JACC: CASE REPORTS VOL. 29, 2024

CARDIO-ONCOLOGY

CASE REPORT: CLINICAL CASE

Management of a Rare Mitral Valve Sarcoma Requiring Valve Replacement and Chemotherapy

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ABSTRACT

A woman with dyspnea is diagnosed with a rare mitral valve primary sarcoma. Patient underwent mechanical mitral valve replacement requiring therapeutic anticoagulation with adjuvant systemic anthracycline-based chemotherapy. The challenges of preventing thromboembolism in a new mechanical prosthesis with risk of bleeding due to cancer and/or its therapies are described. (JACC Case Rep 2024;29:102474) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A 38-year-old woman presented to an outside hospital with progressive dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. Her vital signs were notable for sinus tachycardia and new oxygen requirement. Her clinical course rapidly progressed with acute hypoxic respiratory failure requiring mechanical ventilation. Computed tomography angiography with findings concerning for a mass near the mitral valve (MV) prompted further investigation.

LEARNING OBJECTIVES

- To describe the presentation and management of a rare primary valvular sarcoma.
- To promote the use of echocardiographic contrast material to differentiate tumor from thrombus.
- To recognize the intricacies of surgical valve decision making.
- To discuss the complexity of anticoagulation management for mechanical MVR in cytopenias.

PAST MEDICAL HISTORY

The patient had a reported history of celiac disease, iron-deficiency anemia, and obesity.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included vegetation, thrombus, and atrial myxoma or other atrial tumor.

INVESTIGATIONS

Initial laboratory data were obtained, with normal complete blood count and basic metabolic panel. Her brain natriuretic peptide and D-dimer were elevated.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received March 8, 2024; revised manuscript received May 6, 2024, accepted June 24, 2024.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2024.102474

ABBREVIATIONS AND ACRONYMS

MV = mitral valve

MVR = mitral valve replacement

Computed tomography angiography showed pulmonary edema, bilateral pleural effusions, and a globular filling defect (2.9 × 1.8 cm) adjacent to the MV. Transthoracic echocardiography showed a protruding, solid fixed vegetation (2.9 × 1.8 cm) on the atrial aspect of the posterior leaflet. There was severe mitral stenosis, with a mean diastolic gradient of 18 mm Hg at a heart rate of 99 beats/min and reverse proximal isovelocity surface area by color Doppler (**Figure 1**, Video 1). Administration of ultrasound enhancing agent demonstrated opacification of the MV mass, concerning for vascularized tumor (Video 2). Intraoperative transesophageal echocardiography showed a with large mass attached to the posterior MV leaflet (Videos 3 and 4).

The patient underwent massive excision, and pathologic examination results were notable for an intimal sarcoma (**Figure 2**). There was no evidence of residual MV tumor on postoperative positron emission tomography or a suggestion of metastatic disease.

MANAGEMENT

The patient underwent urgent cardiac surgery for MV mass excision and mitral valve replacement (MVR) with a 29-mm St. Jude medical prosthesis. A postoperative echocardiogram was notable for an elevated MV gradient at 10 mm Hg at heart rate of 100 beats/min, as well as a large pericardial effusion (**Figure 3A**). Given the recent anticoagulation initiation with warfarin, the effusion was discussed with the thoracic surgeons, who recommended conservative management. She was treated with β-blockers, diuretics, and a 4-week course of colchicine, and then showed improvement in volume, MV gradient, and pericardial effusion (**Figure 3B**).

She underwent volume optimization before chemotherapy and showed an improved MV gradient to 8 mm Hg. She started adjuvant chemotherapy with doxorubicin, ifosfamide, and mesna (AIM) 2 months postoperatively. Her anticoagulation was switched

FIGURE 1 CW Doppler Demonstrating Mitral Valve Mean Gradient

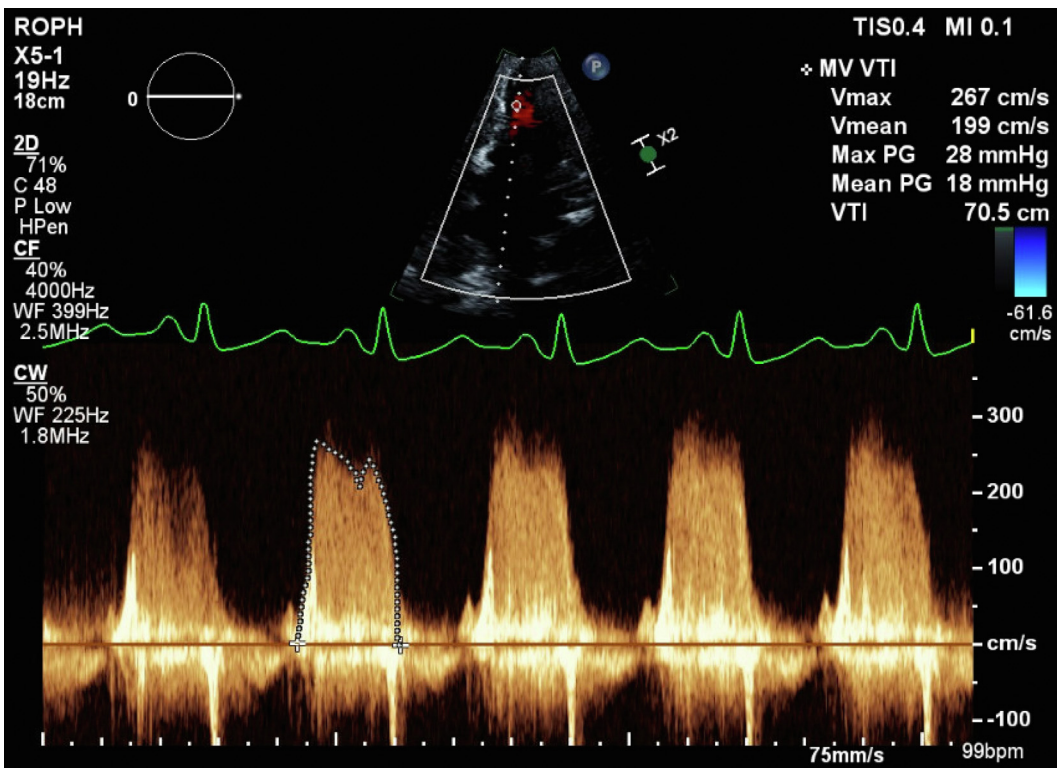
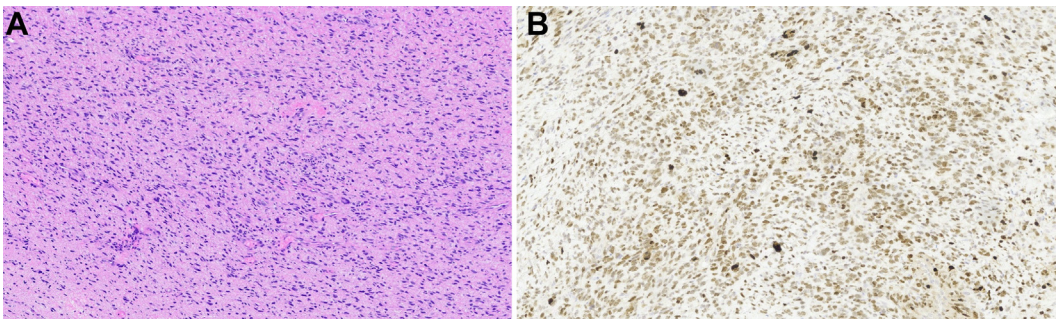


FIGURE 2 **Histologic Results**

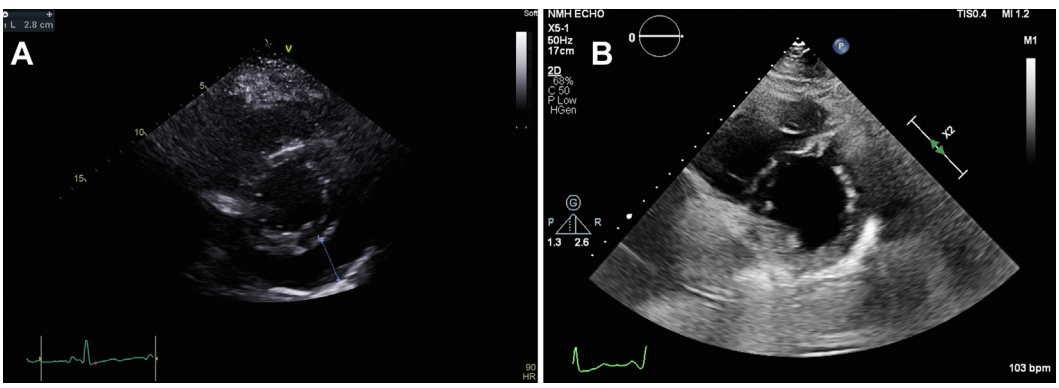


(A) Hematoxylin and eosin staining at ×10 magnification showing high-grade spindle sarcoma with marked cytologic atypia, necrosis, and no specific line of differentiation. (B) Immunohistochemical staining at ×10 magnification showing nuclear positivity for murine double minute clone 2 (MDM2), diagnostic of intimal sarcoma.

from warfarin to therapeutic enoxaparin because of a drug interaction with ifosfamide.

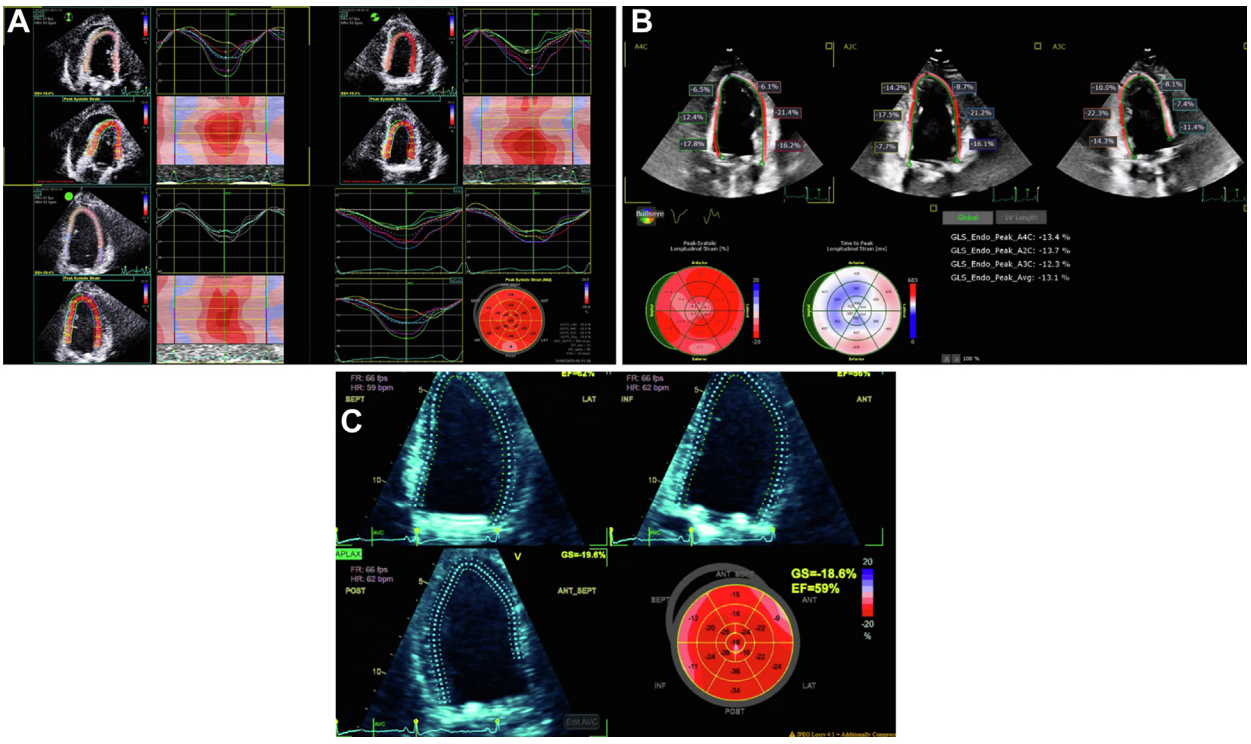
The need for anticoagulation after placement of a new mechanical valve was balanced against the potential risk of bleeding from cancer and/or its therapies. She was admitted through her first 2 cycles of chemotherapy for closer monitoring. The patient had short durations of thrombocytopenia with platelets <50 kμL and anemia with hemoglobin <7 g/dL requiring transfusion. She received bridge therapy with intravenous unfractionated heparin until her blood counts stabilized. She was hospitalized between her first and second cycles of chemotherapy for a gastrointestinal bleed that was treated with supportive management and disruption of anticoagulation for 24 hours. The oncology service reduced the ifosphamide dosage to prevent long durations of thrombocytopenia. Her platelet nadir was noted to be 10 to 50 kμL between day 10 and day 14 of her chemotherapy cycle. A complete blood count was obtained every 48 hours on day 10 and was hospitalized if her platelets were <50 kμL. She was admitted for cycles 3-6 requiring pRBC and platelet transfusions. She didn't receive anticoagulation bridges during these later cycles as she was >3 months from surgery. She completed a total of 6 cycles of chemotherapy over a 4-month span. An echocardiogram was obtained after each cycle of chemotherapy with stable valve hemodynamics. Patient transitioned back to warfarin at completion of chemotherapy.

FIGURE 3 **Evaluation of Pericardial Effusion on Transthoracic Echocardiogram**



(A) Pericardial effusion on postoperative, pre-chemotherapy transthoracic echocardiogram. (B) Transthoracic echocardiogram showing resolution of pericardial effusion.

FIGURE 4 Transthoracic Echocardiogram Surveillance on Anthracycline-Based Chemotherapy



(A) Prechemotherapy EF/GLS (EF 58%/−19.61%). (B) Decrease in EF/GLS (51%/−13.1%) after cycle 5 with cumulative 375 mg/m^2 dose of doxorubicin. (C) Improvement in EF/GLS (59%/−18.6%) after initiation of guideline-directed medical therapy. EF = volumetric fraction of blood ejected from a cardiac chamber with contraction; GLS = measure of myocardial longitudinal length during systole compared to resting length during diastole, it provides early detection of systolic dysfunction.

DISCUSSION

Cardiac neoplasms are rare. The incidence ranges from 0.001% to 0.3%.[1] Malignant primary cardiac tumors account for 10% of cardiac neoplasms. Sarcomas are the most common malignant primary tumor and most frequently arise in the atrium. Primary sarcoma with MV involvement is exceedingly rare, with few case reports in the literature. Primary cardiac sarcomas tend to be aggressive, with a life expectancy of 1 year. There are reports of long-term survival with localized low-grade sarcomas that undergo complete surgical resection.[1,2]

The feasibility of surgical resection in a patient with valvular involvement is complex because of its anatomic location. In many cases of mass with valvular involvement (eg, papillary fibroelastoma), surgical resection is attempted with intention to spare the native valve.[3] This was not possible in this case, so MVR was performed at an outside hospital. There are few documented cases of MV tumors treated with mechanical and bioprosthetic valves, and information regarding their postoperative course is limited.[4] We are unaware of any data explicitly comparing mechanical with bioprosthetic valves in primary cardiac tumors with valvular involvement.

Some younger patients prefer a bioprosthetic MV because of personal preference (eg, pregnancy planning), advances in redo cardiac surgery, and potential valve-in-valve transcatheter MVR in the future. Bioprosthetic MVR requires anticoagulation for 3 to 6 months with a vitamin K antagonist and has a lower thrombotic risk. Mechanical valves have better durability and are a reasonable choice in patients <65 years of age without any known contraindications to anticoagulation and inability to undergo mitral valve repair.[5,6] However, oncology patients with mechanical MVRs have a high thrombotic risk and require permanent anticoagulation, which is a constant threat for patients undergoing antineoplastic therapies because of the risk of bleeding. Disruptions in anticoagulation should be avoided, given the high

incidence of thromboembolism in the first month after surgery (14.8%) in addition to the rare yet deleterious complication of obstructive mechanical prosthetic valve thrombosis (0.3%-1.3%/year).[7,8] The risk of thromboembolism was balanced with the increased risk of bleeding and known pericardial effusion in our patient. Lovenox was continued during transient episodes of thrombocytopenia on the basis of relevant guidelines from the European Society of Cardiology.[9]

FOLLOW-UP

After chemotherapy, the patient feels well and is participating in cardiac rehabilitation. Her echocardiogram demonstrated normal Left ventricular ejection fraction/global longitudinal strain at baseline (**Figure 4A**), which reduced after 5 cycles of chemotherapy (**Figure 4B**) and recovered after guideline-directed medical therapy was started (**Figure 4C**). Patients on anthracycline-based cancer therapies require baseline and close echocardiographic surveillance once they receive a high dose of anthracycline.[9] The initiation of guideline-directed medical therapy may allow patients to continue cardiotoxic cancer therapy, especially if it is given for curative intent, after discussion with a multidisciplinary team.

CONCLUSIONS

We present a rare case of primary sarcoma involving the native MV in a patient who underwent a mechanical MVR before starting systemic chemotherapy. There are no evidence-based guidelines for the management of primary valve malignancy or management of new mechanical valves in patients undergoing chemotherapy. This case highlights the complexity of surgical valve decision making and challenges in anticoagulation management in patients undergoing chemotherapy for active malignancy.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

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

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KEY WORDS anticoagulation, cancer, complication, echocardiography, mitral valve, thrombosis, valve replacement

APPENDIX For supplemental videos, please see the online version of this paper.