Stepwise Use of Multimodality Imaging in a Rare Cardiac Intimal Sarcoma

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INTRODUCTION

Primary cardiac tumors are uncommon, accounting for 0.3% to 0.7% of all cardiac tumors.[1,2] Cardiac intimal sarcomas (CISs) are among the least reported primary cardiac tumors and are frequently misdiagnosed as myxomas, metastases, or thrombi.[3]

Transthoracic echocardiography (TTE) is the initial imaging modality of choice, and tissue biopsy showing *MDM2* gene amplifications is the definitive diagnostic test for CIS.[4] Multimodality imaging with cardiac magnetic resonance imaging (CMR) and combined positron emission tomography and computed tomography (PET/CT) are necessary adjuncts for diagnosis and biopsy planning. CMR is helpful in determining cardiac mass size and location and involvement of adjacent structures.[5] Furthermore, CMR can characterize the tissue of cardiac masses, showing evidence of vascularity or perfusion, inflammation or edema, and necrosis. When combined with PET/CT, CMR offers a powerful imaging capacity to map out the degree of cardiac and extracardiac involvement of masses and help plan therapy.

In this case report, we share an unusual presentation of a rare primary cardiac tumor, demonstrating the need for multimodality imaging for accurate diagnosis and tumor characterization. We also highlight the clinical complexity of treating an aggressive malignancy with right ventricular (RV) myocardial invasion and obstruction.

CASE PRESENTATION

A 68-year-old woman with obesity, hyperlipidemia, remote history of left breast cancer with lumpectomy, radiation, and non-anthracycline-based chemotherapy and a recent diagnosis of right lower extremity melanoma status post excision presented with chest pressure and dyspnea on exertion.

The physical examination was remarkable for a blood pressure of 135/91 mm Hg, a pulse rate of 70 beats/min, an oxygen saturation of 98%, jugular venous distension, and bilateral 1+ pitting edema.

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VIDEO HIGHLIGHTS

Video 1: Two-dimensional TTE, apical four-chamber view, demonstrating the large mass attached to the RV free wall with the moderate-sized pericardial effusion and smaller echogenic mass within the pericardial space.

Video 2: CMR balanced steady-state free precession sequence, axial stack views (superior to inferior displays), demonstrating the 8.0 × 4.9 cm RV mass with anterior and lateral RV wall infiltration.

Video 3: CMR balanced steady-state free precession sequence, sagittal short axis stack views (base to mid), demonstrating the large RV mass with RV outflow tract obstruction.

Video 4: CMR first-pass contrast perfusion sequence, axial view, demonstrating the heterogenous mild uptake of contrast with the RV mass consistent with tumor vascularity.

View the video content online at www.cvcasejournal.com.

Electrocardiography showed T-wave inversions in the anterior leads with concomitant high-sensitivity troponin elevation to 171 pg/mL. Left heart catheterization (Figure 1) showed left anterior descending coronary artery (LAD) bifurcation with distal occlusion of the smaller segment that did not improve with balloon angioplasty, initially concerning for spontaneous coronary artery dissection.

TTE (Figures 2 and 3A, Video 1) demonstrated a 3 × 3 cm mass with contrast perfusion within the right ventricle, moderately reduced RV function, and a mobile pericardial mass with a moderate-sized circumferential pericardial effusion. Initially, these findings were suspicious for metastatic melanoma given the patient's history.

Anticoagulation and antiplatelet therapy were not initiated at this time to prevent tumor thrombi or treat possible spontaneous coronary artery dissection, respectively, given the overall suspicion for metastatic melanoma and its associated hemorrhagic risk.[5]

Other diagnostic considerations included recurrent metastatic breast cancer and primary cardiac masses such as myxomas, sarcomas, and fibroelastomas. Nonneoplastic considerations included thrombus and lipomatous hypertrophy. Repeat TTE 2 weeks later redemonstrated a large heterogenous echogenic mass attached to the RV free wall, septum, and apex, measuring 5.9 × 4.7 cm and elevated right-sided pressures (RV systolic pressure of 97 mm Hg and right atrial pressure of 15 mm Hg).

CMR (Figure 4, Videos 2-4) showed an 8.0 × 4.9 cm mass infiltrating the anterior and lateral wall of the right ventricle and extending exophytically into the adjacent pericardial effusion, with features more suspicious for a malignant myxomatous tumor than metastatic melanoma.

Right heart catheterization with endomyocardial biopsy was performed. Cytopathology (Figure 5) was notable for high-level

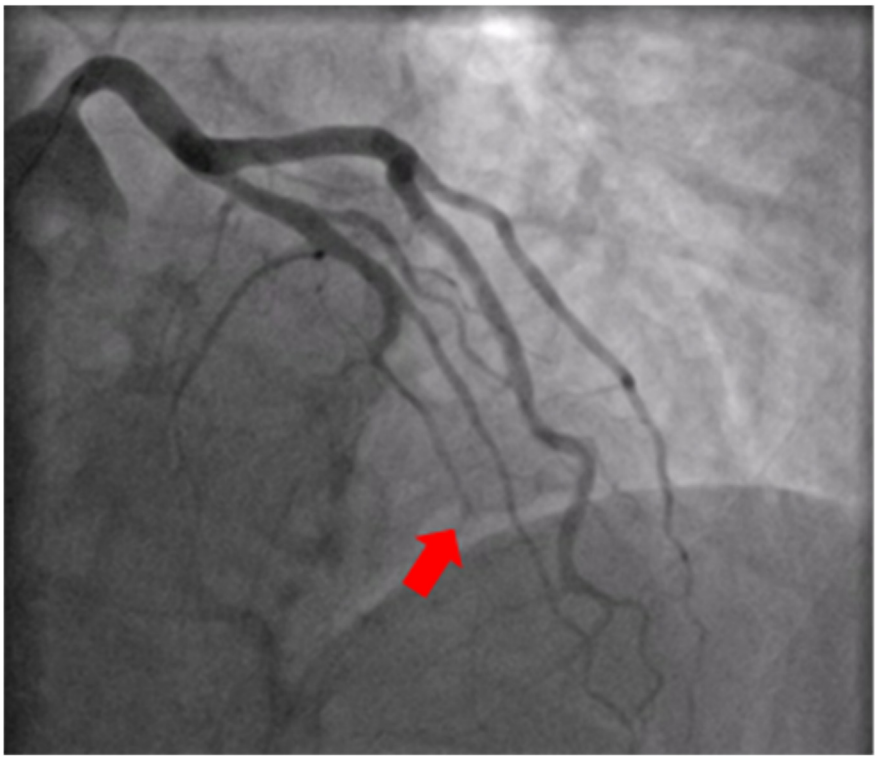

Figure 1 Invasive coronary angiography, left anterior oblique, cranial view, demonstrating mid-LAD bifurcation with occlusion of a smaller caliber segment after balloon angioplasty (*arrow*).

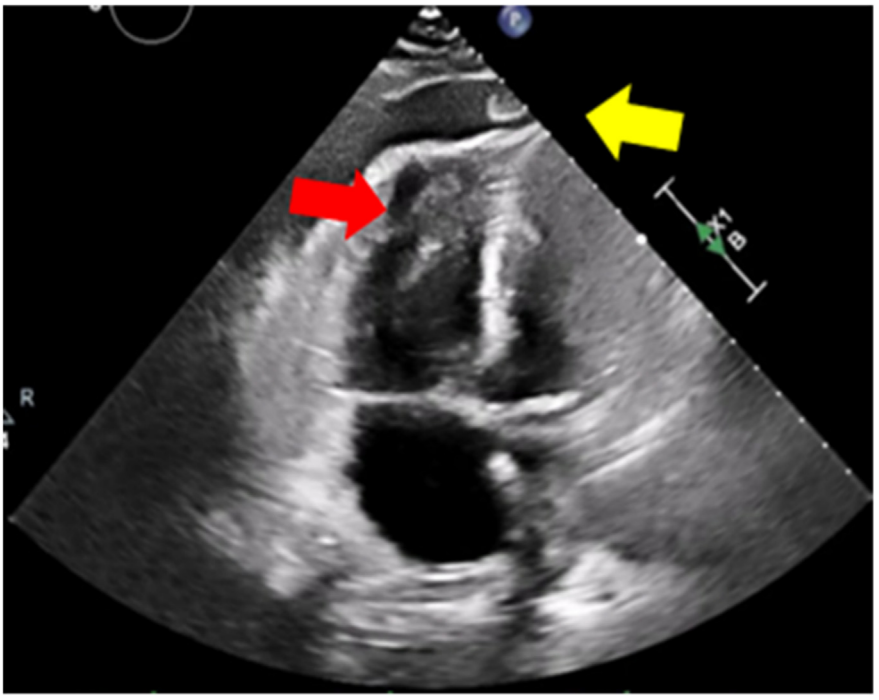

Figure 2 Two-dimensional TTE, apical four-chamber view, systolic phase, demonstrating a large mass attached to the RV free wall (*red arrow*) with a moderate-sized pericardial effusion and a small, contained echogenic mass (*yellow arrow*).

amplification of the *MDM2* (12q15) gene on fluorescence in situ hybridization testing consistent with a well-differentiated liposarcoma or atypical lipomatous tumor.

Ultimately, the patient was diagnosed with primary CIS with extrinsic LAD compression given the tumor's anatomic location on CMR and overall clinical and pathologic findings. The patient was

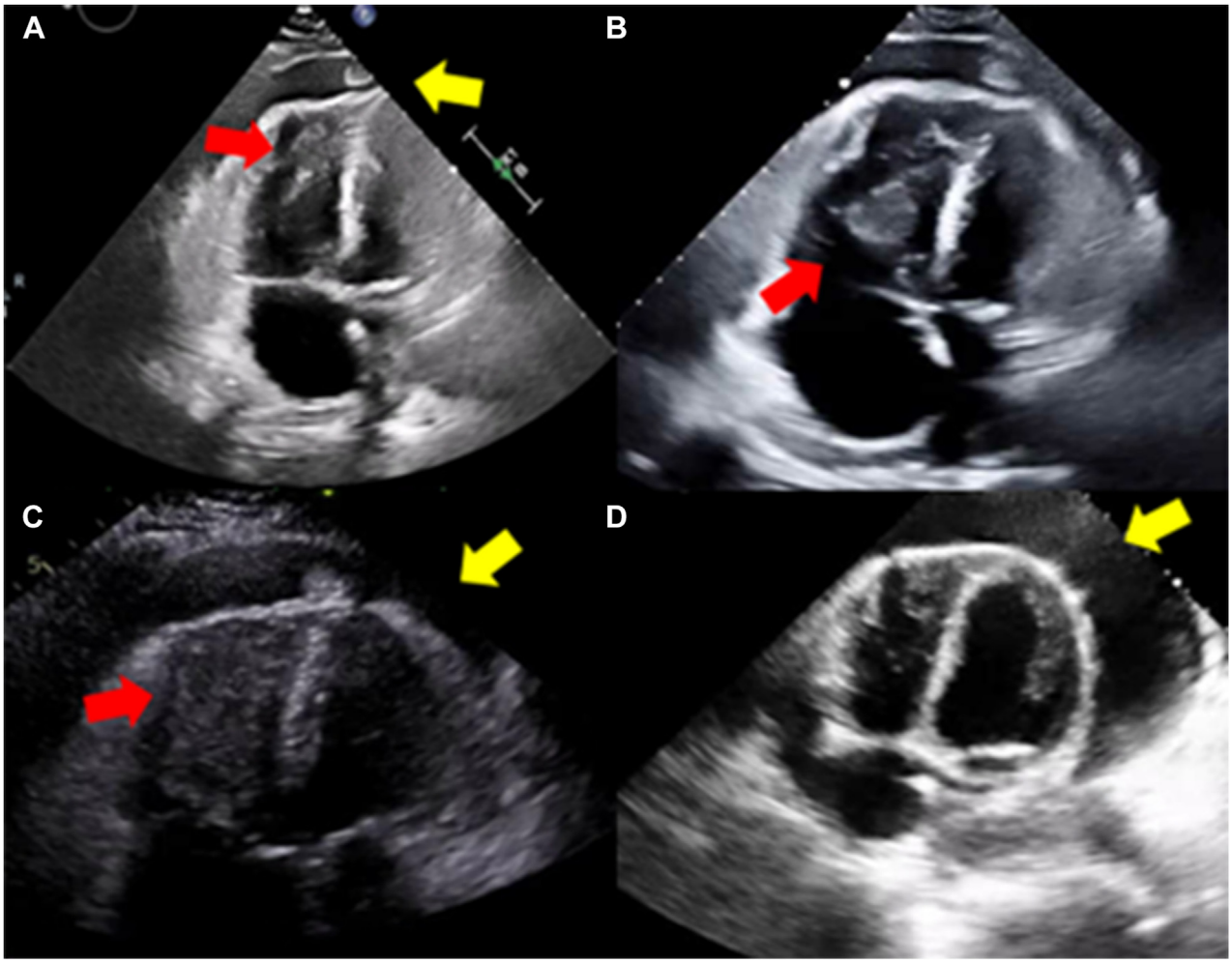

Figure 3 Serial two-dimensional TTE, apical four-chamber views, demonstrating a 5.9 × 4.3 cm mass within the right ventricle (*red arrow*) and a moderate pericardial effusion (*yellow arrow*) at 2 weeks **(A)**; 5.9 × 4.5 cm RV mass (*red arrow*) and moderate pericardial effusion at 5 weeks **(B)**; 5.9 × 4.7 cm RV mass (*red arrow*) and a large pericardial effusion (*yellow arrow*) at 7 weeks **(C)**; and a 6.3 × 5.9 cm RV mass with a very large pericardial effusion (*yellow arrow*) at 20 weeks.

then started on low–molecular weight heparin to minimize the risk for a tumor thrombus and eventually transitioned to a direct oral anticoagulant.

The patient subsequently underwent extensive imaging for staging. Magnetic resonance imaging of the brain, abdomen, and pelvis showed no evidence of metastatic disease. PET/CT redemonstrated the cardiac mass (Figure 6) and noted a possible metastatic lesion at the patient's right femur that was later nondiagnostic for malignancy on core biopsy.

Repeat TTE (Figure 3B) 3 weeks later showed a dilated right atrial cavity with an RV systolic pressure of 64 mm Hg, right atrial pressure of 15 mm Hg, increased transpulmonary gradient, and dilated noncollapsing inferior vena cava indicative of obstructive physiology and volume overload. The patient's medical team withheld diuresis given the patient's tenuous preload dependence in the setting of obstructive physiology and RV failure.

After a multidisciplinary discussion involving cardiac surgery, oncology, and radiation oncology, the patient was discharged home and completed urgent outpatient radiation therapy with a total of 30 Gy of radiation. Surgical resection was deemed prohibitive on the basis of the sarcoma's size, and the patient declined chemotherapy given the unlikelihood of cure and treatment risks. The patient was subsequently admitted twice in the following month with worsening dyspnea and findings suggestive of worsening right heart failure. TTE (Figure 3C) showed newly reduced left ventricular ejection fraction to 25% in addition to continued RV failure and obstructive physiology. Computed tomographic angiography showed new segmental pulmonary emboli despite direct oral anticoagulant compliance. After a multidisciplinary discussion involving cardiology, cardiac surgery, and the institutional pulmonary embolism response team, the patient opted to be discharged home with hospice. Interval TTE 3 months later (Figure 3D) showed a large pericardial effusion with tamponade, and the patient was admitted, underwent successful palliative pericardiocentesis followed by a pericardial window, and was discharged home.

DISCUSSION

CISs are aggressive, with high morbidity and mortality rates.[6] Cardiac sarcomas can be subtyped into angiosarcomas, malignant fibrous cytomas, chondrosarcomas, synovial sarcomas, leiomyosarcomas, intimal

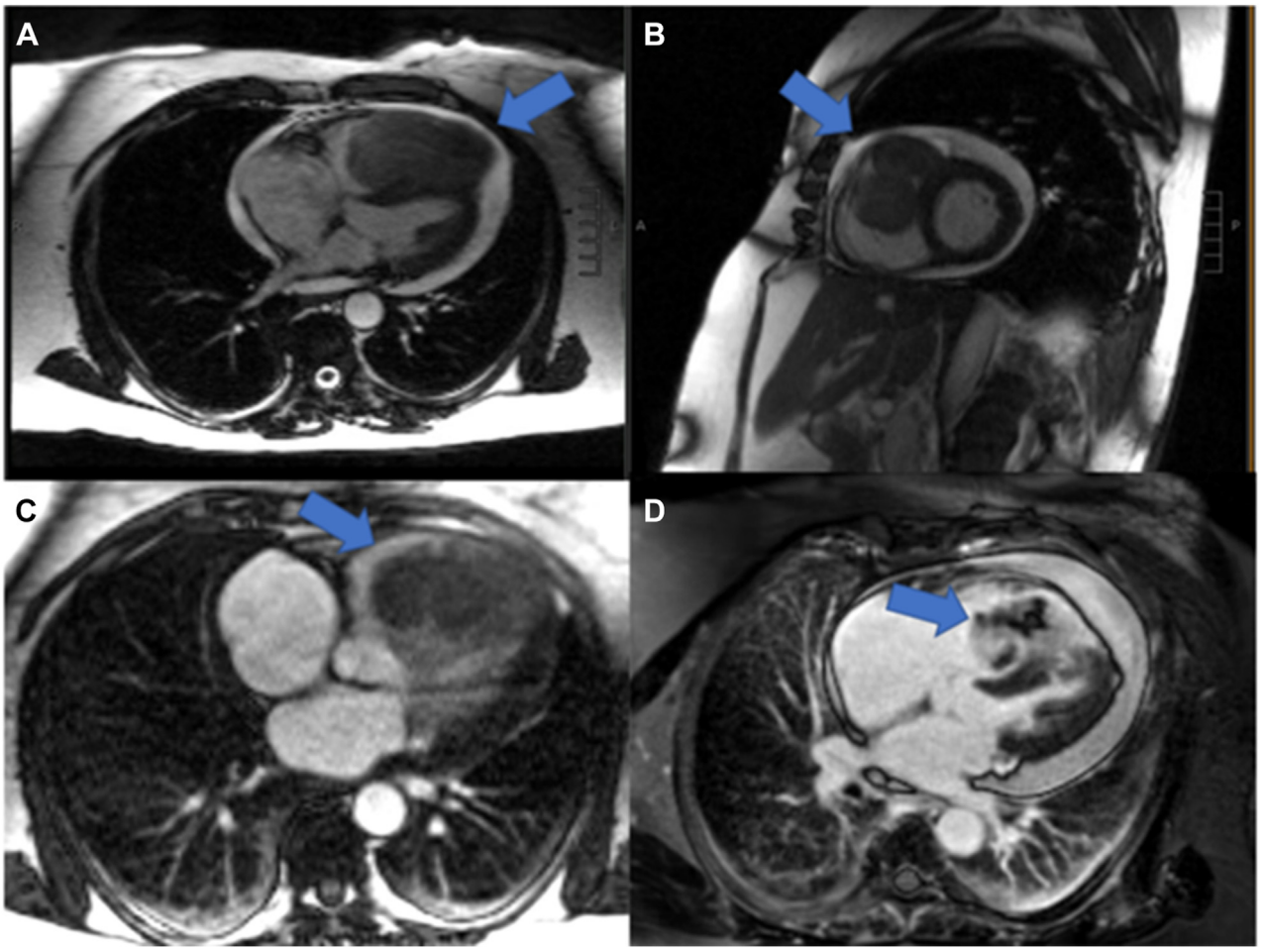

Figure 4 CMR panel with **(A)** balanced steady-state free precession (bSSFP) sequence, axial view, systolic image, demonstrating the 8.0 × 4.9 cm RV mass (*arrow*) with anterior and lateral RV wall infiltration; **(B)** bSSFP sequence, sagittal short-axis view, systolic image of the RV mass (*arrow*) at the level of the RV outflow tract, demonstrating the anatomic predisposition to obstructive physiology; **(C)** first-pass contrast perfusion sequence, axial view, systolic image with heterogenous mild uptake of contrast consistent with tumor vascularity (*arrow*); and **(D)** LGE, axial view, with heterogenous enhancement of the RV and the mass (*arrow*) suggestive of necrosis.

sarcomas, rhabdomyosarcomas, osteosarcomas, and others. Of these, angiosarcomas, undifferentiated sarcomas, and undifferentiated pleomorphic sarcomas are the most prevalent, while cardiac intima sarcomas are extremely rare.[7] Angiosarcomas often affect the right atrium, vena cava, right atrioventricular fissure, left atrial roof, and atrial septum, while the RV outflow tract and the anterior pulmonary artery wall are the typical locations of synovial sarcomas.[8] Malignant fibrous cytomas commonly develop in the left atrium, left atrioventricular fissure, pulmonary veins, and the pulmonary artery's posterior wall, but the preferential location of CIS is less known. The prognosis of cardiac sarcomas, including CISs, is poor, with a median survival time of <1 year.[9] The mean interval between symptom onset and diagnosis, as well as between diagnosis and surgery, is <1 month.[8]

Cardiac sarcoma are also the least reported primary cardiac tumors; however, the proposed marker for CIS, *MDM2*, was one of the most common markers found in an extensive retrospective study of biopsies from patients with primary cardiac sarcomas, suggesting possible underdiagnosis.[4] Püsküllüoglu *et al.*[10] conducted a review of 47 CIS cases, finding that most cases occurred in the left atrium and adjacent valves or myocardium. Our case is unusual in its anatomic location and presentation. Our patient had an RV mass causing distal occlusion of the small segment of a bifurcated LAD, leading to an initial presentation concerning for acute coronary syndrome as well as clinical RV failure. To our knowledge, the literature has one other case that presented as a mass in the right ventricle.[11]

Our patient's risk factors included obesity, hyperlipidemia, melanoma, and prior breast cancer with left chest radiation. Because of the rarity of these tumors, no risk factors for CISs have yet been identified. The other RV CIS case presented with features of volume overload and elevated brain natriuretic peptide, with recurrence of the RV tumor 7 weeks after surgery. One case reported left atrial appendage CIS in a patient with a history of breast cancer who had undergone breast-conserving surgery without irradiation.[12] It is interesting to speculate about a potential relationship between previous chest irradiation or concurrent malignancy and the risk for CIS; this may be a direction for further inquiry.

TTE was the first cardiac imaging study done in our case and led us to suspect metastatic melanoma as the underlying diagnosis on the basis of the patient's history, imaging findings, and the relative scarcity of primary cardiac malignancies. The patient underwent further advanced imaging to characterize the mass (CMR) and identify metastatic lesions (PET/CT). CMR is useful in that it evaluates the relationship between

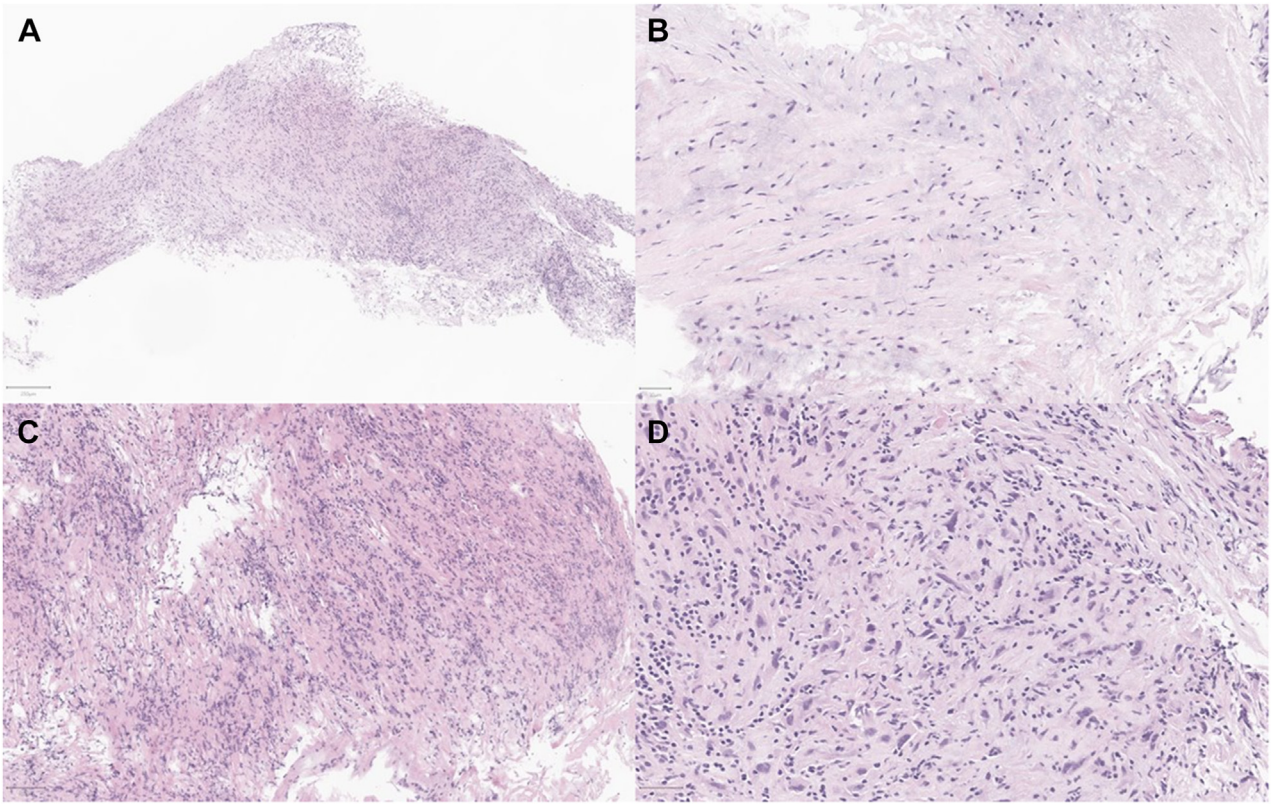

Figure 5 Hematoxylin and eosin sections of the biopsy of the lesion at low power **(A)**, higher power composed of bland spindle cells in a myxoid background **(B)**, abundant mixed inflammation and cystic degeneration **(C)**, and larger cells with hyperchromatic pleomorphic nuclei **(D)**.

cardiac masses and extracardiac structures, allows surgical planning, and is able to differentiate cardiac mass etiologies on the basis of tissue characteristics.[1,13] Features on CMR that are suspicious for malignancy include multiple tumors, a broad base, intramural location, right heart involvement, size > 5 cm, local invasion, and pleural or pericardial effusions. CMR techniques with late gadolinium enhancement (LGE) and T1- and T2-weighted imaging can also help diagnose tumors and determine tumor sequelae. Malignant tumors have significant enhancement on postcontrast T1-weighted imaging, and cardiac tumors with necrosis, edema, and hemorrhage have significant enhancement on T2-weighted images. Malignant tumors often present with moderate, strong, homogenous, or heterogenous enhancement on LGE due to loss of integrity of the tumor cell membranes; however, these findings can also be seen in benign tumors and metastases. PET/CT is invaluable in identifying relationships with extracardiac structures, staging cardiac masses, differentiating between benign and malignant tumors, and determining response to therapy.[1]

Our patient had several features suspicious for malignancy on imaging, including multiple tumors, right heart involvement, size > 5 cm, extensive invasion of local structures (RV anterior and lateral walls, interventricular septum, LAD), and a pericardial effusion. First-pass perfusion on CMR demonstrated heterogenous areas of enhancement on LGE images suggestive of cell-rich and depleted components of the mass and necrosis. CMR also showed T2-weighted hyperintensity and numerous low-intensity foci of LGE, which enhanced in the more delayed long T1- LGE sequences, features more suggestive of a myxomatous tumor rather than metastatic melanoma. We also demonstrated high-level amplification of the *MDM2*-12q15 gene on fluorescence in situ hybridization testing in our patient's endomyocardial biopsy, confirming the diagnosis. *MDM2* amplification has been proposed as a pathologic designation tool for CIS and has been reported in most undifferentiated and primary artery intimal sarcomas.[4] Although we did not test for platelet-derived growth factor receptor–α, other intimal sarcoma cases have also demonstrated amplification and activation of platelet-derived growth factor receptor–α on immunohistochemistry, quantitative polymerase chain reaction, and array comparative genomic hybridization.[14]

Our patient's volume overload, RV failure, and obstructive physiology in the setting of RV intimal sarcoma presented a therapeutic challenge. Interval TTE was critical in monitoring hemodynamic consequences of the patient's tumor and associated pericardial effusion, particularly when the patient presented with new or worsening symptoms. The easy access, safety, and practicality of TTE make it an invaluable follow-up imaging modality. No measures (including diuretics and continuous renal replacement therapy) could have effectively removed fluid without risking at least short-term intravascular volume depletion, leading to a decrease in preload and potential circulatory collapse. We decided that the risk for reducing cardiac preload exceeded the possible benefit of improved volume status.

The mainstay of treatment of malignant cardiac sarcomas is surgery, especially with negative margins (radical surgery).[15] However, it is sometimes difficult to obtain a clear resection margin because of the large tumor size at diagnosis and myocardial size limitations. Radiation and chemotherapy are commonly used in cases in which radical surgery is impossible or metastasis has occurred. The estimated median survival of CIS is 29 months despite using radiation and

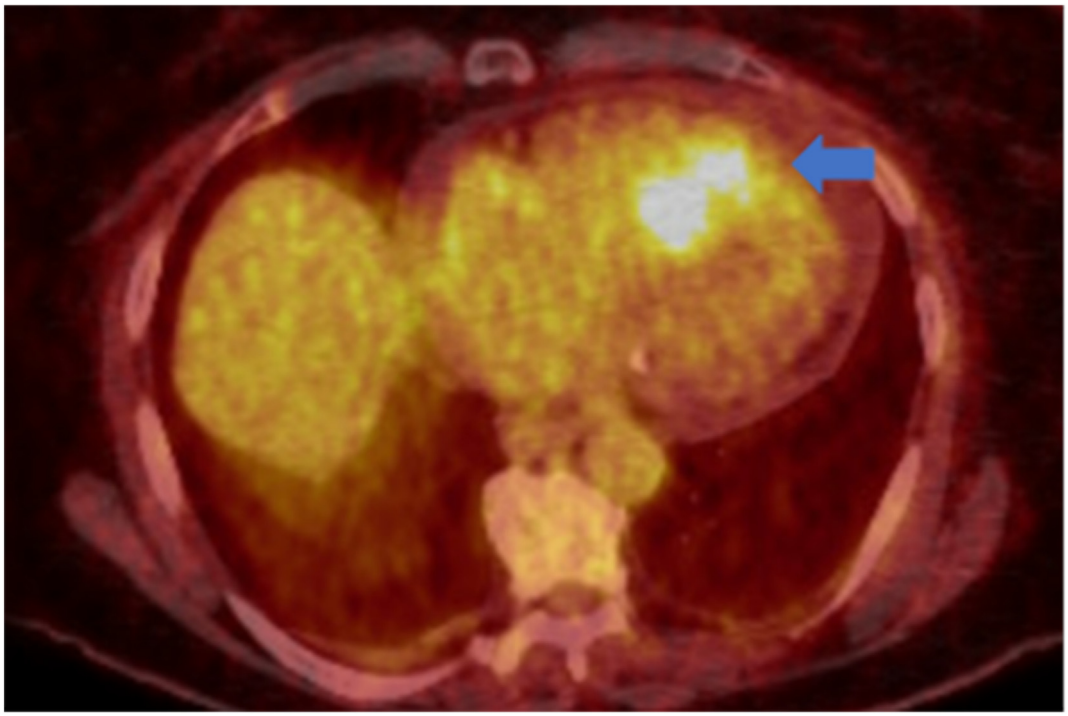

Figure 6 PET/CT fusion axial slice showing a hypermetabolic RV mass (*blue arrow*) with a standardized uptake value of 8.1.

chemotherapy. In our case, surgical therapy was deemed prohibitive because of the extent of mass infiltrating the RV free wall, which would have required resection of the right ventricle at the time of surgery. After a multidisciplinary discussion, the patient opted for radiotherapy alone, as the lesion was within a targetable field, and the oncologists believed that chemotherapy would be ineffective. However, despite the appropriate radiation dose, our patient's cancer progressed, with worsening RV failure, obstructive physiology, and anticoagulation failure, and the patient sought hospice care. Eventually, the patient developed cardiac tamponade and opted for pericardiocentesis followed by pericardial window as a palliative measure.

CONCLUSION

Our case demonstrates an unusual presentation of a CIS and the role of multimodality imaging in diagnosis and therapeutic planning. It also displays the diversity of pathology from a rare and aggressive primary cardiac tumor and the management dilemmas of RV masses. We hope that more research will be devoted to characterizing CISs and identifying treatment targets to improve patients' survival.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

Complete written informed consent was obtained from the patient (or appropriate parent, guardian, or power of attorney) for the publication of this study and accompanying images.

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DISCLOSURE STATEMENT

The authors report no conflict of interest.

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SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.case.2023.06.002.

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