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Case Report

A primary cardiac osteosarcoma: Case report and review of the literature

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ABSTRACT

Primary cardiac osteosarcoma is a rare and aggressive neoplasm that can be difficult to diagnose. We report a case of a previously healthy 49-year-old woman who presented with dyspnea, atrial flutter, and heart failure. A mass was visualized in her left atrium by echocardiography and cardiac computed tomography, and the diagnosis of cardiac myxoma was raised. The patient subsequently underwent surgical resection of the mass and atrial reconstruction. Surprisingly, histological and immunohistological analyses revealed the mass to be an osteosarcoma. The patient received chemotherapy and radiotherapy. Eight months later, she has shown evidence of local recurrence. We briefly discuss primary osteosarcomas in the cardiac cavity and their management.

<**Learning objective:** Primary cardiac tumors are very rare and most likely benign. Malignant tumors constitute less than 25% of primary cardiac neoplasms. However, both primary sarcomas and benign tumors are often found in the left atrium. As a consequence of their location and similar clinical presentation, primary cardiac sarcomas can be easily confused with a benign myxoma, therefore abnormal imaging features (immobility of the mass, neovascularity, multicentricity, calcification and invasion into the heart structures) should raise suspicion for a cardiac sarcoma.>

Introduction

Most cardiac tumors are metastatic tumors, which are 20–40 times more common than primary tumors [1,2]. Most primary tumors of the heart are benign, with atrial myxomas being the most common. Primary malignant heart tumors constitute less than 25% of all primary heart tumors [3], with their prevalence recorded as between 0.001% and 0.030% in one autopsy series [2].

Sarcomas, including angiosarcomas, leiomyosarcomas, and undifferentiated sarcomas [3], make up the bulk of malignant cardiac tumors. Primary cardiac osteosarcomas are extremely rare and account for <10% of all primary cardiac tumors [3,4]. Primary cardiac osteosarcomas exhibit a predilection for the left atrium, whereas the majority of metastatic cardiac tumors (including metastatic osteosarcomas) commonly arise from the right atrium [4]. Clinical manifestations depend on the anatomical site of origin and therefore can mimic different cardiac diseases (heart failure, valvulopathy, arrhythmia, etc.) [2–4].

Osteosarcomas are aggressive with a high incidence of recurrence and metastasis. Even though complete resection can be achieved in some cases, long-term results are usually poor. We present a case of a left atrial osteosarcoma in an adult Peruvian woman with local recurrence despite aggressive surgical and chemoradiotherapeutic management.

Case report

A 49-year-old previously healthy woman presented with progressive dyspnea, orthopnea, and palpitation for eight weeks. Cardiac auscultation revealed a systolic murmur grade 3/6 over the left sternal border. The electrocardiogram showed atrial flutter at 128 bpm with rapid ventricular response. Laboratory investigations, including complete blood cell count, electrolytes, and liver enzymes were within normal range. C-reactive protein was 16.1 mg/dl, lactate dehydrogenase levels 937 U/l and N-terminal-pro-B-type natriuretic peptide 1896 pg/ml.

Transthoracic Doppler-echocardiography revealed a heterogeneous mass in the left atrium, adhering to the atrial wall and posterior leaflet of the mitral valve causing moderate mitral stenosis and mild pulmonary hypertension (Fig. 1). Cardiac computed tomography (CT) confirmed the presence of a solid mass within the left atrium. Systemic CT examination from the head to the lower limbs did not show metastatic disease. A diagnosis of atrial myxoma was considered and surgery scheduled. Intraoperative examination revealed the tumor to be attached to the posterior wall of the left atrium and the posterior mitral leaflet. The atrial mass was partially resected and the atrium reconstructed. Complete resection was not achieved due to the tumor's extension and

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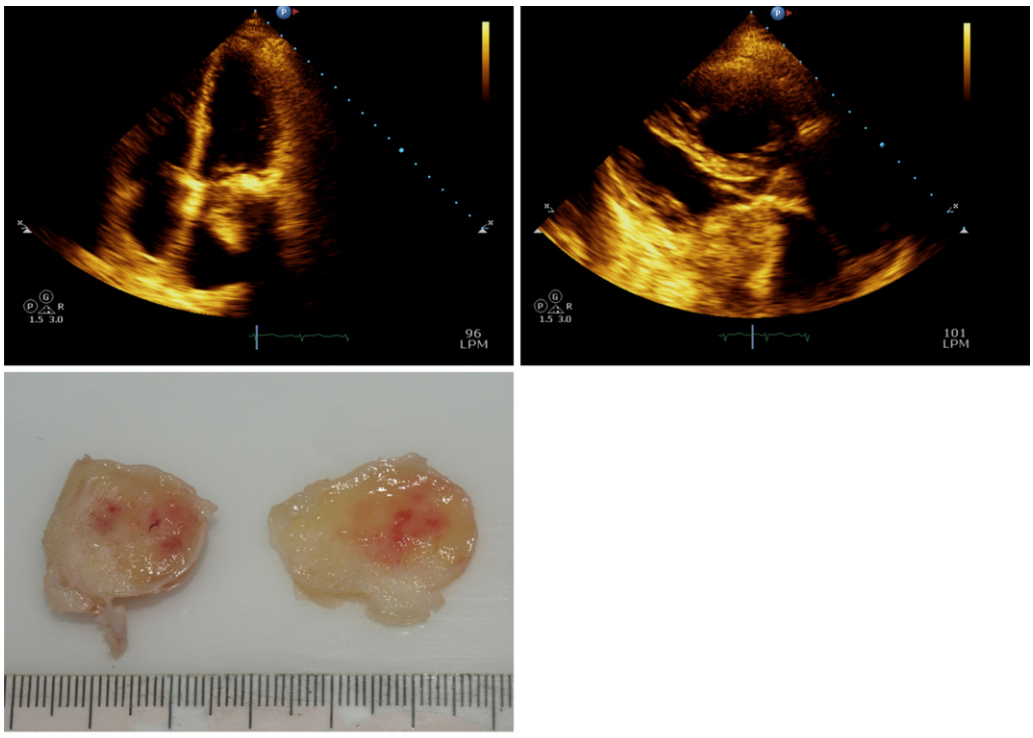

Fig. 1. Top: echocardiographic images showed a large heterogeneous mass causing moderate mitral stenosis. Bottom: cut-section of the tumor was homogeneously grayish-brown with focal areas of hemorrhage.

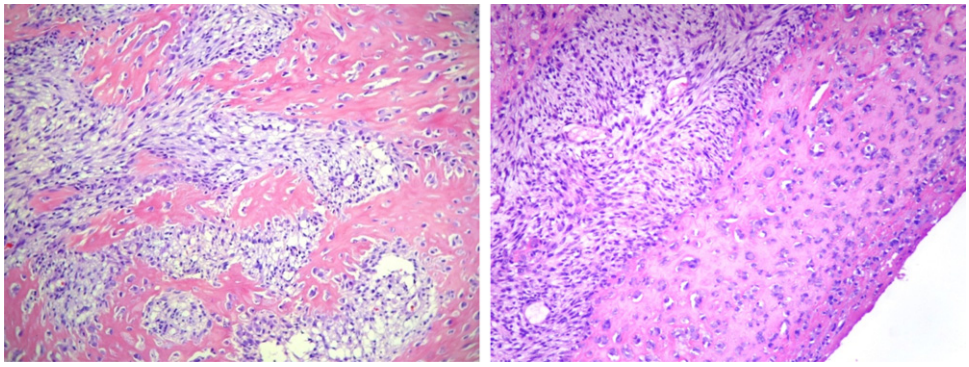

Fig. 2. Hematoxylin and eosin stain (20× magnification) revealed osteoid formation and pleomorphic sarcomatous cellular proliferation.

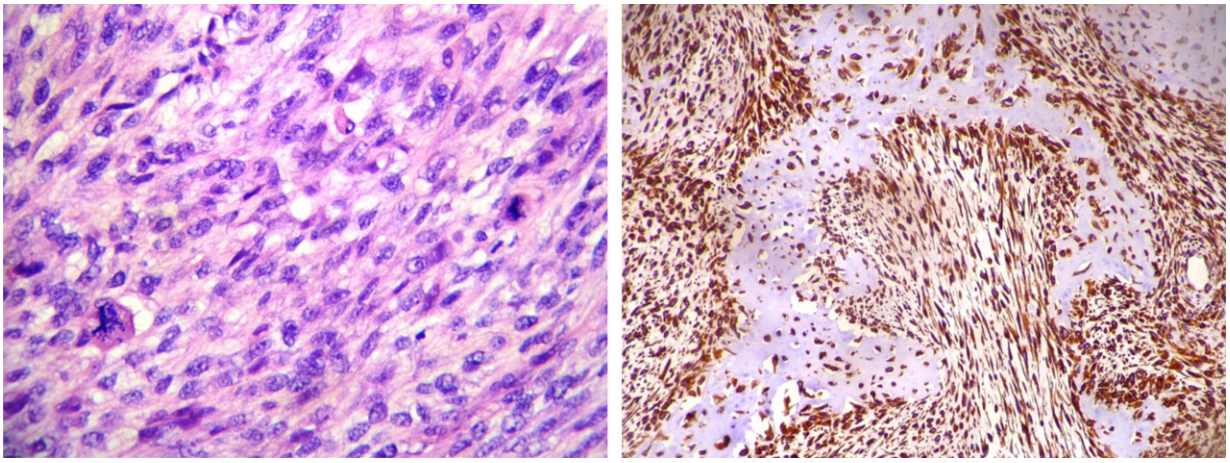

Fig. 3. Left: hematoxylin and eosin stain (40× magnification) showed numerous mitotic figures. Right: the cells stained strongly positive for vimentin (20×).

Table 1
Reported cases of primary cardiac osteosarcoma to date.

Author	Year	Sex/age	Location	Presentation	Histopathology	Metastases
Cumming [5]	1957	M/47	Left atrium, pulmonary vein	Hemoptysis and dyspnea	Osteosarcoma	None
Dorney [6]	1967	M/45	Interatrial septum	Pulmonary edema	Osteosarcoma, osteoclastoma	Posterior mediastinum
Lowry [7]	1972	M/29	Interatrial septum	Congestive heart failure	Osteosarcoma, chondrosarcoma	Lung, liver, and intestine
Yashar [8]	1979	M/17	Left atrium	Mitral stenosis	Osteosarcoma, chondrosarcoma	Recurrence (5 m), lung and anterior mediastinum
Marvasti [9]	1985	M/56	Left atrium	Dyspnea	Osteosarcoma, fibrosarcoma	Bone
Burke [4]	1991	M/24	Left atrium	Syncope	Osteosarcoma, chondrosarcoma	None
		F/43	Left atrium	Myxoma	Osteosarcoma, chondrosarcoma	Thyroid
		F/57	Left atrium, pulmonary vein	Dyspnea	Osteosarcoma	None
		F/40	Left atrium	Pulmonary hypertension	Osteosarcoma, fibrosarcoma	–
		F/24	Left atrium, pulmonary vein	–	Osteosarcoma	–
		M/67	Left atrium	Dyspnea	Osteosarcoma, chondrosarcoma	Lung
		M/45	Left atrium	Myxoma	Osteosarcoma, Chondrosarcoma	–
		F/18	Left atrium	Congestive heart failure	Osteosarcoma, fibrosarcoma	Recurrence (30 m)
		F/23	Mitral valve	Mitral stenosis	Osteosarcoma	Skin
Dan [10]	1997	F/32	Left atrium, mitral valve	Transient ischemic attack	Osteosarcoma, fibrosarcoma	Pleural, muscle, and brain
Jahns [11]	1998	F/66	Left atrium	Syncope	Osteosarcoma, chondrosarcoma, angiosarcoma	Kidney
Zanella [12]	1998	M/32	Left atrium, pulmonary vein	Dyspnea and syncope	Osteosarcoma, fibrosarcoma	Mediastinal vessels
Minami [13]	2000	F/54	Left atrium	Congestive heart failure	Osteosarcoma	None
Yamagishi [14]	2000	F/30	Right ventricle	Dyspnea	Osteosarcoma	None
Nowrangi [15]	2000	M/64	Left venricle	Ventricular tachyarrhythmia	Osteosarcoma	Lung
Lurito [16]	2002	M/14	Right atrium	Congestive heart failure	Osteosarcoma	None
Mathur [17]	2005	M/35	Left atrium	Cardio-pulmonary arrest	Osteosarcoma, chondrosarcoma	Recurrence (12 m)
Koçak [18]	2006	F/34	Left atrium	Dyspnea	Osteosarcoma	None
Bae [19]	2006	F/52	Left atrium, mitral valve	Congestive heart failure	Osteosarcoma, chondrosarcoma	None
Sogabe [20]	2007	F/68	Right ventricle, pulmonary artery	Pulmonary thromboembolism	Osteosarcoma	Recurrence (6 m)
Takeuchi [21]	2007	M/22	Left atrium	Congestive heart failure	Osteosarcoma	Brain, bone, and kidney
Zhang [22]	2008	M/41	Right ventricle	Dyspnea	Osteosarcoma, chondrosarcoma	None
Parwani [23]	2008	F/50	Left atrium	Dyspnea	Osteosarcoma	Recurrence (48 m), intestinal
Forslund [24]	2008	M/75	Right ventricle	Dyspnea and peripheral edema	Osteosarcoma	None
Cabezas-Rodríguez [25]	2009	M/27	Left atrium	Pulmonary edema	Osteosarcoma	None
Dohi [26]	2009	M/20	Right atrium	Dyspnea and peripheral edema	Osteosarcoma, chondrosarcoma	None
Luo [27]	2010	F/42	Left atrium	Dyspnea and chest pain	Osteosarcoma	None
Gomez-Rubin [28]	2010	F/70	Left atrium	Dyspnea	Osteosarcoma	Recurrence (11 m), bone
Ahn [29]	2011	F/47	Left atrium	Dyspnea	Osteosarcoma	Bone
Ye [30]	2011	F/42	Left atrium	Dyspnea	Osteosarcoma, chondrosarcoma	None
Hashimoto [31]	2011	M/67	Left atrium	Congestive heart failure	Osteosarcoma	Intestinal, peritoneal
Present case	2012	F/49	Left atrium, mitral valve	Dyspnea	Osteosarcoma	Local recurrence (8 m)

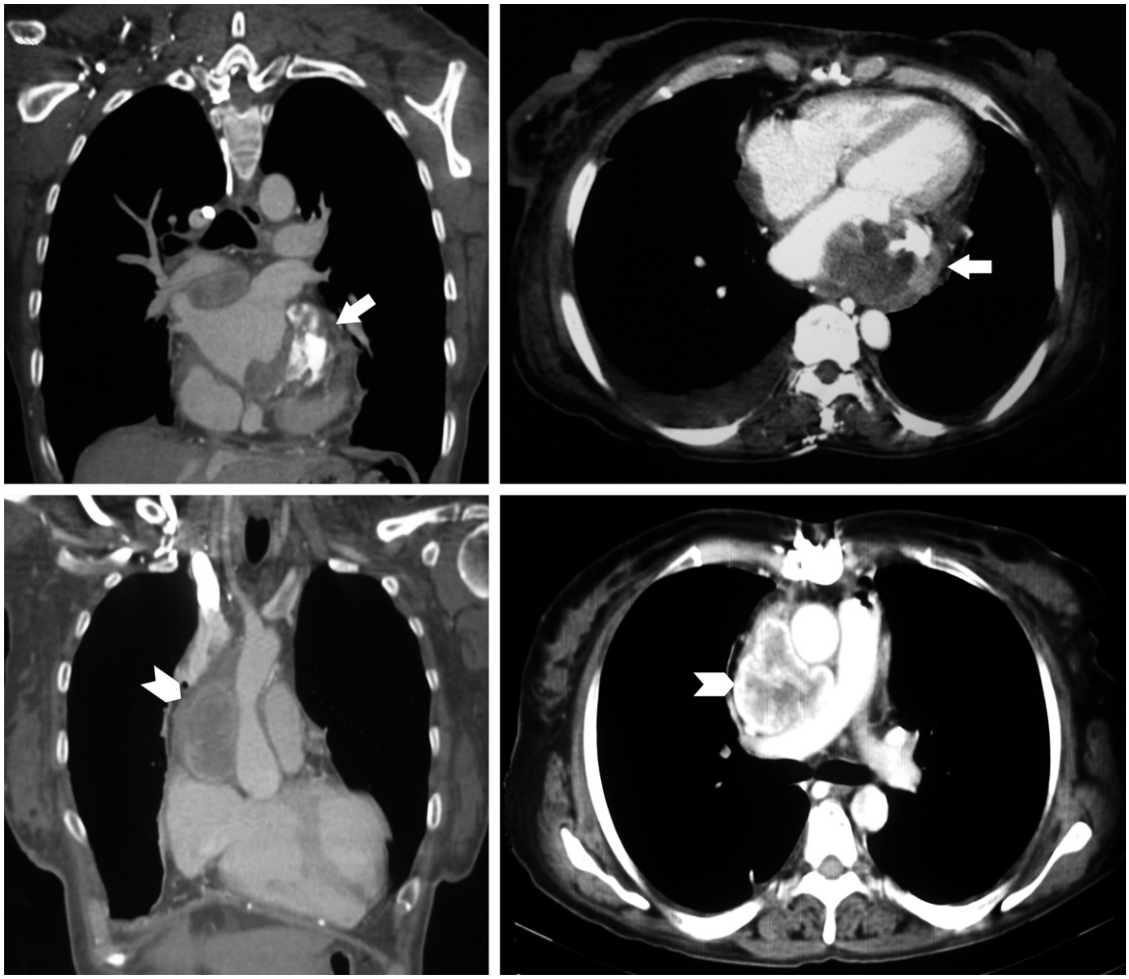

Fig. 4. Thoracic computed tomography images showed a local recurrence 8 months later. Top: recurrent left atrial mass (arrow) appeared adherent to the posterior wall. Bottom: a new tumor (arrowhead) appeared over the right atrium and compressed the superior vena cava.

adhesion to adjacent structures. The patient tolerated the surgery well and was discharged home in stable condition.

Macroscopically, the excised mass measuring 2.5 cm × 2 cm × 1.5 cm was grayish-brown in color, firm in consistency, and contained an area of hemorrhage on the cut section (Fig. 1). Histopathological analyses revealed pleomorphic sarcomatous cell proliferation, eosinophilic osteoid and bone formation (Fig. 2). At 20× magnification, many mitotic figures were noted (Fig. 3), along with foci of hemorrhage. Immunohistochemical studies showed tumor cells were positive for vimentin, but negative for calretinin, smooth muscle actin, desmine, cytokeratin, and S-100 (Fig. 3).

Post-operatively, the patient received chemotherapy consisting of ifosfamide and doxorubicin, as well as radiotherapy amounting to a total dose of 45 Gy over 25 sessions. Periodic check-ups with CT scan assessment were performed. Eight months after the surgery, the patient presented to the emergency room with a history of shortness of breath and 10 kg weight loss. Cardiac CT showed the emergence of two new masses. One mass was located in the right atrium with cephalic extension towards the mediastinum and compression of the superior cava vein. The other mass appeared adherent to the posterior wall of the left atrium (Fig. 4). At this time, the patient was admitted to hospital for supportive care.

Discussion

Primary cardiac osteosarcomas are uncommon tumors, accounting for only 3–9% of all cardiac sarcomas [4]. In 1957, the first report on primary cardiac osteosarcoma was published [5]. Since then, fewer than 50 cases of primary cardiac osteosarcomas have been reported [4–31]. These tumors are slightly more frequent in women, with the average age at diagnosis between the 5th and 6th decade of life (range 14–75 years) (Table 1).

There is no evidence that primary cardiac osteosarcomas represent malignant transformation of benign tumors, despite the fact that both osteosarcoma and benign tumor are often found in the left atrium [9,11]. The tumor's cell of origin has yet to be clearly identified. Currently, it is believed that they arise from undifferentiated mesenchymal stem cells in the endocardium that transform into active osteoblasts secondary to over-expression of specific genes [12,24]. Clinical manifestations of cardiac tumors depend on their anatomical location and reflect the degree of obstruction, invasion, and embolization of specific intracardiac structures [4,16]. Most patients present with dyspnea secondary to mitral valve obstruction, although arrhythmias and pericardial tamponade are seen as well [3,4,28]. Our patient presented with heart failure, arrhythmia (atrial flutter) and valvulopathy (mitral stenosis).

Preoperative suspicion of malignant cardiac neoplasm is crucial in planning extensive resection. Currently, echocardiography cannot reliably differentiate an osteosarcoma from a myxoma, but certain characteristics including large size, immobility of the mass, neovascularity, absence of a clear pedicle, multicentricity, calcification and invasion into the pulmonary veins, valvular structures, and atrial septum may suggest malignancy [12,32]. Cardiac osteosarcomas have been reported on cardiac CT as a low attenuation

mass with dense calcification [12]. However, calcification may also be minimal or absent (as in our case), and is seen in other types of cardiac tumors including myxomas, fibromas, rhabdomyomas, and teratomas [1,2,32]. Unambiguous imaging-based diagnosis therefore remains challenging, with serial echocardiograms and CTs being the most reasonable strategy to differentiate myxoma-like lesions.

The specific diagnosis of osteosarcoma is established through histological and immunohistochemical studies. Osteosarcomas are a heterogeneous group of tumors containing malignant, bone-producing cells [3,4,12]. Macroscopically, the tumor may be well circumscribed and pseudoencapsulated, with infiltration into the surrounding tissues. Calcification, necrosis, or hemorrhage within the tumor can be seen. On histology, the tumor contains variable amounts of spindle cells, osteoid, bone, and cartilage. Depending on the predominant component, osteosarcomas can be subgrouped into osteoblastic, chondroblastic, and fibroblastic types [4,12]. Recognition of a sarcomatoid tumor featuring malignant osteoid allows confident identification of osteosarcoma [12]. Multiple previous studies have established the similarity between immunophenotype of extra-skeletal osteosarcomas and skeletal osteosarcomas [33]. These tumors are uniformly positive for vimentin and sometimes show positivity for alpha-actin smooth muscle [4,12,22]. Burke et al. reported that histological grading is useful for predicting outcome, with increased nuclear atypia correlating with a worse prognosis [3]. Severe nuclear atypia and high mitotic activity were observed in our case, and the patient showed local tumor recurrence 8 months after surgery.

Osteosarcomas grow rapidly and behave aggressively. Recurrence and metastasis are common features of cardiac osteosarcomas. The prognosis is poor with a survival rate of about 15% [3]. Better survival rates are associated with the absence of necrosis and low mitotic count. However, the latter may reflect early diagnosis rather than different behavior. In addition, metastasis to distant organs including the skin, brain, thyroid, lung, stomach, liver, kidney, muscle, and bone have been reported [4,7,10,11,15,21,28,29,31]. No standard therapy exists due to the tumor's low incidence rate. Since cardiac muscle exhibits a low tolerance to chemotherapy, surgery is the first-line treatment for malignant cardiac tumors, and is the only therapy that has demonstrated prolonged survival in these patients [1]. Recently, heart transplantation has emerged as an alternative approach for unresectable tumors, in patients with no evidence of distant metastasis [34].

In summary, as a consequence of their location, primary atrial cardiac osteosarcoma can be easily confused with a benign myxoma, therefore abnormal imaging features should raise suspicion for a cardiac sarcoma. Due to the usually aggressive behavior of this tumor, early detection and aggressive surgical resection may result in a longer survival time.

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