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EDITORIAL COMMENT

Gaining Insights Into Lipomatous Hypertrophy of the Interatrial Septum

A Step Forward*

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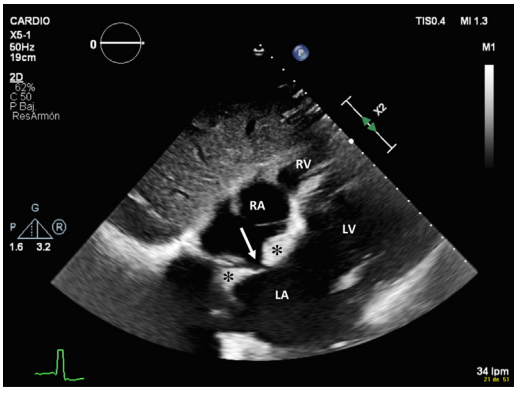
Cardiac tumors have remained a conundrum over the centuries, partly because of their low incidence and partly because of their heterogeneous clinical presentation and overall poor prognosis. The first historical description of a clinical picture compatible with a cardiac tumor (probably a melanoma metastasis) has been attributed to a woman who was important in English and European history, Catherine of Aragon. The 16th-century chronicle reported that "the embalmer sliced the heart in half and washed it through several times, but it remained stubbornly dark. Another strange black body was attached to it." It is not surprising that cardiac tumors present significant challenges at all stages of their disease course, from clinical suspicion supported by imaging techniques, to confirmation with biopsy or surgery, and, finally, to management (1).

Cardiac tumors can be classified as primary or metastatic, with metastatic tumors almost 20 times more common in clinical practice than primary tumors. Of these cardiac tumors, 80% of primary tumors are benign, and 20% are malignant, with an incidence of <0.03% at necropsy (2). Metastatic tumors result from local tumor invasion or metastases from another malignant disease. A third type of lesion, including a vegetation or thrombus, mimics a tumor.

In general, the specific signs and symptoms of cardiac tumors are determined by the location of the tumor in the heart. Heart failure, syncope, systemic embolization, intracardiac obstruction, arrhythmias, pericardial effusion with or without tamponade, and constitutional symptoms are some of the classical presentations of this condition (3). Such clinical features are shared with other possible diagnoses. A high index of clinical suspicion remains critical for early recognition and appropriate diagnostic workup. Early diagnosis and differentiation from other clinical conditions are critical to facilitate initiation of appropriate therapy. A correct diagnosis may be challenging given the variability in presentation, but

FIGURE 1 Lipomatous Hypertrophy of the Interatrial Septum on Transthoracic Echocardiography



Images of lipomatous hypertrophy of the interatrial septum **(asterisks),** with characteristic sparing of the fossa ovalis **(arrow).** Subcostal 4-chamber view. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

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FIGURE 2 **Imaging Characteristics and Differential Diagnosis of Cardiac Masses on the Basis of Echocardiography, CT, and CMR**

	Echocardiography	Computed Tomography	Magnetic Resonance Imaging
Benign masses	**Myxoma**		
	Heterogeneous mobile mass pedunculated in the region of the fossa ovalis. Partially enhanced with contrast.	Pedunculated, mobile, heterogeneous, low attenuation, 10% calcified.	Hypointense, mobile. Heterogeneous after contrast enhancement.
	LHIS		
	Fatty infiltration of the atrial septum, preserving the fossa ovalis.	"Dumbbell-shaped" mass involving the interatrial septum with sparing of the fossa ovalis, homogenous appearance with sharp margins, fatty attenuation (density<-50 HU), and no or minimal contrast enhancement.	Nonencapsulated, immobile, hyperintense mass, without stalk. No uptake after contrast enhancement.
	Fibroma		
	Demarcated, noncontractile and solid, highly echogenic mass. No enhancement with contrast.	Homogenous, low attenuation, minimal enhancement, central calcification.	Hypo/isointense, solitary, noncontractile mass that often narrows the ventricular cavity. Hyperenhancement after contrast Enhancement.
	Lipoma		
	Homogeneous, broad-based, immobile, without a pedicle and encapsulated; most often small in size. No enhancement with contrast.	Smooth, encapsulated, fat attenuation, no enhancement.	Arise from the epicardium or endocardium; when originates from the endocardium, it manifests decreased mobility and a broad base of attachment. No uptake after contrast enhancement.
	Rhabdomyoma		
	Small, well-circumscribed (multiple) nodules or a pedunculated mass. No enhancement with contrast.	Smooth, multiple, attenuation similar to myocardium.	Multiple well circumscribed and vary from a few mm to a few cm in size. No/minimal uptake after contrast enhancement.
	Angiosarcoma		
	Lobulated masses, distinctly heterogeneous with an area of necrosis or hemorrhage. Hyperenhancement with contrast.	Broad base, irregular, heterogeneous, low attenuation, infiltrative, pericardial effusion,	Isointense. Heterogeneous uptake after contrast enhancement.
Malignant masses	**Rhabdomyosarcoma**		
	Arise from any cardiac structure, initially invade the pericardium. Hyperenhancement with contrast.	Irregular, low attenuation, infiltrative.	Isointense that involves multiple sites within the heart, including the valves. Homogeneous uptake after contrast enhancement.
	Sarcoma		
	Broad-based mass, with heterogeneous echogenicity. Hyperenhancement with contrast.	Large, fat and soft tissue attenuation, mild contrast enhancement, infiltrative.	Isointense mass. Heterogeneous after contrast enhancement.
	Lymphoma		
	Homogeneous, infiltrating masses leading to wall thickening or as nodular masses. Hyperenhancement with contrast.	Typically demonstrates thickening and nodularity. Often demonstrate enhancement.	Isointense, pericardial effusion. No/ minimal uptake after contrast enhancement.
	Metastatic mass		
	The pericardium is more frequently involved with metastases. Pericardial effusion. Hyperenhancement with contrast.	Pericardial metastasis can appear as pericardial thickening, disruption, or effusion. Often demonstrate enhancement.	Typical involvement is the pericardium. Heterogeneous after contrast enhancement.
Pseudotumor	**Thrombus**		
	Variable size. May be homogeneously echogenic or may have heterogeneous texture with lucent areas. No enhancement with contrast.	Hypodense, low attenuation filling defect in a contrast pool within a cardiac chamber. Chronic thrombi may develop spotty calcifications.	Isointense/ hypointense mass (if recent thrombus). Typically localized near a wall motion abnormality (after infarction) or in the left atrial appendage. No uptake after contrast enhancement.
	Pericardial cyst		
	Echolucent mass adjoining the cardiac border. Frequently septated. No enhancement with contrast.	Thin-walled structures sharply demarcated, homogenous appearance, attenuation similar to water (-10 to 20 HU). Non-enhancing lesions with contrast.	Encapsulated fluid-filled structure typically located in the right pericardiophrenic angle.

our knowledge of the disease has advanced relatively quickly, mostly because of the adoption of different imaging techniques (**Figure 1**). Cardiac tumors and tumor-like lesions are mainly diagnosed by echocardiography (transthoracic and transoesophageal), computed tomography (CT), and cardiac magnetic resonance (CMR). CMR generally is preferred over CT (4). In addition to providing detailed anatomic images and no radiation, T_1- and T_2-weighted CMR sequences reflect the chemical microenvironment within a tumor and offer clues to the possible type of tumor that is present (**Figure 2**). Endomyocardial biopsy is sometimes enough to make a diagnosis in right-sided mases. Surgical biopsy, which is performed only if necessary, leads to a definitive diagnosis in most cases. In patients with a pericardial effusion, pericardial fluid analysis can be helpful to establish the diagnosis and guide symptomatic treatment in some cases (e.g., metastatic melanoma, lymphoma).

Treatment depends on the type of tumor. Although surgery is indicated in patients with symptomatic benign tumors, in the case of unresectable malignant disease (e.g., cardiac lymphoma), systemic chemotherapy and radiotherapy are often combined. The prognosis varies according to the underlying condition and clinical picture (5).

The goals of the initial evaluation are to determine the following: whether a cardiac tumor is present; the location of the lesion within the heart; whether the tumor is benign or malignant, and whether there are any relevant clinical signs or symptoms. This information is critical in planning further evaluation and management.

In the current setting of the coronavirus disease-2019 pandemic and the risk of virus transmission, reliance on echocardiography, CMR, and endomyocardial biopsy may present a barrier to early diagnosis and treatment, depending on availability, awareness, clinical evolution, and progression of the pandemic in the patient's geographic location. Some clinicians may be less likely to propose certain diagnostic techniques and therapies for minimally symptomatic patients or for patients with many comorbidities.

In this issue of *JACC: Case Reports,* Yavar et al. (6) illustrate the challenges that this diagnosis presents. Their patient, a 55-year-old woman, presented with complete heart block during a routine evaluation before surgery. An extensive evaluation suggested a primary cardiac tumor involving the interatrial septum with a complex pericardial effusion and apparent pericardial masses. Open thoracic surgery revealed lipomatous hypertrophy masquerading as an invasive tumor.

Some investigators have stated that the term *lipomatous hypertrophy of the interatrial septum (LHIS)* is inappropriate, for many reasons. The lesion is not a lipoma or hypertrophy because the fat infiltrates the cardiac tissue and is not encapsulated.

LHIS can defined as a circumscribed, fatty mass characterized by fatty deposits that infiltrates the interatrial septum with a thickness of >2 cm. It should be considered in the differential diagnosis of any atrial cardiac tumor. LHIS was first described in 1964 by Prior (7), who reported a nonencapsulated LHIS in a post-mortem examination. In 1982, the first case of LHIS in a patient whose diagnosis was established by cardiac tomography was reported (8).

The differential diagnosis of LHIS begins with imaging techniques, thus limiting the need for histological examination in most cases. Myxomas are the most common primary cardiac tumors, representing almost 50% of all cases. Myxomas are also located in the atria, arising from the interatrial septum in close proximity to the foramen ovale. Conversely, in LHIS the foramen ovale is preserved. Unlike rhabdomyomas and fibromas, which are common in infants and children, LHIS is also common in obese or older people, with higher incidences in women and in patients with metabolic disorders such as cerebrotendinous xanthomatosis or mediastinoabdominal lipomatosis. LHIS has also been described in patients receiving long-term parenteral nutrition (9).

Clinically, LHIS has been associated with atrial arrhythmias. The infiltrated septum may play a central role as an both ectopic source and a zone of re-entry, with autonomic tone being a key regulator. Disturbances in conduction related to fat infiltration, inflammation, tissue fibrosis, and/or connexin abnormalities (interfering with the architecture of atrial myocytes) would predispose patients to atrial arrhythmias (10). Finally, LHIS can lead to a mutation to a malignant tumor, which was the cause of death in a study series (11).

The case described by Yavar et al. (6) is challenging, for several reasons. First, there is a lack of evidence-based recommendations for diagnosis of this condition. Second, the use of advanced techniques such as positron emission tomography is able to point to a diagnosis of metastatic tumors, atrial myxoma, or LHIS but cannot differentiate among them. Third, open surgery may be necessary as the final diagnostic and therapeutic maneuver, as in this case. Fourth, in patients with cardiac arrhythmias, atrial arrhythmias, and atrioventricular block, as in this case, the use of cardiac imaging is useful to explore the presence of LHIS. Fifth, operative

intervention should be limited to patients with severe symptoms (9).

In conclusion, this case illustrates how diverse diagnostic modalities (echocardiography, CT, CMR, positron emission tomography) and surgical techniques are essential for guiding diagnosis and how they can be used in combination for successful definitive treatment.

AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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REFERENCES

1. Tremlett G. Catherine of Aragon. London, United Kingdom: Faber & Faber, 2010.

2. Reynen K. Frequency of primary tumors of the heart. Am J Cardiol 1996;77:107.

3. Molina J, Edwards J, Ward H. Primary cardiac tumors: experience at the University of Minnesota. Thorac Cardiovasc Surg 1990;38 Suppl 2:183–91.

4. Kassi M, Polsani V, Schutt RC, et al. Differentiating benign from malignant cardiac tumors with cardiac magnetic resonance imaging. J Thorac Cardiovasc Surg 2019;157:1912–22.e2.

5. Heyer CM, Kagel T, Lemburg SP, Bauer TT, Nicolas V. Lipomatous hypertrophy of the interatrial septum. Chest 2003;124:2068–73.

6. Yavar Z, Gilge JL, Patel PJ, et al. Lipomatous hypertrophy of the interatrial septum manifesting as third degree atrioventricular block. J Am Coll Cardiol Case Rep 2020;2:2235–9.

7. Prior JT. Lipomatous hypertrophy of cardiac interatrial septum. A lesion resembling hibernoma, lipoblastomatosis and infiltring lipoma. Arch Pathol 1964;78:11–5.

8. Isner JM, Swan CS, Mikus JP, Carter BL. Lipomatous hypertrophy of the interatrial septum: in vivo diagnosis. Circulation 1982;66:470–3.

9. Xanthos T, Giannakopoulos N, Papadimitriou L. Lipomatous hypertrophy of the interatrial septum: a pathological and clinical approach. Int J Cardiol 2007;121:4–8.

10. Nattel S, Heijman J, Zhou L, Dobrev D. Molecular basis of atrial fibrillation pathophysiology and therapy: a translational perspective. Circ Res 2020;19(127):51–72.

11. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 20-1997. A 74-year-old man with progressive cough, dyspnea, and pleural thickening. N Engl J Med 1997;336:1895–903.

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