is used for initial screening for a cardiac tumor but generally is not helpful for obtaining a tissue diagnosis and is an invasive test. Similar to transthoracic echocardiography, transesophageal echocardiography often misses structures in the posterior sections of the left and right atrium and apical ventricular masses. It can initially help to determine implantation site and mobility of the tumor and can discriminate between vegetation, thrombi, and tumor.

Computed tomography angiography: Ultrafast CTA is especially useful for assessing blood supply to the tumor and for assessing extrathoracic cardiac metastasis.

Magnetic resonance imaging: MRI is excellent to assess size, shape, and three-dimensional relationships to other cardiac structures (Araoz, Eklund, Welch, & Breen, 1999; Gilkeson & Chiles, 2003; Sparrow, Kurian, Jones, & Sivananthan, 2005; Thakrar et al., 2009). It is particularly useful in distinguishing among tumor, thrombus, and pseudotumor and is likely the best choice for assessing cardiac tumors because of its high contrast and spatial resolution (Hoey, Mankad, Puppala, Gopalan, & Sivananthan, 2009;

Shah, 2010). Although it can give a clue to tissue pathology, it cannot determine histology, and a cardiac biopsy may be necessary.

Angiography: Angiograms are useful for defining coronary and anomalous blood supply to the tumor, which is extremely important for surgical excision. However, the healthcare professional performing the procedure must be careful not to dislodge tumor fragments during manipulation of catheters and dye injection. Transeptal puncture and left ventriculograms are relatively contraindicated for fear of tumor dissemination but can be beneficial if safely done. The ideal imaging modality is likely a combination of all these methods, as each provides different information to the clinician.

Conclusion

Cardiac tumors are rare. Although tumors of the heart usually are benign, malignant cardiac tumors are very serious and must be diagnosed and treated early in the disease process. Advanced surgical techniques and novel systemic therapies are necessary for treatment.

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