

Cardiac sarcoma - a fatal disease: report of 2 cases

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Abstract: Cardiac sarcomas are malignant tumors that almost always have a short and fatal course, making the diagnosis challenging. In most patients, the diagnosis is late, and survival is limited, mainly due to previously existing and undetected metastases. The therapeutic approach includes surgery, chemotherapy, and radiation therapy, alone or in combination, but because the tumor is rare there are no randomized studies to guide treatment. We report 2 cases of cardiac sarcoma in which a right-side heart sarcoma resection was performed in our hospital. These two tumors share a tendency to metastasis, histologically documented, thus being at high fatal risk.

Key Words: angiosarcoma, pleomorphic sarcoma, undifferentiated sarcoma.

Primary cardiac sarcomas are rare and represent 20% of all primary cardiac tumors [1]. Symptoms depend on the chambers and the cardiac structures involved. Transthoracic echocardiography is commonly used to identify a cardiac mass [2, 3]. The diagnosis of cardiac sarcoma requires adequate sampling and careful use of ancillary diagnostic techniques. In the most recent histologic classifications, angiosarcoma is the most common malignant tumor of the heart with recognizable differentiation. Undifferentiated sarcomas account for one-third of all cardiac sarcomas and have been included in the pleomorphic sarcoma subgroup [4].

Elective cardiac sarcoma therapy consists of complete surgical excision, when possible, followed by radiation and chemotherapeutic regimen [5]. Prognosis of cardiac sarcomas is very poor, with mean survival ranging from 9.6 to 16.5 months. A less aggressive course seems related to left atrium location, a low histologic grading with scarce cellular pleomorphism and low-mitotic activity, absence of necrosis, myxoid tumor appearance, and absence of metastasis at diagnosis [6].

Case Report 1

A 36-year-old female presented to our hospital with radiographic and echocardiographic examinations revealing a right ventricular tumor spreading to the interventricular septum and right ventricular wall. The

tumor was surgically approached by medial sternotomy, but complete tumor resection was not possible because of the extensive tumor infiltration. The palliative intervention, consisting in partial excision of the tumor mass, aimed at releasing the right ventricular outflow tract.

Macroscopically, the tumor corresponded to a firm polypoid mass (Figure 1a), with large endocardial base, infiltrating the ventricular septum and projecting into the right ventricular cavity. The bulky tumor compressed the pulmonary valve, occluding the pulmonary artery orifice as well. The tumor had variegated appearance due to the presence of areas of necrosis and hemorrhage.

Histological examination (Figure 1b) of the tumor revealed a high grade cardiac sarcoma, without evidence of specific lines of differentiation. Microscopic study showed a heterogeneous hypercellular tumor, consisting of spindle cells, interspersed focally with multinucleated giant cells. The dominant histological feature of the tumor was marked cellular pleomorphism and increased mitotic activity. Immunohistochemical evaluation (Figure 1d) revealed a positive immunoreactivity to vimentin, suggesting a fibroblastic origin, and negative immunoreactivity to desmin and mesothelial markers, excluding a smooth muscle and mesothelial origin.

These findings were suggestive of a pleomorphic undifferentiated cardiac sarcoma.

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Another important feature of the tumor was the tendency to pulmonary thromboembolism, supported by the presence of tiny tumor nodules (Figure 1c) dislodged from the tumor mass without evidence of metastases. The thrombotic status was explained by the hypercoagulate status associated to cardiac tumor.

Regardless of histology, malignant cardiac tumors have a poor prognosis when tumor resection is difficult, they are undifferentiated, have areas of necrosis, and high mitotic index. In this case adjuvant chemotherapy has a limited value, and radiation therapy is restricted by adverse cardiac effects.

evidenced. Global systolic function was preserved with an ejection fraction above 60%. Small pleural and pericardial effusions were observed. These findings were suggestive of right atrial myxoma. No metastases were seen.

Coronary angiography showed a double source of tumor vascularisation: from LCX and RCA. The likelihood of an angiosarcoma was high.

The intraoperative findings showed a mobile, solid, gray-pinkish, tumor mass of moderate consistency, attached to the atrial septum on a large base (Figure 2a). The tricuspid orifice and leaflets were morphologically

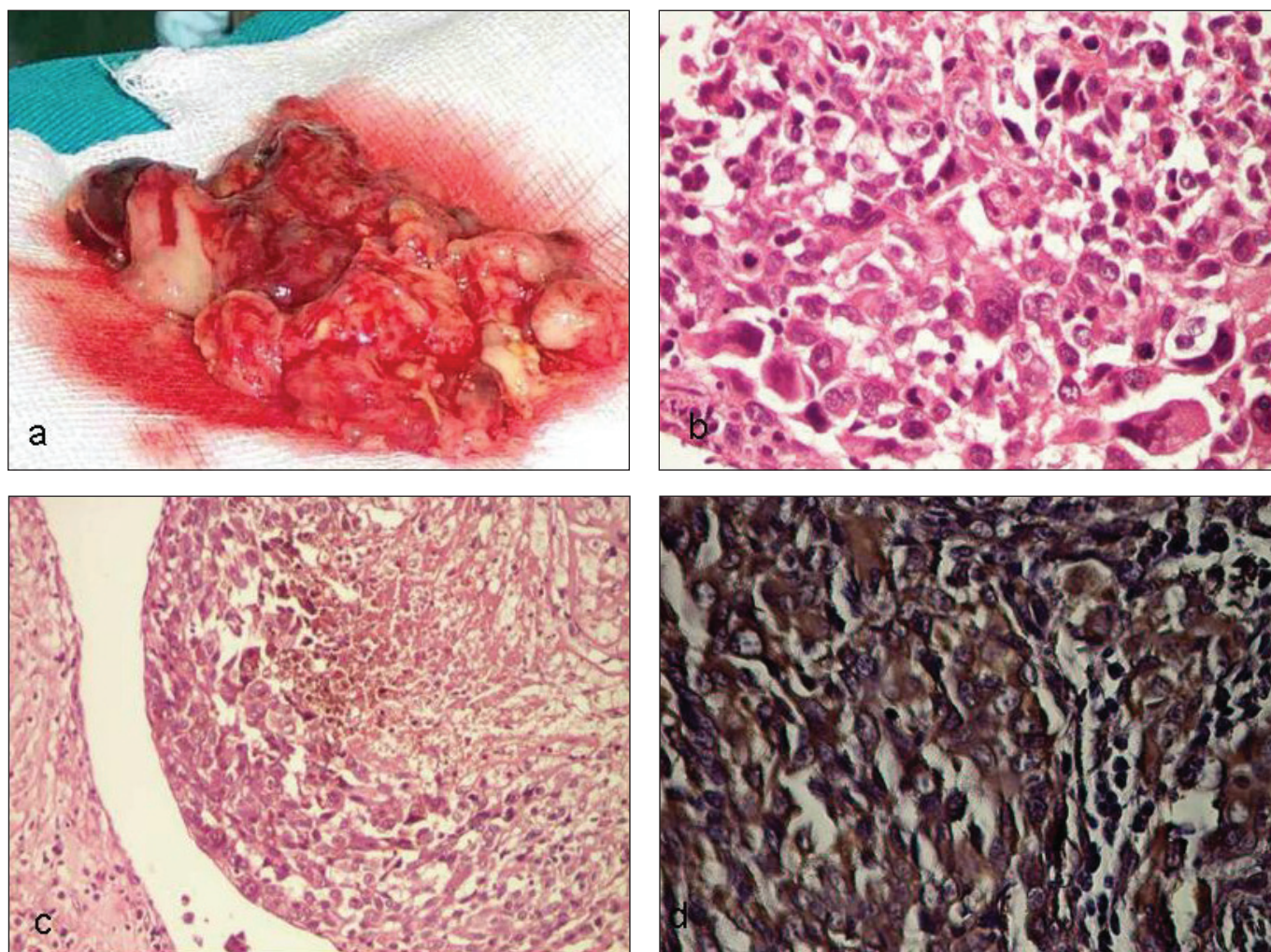


Figure 1: Cardiac fibrosarcoma: 1a - Gross polypoid tumoral appearance; 1b - Pleomorphic tumoral cells and multinucleated giant cells (HE, 40x); 1c - Right ventricle: intracavitary tumoral embolus (HE, 20x); 1d - Focal positive immunoreactivity for vimentin in tumoral cells, 40x.

Case Report 2

A 58-year-old male presented to our hospital for cardiac assessment. The patient had a 4-year history of recurrent pericarditis of unknown etiology, which responded to prednisone administration. At presentation he complained of progressive exertion dyspnea.

The clinical picture was normal except for shortness of breath. Blood reports were normal, except a mild anemia. Initial ECG and chest X-ray were unremarkable but, later, a second review of chest X-ray raised the suspicion of mild pericardial effusion. On transthoracic echocardiography, a lobulated mass of 3x2 cm in size, attached to the interatrial septum was

normal. Histology (Figure 2b) revealed a low-grade angiosarcoma, with a low mitotic index and nuclear pleomorphism, infiltrating locally the tumor base. Necrotic foci and hemorrhagic infiltration were focal tumor features. Tumor emboli detachment was also seen (Figure 2c). Immunohistochemistry confirmed that tumor cells were positive for CD34 and CD31 vascular markers (Figure 2d).

The postoperative transthoracic echocardiography showed normal sized and free cavities, left ventricle with normal global systolic function, pericardium without fluid, and intact intraatrial septum. Abdominal ultrasound was normal. The early course was uneventful and the patient

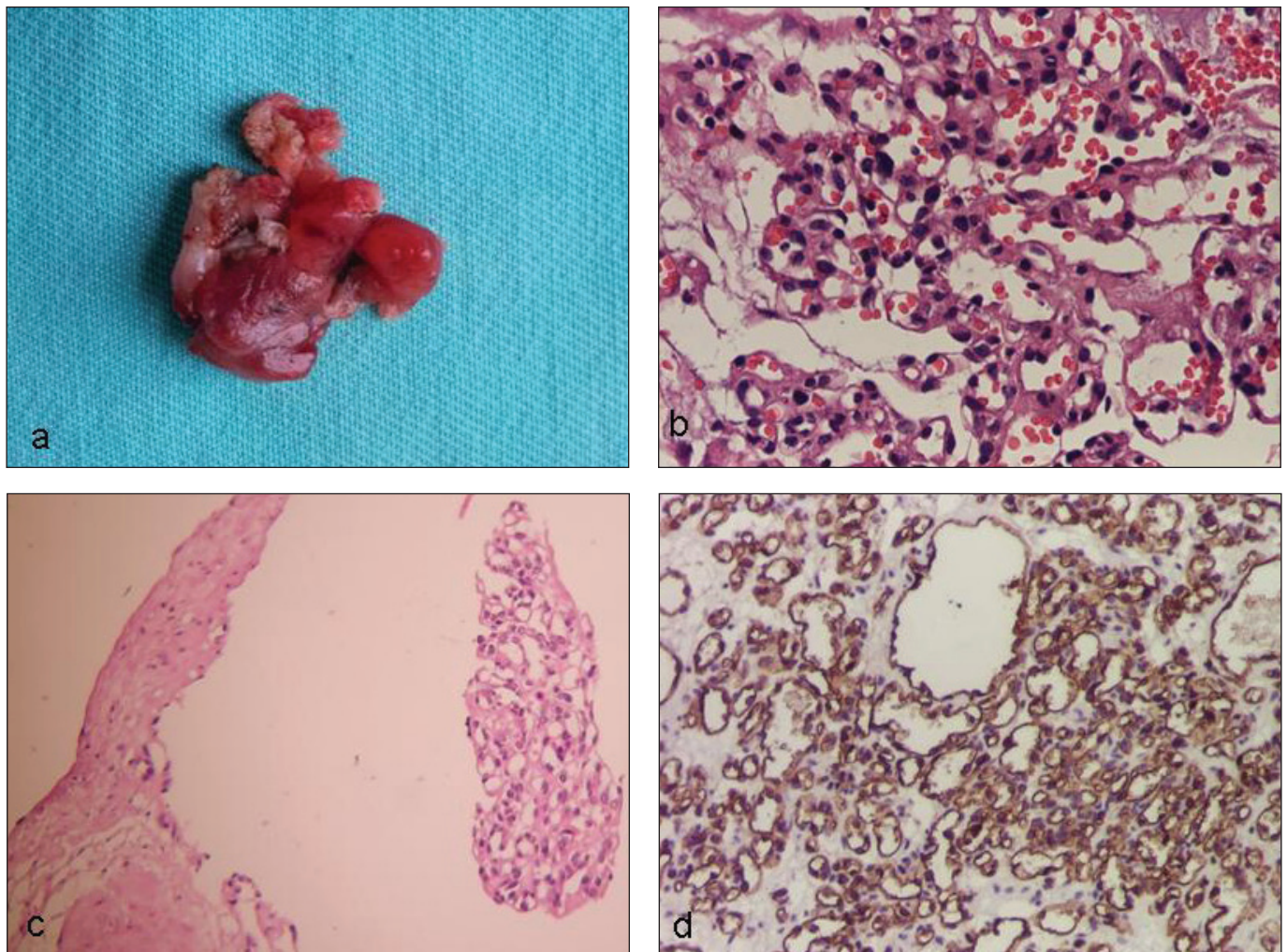


Figure 2: Cardiac angiosarcoma: 2a - Gross appearance of a solid, lobulated, pinkish, tumoral mass with hemorrhagic foci; 2b - Pleomorphic tumoral cells form vascular structures containing erythrocytes (HE, 40x); 2c - Right atrium: intracavitary tumoral embolus (HE, 10x); 2d - Diffuse positive immunoreactivity for CD34 in tumoral cells, 20x.

was discharged from hospital in good condition, CT exams and cancer treatment being recommended.

Discussions

Primary cardiac neoplasms are extremely rare, with an autopsy prevalence of 0.001- 0.28%. In adults, about 25% of primary tumors of the heart are malignant; angiosarcoma accounts for 35% to 40% of them, being the most common primary cardiac malignant tumor, followed by fibrosarcoma, representing 33% of cardiac sarcomas [3]. Because they are so rare, often they are missed or misdiagnosed.

The diagnosis of cardiac sarcoma is complicated by the fact that most cardiac tumors cause a variety of nonspecific clinical manifestations. The diagnosis of cardiac sarcoma is often not made preoperatively or even antemortem. It is overlooked because of the rarity of the lesion and the nonspecific nature of signs and symptoms [2]. Bloody pericardial effusion may cause cardiac failure. Myocardial involvement may lead to heart failure, as well. Endomyocardial masses cause valvular obstruction or insufficiency. Tumor fragments may embolize from the right side of the heart to the lungs and cause dyspnea. Local extension of the tumors may cause signs and symptoms such as superior vena cava syndrome [4].

So, the diagnosis was delayed, being suggested, in the first case, by the markedly increase of tumor mass with obstruction of pulmonary ejection tract, and, in the second case, by recurrent pericardial effusions of unknown cause.

Imaging studies are an important tool in preoperative tumor diagnosis. Nowadays, advances in diagnostic techniques have facilitated accurate, noninvasive assessment of cardiac sarcomas [7, 8]. In cardiac tumors, the challenge is not only to differentiate between primary or secondary, and malignant or benign tumors, but also between neoplastic and non-neoplastic lesions. Imaging modalities are required for rapid diagnosis and staging, as well. Transthoracic echocardiography is the preferred diagnostic procedure for noninvasive imaging of cardiac tumors [9, 10]. Preoperative investigations did not reveal any metastases in any of the cases.

A diagnosis of cardiac tumor was made postoperatively by morphological examination in both cases. Although endomyocardial biopsy provides tissue to use in diagnosis, this biopsy is not absolutely necessary preoperatively because cardiac tissue is obtained during surgical exploration [11, 12]. Microscopic examination performed on pieces of surgical excision was essential in the diagnosis, revealing in the first case a pleomorphic

undifferentiated fibrosarcoma, and in the second case a differentiated angiosarcoma. A common histological feature in both our cases was the tendency of embolization, demonstrated histologically.

Fibrosarcomas have an infiltrative growth pattern. No cardiac chamber predilection has been noted. However, cardiac valvular involvement is found in as many as 50% of lesions [7]. In the case one, we showed a pulmonary orifice occlusion due to pulmonary ejection tract involvement.

Nearly 80% of cardiac angiosarcomas arise as mural masses in the right atrium [12], especially the free wall, the interatrial septum being a rare location. Typically, they completely replace the atrial wall and fill the entire cardiac chamber. They may invade adjacent structures (e.g., vena cava, tricuspid valve). In the case two, the tumor invaded the venous sinus impeding venous returning. The coronary venous sinus involvement was a cause of pericardial effusion by venous engorgement, without effects on venous returning due to the presence of an adequate collateral circulation with anterior cardiac veins and thebesian veins.

The prognosis of malignant cardiac tumors is generally the same: almost all cardiac sarcomas are rapidly fatal. Orlandi suggested that age, gender, presence of differentiation, and histologic type do not affect prognosis. A low level of mitotic activity and any therapy were the only significant factors affecting survival rate. Although the prognosis in patients with cardiac sarcomas is dismal, histologic grading is useful in predicting outcome, as has been shown for soft tissue sarcomas of other sites [11].

In pleomorphic undifferentiated fibrosarcoma, statistics showed that the average survival is of 6 months since diagnosis [7, 11]. Mayer noted that undifferentiated cardiac sarcomas and non-removable malignant tumors have a poor prognosis [7]. The presence of tumor necrosis and high mitotic rate are also indicative of poor prognosis. Orlandi reported a higher survival in relation to applied therapeutic modality [11].

In the first case, the partial tumor removal was correlated with an immediate good course reflected in the improvement of cardiac function due to releasing of the pulmonary outflow tract. However, further development was

unfavorable, with a 3-month post-surgical survival due to progressive deterioration of cardiac function by progressive local recurrent tumor invasion. Since admission, the patient was clinically in extremis, with progressive ventricular dysfunction.

Generally, angiosarcoma is characterized by a short clinical course, given its aggressive behavior, and delayed diagnosis, due to the non-specific clinical picture and its rarity [4, 12]. Brooks appreciates that the average survival from initial symptoms to death is less than 9 months, and the features associated with longer survival include: left-sided tumor, complete tumor resection, post-operative adjuvant therapy, tumors with less than 10 mitoses/HPF, and absent necrosis [4]. In the second case, although the tumor was completely removed and well differentiated, the tendency to metastasis observed histologically made it a poor prognosis tumor.

The usual scenario of progressive cardiac sarcomas is rapid metastases, tamponade, and cardiac heart failure. These most frequent causes of death are a good illustration for the therapeutic dilemma faced with this neoplasia.

So, what is the management of these life threatening tumors? The question of a new therapeutic strategy combining surgery with radiotherapy and chemotherapy is under debate. Complete or partial excision of primary or metastatic cardiac sarcoma can provide hemodynamic improvement and relief from congestive heart failure. Postsurgical adjuvant radiation and chemotherapy have not proven consistently beneficial [13, 14]. However, they can be beneficial in improving the symptoms and quality of life. The role of orthotopic heart transplantation for malignant cardiac tumors continues to be debated.

Conclusion

We presented two right cardiac sarcomas, the first with signs of pulmonary tract obstruction, and the second with pericardial effusions at presentation. These tumors are both rapidly fatal, having in common histologically documented pulmonary embolization at diagnosis. Cardiac sarcomas are rarely cured, but prolonged survival or significant palliation is possible with surgical resection.

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