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INTERVENTION AND SURGERY

CASE REPORT: CLINICAL CASE

Surgical Resected Cardiac Angiosarcoma in a 75-Year-Old Patient With a Mitral Valve Bioprosthesis

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ABSTRACT

A 75-year-old patient with a history of mitral and aortic valve replacement surgery 7 years ago, presented with progressive dyspnea. Transesophageal echocardiogram showed a mass suggestive of bioprosthetic mitral valve thrombosis. We present the investigation process using imaging, surgical findings, nuclear medicine, and histopathology that result in the diagnosis of cardiac angiosarcoma. (JACC Case Rep. 2024;29:102923) © 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/).

HISTORY OF PRESENTATION

A 75-year-old man presented to the emergency department with a report of progressive dyspnea on exertion over the past 2 weeks. The patient denied fever, chills, or recent dental interventions.

TAKE-HOME MESSAGES

- This case highlights the importance of multidisciplinary work team for the differential diagnosis of primary cardiac tumors.
- Cardiac masses in prosthetics valves diagnosed on transthoracic echo should prompt surgery and histological examination to establish definitive diagnosis.

PAST MEDICAL HISTORY

The patient had received aortic (25 mm) and mitral (29 mm) valve replacements (both Carpentier Perimount Magna Ease, Edwards Lifesciences) with bioprostheses and left atrial appendage exclusion 7 years ago due to severe aortic and mitral stenosis and atrial fibrillation. He had experienced several episodes of acute heart failure in the previous months, which had been resolved medically. The patient was on oral anticoagulation with acenocoumarol, but had had poor anticoagulation control of international normalized ratio.

DIFFERENTIAL DIAGNOSIS AND INVESTIGATIONS

The transthoracic echocardiogram (**Figure 1A**) showed that the aortic prosthesis had no signs of dysfunction,

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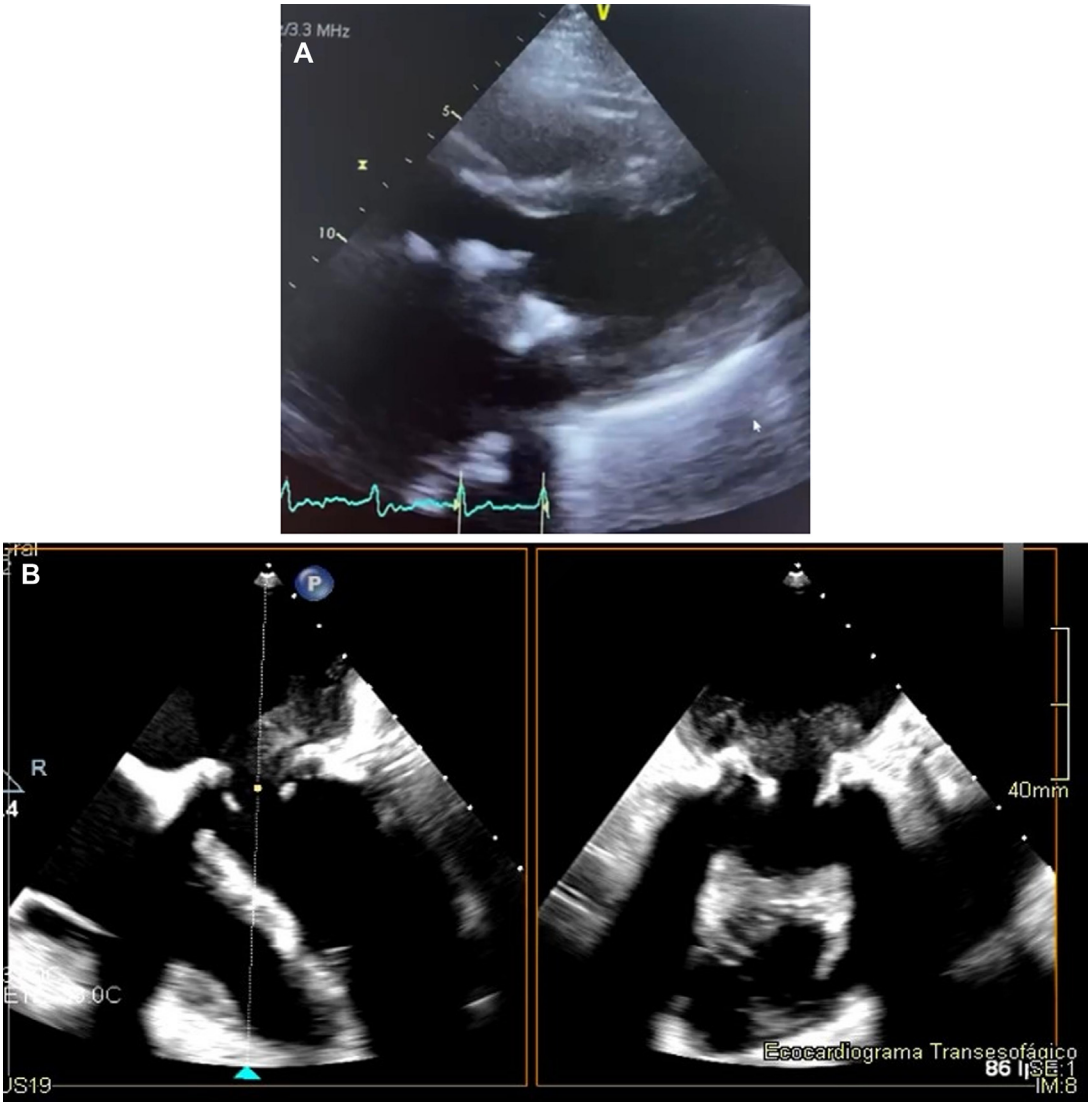
ABBREVIATIONS AND ACRONYMS

FDG = fluorodeoxyglucose F 18

although the mitral bioprosthesis had a mild mitral transprosthetic regurgitation and severe mitral stenosis with a mean gradient of 8 and valve area of 0.7 cm^2. Coronary angiography was normal.

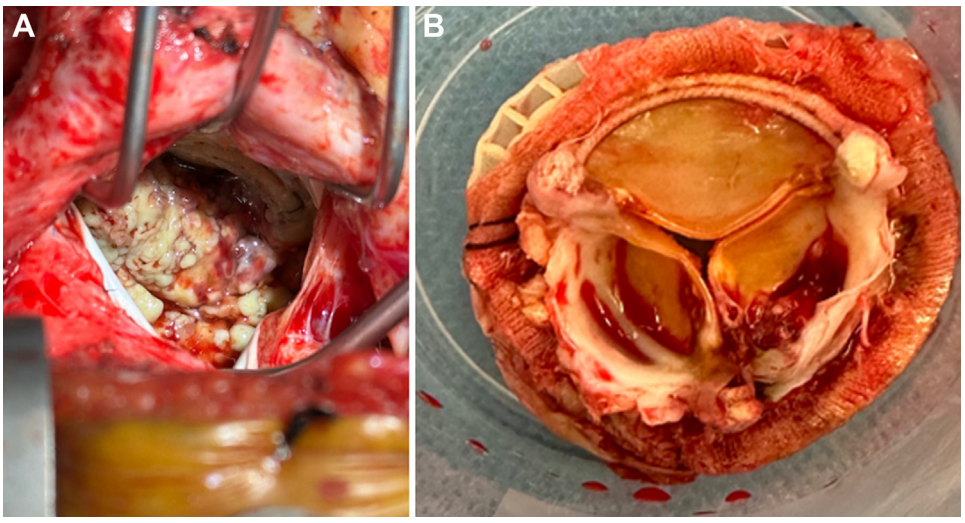
The transesophageal echocardiogram (**Figure 1B**) showed a heterogenous mass (38 × 27 × 20 mm) suggestive of large thrombus on the posterior and lateral aspects of the mitral prosthesis, which partially blocked the posterolateral and posteromedial leaflets (Video 1). Severe mitral prosthetic obstruction with mean gradient of 16 mm Hg, an effective area of 0.81 cm^2, and moderate intraprosthetic regurgitation was described. There was no

FIGURE 1 Echocardiogram



(A) Presurgery transthoracic echocardiogram shows severe mitral stenosis with mitral annular calcification, in the referring hospital. (B) Presurgery transesophageal echocardiogram demonstrates a heterogeneous mass, which involves mitral annular bioprosthesis.

FIGURE 2 Macroscopic Findings



(A) Intraoperative findings of the mitral valve prosthesis viewed from the left atriotomy. (B) Macroscopic findings of the mitral valve prosthesis after mitral valve replacement surgery showing a large vegetation fully adhered to the bioprosthesis.

evidence of residual flow inside the left atrial appendage. Given the imaging findings and previous medical history, thrombosis of mitral bioprosthesis was the first differential diagnosis. After a Heart Team discussion, a surgical replacement of the mitral valve was programmed in an urgent basis.

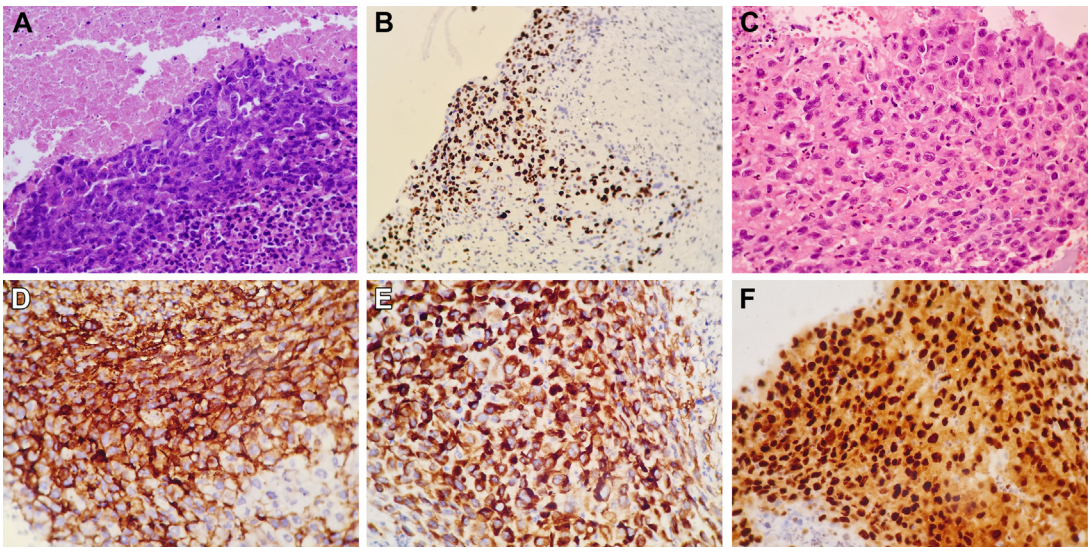
MANAGEMENT

Intraoperative findings (Figure 2) included a large mass on the atrial aspect of the mitral prosthesis that almost occluded it. The prosthetic mass resembled a large vegetation, which was fully adhered to the ring and the leaflets of the prosthesis with minimal extension to the endocardium close to the base of the remanent of the left atrial appendage. Given the potential diagnosis of endocarditis, tissue samples were obtained for microbiology and pathology analyses. The mitral bioprosthesis was replaced with a 27-mm St. Jude MS (Abbott Vascular) mechanical mitral valve. During the procedure, surgeons confirmed the occlusion of the left atrial appendage and ruled out the presence of thrombi or vegetations in any other region of the left atrium or left ventricle. The intraoperative transesophageal echocardiogram showed normal function of the mitral and aortic prostheses.

The patient had an uneventful immediate postoperative course. Daptomycin, rifampin, and gentamicin were started given the high suspicion of endocarditis. Blood cultures, valve prosthesis cultures, intraoperative tissue cultures (mass vs thrombus), and RNA assays were all negative for bacterial growth. The pathologic examination of the mitral mass and valve leaflets (Figure 3A) demonstrated a highly cellular epithelioid neoplastic proliferation with abundant foci of necrosis and mitotic figures. The neoplastic cells tested positive for vascular markers such as CD31, D2-40, factor VIII, WT-1, and ERG with immunohistochemical stains. The total proliferative index (Ki67) was 60%. Such findings were compatible with an endothelial angiosarcoma (Figure 3B).

A fluorodeoxyglucose F 18 (FDG)-positron emission tomography/computed tomography scan (Figure 4) was performed after surgery to look for primary tumors. The scan demonstrated bone involvement at first right costal arch (maximum standardized uptake value: 8.4). There was also a cardiac uptake at the left atrial appendage, which was difficult to interpret given the surgical inflammation. Additionally, there were unspecific FDG uptake at D12 and L1 vertebral bodies, interpreted as fractures. So, the FDG-positron emission tomography findings were not clearly related to the tumor (Video 2). Magnetic resonance imaging showed compression fracture of the L1 vertebral body and degenerative changes in the lumbar spine. The Sarcoma Committee ruled out distant disease. Antibiotic treatment was discontinued and paclitaxel treatment was initiated.

FIGURE 3 Histological Findings



(A) Histological findings revealed a highly cellular neoplastic proliferation with epithelioid morphology and abundant necrosis (hematoxylin and eosin stain). The cells are large, with abundant cytoplasm and severe nuclear atypical features such as irregular membranes, conspicuous nucleoli, and pleomorphism. (B) The mean Ki67 proliferation index is >50%. In this field, the Ki67 proliferative index is ~70% (original magnification: 200×). (C) Diffuse neoplastic proliferation of epithelioid cells with marked atypia and frequent mitotic activity (hematoxylin and eosin, original magnification: 400×). (D) Immunohistochemical staining showed that the neoplastic cells were positive for vascular markers such as D2-40 (original magnification: 400×), (E) WT-1 (original magnification: 400×), and (F) ERG (original magnification: 400×).

DISCUSSION

Cardiac masses are space-occupying lesions located within the cardiac cavities or adjacent to the pericardium. Some cardiac masses are more frequently diagnosed such as clots, vegetations, and common benign tumors such as myxomas. Malignant primary or metastatic tumors are extremely rare. Cardiac angiosarcoma is an uncommon malignant that accounts for approximately 25%-30% of all primary cardiac malignancies. It is considered to be the most fatal and aggressive primary cardiac malignancy.[1]

In patients with prosthetic valves, the most important etiologies of cardiac masses within the valve apparatus are either thrombus or vegetations. Our patient did not report fever, chills, or any other signs suggestive of infection (ie, endocarditis). The patient had a biological mitral prosthesis and a history of atrial fibrillation with poor anticoagulation control, so the clinical presentation was highly suggestive of prosthesis valve thrombosis. However, the macroscopical surgical findings were not compatible with thrombus, so the main diagnosis was ruled out in the operating room. The cardiac mass was located within the biological prosthetic mitral valve leaflets, and the macroscopical appearance was very similar to endocarditis vegetations. There were no other masses identified in any additional cardiac tissues.

Patients with cardiac prosthesis are at risk of endocarditis and the nonspecific, indolent, and subtle history of the patient, ruled in subacute endocarditis once again. The mass was sent to the microbiology department, so that bacterial or fungal cultures could guide antibiotic treatment. The cardiology department started empirical parental antibiotics.

The histopathological result was very unexpected, as the final diagnosis was cardiac angiosarcoma, especially when the mass anatomically directly originated in the prosthetic tissue. Tumors located in foreign vascular materials are, to our knowledge, exceptional. There is a single case reported of a sarcoma associated with silver-coated mechanical heart valve prosthesis in 2001 by Grubitzsch et al.[2] In fact, sarcomas associated with bioprosthetic valves have not been described. It is impossible to speculate about any cause-and-effect relationship and potential mechanisms, because it is a single case. Still, it is well known that degeneration of bioprosthetic valves is an irreversible process that involves the host immune response. Inflammation predisposes to the development of cancer and promotes all stages of tumorigenesis. This could have been the trigger for

malignant cell growth in our patient. Nevertheless, the tumorigenesis mechanisms are incompletely unknown.

The differential diagnosis for cardiac sarcomas includes thrombus, vegetations (ie, endocarditis), metastases, and other causes of intracardiac masses. In our patient, the cardiac mass final and unpredictable diagnosis was angiosarcomas, which gives more uncertainty about the origin of the tumor and whether we achieved a free margin resection only by resecting the evident mass and replacing the valve. Given the imaging findings, it is most likely that the cardiac mass was a primary tumor and not a metastasis.

In reference to the patient prognosis, Blindaru et al[3] reported a case of surgical resection of a giant cardiac angiosarcoma before even initiating chemotherapy because of the patient's hemodynamic instability. They concluded that surgical treatment should be an important alternative when functionality is not affected by complete surgical resection. Surgical resection with an R0 margin is considered the goal; however, chemotherapy and radiotherapy postsurgery may improve the outcomes.[4] In our case, it is not possible to determine whether a complete resection was achieved because the presurgical diagnosis was not angiosarcoma, and we did not assess disease-free margins.

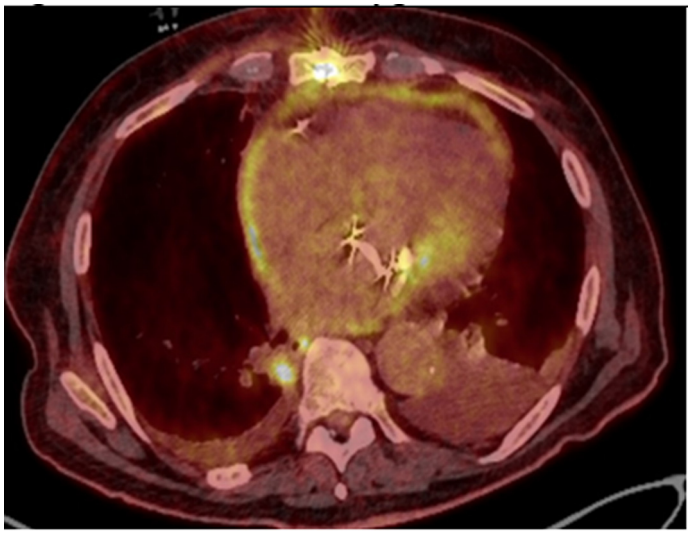
In our patient, the entire mass was resected; therefore, we believe a macroscopically complete and free margin was achieved. It was not necessary to perform reconstruction of structures as the tumor was in the atrial area of the 25-mm Perimount Magna Ease bioprosthetic mitral valve, and it was entirely replaced with a 27-mm St Jude MS mechanical mitral valve.

Postoperative treatment often includes chemotherapy and radiotherapy to control tumor growth and manage metastases. Combining these therapies with surgery can provide palliative benefits and potentially extend survival. In fact, a systematic literature review has found that median overall survival increased from 6 months with surgery alone to 13 months and 27 months with adjuvant chemotherapy and chemoradiotherapy, respectively.[5] Our patient is currently receiving postoperative treatment with paclitaxel.

FOLLOW-UP

The patient was transferred to the oncology department the same day the diagnosis was made. After an improvement of renal function, the patient was a candidate for the second-line treatment of angiosarcoma. The patient had no tumor-related symptoms apart from asthenia, anorexia, and pain. He started chemotherapy with paclitaxel. The patient remained alive and disease-free 3 months after the procedure.

FIGURE 4 Fluorodeoxyglucose F 18-Positron Emission Tomography



Postsurgery fluorodeoxyglucose F 18-positron emission tomography showing bone uptake that was not correlated with metastasis later on.

CONCLUSIONS

Cardiac masses are rare, but can include benign tumors, malignant tumors (primary and secondary) and tumor-like conditions such as thrombus or vegetations. We have learned cardiac tumors should be part of the differential diagnosis of any space-occupying mass; however, angiosarcoma in a biological prosthetic valve is an unpredictable diagnosis. Surgical resection is the gold standard and most important prognostic factor for angiosarcoma treatment. Overall, whereas surgical resection combined with adjuvant therapies offers the best available option, the prognosis for cardiac angiosarcoma remains poor.

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KEY WORDS cancer, imaging, mitral valve, nuclear medicine, positron emission tomography, postoperative, thrombosis, valve replacement

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