Incidental Left Atrial Mass on Transesophageal Echocardiogram During Evaluation of Severe Mitral Regurgitation

Carly Fabrizio, DO, Ahmed Abuzaid, MD, Pragya Ranjan, MD, Stephen Meng, MD, Audrey Sernyak, MD, and Erik Marshall, MD, *Newark, Delaware*

INTRODUCTION

An asymptomatic middle-age female was found to have a new prominent systolic murmur on routine physical exam. Transthoracic echocardiogram (TTE) revealed normal left ventricular systolic function and a thickened mitral valve (MV) with severe mitral regurgitation (MR). An echocardiogram performed following an episode of vasovagal syncope 8 years previously had shown a normal MV. Subsequent transesophageal echocardiogram (TEE) confirmed a thickened MV with severe regurgitation as well as a 1.2 × 1.2 cm mass attached to the left atrial (LA) free wall just above the orifice of the appendage. This case explores the etiology of the mass and its relationship to the abnormal MV.

CASE PRESENTATION

A 51-year-old woman with a history of systemic hypertension was found to have a new systolic murmur on an annual routine physical exam by her primary care physician. She was asymptomatic and was exercising regularly to high levels without difficulties. Vital signs revealed a temperature of 36.6°C, regular pulse at 96 beats per minute, blood pressure of 146/95 mm Hg, and normal pulse oximetry. Physical examination was significant for an apical grade 2/6 holo-systolic murmur. She was referred for a TTE, which revealed borderline LA enlargement, a thickened mitral valve (MV) with severe MR, and preserved left ventricular systolic function with an ejection fraction (EF) of 65%. No other valve abnormality was noted (Figure 1). A prior echocardiogram had been performed 8 years previously due to an episode of vagal syncope. This study revealed a normal MV without significant regurgitation. Given the severity of her MR with an unspecified mechanism, she underwent a TEE. The TEE showed thickened MV leaflets without evidence of prolapse and confirmed the severe MR with normal EF. It also demonstrated a 1.2 × 1.2 cm echodensity with a broad base attached to the LA wall just above the atrial appendage with mobile components. This mass was not seen on her TTE (Figure 2, Videos 1, 2, and 3). Subsequent workup including blood cultures, inflammatory markers, and rheumatologic markers were all normal. Whether the mass and the MV abnormalities were related was unclear at this point. Given there was no evidence of infection or reason for thrombus, the mass was thought to likely be a tumor. However, the location was not typical for a myxoma or fibroelastoma, the two most common benign cardiac masses.

A cardiac magnetic resonance (CMR) was performed to further classify the characteristics of the mass. CMR showed a 1.3 × 1.2 cm LA mass with polypoid frond-like appearance along the left superolateral wall adjacent to the atrial appendage with intermediate T1 weighted sequence signal and mildly hyperintense T2 signal with avid gadolinium enhancement (Figure 3). A computed tomography (CT) of the chest, abdomen, and pelvis revealed two 4 mm pulmonary nodules at the right lower and left lower lung lobes with no focal regions of consolidation in the lungs. One consideration in trying to link the valve abnormality to the mass was the possibility of a bronchial carcinoid tumor. These neuroendocrine tumors have surface somatostatin receptors and can be imaged using Gallium-Dotatate positron emission tomography (PET)/CT scan. Although the patient did not have symptoms to suggest systemic carcinoid syndrome, a Dotatate PET/CT was performed and 5 hydroxyindoleacetic acid (HIAA) levels and chromogranin were obtained. The scan revealed tracer localization corresponding to the known LA mass without any other structures including the cardiac valves, intestines lungs, or mediastinum including a previously found pulmonary nodule (Figure 4). The 5 HIAA and chromogranin levels were normal.

Two weeks prior to the planned surgery for removal, the patient developed progressive dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. She was admitted for decompensated left-sided heart failure. After medical stabilization, preoperative chest CT showed increased LA mass size (2.3 × 2 cm) with no pericardial effusion or extracardiac extension. Given the clinical picture and progression of mass size, surgery was planned on the following day. An intraoperative TEE confirmed the increase in mass size (2.2 × 5.1 cm) with prolapse into the left ventricle in diastole resulting in obstruction of the MV inflow (Figure 5, Video 4). Intraoperative assessment of the mass showed it was attached to the left atrium between the orifice of the LA appendage and the left upper pulmonary vein. Frozen section was highly suspicious for sarcoma. The mass was debulked. Adjacent LA wall was excised, and autologous pericardium was fashioned to close the defect. The MV anterior and posterior leaflets were excised, and a bioprosthetic valve (Edwards, pericardial valve) was placed in the mitral position.

Histopathology revealed a diagnosis of an undifferentiated high-grade pleomorphic sarcoma. The tumor had a solid and papillary proliferation of malignant epithelioid cells showing moderate cytologic atypia and mitotic activity with negative immunohistochemistry for vascular derivation (CD31, CD34; rules out angiosarcoma) and negative keratin staining (rules out carcinoma) and other specific stains (rules out any lineage specific differentiation). Cytogenic testing did not demonstrate MDM2 amplification. The MV pathology revealed myxomatous degeneration with no evidence of malignancy, and the

From the Heart and Vascular Institute, Christiana Care Health System, Newark, Delaware.

Keywords: Severe mitral regurgitation, Left atrial mass, Cardiac sarcoma

Conflicts of interest: The authors reported no actual or potential conflicts of interest relative to this document.

2468-6441

https://doi.org/10.1016/j.case.2018.10.002

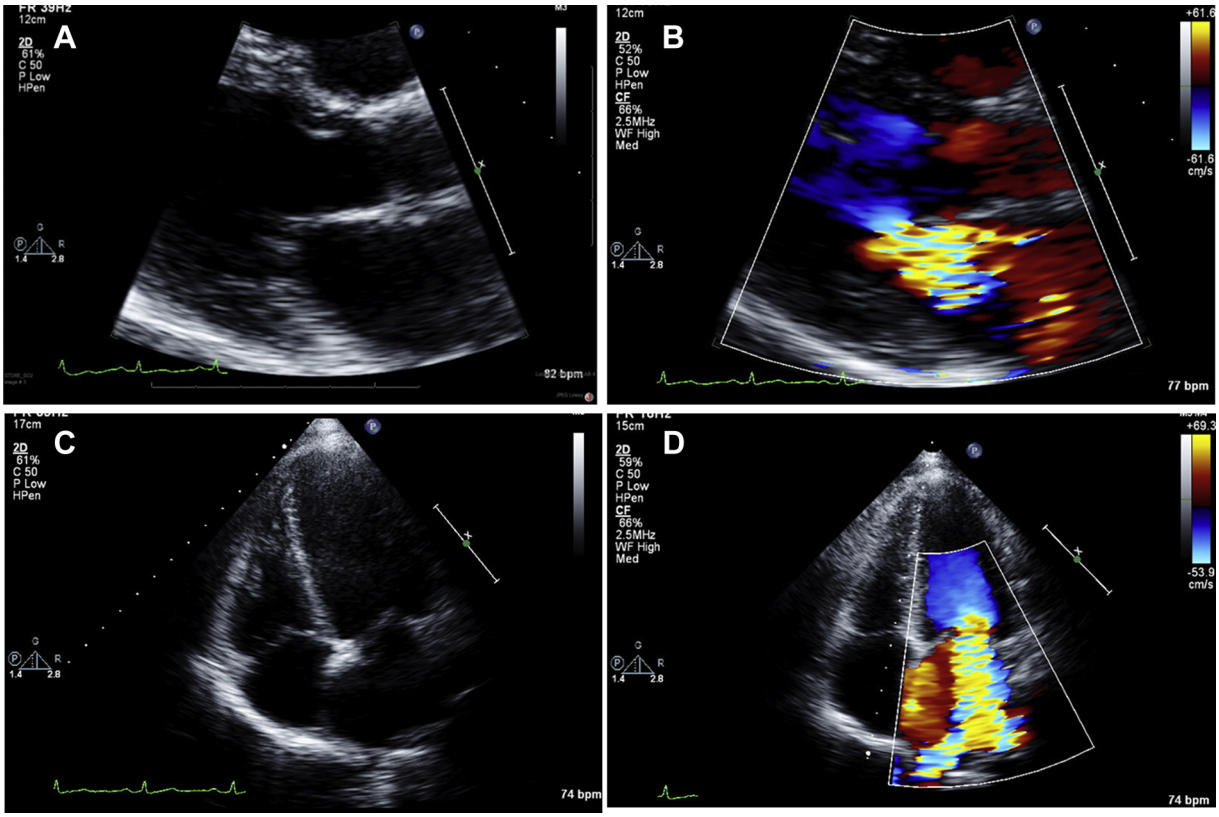

Figure 1 **(A-D)** Transthoracic echocardiogram (TTE), parasternal long-axis view without **(A)** and with color Doppler **(B)**, showing severe mitral regurgitation. TTE apical four-chamber view **(C-D)** again showing severe mitral regurgitation.

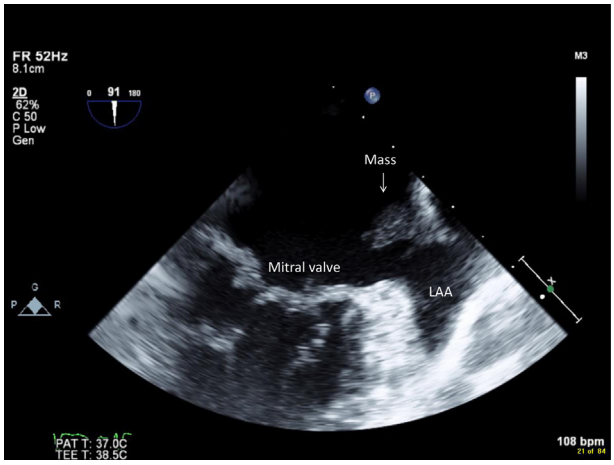

Figure 2 Transesophageal echocardiogram midesophageal window, commissural view showing a 1.2 × 1.2 cm echodensity attached to the left atrial wall just above the left atrial appendage (LAA) but not within the appendage. Also notice the thickened mitral valve leaflets.

LA wall was negative for malignancy. Her postoperative course was uneventful, and she was subsequently started on systemic chemotherapy by the oncology team.

DISCUSSION

Heart murmurs are commonly encountered on physical examination in the outpatient setting. Two-dimensional echocardiography is a reasonable initial evaluation for an asymptomatic patient who has an otherwise unexplained murmur on a routine examination.[1] When MR is encountered on echocardiogram, it is essential to decipher whether the mechanism of regurgitation is due to an intrinsic abnormality of the valve apparatus (primary MR) or whether there is a secondary cause resulting in a normal MV functioning abnormally, such as severe left ventricular dysfunction leading to papillary muscle displacement, leaflet tethering, and inadequate coaptation (secondary MR).[2] In this case the etiology of the MR was clearly primary. This is in stark contrast to an echo 8 years previously, which revealed a normal MV. Mitral leaflet thickening without prolapse or stenosis can be seen in patients with rheumatic valve disease, radiation heart disease, and carcinoid and those taking certain drugs such as Fen-phen. The patient had never taken these drugs, had never had rheumatic fever or radiation, and had no symptoms to suggest the carcinoid syndrome.

If the etiology or severity of MR is in question, follow-up imaging with TEE can help identify structural abnormalities of the valve apparatus. In the case under discussion, there was concern for a primary MV pathology that was not clearly defined on TTE. Therefore, a TEE was performed and a subsequent LA mass was observed. Cardiac masses can be thrombus, most frequently located in the atria, in particular the appendage, myxomas (most common primary cardiac tumor), other benign cardiac tumors (lipoma, rhabdomyoma, papillary fibroelastoma, cardiac hemangioma), or secondary cardiac tumors (i.e., metastasis).

Primary cardiac tumors are an extremely rare occurrence; approximate incidence ranges from 0.001% to 0.003% on autopsy series. Secondary cardiac tumors from metastasis are 30–50 times more common.[3,4] Most cardiac tumors are benign, with about 10% being malignant.[5] Malignant cardiac tumors can be characterized as

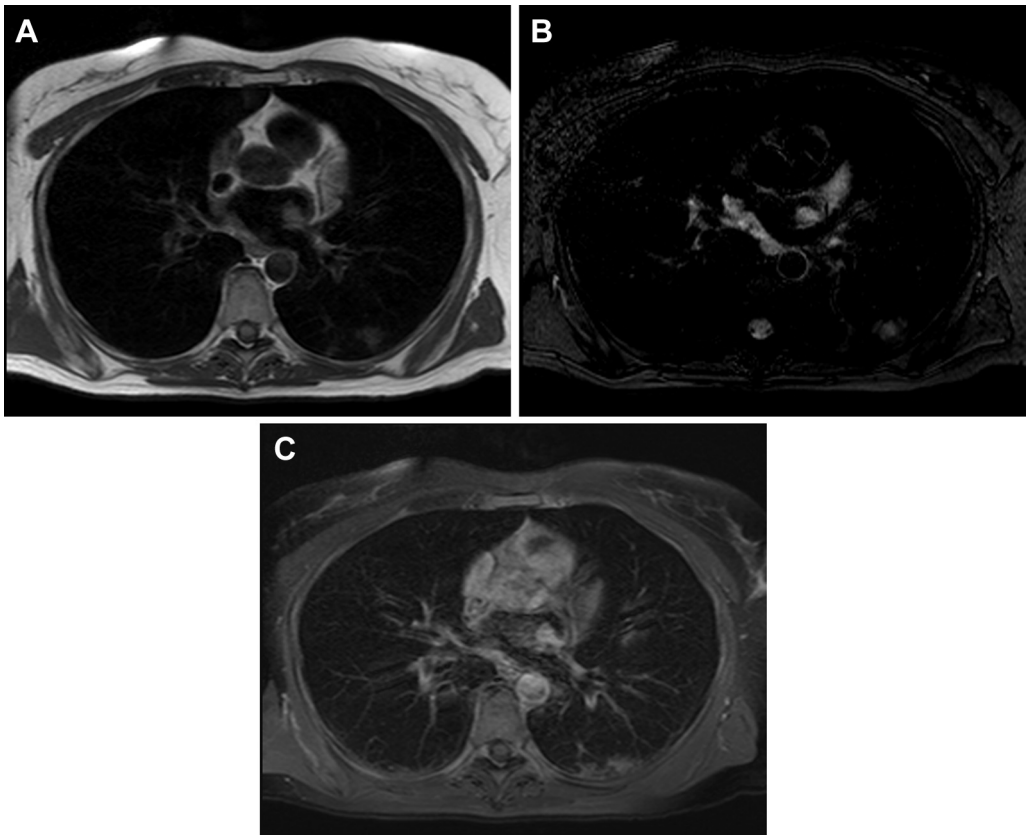

Figure 3 **(A-C)** Cardiac magnetic resonance images demonstrate left atrial mass along the left superolateral wall, adjacent to the atrial appendage base, measuring 1.3 × 1.2 cm, of intermediate T1 signal intensity **(A)**, mildly hyperintense T2 signal intensity **(B)**, and with avid enhancement on postcontrast fat-suppressed T1-weighted images obtained after the intravenous administration of 13 mL of gadolinium-based contrast (MultiHance; **C**).

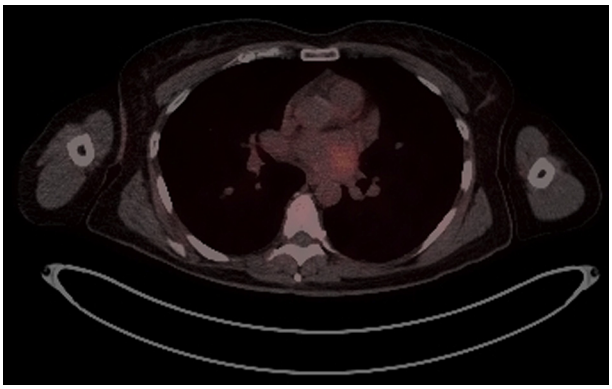

Figure 4 Positron emission tomography/computed tomography tumor imaging with Gallium-68 Dotatate, 5.4 mCi showing abnormal tracer localization corresponds to the known left atrial mass. This finding is most compatible with somatostatin receptor-rich lesions, e.g., cardiac carcinoid.

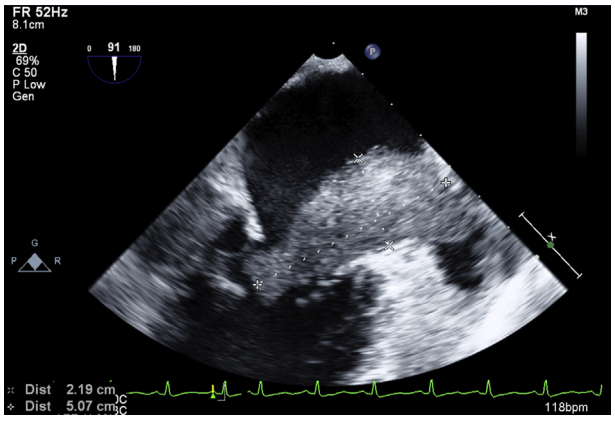

Figure 5 Transesophageal echocardiogram (TEE) midesophageal window, two-chamber view showing left atrial mass with significant growth (5.1 × 2.2 cm) compared with the previous TEE 6 weeks ago. There is prolapse of the mass into the left ventricle during systole resulting in obstruction of the mitral valve.

sarcomas (undifferentiated sarcoma, angiosarcoma, leiomyosarcoma, rhabdomyosarcoma, myxofibrosarcoma, osteosarcoma, synovial sarcoma), germ cell tumors (teratoma, yolk sac tumors), and lymphoma.[6] Cardiac sarcomas are typically asymptomatic until they are advanced. The mass itself may manifest by obstructing blood flow and interfering with the valve function as was observed just prior to surgery in this case, local invasions causing arrhythmias, pericardial effusion or tamponade, embolic phenomena, and finally symptoms such as dyspnea, syncope, chest pain, and weight loss. Undifferentiated sarcomas have no specific histology and typically mimic myxomas. The incidence has

been reported to be up to 24%, most commonly presenting in the left atrium. Valve involvement is common, and the average age of diagnosis is 45 years old.[7]

When a cardiac tumor is found on routine imaging, there are multiple imaging modalities that can be used to help determine the location, size, extent of tumor infiltration, and whether it is likely to be benign or malignant in origin. TTE and TEE are the appropriate modalities to begin cardiac mass classification. CT angiography is helpful to detect myocardial infiltration, compression of cardiac chambers, pericardial and great vessel involvement, calcification within the tumor, fat depiction, and vascularization of the mass.[7,8] CMR is the best modality to characterize soft tissue, assess infiltration, and accurately determine cardiac function.[9] In the case discussed, the CMR was suggestive of myxoma. Myxomas and undifferentiated sarcomas can have isointense T1 and hyperintense T2 signals, making it difficult to differentiate, especially since the left atrium is a common site for both.[10]

In this patient, the findings of the MV raised the possibility of a metastatic carcinoid tumor. Carcinoid tumors can arise outside the gastrointestinal tract and may not produce the carcinoid syndrome. In particular, carcinoids arising from the pulmonary bronchi can metastasize to the left heart and cause isolated left-sided valvulopathy without causing the carcinoid syndrome.[11] Dotatate PET/CT imaging detects hormonally active tissues, specifically NET activity.[12] While this scan was positive, 5 HIAA levels were normal. Can a poorly differentiated sarcoma produce a metabolically active substance that resulted in the valvulopathy as well as a positive Dotatate scan yet have a negative 5 HIAA? Or was the MV finding a "red herring" and by coincidence the mass was discovered? Unfortunately, we may never know the answer.

Ultimately, the diagnosis of cardiac sarcoma portends a poor prognosis. Mean survival for most cardiac sarcomas is between 9 and 11 months, with some studies showing up to 24% survival at 3 years.[13] Survival in these patients is improved after resection and adjuvant therapy.[14]

CONCLUSION

This case demonstrates the importance of multimodality imaging. Echocardiography is an accurate, noninvasive imaging modality that helps to further classify valvular heart disease, such as MR. When the etiology of MR is not evident and there is a need to further visualize the MV apparatus, TEE can be a helpful adjunct. Finally, cardiac tumors have a broad differential diagnosis. Systematic approaches to further classify cardiac masses in a noninvasive way with CT, magnetic resonance imaging, or PET/CT are necessary and should be considered when echocardiography is nondiagnostic.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2018.10.002.

REFERENCES

1. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:e57-185.
2. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2017;70:252-89.
3. Reynen K. Frequency of primary tumors of the heart. Am J Cardiol 1996;77:107.
4. Lam KY, Dickens P, Chan AC. Tumors of the heart. A 20-year experience with a review of 12,485 consecutive autopsies. Arch Pathol Lab Med 1993;117:1027-31.
5. Basso C, Rizzo S, Valente M, Thiene G. Cardiac masses and tumors. Heart 2016;102:1230-45.
6. Abels B, Pfeiffer S, Stix J, Schwab J. Multimodal imaging for the assessment of a cardiac mass: a case of primary cardiac sarcoma. Radiol Case 2017;11:11-9.
7. Shanmugam G. Primary cardiac sarcoma. Eur J Cardiothoracic Surg 2006;29:925-32.
8. Kassop D, Donovan MS, Cheezum MK, Nguyen BT, Gambill NB, Blankstein R, et al. Cardiac masses on cardiac CT: a review. Curr Cardiovasc Imaging Rep 2014;7:9281.
9. Patel RD, Lim RP, Axel L, Srichai MB. Diagnostic utility of cardiac MRI in clinical evaluation of cardiac masses with histopathological correlation. J Cardiovasc Magn Reson 2012;14(Suppl 1):298.
10. Butany J, Nair V, Naseemuddin A, Nair GM, Catton C, Yau T. Cardiac tumours: diagnosis and management. Lancet Oncol 2005;6:219-28.
11. Yuan SM. Valvular disorders in carcinoid heart disease. Braz J Cardiovasc Surg 2016;31:400-5.
12. Mojtahedi A, Thamake S, Tworowska I, Ranganathan D, Delpassand ES. The value of 68Ga-DOTATATE PET/CT in diagnosis and management of neuroendocrine tumors compared to current FDA approved imaging modalities: a review of literature. Am J Nucl Med Mol Imaging 2014;4:426-34.
13. Bakaeen FG, Reardon MJ, Coselli JS, Miller CC, Howell JF, Lawrie GM, et al. Surgical outcomes in 85 patients with primary cardiac tumors. Am J Surg 2003;186:641-7.
14. Zhang PJ, Brooks JS, Goldblum JR, Yoder B, Seethala R, Pawel B, et al. Primary cardiac sarcomas: a clinicopathologic analysis of a series with follow-up information in 17 patients and emphasis on long-term survival. Hum Pathol 2008;39:1385-95.