Cancer and the Heart

Primary Cardiac Tumors

Monika J. Leja, MD
Dipan J. Shah, MD
Michael J. Reardon, MD

Primary cardiac tumors are a rare entity whose incidence, according to surgery and autopsy reports, is 0.3% to 0.7% of all cardiac tumors.[1] Metastasis to the heart from other primary cancers is 30 times more common. Only 25% of primary cardiac tumors are malignant, and, of these, 75% are sarcomas. Malignant primary cardiac sarcomas are usually located in the right atrium and are most commonly angiosarcomas. In the left atrium, the most common malignant tumors are pleomorphic sarcoma (also known as malignant fibrous histiocytoma) and leiomyosarcoma.[2] Malignant primary cardiac tumors, which often strike a young patient population, have a dismal prognosis: without surgical resection, the survival rate at 9 to 12 months is only 10%.

Symptom presentation for cardiac tumors is quite varied, but it is dependent upon tumor location and size, rather than upon histologic characteristics. Presentation includes congestive heart failure from intracardiac obstruction, systemic embolization, constitutional symptoms, and arrhythmias. Left atrial sarcomas tend to be more solid and less infiltrative than right-sided sarcomas; consequently, they tend to metastasize later. They usually present with symptoms of blood-flow obstruction and substantial, life-threatening congestive heart failure. Right-sided cardiac tumors are usually malignant and appear as bulky, infiltrative masses that grow in an outward pattern. These are usually fast-growing tumors that metastasize early and do not present with congestive heart failure until late in the disease.[3]

The genetics of primary cardiac tumors is poorly understood. Although several complexes with genetic links (such as Carney complex) have been associated with benign primary cardiac myxomas, there are no demonstrable associations with malignant sarcomas. There is, however, some small amount of information on sarcoma overall. Sarcomas generally reside in 2 groups: specific gene alterations with simple karyotypes or nonspecific gene alterations with complex karyotypes. Most simple alterations—such as rhabdomyosarcomas and Ewing, synovial, and gastrointestinal stromal tumors—are the result of chromosomal translocations. Pleomorphic sarcomas and leiomyosarcomas are probably the result of nonspecific translocations.[4-6]

The diagnosis of cardiac tumors relies heavily on the use of multiple imaging techniques, including cardiac computed tomography (CT), cardiovascular magnetic resonance (CMR), and echocardiography. Important imaging data to collect include information on the size of the intracardiac mass, the mobility of the mass (an important predictor of prognosis and embolic potential), myocardial invasion, and cardiac chamber location. These factors will provide the means to diagnosis and prognosis. Other important data to collect include the mechanism of tumor implantation, the relationship of the tumor with adjacent structures, the surgeon's route of access to the heart, left ventricular ejection fraction, and the dimensions of the affected chamber.

Two-dimensional (2-D) transthoracic echocardiography (TTE) has been a common imaging technique in the evaluation of the heart, but it has several disadvantages during the imaging of cardiac tumors. These include a restricted field of view, incomplete ability to evaluate the mass when the body habitus is unfavorable, and poor ability to characterize tissue. Three-dimensional (3-D) TTE has many advantages over 2-D TTE in imaging cardiac tumors by allowing for the acquisition of full volumes, live 3-D images, and 3-D zoom (smaller, magnified, pyramidal data at higher resolution). Three-dimensional TTE is much better at evaluating mass volume. Two-dimensional TTE and transesophageal echocardiography underestimate mass by as much as 24%.[7,8] Three-dimensional TTE reveals more information on the type of tumor and site of attachment, surface features, and the tumor's spatial relationships to surrounding structures.

Cardiovascular magnetic resonance will probably become a staple imaging technique for cardiac tumors for several reasons, including its excellent spatial and contrast

Presented at the First International Conference on Cancer and the Heart; from The University of Texas MD Anderson Cancer Center and the Texas Heart Institute at St. Luke's Episcopal Hospital; Houston, 3–4 November 2010.

Section Editor: *Edward T.H. Yeh, MD*

From: *Departments of Cardiology, The University of Texas MD Anderson Cancer Center (Dr. Leja), and the Methodist DeBakey Heart & Vascular Center (Drs. Reardon and Shah); Houston, Texas 77030*

Address for reprints: *Monika J. Leja, MD, Department of Cardiology, The University of Texas MD Anderson Cancer Center, Unit 1451, 1515 Holcombe Blvd., Houston, TX 77030*

E-mail: *mleja@mdanderson.org*

resolution (with no radiation exposure) and its ability to obtain a wide field of view and to perform multiplanar imaging. Cardiovascular magnetic resonance can identify, with high specificity, cardiac masses that do not require excision: pseudotumors, thrombi, lipomas, lipomatous hypertrophy, and papillary fibroelastomas. Most other cardiac tumors will require tissue diagnosis to aid in the establishment of a treatment plan.[9,10]

At MD Anderson Cancer Center, we recommend a multiple-technique approach to the imaging of cardiac tumors, consisting of cardiac CT, CMR, 3-D TTE, and positron emission tomography (PET). If the mediastinal mass is within the heart, we recommend 3-D TTE and baseline CMR for tissue characterization, with routine CMR follow-up every 2 to 3 months for staging and monitoring the tumor growth. A CT of the chest with contrast agent should also be completed every 3 months in order to monitor lung metastasis, because the lung is the most common area of spread. Should CMR and TTE fail to characterize the cardiac mass at the outset, a definitive biopsy is best obtained if it can be done safely. This will not only diagnose the tumor but exclude benign masses and other malignant tumors, such as lymphoma, that are best treated nonsurgically.

When possible, surgical excision in combination with systemic chemotherapy remains the best treatment for malignant cardiac tumors. The principal problem with surgical resection of primary cardiac tumors has been the tumor's extensive involvement of cardiac structures, which makes access difficult—the involvement of left-sided posterior structures especially impedes adequate resection. Benefit has been shown in the resection of left atrial sarcomas and pulmonary artery sarcomas,[11,12] but resection of right atrial sarcomas has not shown overall improvement in survival. However, increased survival rates were observed in patients when negative surgical margins were achieved in right-sided resections. In a retrospective review of 54 patients who had undergone extensive resection of the right atrium for sarcoma (with bovine pericardial reconstruction), Reardon and colleagues[13,14] reported a 30-day mortality rate of 9%, with a survival benefit for patients whose tumors were resected with negative surgical margins but not for patients with positive surgical margins (median survival, 27 vs 4 mo, respectively). The overall 5-year survival rate was 17%, and the median overall survival duration was 9 months. Complete resection remains a technical challenge. Metastatic disease remains the challenge in malignant disease, and a biologic approach will be necessary.

In conclusion, primary cardiac tumors are a rare entity; howver, if malignant, they are a lethal threat to an often youthful patient population. The use of multiple imaging techniques—CMR, 3-D TTE, PET, and cardiac CT—is the key to early diagnosis. We recommend referral to experienced centers for aggressive and early treatment with early surgical intervention and systemic chemotherapy.

References

1. Bisel HF, Wroblewski F, Ladue JS. Incidence and clinical manifestations of cardiac metastases. J Am Med Assoc 1953; 153(8):712-5.
2. Glancy DL, Morales JB Jr, Roberts WC. Angiosarcoma of the heart. Am J Cardiol 1968;21(3):413-9.
3. Esaki M, Kagawa K, Noda T, Nishigaki K, Gotoh K, Fujiwara H, et al. Primary cardiac leiomyosarcoma growing rapidly and causing right ventricular outflow obstruction. Intern Med 1998;37(4):370-5.
4. Carney JA, Gordon H, Carpenter PC, Shenoy BV, Go VL. The complex of myxomas, spotty pigmentation, and endocrine overactivity. Medicine (Baltimore) 1985;64(4):270-83.
5. Ginsberg JP, de Alava E, Ladanyi M, Wexler LH, Kovar H, Paulussen M, et al. EWS-FLI1 and EWS-ERG gene fusions are associated with similar clinical phenotypes in Ewing's sarcoma. J Clin Oncol 1999;17(6):1809-14.
6. Francis P, Namlos HM, Muller C, Eden P, Fernebro J, Berner JM, et al. Diagnostic and prognostic gene expression signatures in 177 soft tissue sarcomas: hypoxia-induced transcription profile signifies metastatic potential. BMC Genomics 2007;8:73.
7. Asch FM, Bieganski SP, Panza JA, Weissman NJ. Real-time 3-dimensional echocardiography evaluation of intracardiac masses. Echocardiography 2006;23(3):218-24.
8. Ahmed S, Nanda NC, Miller AP, Nekkanti R, Yousif AM, Pacifico AD, et al. Volume quantification of intracardiac mass lesions by transesophageal three-dimensional echocardiography. Ultrasound Med Biol 2002;28(11-12):1389-93.
9. Hoey ET, Mankad K, Puppala S, Gopalan D, Sivananthan MU. MRI and CT appearances of cardiac tumours in adults. Clin Radiol 2009;64(12):1214-30.
10. Gilkeson RC, Chiles C. MR evaluation of cardiac and pericardial malignancy. Magn Reson Imaging Clin N Am 2003;11 (1):173-86, viii.
11. Blackmon SH, Patel AR, Bruckner BA, Beyer EA, Rice DC, Vaporciyan AA, et al. Cardiac autotransplantation for malignant or complex primary left-heart tumors. Tex Heart Inst J 2008;35(3):296-300.
12. Blackmon SH, Rice DC, Correa AM, Mehran R, Putnam JB, Smythe WR, et al. Management of primary pulmonary artery sarcomas. Ann Thorac Surg 2009;87(3):977-84.
13. Reardon MJ. Malignant tumor overview. Methodist Debakey Cardiovasc J 2010;6(3):35-7.
14. Vaporciyan A, Reardon MJ. Right heart sarcomas. Methodist Debakey Cardiovasc J 2010;6(3):44-8.