Cardiac pleomorphic sarcoma after placement of Dacron graft

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Primary cardiac tumors, either benign or malignant, are very rare. The combined incidence is 0.002% on pooled autopsy series.[1] The benign tumors account for 63% of primary cardiac tumors and include myxoma, the most common, and followed by papillary fibroelastoma, fibroma, and hemangioma. The remaining 37% are malignant tumors, essentially predominated by sarcomas.[1]

Although myxoma is the most common tumor arising in the left atrium, we present a case that shows that sarcoma can also arise from the same chamber. In fact, sarcomas could mimic cardiac myxoma.[2] The cardiac sarcomas can have similar clinical presentation and more importantly can share similar histopathological features. Sarcomas may have myxoid features.[2] Cases diagnosed as cardiac myxomas should be diligently worked up to rule out the presence of sarcomas with myxoid features. In addition, foreign bodies have been found to induce sarcomas in experimental animals.[3,4] In particular, 2 case reports have described sarcomas arising in association with Dacron vascular prostheses in humans.[5,6] We present here the case of a patient who was diagnosed with cardiac pleomorphic sarcoma 8 years after the placement of a Dacron graft.

Case presentation and summary

A 56-year-old woman with history of left atrial myxoma status after resection in 2005 and placement of a Dacron graft, morbid obesity, hypertension, and asthma presented to the emergency department with progressively worsening shortness of breath and blurry vision over period of 2 months. Acute coronary syndrome was ruled out by electrocardiogram and serial biomarkers. A computed-tomography angiogram was pursued because of her history of left atrial myxoma, and the results suggested the presence of a left atrial tumor. She underwent a transesophageal echocardiogram, which confirmed the presence of a large left atrial mass that likely was attached to the interatrial septum prolapsing across the mitral valve and was suggestive for recurrent left atrial myxoma (Figure 1). The results of a cardiac catheterization showed normal coronaries.

The patient subsequently underwent an excision of the left atrial tumor with profound internal and external myocardial cooling using antegrade blood cardioplegia under mildly hypothermic cardiopulmonary bypass. Frozen sections showed high-grade malignancy in favor of sarcoma. The hematoxylin and eosin stained permanent sections showed sheets of malignant pleomorphic spindle cells focally arranged in a storiform pattern. There were areas of necrosis and abundant mitotic activity. By immunohistochemical (IHC) stains, the tumor cells were diffusely positive for vimentin, and negative for pancytokeratin antibody (AE1/AE3), S-100 protein, Melan-A antibody, HMB45, CD34, CD31, myogenin, and MYOD1. IHC stains for CK-OSCAR, desmin, and smooth muscle actin were focally positive, and a ki-67 stain showed a proliferation index of about 80%. The histologic and IHC findings were consistent with a final diagnosis of high-grade undifferentiated pleomorphic sarcoma (Figure 2).

A positron emission tomography scan performed November 2013 did not show any other activity. The patient was scheduled for chemotherapy with adriamycin and ifosfamide with a plan for total of 6 cycles. Before her admission for the chemotherapy, the patient was admitted to the hospital for atrial fibrillation with rapid ventricular response and had multiple complications requiring prolonged hospitalization and rehabilitation. Repeat imaging 2 months later showed diffuse metastatic disease.

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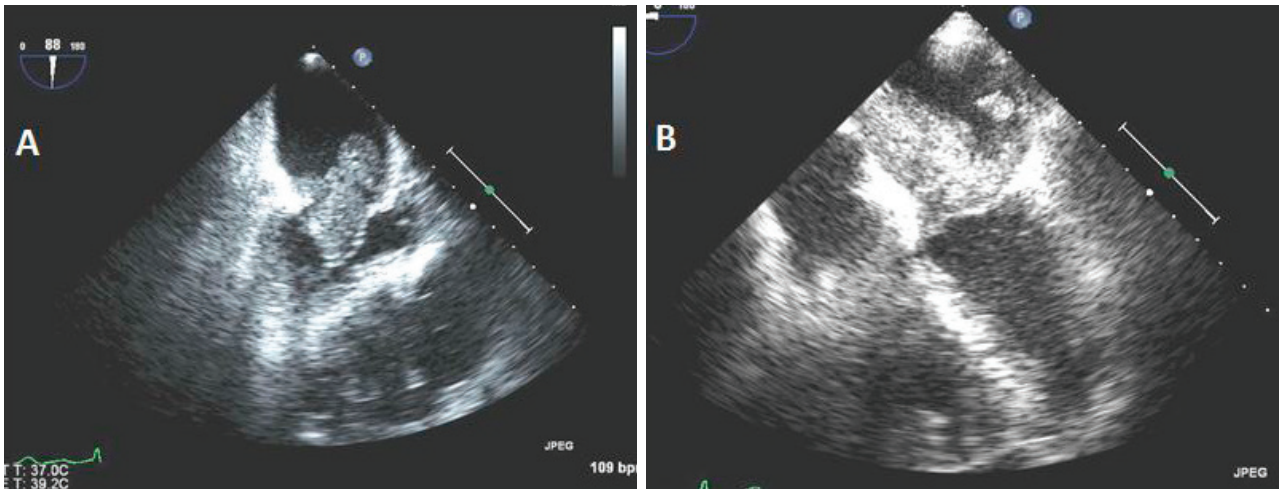

FIGURE 1 A transesophageal echocardiogram confirmed the presence of a large left atrial mass: **A,** 2 chamber view, and **B,** 4 chamber view.

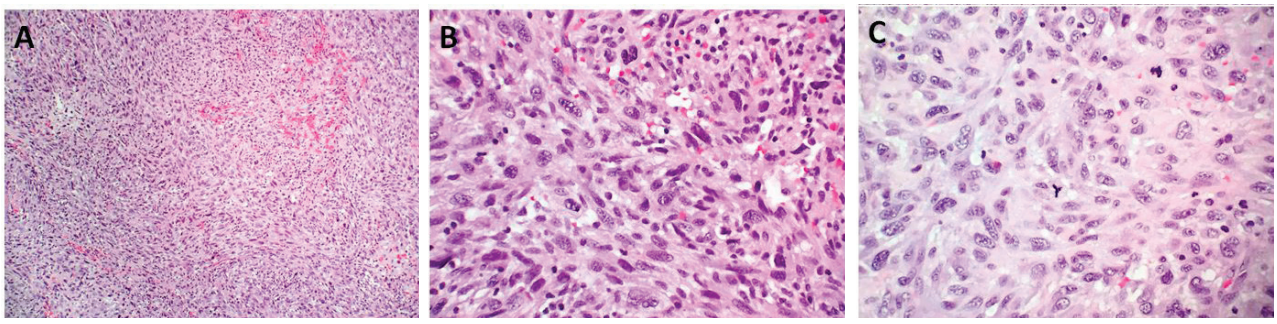

FIGURE 2 Undifferentiated pleomorphic sarcoma showing: **A,** pleomorphic spindle cells arranged in a storiform pattern (H&E, x100); **B,** markedly pleomorphic spindle cells at high magnification (H&E, x400); **C,** an atypical mitotic figure in the center (H&E, x400).

However, her performance status had declined and she was not eligible for chemotherapy. She was placed under hospice care.

Discussion

This case demonstrates development of a cardiac pleomorphic sarcoma, a rare tumor, after placement of a Dacron graft. Given that foreign bodies have been found to induce sarcomas in experimental animals,[3,4] and a few case reports have described sarcomas arising in association with Dacron vascular prostheses, [5-10] it seems that an exuberant host response around the foreign body might represent an important intermediate step in the development of the sarcoma.

There is no clearly defined pathogenesis that explains the link between a Dacron graft and sarcomas. In 1950s, Oppenheimer and colleagues described the formation of malignant tumors by various types of plastics, including Dacron, that were embedded in rats. [3,4] Most of the tumors were some form of sarcomas. It was inferred that physical properties of the plastics may have some role in tumor development. Plastics in sheet form or film that remained in situ for more than 6 months induced significant number of tumors compared with other forms such as sponges, films with holes, or powders.[3,4] The 3-dimensional polymeric structure of the Dacron graft seems to play a role in induction of sarcoma as well. A pore diameter of less than 0.4 mm may increase tumorigenicity.[11] The removal of the material before the 6-months mark does not lead to malignant tumors, which further supports the link between Dacron graft and formation of tumor. A pocket is formed around the foreign material after a certain period, as has been shown in histologic studies as the site of tumor origin.[9,10]

At the molecular level, the MDM-2/p53 pathway has been cited as possible mechanism for pathogenesis of intimal sarcoma.[12,13] It has been suggested that endothelial dysplasia occurs as a precursor lesion in these sarcomas.[14] The Dacron graft may cause a dysplastic effect on the

endothelium leading to this precursor lesion and in certain cases transforming into sarcoma. Further definitive studies are required.

The primary treatment for cardiac sarcoma is surgical removal, although it is not always feasible. Findings in a Mayo clinic study showed that the median survival was 17 months for patients who underwent complete surgical excision, compared with 6 months for those who complete resection was not possible.[15] In addition, a 10% survival rate at 1 year has been reported in primary cardiac sarcomas that are treated without any type of surgery.[16]

There is no clear-cut evidence supporting or refuting adjuvant chemotherapy for cardiac sarcoma. Some have inferred a potential benefit of adjuvant chemotherapy although definitive conclusions cannot be drawn. The median survival was 16.5 months in a case series of patients who received adjuvant chemotherapy, compared with 9 months and 11 months in 2 other case series.[17,18,19] Multiple chemotherapy regimens have been used in the past for treatment. A retrospective study by Llombart-Cussac colleagues, analyzed 15 patients who had received doxorubicin-containing chemotherapy, in most cases combined with ifosfamide or dacarbazine. [20] Resection was complete in 6 patients and incomplete in 9. The patients were given chemotherapy within 6 weeks of surgery. Five patients developed metastatic disease during therapy. The median interval to first relapse was 10 months and overall median survival was 12 months in these patients.[20] Other regimens that have been used for treatment are mitomycin, doxorubicin, and cisplatin (MAP); doxorubicine, cyclophosphamide, and vincristine (DCV); ifosfamide and etoposide (IE); ifostamide, doxorubicin, and decarbazine; doxorubicin and paclitaxel, and paclitaxel alone.[4] Of those, a patient with on the IE survived the longest, 32 months.

Radiation showed some benefit in progression-free survival in a French retrospective study.[21] Radiation therapies have been tried in other cases, as well in addition to chemotherapy. However, there is not enough data to support or refute it at this time.[15,17,20] Several sporadic cases reported show benefit of cardiac transplantation.[21,22]

Conclusion

In consideration of the placement of the Dacron graft 8 years before the tumor occurrence, the anatomic proximity of the tumor to the Dacron graft, and the association between sarcoma with Dacron in medical literature, it seems logical to infer that this unusual malignancy in our patient is associated with the Dacron prosthesis.

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