

Recurrent Undifferentiated Pleomorphic Sarcoma in the Left Atrium



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INTRODUCTION

Primary malignant tumors represent a substantial minority of the masses in the heart, although metastatic disease is more common. They exhibit nonspecific symptoms and presentation usually occurs in the later stages of the disease. The initial diagnostic approach is to use transthoracic echocardiogram, and other advanced imaging techniques, such as cardiac computed tomography and magnetic resonance imaging, may provide further anatomic and tissue characterization. The overall prognosis is poor even with surgical resection. We present a case of a very aggressive malignant primary cardiac tumor with early recurrence despite surgical resection.

CASE PRESENTATION

A 31-year-old male patient presented with a 9-month history of weight loss, malaise, weakness, and worsening functional class (New York Heart Association III–IV), productive cough with clear sputum without fever, presyncopal episodes, palpitations, and more recently right-sided amaurosis fugax. This particular symptom was the main reason for visiting the emergency department.

On admission, physical examination showed blood pressure of 120/80 mm Hg, a heart rate of 98 beats/min, a respiratory rate of 21 breaths/min, oxygen saturation of 93% on room air, rapid heart sounds, a grade II/VI systolic ejection murmur with an early diastolic rumble, clear lung fields, no abdominal abnormalities, no pitting edema, and normal neurologic findings without significant visual impairment.

Basic laboratory tests showed hemoglobin of 8.9 g/dL with normal electrolyte levels and renal function. The patient was in sinus rhythm at the time of admission. Initially, chest computed tomography was negative for pulmonary embolism but showed a mass located in the left atrium (Figure 1).

Transthoracic echocardiography (TTE) demonstrated normal left ventricular function and severe left atrial enlargement with a giant mass protruding into the left ventricle and causing severe functional mitral valve stenosis (Videos 1–3, Figure 2).

TTE also showed right ventricular dilatation with moderate systolic dysfunction (Video 4), severe tricuspid insufficiency, and severe pulmonary hypertension with pulmonary artery systolic pressure of

100 mm Hg (Figure 3). Differential diagnosis included myxoma, thrombus, or malignant tumor. The lack of septal attachment made the diagnosis of myxoma less likely.

Because the patient was experiencing a transient ischemic attack with imminent risk for systemic embolization and worsening functional class, he was taken for emergent surgery the day after admission. Surgical findings included a large infiltrative mass of 5 × 5 cm with irregular borders that originated in the lumen of the left inferior pulmonary vein, which was patent (Figure 4). The mass was resected, and the mitral valve was repaired with annuloplasty (moderate mitral regurgitation was present during perioperative transesophageal echocardiography; no data on mitral valve gradient after the initial repair were available). There was no reconstruction of the pulmonary veins.

Histologic examination demonstrated a poorly differentiated high-grade malignant tumor with evidence of epithelioid and spindle-shaped cells with marked atypia and nuclear pleomorphism, abundant atypical mitosis, extensive necrosis, and hemorrhage. The histologic picture corresponded to a poorly differentiated tumor with a high degree of malignancy (Figure 5). Immunohistochemical study reported an undifferentiated pleomorphic sarcoma.

Hematology/oncology was consulted to start adjuvant chemotherapy, but just 1 month after discharge the patient was readmitted because of myalgia of the upper and lower extremities associated with headache and palpitations. New TTE showed a solid mass with ovoid morphology of 3.7 × 3.6 cm adhered to the lateral and posterior aspect of the left atria adjacent to the mitral valve ring, resulting in severe mechanical obstruction with a mean gradient of 23 mm Hg associated with moderate regurgitation and pulmonary artery systolic pressure of 100 mm Hg in addition to moderate right ventricular dysfunction (Videos 5–7, Figures 6 and 7). It was considered recurrence of the pleomorphic sarcoma.

Because of rapid recurrence, the patient was transferred to palliative care and died 4 weeks after the second TTE.

DISCUSSION

Primary malignant cardiac tumors are rare and usually fatal. The prognosis of these lesions remains bleak despite newer imaging modalities. The reasons for this discouraging prognosis include the advanced staging of the tumor when clinically evident, associated with nonspecific symptoms. Also, there is a lack of knowledge regarding optimal therapy, although it is very rare, and it is usually too late for chemotherapy or radiation treatment when diagnosed.¹

Given the low incidence of this particular condition, there are no studies that report predisposing factors for undifferentiated pleomorphic sarcoma. Likewise, there is no hypothesis regarding why it originates in the pulmonary veins. Studies have focused on reporting the presentation, diagnosis, management, and follow-up of these patients.

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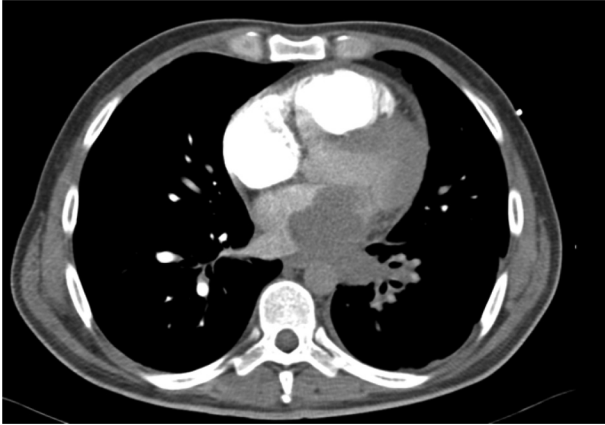


Figure 1 Axial reconstruction of computed tomography showed a mass with irregular contours attached to the left inferior pulmonary vein protruding into the mitral valve.

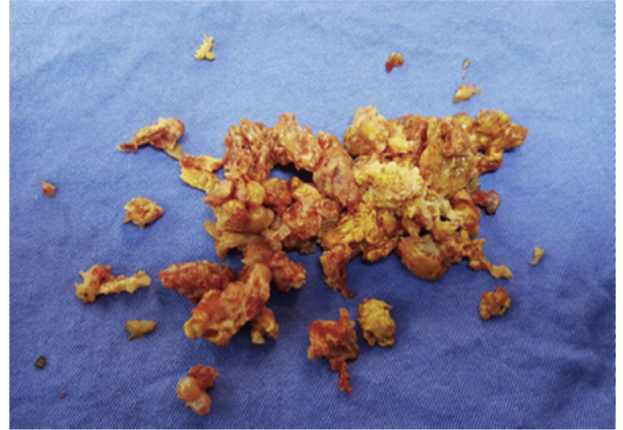


Figure 4 Gross specimen of the mass excised with irregular borders.

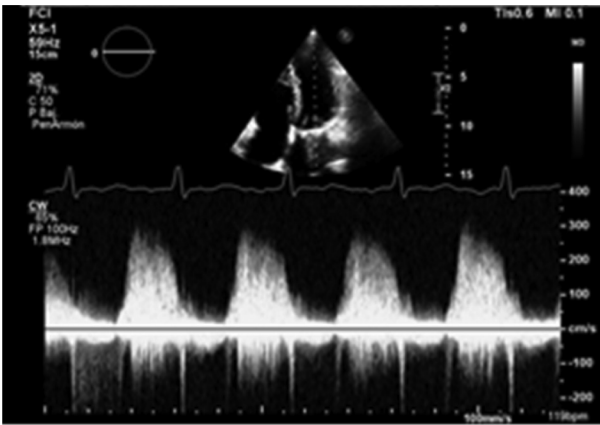


Figure 2 Increased transmittal mean gradient of 14 mm Hg.

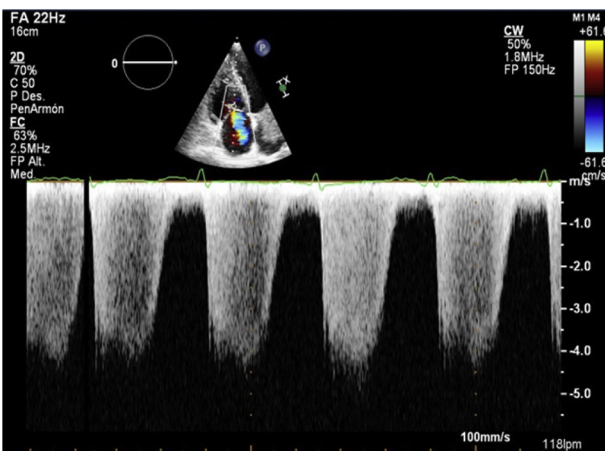


Figure 3 Continuous-wave Doppler at the tricuspid valve showing severe pulmonary hypertension with pulmonary artery systolic pressure of 100 mm Hg.

According to Simpson *et al.*² at the Mayo Clinic Cancer Center, during a 32-year follow-up of malignant primary heart tumors, only 6% had poorly differentiated sarcomas. These results contrast the findings of a retrospective French study of the Sarcoma Group with

a follow-up period of 33 years, in which 36% of all tumors were poorly differentiated sarcomas.³ This information could suggest a hypothesis regarding genetic and environmental predisposition in the European population for this particular type of tumor.

This particular type of sarcoma occurs in adults, without gender predilection, and can appear in any heart chamber,⁴ although they occur more frequently in the left atrium, as evidenced by the study by Simpson *et al.*,² in which the majority of localization was in the left atrium (47%), followed by the right atrium (21%).

Dyspnea on exertion was the most frequent symptom, presenting in 79% of cases, followed by chest pain (38%), cough (21%), hemoptysis (12%), embolic events (9%), and syncope (6%).^{2,5,6} Findings on TTE were abnormal in all 34 patients in the Mayo Clinic review, showing cardiac masses in 30 patients and pericardial effusion in the remaining four patients.² Intracavitary location of the tumor may cause obstruction to the heart valves, as was noticeable in our patient, with a high gradient across the mitral valve resulting in severe pulmonary hypertension. Depending on the location of sarcoma, a variety of manifestations may present, including heart failure, second- or third-degree atrioventricular block, atrial tachycardia, and stroke.⁶

TTE plays a very important role in the diagnosis of this pathology, allowing the detection of predictive features of malignancy such as location in the right- or left-sided chambers, broad base, infiltration of adjacent structures, and pericardial effusion.

There are other complementary diagnostic methods, such as magnetic nuclear imaging, which shows greater sensitivity and specificity for cardiac masses.⁷ For cardiac sarcomas, classic magnetic resonance imaging findings include isointensity in T1-weighted images, hyperintensity in T2-weighted images, and variable late gadolinium enhancement distribution.

The histologic diagnosis of sarcomas can be difficult and requires expertise and the availability of immunohistochemical analysis.⁷

The optimal treatment approach for this type of cancer is not standardized. Complete surgical removal should be performed if possible. Surgery is often palliative to ameliorate obstruction, and adjuvant chemotherapy and radiotherapy have been reported to prolong survival but rarely provide cure.⁶

Cardiac sarcomas rapidly infiltrate all layers of the heart and further invade adjacent mediastinal structures. Donsbeck *et al.*⁴ reported that metastases were the cause of the death in 25% of cases, and the most common cause of death (50%) was local recurrence of the tumor.

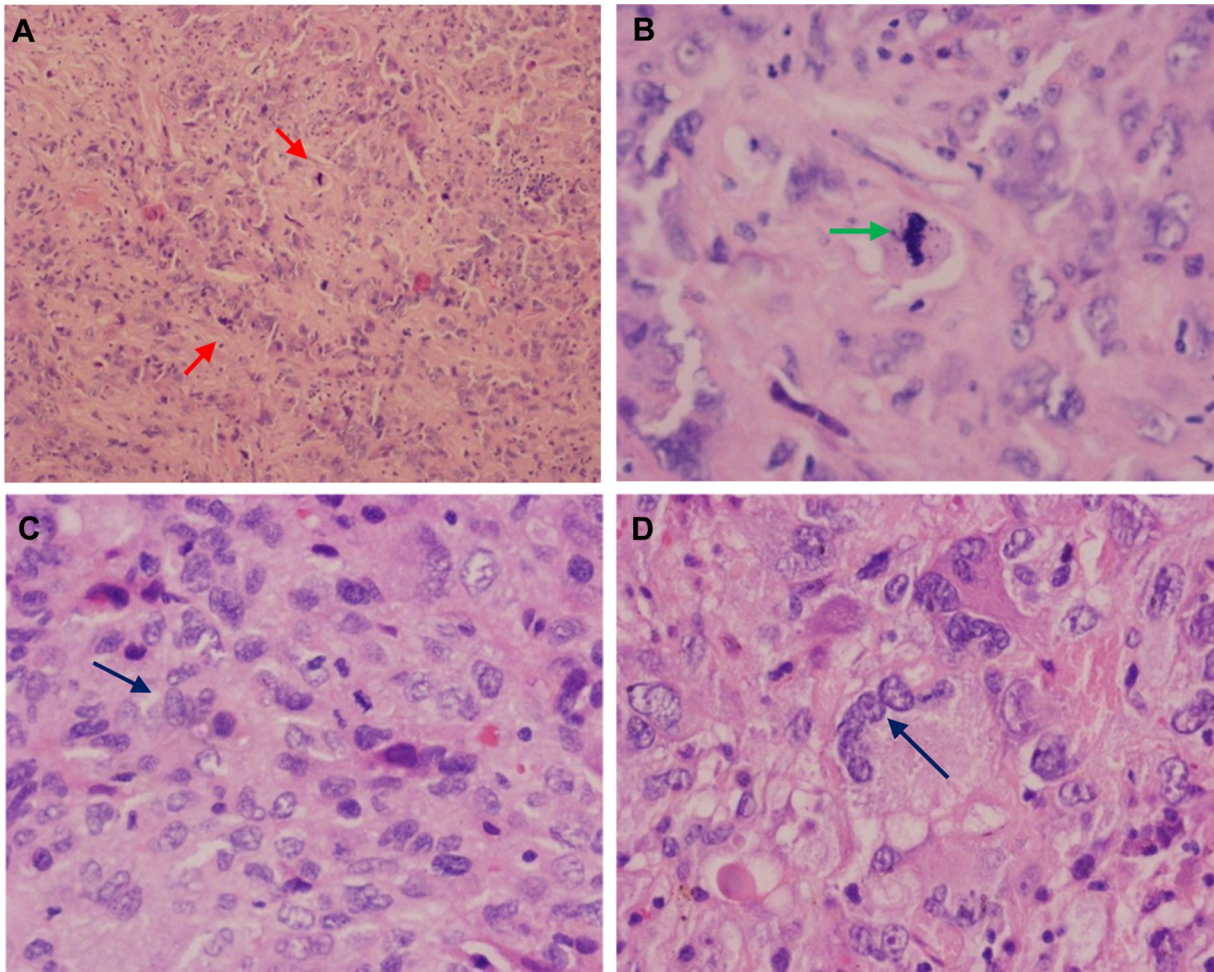


Figure 5 (A) Hematoxylin and Eosin, 10 \times : high-grade tumor lesion, cells with marked atypia and nuclear pleomorphism with abundant atypical mitosis (red arrow). (B) Hematoxylin and eosin, 40 \times : nuclear pleomorphism, atypical mitosis (green arrow). (C,D) Hematoxylin and eosin, 40 \times : giant multinucleated tumor cells and bizarre nucleus (blue arrow).

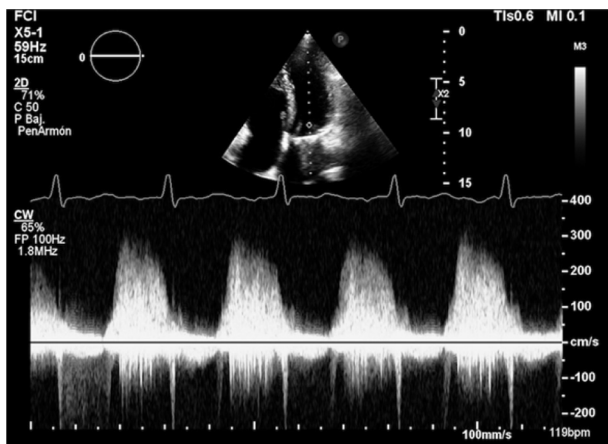


Figure 6 Increased transmittal mean gradient of 23 mm Hg.

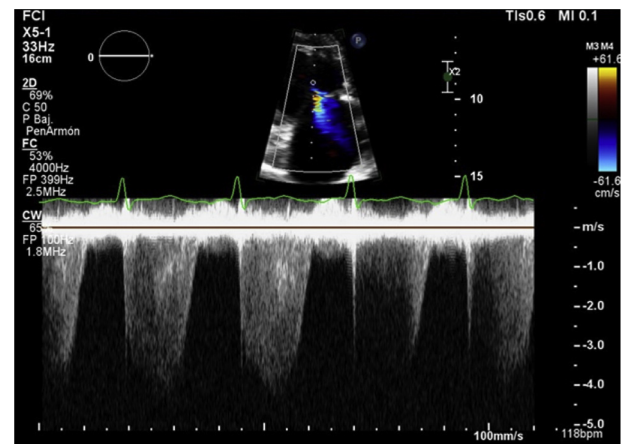


Figure 7 Continuous-wave Doppler at the tricuspid valve showing moderate pulmonary hypertension, pulmonary artery systolic pressure 100 mm Hg.

The major problem during surgical treatment of this malignancy is the extensive involvement precluding complete resection, with a high risk for recurrence. An alternative treatment reserved for left-heart sarcomas might be autotransplantation, which consists of removing the heart and resecting the tumor with sufficient margins, followed by re-implantation. This has been performed successfully by well-trained teams with 1.4% operative mortality.³

Cardiac transplantation is an option for inoperable sarcomas but is not routinely considered because of concern for recurrence and the possibility that immunosuppression may stimulate further tumor growth or a new neoplasia.¹

The level of evidence for the optimal multimodality management is low because of disease rarity. Therefore, the optimal management for cardiac sarcomas is often extrapolated from soft-tissue sarcoma therapies.³ So far there is no management protocol or follow-up for these cases, although routine TTE is often recommended every 3 months after surgical resection.

A multimodality treatment, including preoperative and/or postoperative chemotherapy in addition to radiotherapy, was associated with improvement in progression-free survival. Chemotherapy alone was significantly associated with improved survival only in nonoperated patients but not in those with surgical resection.³ Treatment with first-line chemotherapy for undifferentiated pleomorphic sarcoma has been described with doxorubicin plus ifosfamide, and second-line treatment includes trabectedin-gemcitabine plus docetaxel-pazopanib.⁷

The median survival rate, as reported in previous studies, ranged from 6 to 16 months.⁴

CONCLUSION

Primary malignant cardiac tumors are an uncommon and usually fatal pathology. This case is the first one published from Latin America. Its nonspecific clinical presentation and diagnosis in advanced stages of the disease are responsible for its very poor prognosis and high recur-

rence rate, as seen in our patient. The most commonly described symptom is dyspnea, and the most frequent finding on TTE is a mass at the level of the atria, although the tumor may have a different primary location, which may explain other symptoms, such as heart failure and atrioventricular block during presentation. The initial treatment is complete surgical resection, and adjuvant chemotherapy and radiotherapy are often palliative therapeutic options, given that survival after diagnosis is ≤ 1 year.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.case.2017.07.003>.

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