

Cardiac Lymphoma Presenting as Subacute Progressive Dyspnea: A Case Report and Review of the Literature on the Pathophysiology and Imaging of Intracardiac Tumors



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INTRODUCTION

Here we describe the case of a 64-year-old man presenting with a 1-month history of progressive dyspnea on exertion. Notable physical exam findings included elevated jugular venous pressure, bradycardia, and softened heart sounds. A preliminary echocardiogram revealed a large intracardiac mass and a moderate pericardial effusion, in the absence of pericardial tamponade physiology. Transesophageal echocardiogram (TEE) showed invasion by the mass of the right chambers and documented infiltration of the atrial septum. Flow cytometry examination of the pericardial fluid revealed B-cell lymphoma. Further evaluation confirmed primary cardiac lymphoma. While cardiac involvement is relatively common in the setting of lymphoma, primary cardiac lymphomas are exceedingly rare, accounting for only 1% of primary cardiac tumors.

CASE PRESENTATION

A 64-year-old white man with past medical history notable only for heavy smoking presented to an outpatient pulmonary clinic complaining of progressive dyspnea over 1 month. He was initially diagnosed with chronic obstructive pulmonary disease and started on daily tiotropium and albuterol, as needed. His symptoms continued to worsen, despite compliance with his prescribed regimen, and he soon developed weight gain and bilateral lower extremity edema. A preliminary transthoracic echocardiogram (TTE) revealed a large cardiac mass, which prompted referral to our institution. Prior to his scheduled appointment at our hospital, the patient's shortness of breath aggravated to the extent that he was compelled to present urgently to the emergency department of our institution. Review of systems was positive for occasional palpitations, orthopnea, and drenching night sweats for the past three nights. Initial vital signs were regular heart rate of 48 beats per minute (bpm), respiratory rate of 16, oxygen saturation of 96% on room air, blood pressure of

122/89 mm Hg, and temperature of 97.2°F. Physical exam was notable for an obese man in mild distress, evident jugular venous pulsations to the mandible, softened heart sounds, and decreased breath sounds in the lower lung fields. Laboratory workup revealed hyponatremia (128 mmol/L), hypochloremia (91 mmol/L), and elevated hemoglobin and hematocrit (17.2 gm/dL and 53%, respectively). A chest x-ray revealed an enlarged cardiac silhouette (Figure 1). An electrocardiogram documented complete heart block and a junctional escape rhythm at 56 bpm. A bedside TTE disclosed a large intracardiac mass (6.7 × 4.15 cm), which extended from the right atrium (RA) into the right ventricle (RV), causing severe tricuspid valve obstruction, a moderate pericardial effusion, and a preserved ejection fraction (Figure 2, Videos 1-4). After admission to the cardiac care unit, the patient underwent a TEE, which confirmed the invasion by the mass of the RA and RV chambers and documented infiltration of the atrial septum, with visualization of a smaller mass (3 × 3 cm) in the left atrium (LA). The obstruction of the tricuspid valve orifice, virtually complete, resulted in elevated transvalvular diastolic gradient (11 mm Hg) and contributed, along with the moderate pericardial effusion, to impaired RV filling (Figure 3, Videos 5-7). Echo-Doppler showed exaggerated respiratory variation in early diastolic inflow velocities through the mitral and tricuspid valves in absence of overt pericardial tamponade physiology. Cardiac magnetic resonance imaging (CMRI) ruled out the concurrent presence of additional lesions and confirmed extensive invasion by the cardiac mass of the RA and the RV, with virtual obliteration of

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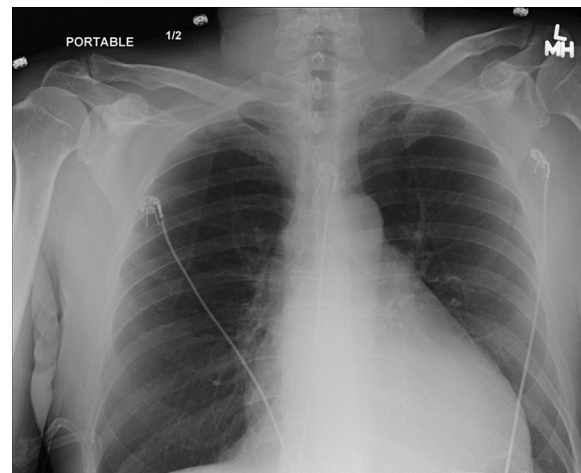


Figure 1 Chest x-ray showing cardiomegaly, in absence of any other major abnormalities.

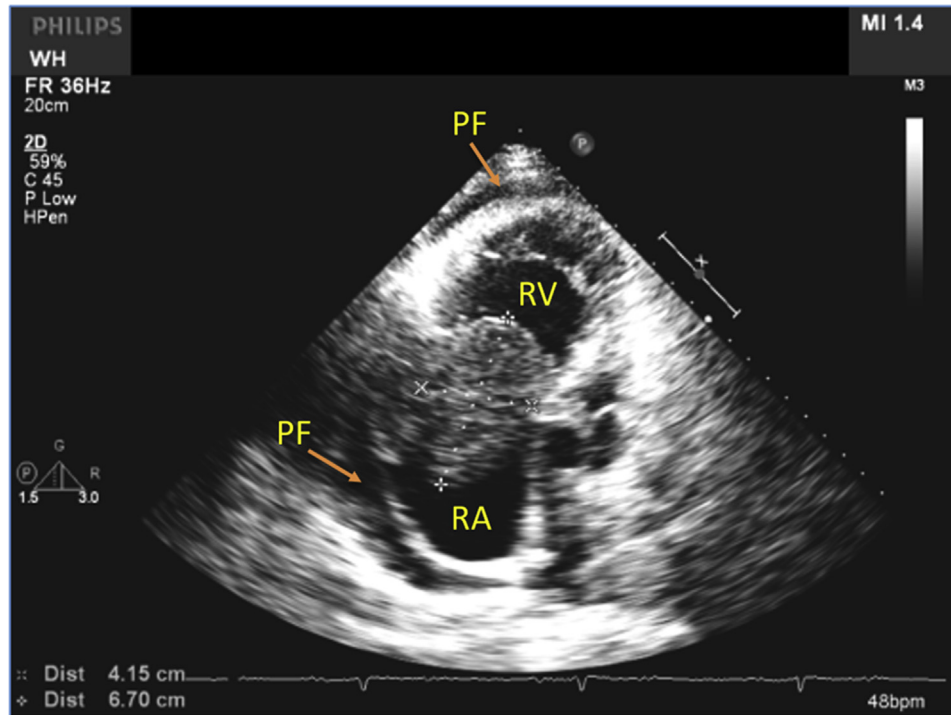


Figure 2 Two-dimensional TTE parasternal view showing the RV and the RA. The tricuspid valve is occupied by a large mass measuring 4.15 × 6.7 cm. Pericardial fluid (PF) surrounding the RV and RA is indicated by orange arrows.

the RV inflow tract (Figure 4, Videos 5-7). Delayed contrast enhancement exposed areas of focal enhancement within the mass, consistent with necrosis. The patient was subsequently evaluated for surgical resection of the cardiac mass and deemed inoperable. Ten days after admission, due to the progressive enlargement of the pericardial effusion causing impending cardiac tamponade, he underwent pericardial window and drain placement with drainage of a total amount of 600 mL of fluid. On gross inspection, a white infiltrate was noted on the heart. The pericardial fluid was sent for flow cytometry evaluation, which disclosed findings consistent with B-cell lymphoma. Bone marrow biopsy was negative for lymphoma cells, which confirmed the diagnosis of primary cardiac involvement. After consulting with hematology services, he received 3 days of chemotherapy with a rituximab, cyclophosphamide, vincristine, and doxorubicin regimen. Prior to discharge, which occurred 1 week after, he elected to follow up with his local cardiologist at an outside facility, due to the distant geographical location of his domicile from our institution.

DISCUSSION

Cardiac tumors may be primary (benign or malignant) or metastatic (malignant). Based on the World Health Organization histologic classification of tumors of the heart,¹ the estimated frequency of cardiac tumors is exceedingly rare, ranging from 0.0017% to 0.33%. Review of 22 autopsy-based series of primary cardiac tumors disclosed a frequency of 0.021% in a population of 731,309 patients.² In a 20-year (1972–1991) review of 12,485 autopsy cases, there was a 0.056% incidence of primary tumors and a 1.23% incidence of secondary tumors.³ Although the above data may express some degree of referral bias and therefore reflect inaccurately population-based incidence rates, it is common consensus to consider primary

benign tumors three- to four-fold more frequent than their malignant counterparts and metastatic tumors 30 to 40 times more common than primary tumors. While preponderantly epicardial, secondary cardiac tumors can also be myocardial or endocardial.⁴ Lung and breast carcinoma, soft-tissue sarcoma, and renal cancer are common sources of metastases to the heart. For unclear reasons, melanoma is also a tumor with a high proclivity to metastasize to the heart. Leukemia and lymphoma, in turn, often engender cardiac metastases, which, not uncommonly, remain clinically silent.^{3,4}

Atrial myxoma is the most common cardiac tumor, accounting for approximately 30% of all primary cardiac tumors (see Table 1). Myxomas manifest in 90% of the cases as a solitary LA mass, affecting more commonly women between the ages of 50 and 70 years.⁵ A list of other less common primary benign tumors is provided in Table 1. Indeed, the majority of malignant primary cardiac tumors are sarcomas, mostly angiosarcomas or less frequently rhabdomyosarcomas.⁶ They are common between the third and fifth decades of life and, once again, develop most often in the RA. While up to 20% of patients with lymphoma may have metastatic involvement of the heart, primary cardiac lymphomas (which, by definition, must involve exclusively the heart and/or the pericardium) are extremely rare, accounting for 1% of all primary cardiac masses.³ However, their incidence in the last 30 years is slightly increased, since they have been diagnosed as one manifestation of the acquired immunodeficiency syndrome, as well as in transplant recipients receiving immunosuppressive drugs.^{7,8}

Imaging plays a chief role in the diagnosis and management of cardiac masses. Echocardiography provides images of both the myocardium and cardiac chambers as well as crucial information regarding size and mobility of the cardiac mass, degree of obstruction to the circulation, and likelihood of systemic embolization.⁹ Although TTE can be rather informative per se in the identification of a tumor, TEE is usually

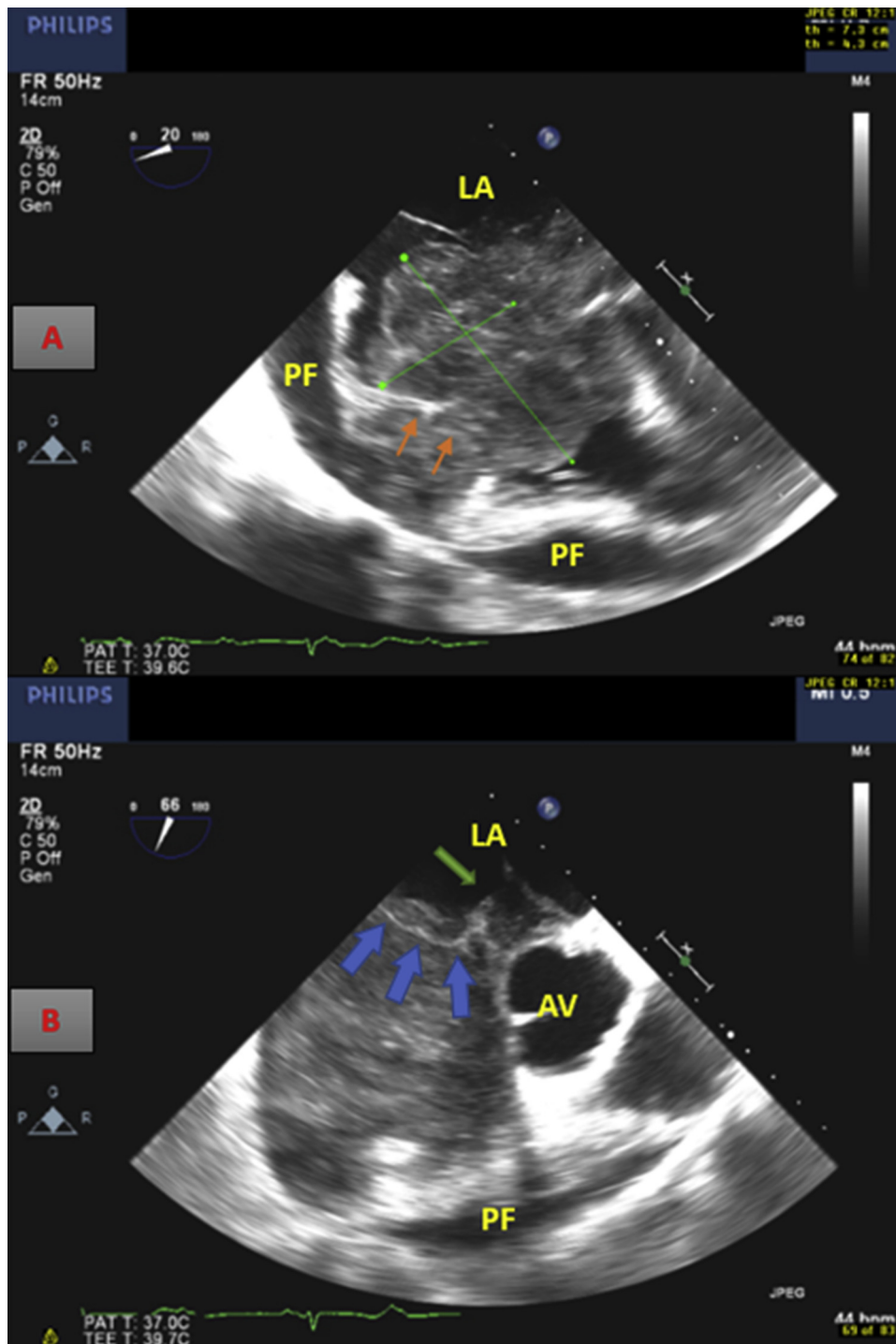


Figure 3 Two-dimensional TEE views confirming in *panel A* the invasion by the mass of the RA with infiltration of the RA wall (*orange arrows*) and documenting in *panel B* the infiltration of the atrial septum (*blue arrows*), with visualization of a smaller mass (3×3 cm; *green arrow*) in the LA. AV, Aortic valve; PF, pericardial fluid.

combined because of a higher diagnostic utility, mainly due to the proximity of the esophagus to the heart, the lack of intervening anatomic structures (such as ribs, muscles, and lungs), and the ability to use high-frequency imaging transducers affording superior spatial resolution.⁹ The combination of echocardiography plus CMRI or computed tomography may be useful in the differential diagnosis of thrombi versus tumors in the case of lesions arising from a heart valve.¹⁰

Primary cardiac tumors may originate from any cardiac tissue. Frequently, they develop in the myocardium or endocardium, but they may also derive from valve tissue, cardiac tissue, or pericardial connective tissue. Cardiac tumors have five common manifestations, including heart failure, embolization, conduction abnormalities, pericardial disease, and systemic symptoms (such as weight loss, fever, and night sweats). Less commonly, they can be clinically silent and only

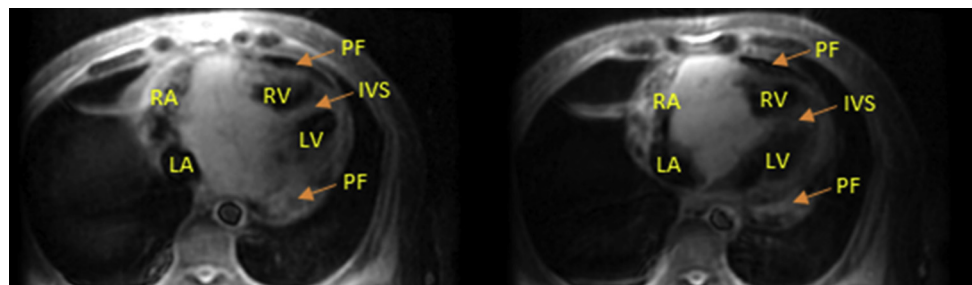


Figure 4 The cardiac mass (11.7 × 6.2 × 5.1 cm), as documented by CMRI, invades the RA, the LA, and the RV with virtual obliteration of the RV outflow tract. Pericardial fluid (PF) is also seen. IVS, interventricular septum.

Table 1 Most common cardiac tumors, primary and metastatic

Benign primary tumors (75% of all primary)	Malignant primary tumors (25% of all primary)	Metastatic tumors (30- to 40-fold more common than primary)
Myxomas (30)	Sarcomas (16)	Lung carcinoma
Papillary fibroelastomas (10)	Angiosarcoma (8)	Breast carcinoma
Lipomas (10)	Rhabdomyosarcoma (5)	Soft-tissue sarcoma
Rhabdomyomas (6)	Fibrosarcoma (3)	Renal carcinoma
Fibromas (3)		Melanoma
Angioma/hemangiomas (3)	Pericardial mesothelioma (3)	
Teratomas (1)	Leiomyosarcoma (1)	
Paragangliomas (<1)	Primary lymphomas (1)	
Pericardial cysts (<1)		

Benign tumors outnumber malignant ones by a ratio of approximately 3 to 1. Roughly 75% of primary tumors are benign in origin, with myxomas being by far the most frequent tumors, accounting for 30% of all primary cases. The remaining 25% of primary tumors are malignant. Among these, sarcomas (angiosarcomas, rhabdomyosarcomas, and fibrosarcoma) are the most frequent malignant tumors, accounting for one-fourth of all primary tumors and over 50% of malignant ones. Secondary tumors are considerably more frequent than primary cardiac tumors, and approximately 15% of patients with any form of cancer develop cardiac metastases. Carcinoma of the breast, lung, esophagus, and pancreas, malignant melanoma, and malignant lymphoma are mentioned most frequently in the literature as the primary tumors. For unclear reasons, melanomas metastasize to the heart in more than 50% of the cases (modified from reference 15).

diagnosed incidentally. The clinical presentation of cardiac tumors is dictated by their size, location, and modality of progression (infiltration vs volume expansion) rather than their histopathological type.¹¹ From a pathophysiological standpoint, the neoplastic mass can disrupt valvular function or obstruct the ostium of a coronary artery, leading to decreased coronary flow and potentially causing angina, myocardial infarction, syncope, arrhythmias, heart failure, or even sudden cardiac death. Ventricular invasion can cause impaired contractility or conduction abnormalities and can lead to heart block (as observed in this case) or tachyarrhythmias.¹² Embolization can occur with any cardiac mass but is most commonly associated with myxomas, which are friable and therefore more prone to undergo spontaneous fragmentation. While left-sided embolization manifests with acute or recurrent cerebrovascular attacks, embolization to the lungs can cause acute pulmonary embolism or chronic embolic disease, finally resulting in pulmonary hypertension, secondary to occlusion of the pulmonary vasculature.¹³ Pericardial involvement is more commonly observed with metastatic tumors and can manifest as pericarditis, pericardial effusion and cardiac tamponade, and constrictive pericarditis.

Treatment of benign primary tumors is surgical excision, which is associated with a survival rate of 95% at 3 years.¹⁴ In the case of fibroelastoma originating from valvular tissue, repair/replacement of the affected valve may also be necessary. Serial echocardiographic

assessment is conventionally performed to monitor for recurrence. Rhabdomyomas can represent exceptions to the surgical approach, as they often regress spontaneously, without requiring treatment. Due to the poor prognosis, treatment of malignant primary tumors is typically palliative, including radiation therapy, chemotherapy, and management of associated complications. Finally, the treatment of metastatic cardiac tumors (usually chemotherapy or palliation) is contingent upon the nature of the primary tumor.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.case.2016.11.004>.

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