

Title:

Recurrent Undifferentiated Pleomorphic Sarcoma in the Left Atrium.

Case presentation

A 31-year-old male patient presented with a 9-month history of weight loss, malaise, weakness, and worsening functional class NYHA III-IV, productive cough with clear sputum without fever, pre-syncopal episodes, palpitations and more recently right sided amaurosis fugax. This particular symptom was the main reason for visiting the emergency room.

On admission, physical examination showed BP 120/80 mmHg, HR 98 bpm, RR 21, SAO2 93% on room air, rapid heart sounds, II/VI systolic ejection murmur with and early diastolic rumble, clear lung fields, no abdominal abnormalities, no pitting edema and normal neurological exam without significant visual impairment.

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

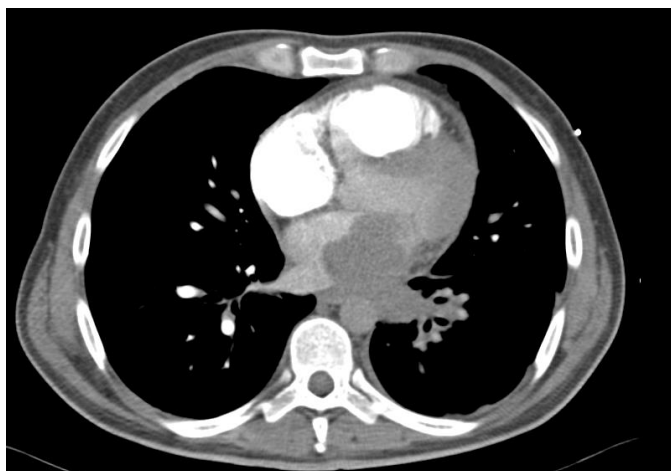


Figure 1. Axial reconstruction of the computed tomography showed a mass with irregular contours attached to left inferior pulmonary vein protruding in the mitral valve

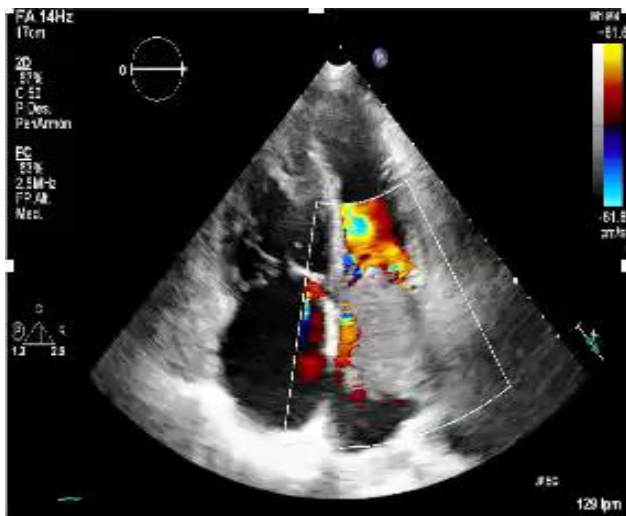
Trans-thoracic echocardiogram (TTE) demonstrated normal left ventricular function, severe left atrial enlargement with a giant mass protruding into the left ventricle and causing severe functional mitral valve stenosis (Video 1, 2, 3). (Figure 2).



Video 1. Parasternal long axis view with evidence of left atrial mass of irregular contours.



Video 2. Apical-4 chamber view showing left atrial mass with severe obstruction of the mitral outflow tract and right ventricular dilatation.



Video 3. Apical-4 chamber view. Mass in the left atrium that protrudes at the level of the mitral valve generating severe mitral stenosis.

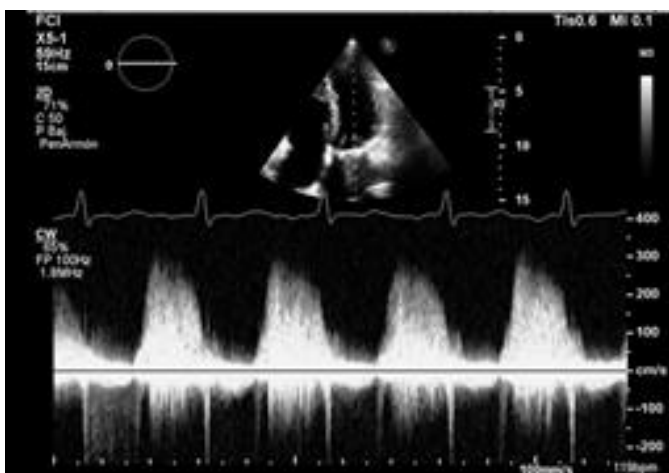
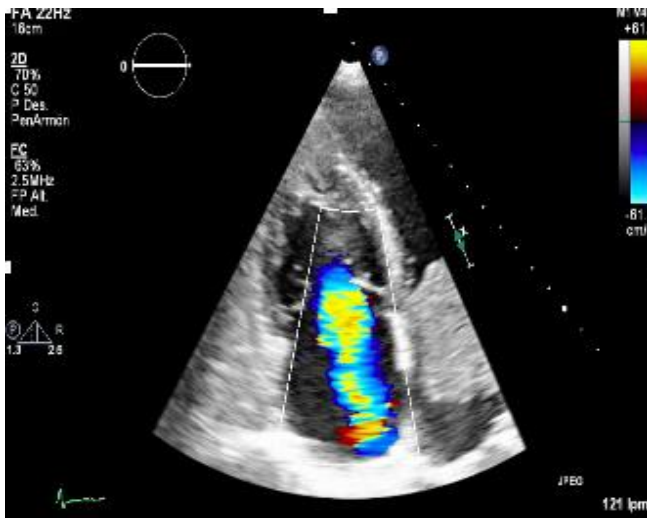


Figure 2. Increased trans-mitral mean gradient of 14 mmHg.

It also showed right ventricular dilatation with moderate systolic dysfunction (Video 4), severe tricuspid insufficiency and severe pulmonary hypertension with pulmonary artery systolic pressure (PSAP) of 100 mmHg. (Figure 3). Differential diagnosis included myxoma, thrombus or malignant tumor. The lack of septal attachment made the diagnosis of myxoma less likely.



Video 4. Apical-4 chamber view. Right ventricular dilatation with moderate systolic and severe tricuspid regurgitation dysfunction.

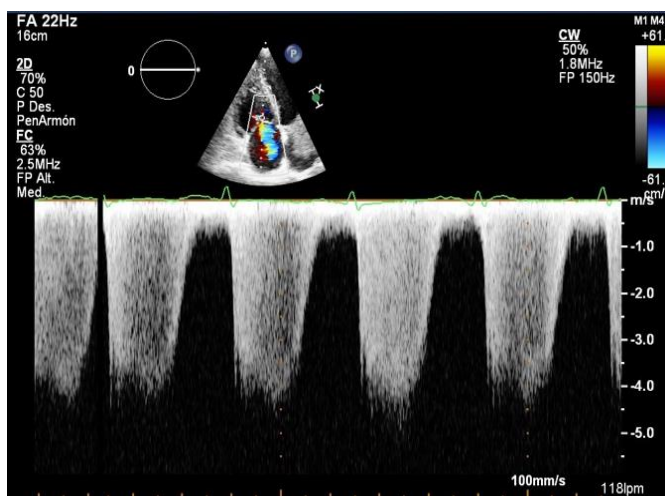


Figure 3. Continuous wave Doppler at the tricuspid valve showing severe pulmonary hypertension with pulmonary artery systolic pressure (PSAP) of 100

mmHg.

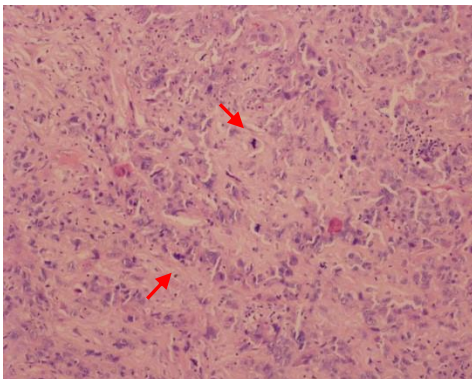
Due to the fact the patient was experiencing transient ischemic attack with imminent risk of systemic embolization and worsening functional class, he was taken to emergent surgery the next day after admission. Surgical findings included a large infiltrative mass of 5 x 5 cm with irregular borders that originated in the lumen of the left inferior pulmonary vein, which was patent (Figure 4). The mass was resected and mitral valve was repaired with annuloplasty (moderate mitral regurgitation was present during peri-operative trans-esophageal echocardiogram. No data on the mitral valve gradient after the initial repair). There was no reconstruction of was the pulmonary vein.



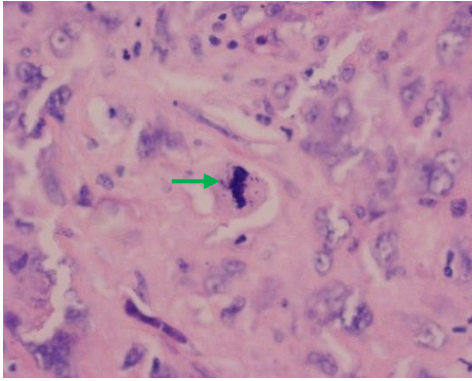
Figure 4. Gross specimen of the mass excised with irregular borders

Histological 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 histological picture corresponded to a poorly differentiated malignant tumor with a high-degree of malignancy (Figure 5). Immunohistochemical study reports undifferentiated pleomorphic sarcoma.

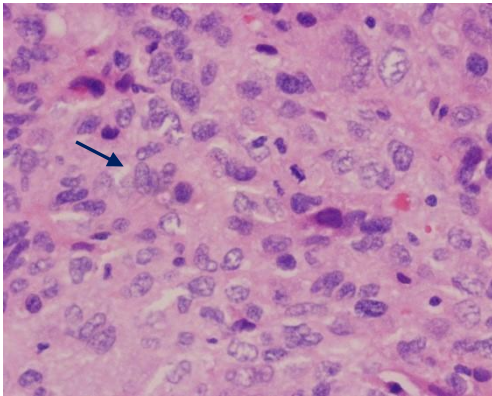
FIGURE 5



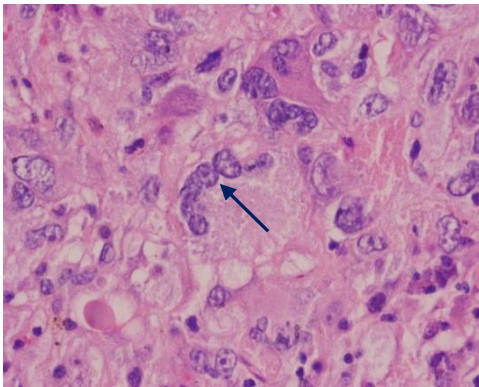
Panel A



Panel B



Panel C



Panel D

Figure 5. *Panel A:* H&E, 10x, High-grade tumor lesion, cells with marked atypia and nuclear pleomorphism with abundant atypical mitosis (red arrow). *Panel B:* H&E, 40x: Nuclear pleomorphism, atypical mitosis (green arrow). *Panel C and D:* H&E, 40x Giant multinucleated tumor cells and bizarre nucleus. (blue arrow).

Hematology Oncology was consulted for starting adjuvant chemotherapy but just 1 month after discharge he was re-admitted again due to myalgias of upper and lower extremities associated with headache and palpitations. A new TTE showed a solid-mass with ovoid morphology of 3.7 x 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 mmHg associated with moderate regurgitation and PSAP of 100 mmHg in addition to moderate right

ventricular dysfunction (Video 5,6,7), Figure 6,7. It was considered recurrence of the pleomorphic sarcoma.



Video 5. Parasternal long axis view with evidence of left atrial mass of irregular contours



Video 6. Apical-4 chamber view, showing left atrial mass with severe obstruction of the mitral outflow tract

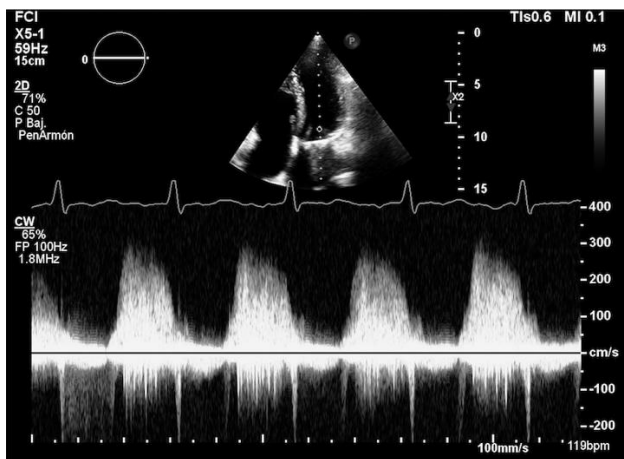
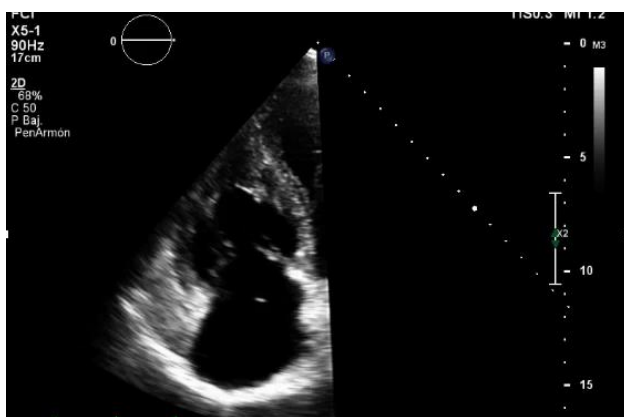


Figure 6. Increased trans-mitral mean gradient of 23 mmHg.



Video 7. Apical-4 chamber view. Right ventricular dilatation and moderate dysfunction.

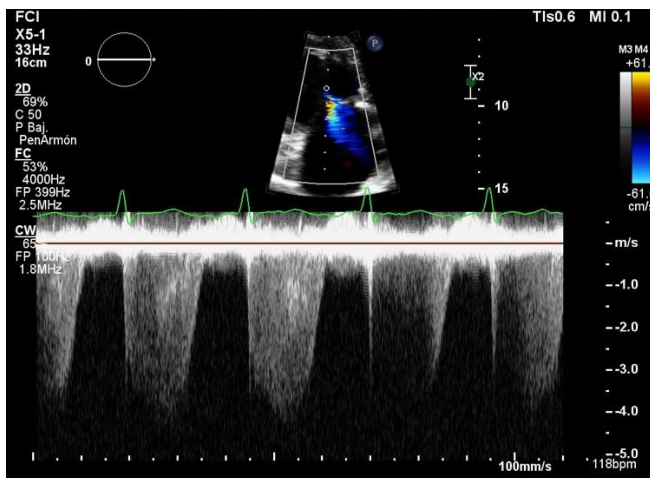


Figure 7. Continuous wave Doppler at the tricuspid valve showing moderate pulmonary hypertension, PSAP 100 mmHg.

Due to rapid recurrence the patient was put in palliative care and expired 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 are the advanced staging of the tumor when clinically evident, associated with nonspecific symptoms. Also, there is lack of knowledge regarding optimal therapy granted 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 about why it originates in the pulmonary veins. Studies have focused on reporting the presentation, diagnosis, management, and follow-up of these patients.

According to Simpson and colleagues at the Mayo Clinic Cancer Center, during a 32 year follow-up of malignant primary heart tumors, only 6% had poorly differentiated sarcomas (2). These results contrast the findings of a retrospective French study of the Sarcoma Group with a follow-up 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 sarcomas occur 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, where the majority of the localization was in the left (47%) followed by the right atrium (21%). (2)

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). The TTE was abnormal in all 34 patients in the Mayo Clinic review showing a cardiac mass in 30 patients and pericardial effusion in the remaining 4 patients (2). Intra-cavitary 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 AV 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/left sided chambers, broad base, infiltration of adjacent structures and pericardial effusion.

There are other complementary diagnostic methods such as magnetic nuclear imaging (MRI), which shows a greater sensitivity and specificity for cardiac masses (7). For cardiac sarcomas, classic MRI findings include iso-intensity in T1 weighted images, hyper-intensity in T2 and homogenous late gadolinium enhancement distribution.

The histological diagnosis of sarcomas can be difficult and requires expertise and the ability of immuno-histochemical tool panel.(7)

The optimal treatment approach for this type of cancer is not standard. A 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 reported 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. (4)

The major problem during surgical treatment of this malignancy is the extensive involvement precluding complete resection with a high recurrence risk. An alternative treatment reserved to left-heart sarcomas might be auto-transplantation, which consists of removing the heart, resecting the tumor with sufficient margins

followed by re-implantation. This has been performed successfully in well-trained teams with a 1.4% operative mortality. (3)

Cardiac transplantation is an option for inoperable sarcomas, but is not routinely considered due to 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 multi-modal management is low due to disease rarity. Therefore, the optimal management for cardiac sarcomas is often extra-polated from soft-tissue sarcomas 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 multi-modal treatment including preoperative and/or post-operative chemotherapy in addition to radiotherapy was associated with improvement in progression-free survival. Chemotherapy alone was significantly associated with improved survival only in non-operated patients but not in those with surgical resection (3). Treatment with first-line chemotherapy for undifferentiated pleomorphic sarcoma is described with doxorubicin plus ifosfamide and second-line includes trabectedine-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 in Latin America. Its nonspecific clinical presentation and the diagnosis in advanced stages of the disease are responsible for its very poor prognosis and high recurrence rate as seen in our patient. The most commonly described symptom is dyspnea and the most frequent TTE finding is a mass at the level of the atria although the tumor may have different primary location which may explain other symptoms such as heart failure and AV block during presentation. The initial treatment is complete surgical resection and adjuvant chemotherapy and radiotherapy are often palliative therapeutic options, granted the survival after diagnosis is one year or less.

Conflict of interests

The authors declare no conflict of interest.

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