

Metastatic pleomorphic sarcoma to left atrium

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Abstract

Although several thousand patients are diagnosed with sarcoma annually in the United States, metastases to the heart are very uncommon. In this case report, an overall low frequency cancer presents masquerading with common cardiac symptomology. This case illustrates the importance for detailed diagnostic cardiac evaluations and heightened suspicion by physicians to consider metastatic disease to the heart in cancer patients with cardiovascular complications. Also discussed is a review of surgical and chemotherapeutic options for this problem.

Introduction

A 53-year-old Caucasian gentleman presented with progressive lower back pain, urinary and bowel incontinence, and lower extremity swelling over a one month period. He had been diagnosed six months prior at an outside institution with a high-grade pleomorphic sarcoma with focal myxoid and epithelioid elements of the duodenum. Small bowel resection was performed because of bowel obstruction. Perioperatively, the patient suffered a myocardial infarction (MI) due to focal narrowing of the left anterior descending artery and a drug-eluting stent was placed during cardiac catheterization. Post-operative transthoracic echocardiogram (TTE) was interpreted as mild mitral valve thickening, with flail chordae tendineae and an estimated ejection fraction of 35-40%. After discharge, the patient was lost to follow-up.

Case Report

On presentation to our facility, physical examination revealed normal lower extremity

strength, focal tenderness over the sacrum, pitting edema in the lower extremities and a murmur of mitral regurgitation with basilar crackles and dullness. Computed tomography (CT) showed a wedge-shaped splenic infarct and magnetic resonance imaging (MRI) of the spine demonstrated osseous metastatic disease involving the vertebral bodies, with epidural and neuroforaminal tumor extension in the sacrum. A TTE was performed in anticipation of chemotherapy with adriamycin and revealed a large vegetation attached to the anterior leaflet of the mitral valve with prolapse into the left atrium and ventricle (Figure 1A, arrow) and hypoechoic regions within the cardiac tissue (Figure 1A, arrowhead). The patient was taken to the operating room to remove the vegetation, biopsy the hypoechoic mass and replace the mitral valve. A 9 cm vegetation was excised from the anterior mitral valve leaflet (Figure 1B, left and middle). Intraoperatively, the patient was noted to have diffuse disease throughout the atrial septum and mitral valve (Figure 1B, right) and the procedure was terminated. Post-operative cardiac MRI showed a lobulated cardiac mass infiltrating the atrial septum, the posterior aortic wall and the posterior aspect of the anterior mitral valve annulus. In the axial plane, the mass measured at least 5.3 x 2.2 cm and extended to the superior portion of the left atrium near the entry of the right superior pulmonary vein (Figure 1C; mass indicated with arrowheads). Histology of the atrial mass revealed a high-grade pleomorphic sarcoma, metastatic to heart. Low power frozen sections of the atrial wall showed hypercellularity (Figure 2A). Medium and high power frozen (Figure 2B and C) and permanent (Figure 2D) sections showed tumor giant cells (indicated with arrowheads) among spindled and epithelioid

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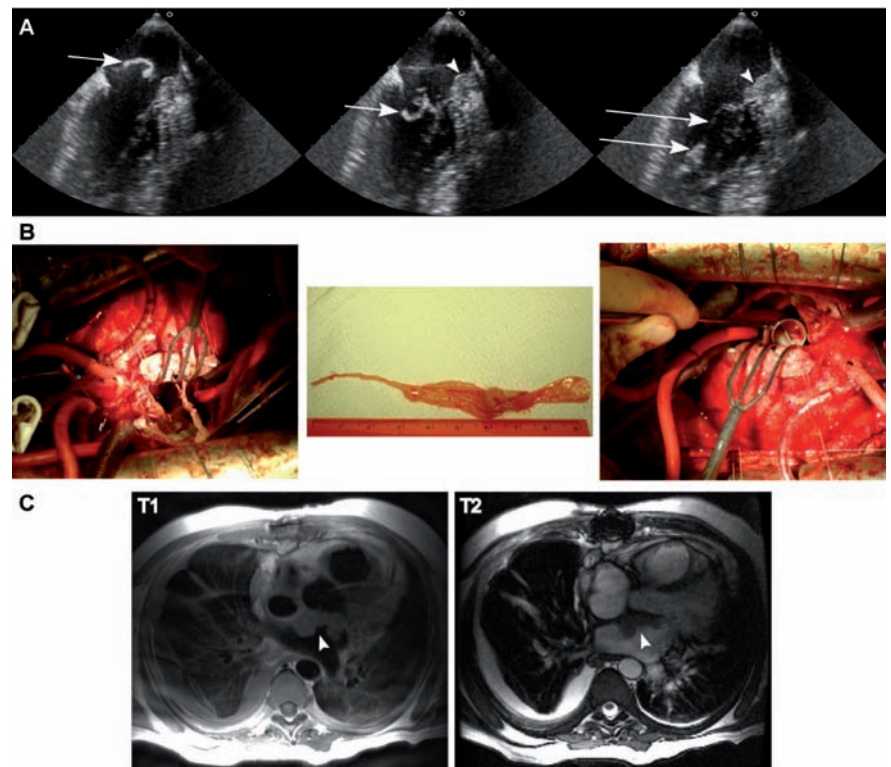


Figure 1. Echocardiography (A) performed before excision of vegetation (B) and post-operative cardiac MRI (C).

tumor cells. The atrial mass was immunohistochemically positive for vimentin, confirming mesenchymal differentiation (Figure 2E). Immunohistochemical stains for other markers, including CD117, AE1/AE3, desmin, myogenin, caldesmon, S100, HMB-34, calretinin, CD31 and CD34 were negative (Figure 2F).

A diagnosis of metastatic cardiac sarcoma was established and treatment with gemcitabine and docetaxel was initiated. Adriamycin-based therapy was not considered secondary to the patient's reduced cardiac function (37% ejection fraction). Five weeks after initiating chemotherapy, the patient was admitted for worsening lower extremity edema but denied shortness of breath, orthopnea, paroxysmal nocturnal dyspnea, chest pains, palpitations, weight gain, or symptoms of transient ischemic attacks. Electrocardiogram revealed atrial flutter at 119 beats per minute with 2:1 block and the old anterolateral infarct. The patient declined cardioconversion and was treated with amiodarone. At the time of preparation of this report, the patient was tolerating palliative gemcitabine and docetaxel chemotherapy.

Discussion

Soft-tissue sarcomas are a diverse mix of cancers with an incidence of 10,390 new cases diagnosed annually in the United States.¹ Despite aggressive treatment with surgery, radiation and chemotherapy, outcomes remain suboptimal as 3,680 (35%) soft-tissue sarcoma patients die annually.¹ Death secondary to metastases is common and sites of metastases vary depending on the type of soft-tissue sarcoma with most types showing a predilection for the lungs. Metastatic involvement of the heart by soft-tissue sarcoma has been reported in the literature but most cases of cardiac involvement occur in the setting of widespread metastases.² Our patient is among the first reported cases of an epithelioid high-grade pleomorphic sarcoma metastatic to the heart in absence of known widespread metastases.

Familiarity with the unique characteristics of the soft-tissue sarcomas will enable a physician to identify expected patterns of metastatic spread. One should be suspicious of cardiac metastases in a soft-tissue sarcoma patient who suddenly develops unexplained congestive heart failure, new cardiac murmurs, arrhythmias or embolic phenomena. For such patients, metastatic cardiac disease should be included in the differential diagnosis and further evaluation with electrocardiograms, echocardiograms, and cardiac MRI should be made. Accurate imaging of cardiac cancer is very important in the multimodal medical and surgical management of metastatic cardiac

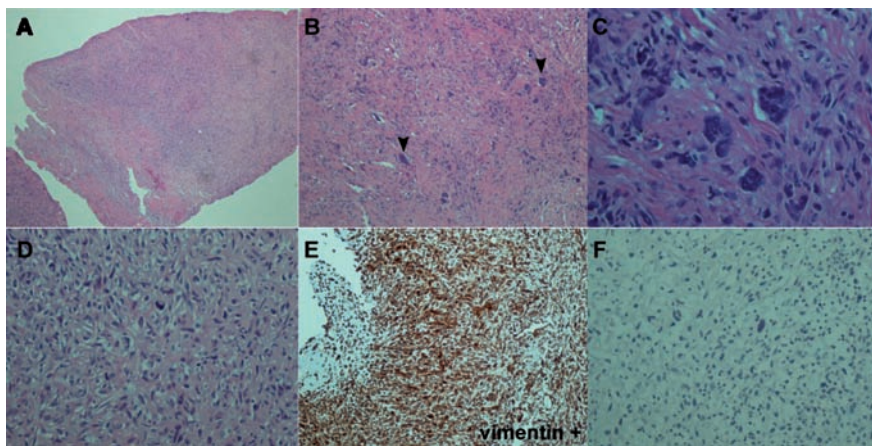


Figure 2. Histology of atrial mass.

sarcoma.³ In this patient, cardiac metastasis was only incidentally discovered during pre-chemotherapy cardiac evaluation. However, several aspects of this patient's clinical course suggested the presence of this diagnosis. The patient's initial myocardial infarction prompted cardiac catheterization, which showed luminal narrowing assumed to be secondary to atherosclerotic disease. Yet, on repeat studies, the patient had no evidence of significant atherosclerotic disease. The patient's infarct likely resulted from an embolic event originating from the large mitral valve vegetation or from extrinsic compression of the artery by tumor. The splenic lesions noted on CT scans likely represent distant emboli with infarction. Finally, review of the outside hospital TTE abnormalities noted after the patient's perioperative MI indicated that he had cardiac metastases at initial presentation. A high degree of suspicion for cardiac involvement by sarcoma may have hastened a correct diagnosis.

Conclusions

Management of metastatic sarcoma to the heart remains a difficult task. Some reports discuss surgical resection of cardiac metastatic lesions with variable success,^{4,5} while others report the use of cardiac transplantation.⁶ In this case, surgical excision was attempted, but the extensive infiltrating nature of the tumor prohibited complete debridement leaving systemic therapy as the only viable option. There are several generally accepted systemic therapies for metastatic sarcoma with most regimens including doxorubicin as a single agent⁷ or in combination with other drugs. The most widely employed combination chemotherapy regimens are doxorubicin/dacarbazine,^{8,9} doxorubicin/ifosfamide/mesna^{10,11} mesna/doxorubicin/ifosfamide/dacarbazine,¹² ifosfamide/epi-

rubicin/mesna,¹³ and gemcitabine/docetaxel.¹⁴⁻¹⁶ However, the use of doxorubicin was felt to be contraindicated due to the depressed cardiac function in this patient. If a sarcoma expresses CD117, imatinib would be a viable treatment option due to the drug's oral administration, favorable toxicity profile, and anti-tumor activity on some subsets of sarcoma, particularly gastrointestinal stromal tumors.¹⁷⁻¹⁹ Expression of this marker is felt to be favorable due to this relationship. Thus far, reports do not associate imatinib with induction of cardiac failure.²⁰ Unfortunately our patient's cardiac tumor did not express CD117 and the drug was not a treatment option. Since metastatic sarcoma to the heart is a rare occurrence, no prospective or randomized trials exist to help guide treatment. In fact, there are no data to show whether systemic treatment of unresectable cardiac sarcomas significantly improves duration or quality of life. In the setting of congestive or restrictive heart failure, many of the first-line chemotherapy options are not feasible for fear of therapy worsening cardiac function. In our case, gemcitabine/docetaxel chemotherapy was felt to be an active regimen with controllable toxicity and without potential devastating cardiac side effects. Tolerance to the treatment regimen thus far has been acceptable and the patient is continuing this chemotherapy.

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