

## Cardiac angiosarcoma: an unexpected diagnosis

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### ABSTRACT

Cardiac angiosarcoma is a rare entity. The incidence through autopsy findings ranges between 0.001% and 0.03%. The disease usually presents with non-specific symptoms, although asymptomatic cases are frequent; therefore, diagnosis is unexpected and consequently delayed. The authors report the case of a middle-aged man with a recent onset cough and dyspnea. He sought medical care several times without receiving a definite diagnosis until a plain chest radiography was taken showing a mediastinal enlargement, which was the reason why he was hospitalized for clinical investigation. During the diagnostic workup, an echodopplercardiogram and a thoracic computed tomography were performed, showing a heterogeneous soft-tissue mass infiltrating the pericardium and the anterior atrial wall. Multiple and scattered pulmonary nodules were also present. A pulmonary nodule was biopsied, which revealed an angiosarcoma. The clinical features added to the radiological and histological findings permitted the diagnosis of right atrial angiosarcoma. The authors highlight the unexpected pattern in the presentation of cardiac tumors.

### Keywords

Hemangiosarcoma; Heart Neoplasms, Incidental Findings.

### CASE REPORT

A 63-year-old male patient sought the medical facility complaining of recent productive cough and dyspnea. His past medical history included pulmonary tuberculosis, which was treated few years before, and smoking of 15 packs/year. He had sought medical care several times during the prior 2 months, but was always treated with symptomatic medication until a plain chest radiography was taken, which showed mild mediastinal enlargement and a bulging on the right atrium contour (Figure 1). This was the reason for the hospital admission and clinical investigation.

The initial physical examination revealed an afebrile patient, who presented normal hemodynamic parameters and no peripheral edema. Lung examination was normal, and cardiac auscultation revealed an ejection murmur. Raised jugular venous pressure and hepatomegaly were also observed. The remaining examination was normal and the initial laboratory workup was unremarkable.

The echodopplercardiogram showed pericardium thickening with mild effusion and a left ventricular ejection fraction of 60%. Thoracic computed

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tomography (CT) showed a mass with soft tissue attenuation infiltrating the pericardium and the anterior wall of the right atrium (Figure 2) and multiple, bilateral, scattered, solid pulmonary nodules measuring up to 2.6 cm.

The magnetic resonance imaging (MRI) also showed a mass with heterogeneous distinction diffusely involving the pericardium, with compression/invasion of the right ventricle's outflow tract, pulmonary artery and superior vena cava (Figures 3 and 4).

The pericardium was biopsied, but the histological examination did not reveal evidence of malignancy. A



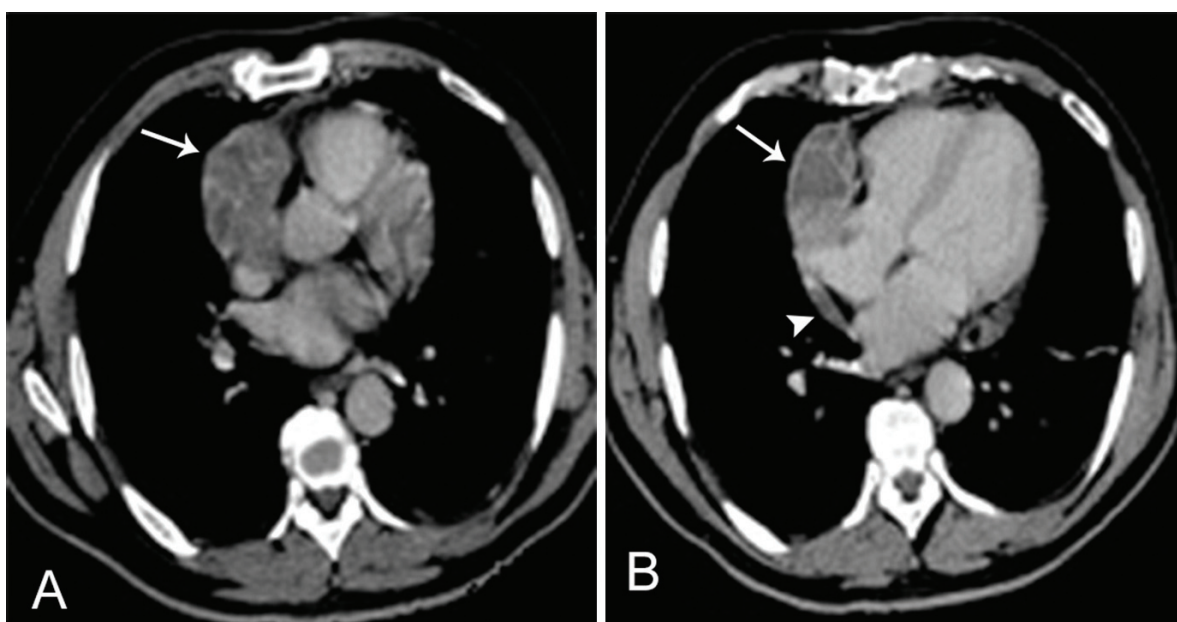
**Figure 1.** Plain chest radiography showing a mediastinal enlargement with a bulging along the right atrium contour.

pulmonary nodule was subsequently biopsied, which showed a mesenchymal malignancy represented by sinusoidal vascular channels filled with red blood cells and lined with atypical endothelial cells (Figure 5A). The immunohistochemical profile showed positivity for CD31, CD34 (Figure 5B), while Desmin and S100 Protein were negative, rendering the diagnosis of angiosarcoma. Adding the radiological and clinical findings to the histological clues, the final diagnosis was metastatic angiosarcoma primary to the right atrium.

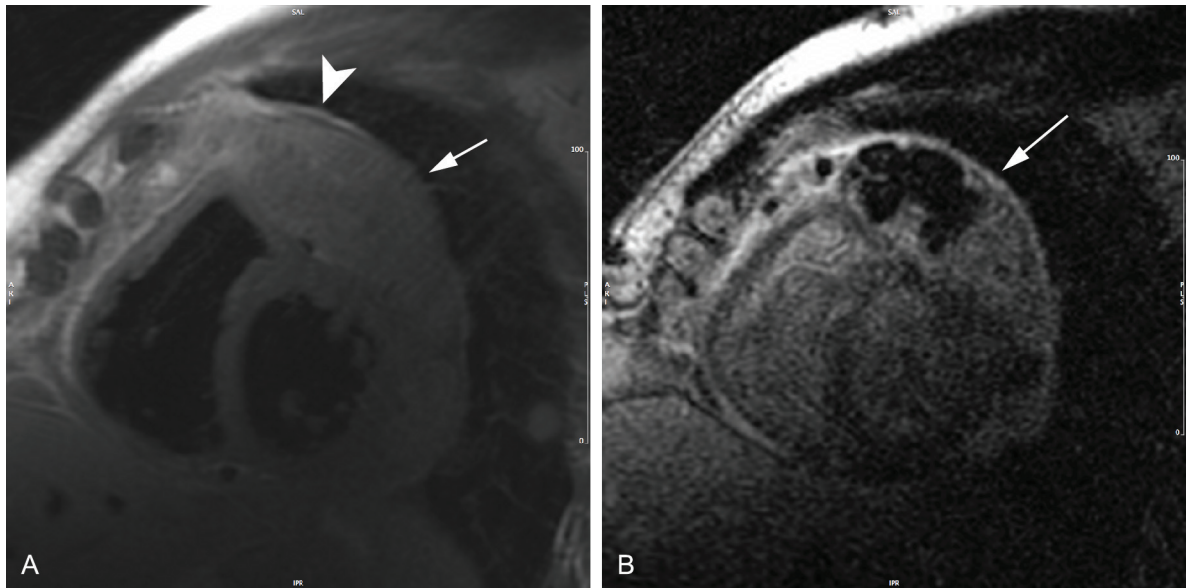
The patient received chemotherapy with doxorubicin 25 mg/m<sup>2</sup> from day 1 to 3, and ifosfamide 2000 mg/m<sup>2</sup> from day 1 to 5 every 21 days. After two cycles, CT showed reduction in the size of the pulmonary nodules (from a maximum of 2.6 cm down to a maximum of 1.8 cm). Before the third cycle of chemotherapy, the patient was admitted to the emergency department with a pulmonary infection. Despite intensive care, he developed refractory septic shock and died after 24 days.

## DISCUSSION

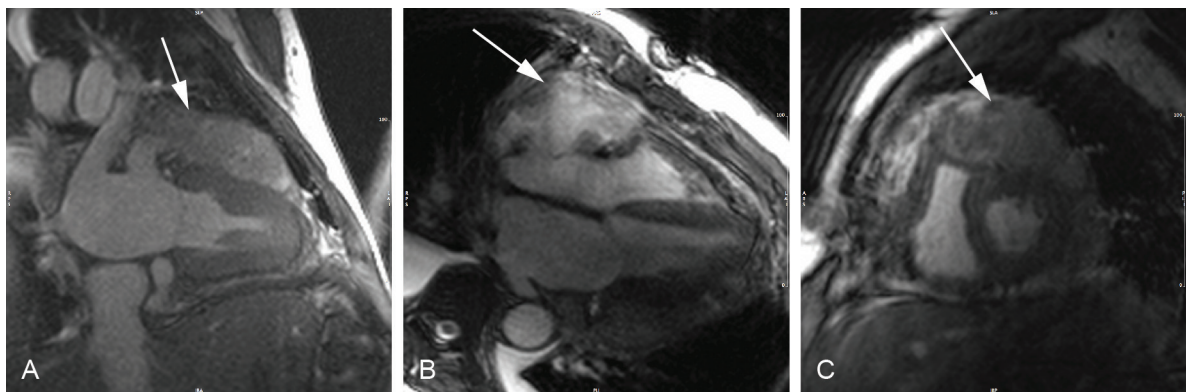
Primary cardiac tumors are extremely rare. The incidence of these tumors in autopsy findings ranges from 0.001% to 0.03%.<sup>1</sup> About 80% of the tumors are benign, and are represented



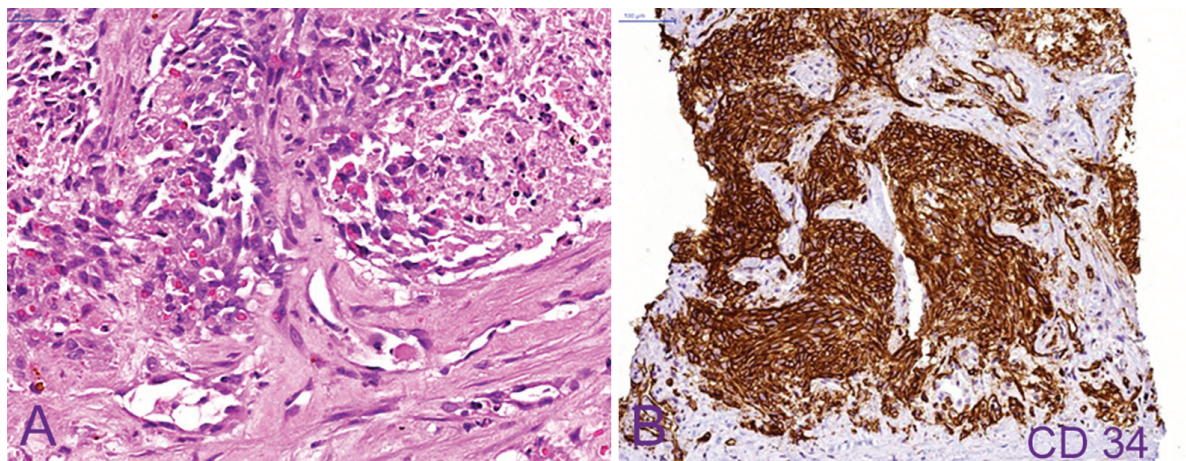
**Figure 2.** Axial computed tomography of the thorax. **A, B** - Soft tissue attenuating mass infiltrating the anterior wall of the right atrium (arrows); and in B, the pericardium (arrowhead).



**Figure 3.** Cardiac MRI. **A** - T2 weighted image - (short axis double sequences) Heterogeneous mass with right atrium isosignal in the pericardial cavity (arrow) and a small area with slightly increased signal that can represent pericardial effusion (arrowhead); **B** - T2 weighted image - (after administration of gadolinium) Heterogeneous enhancement of the mass (arrow), consistent with tumor.



**Figure 4.** Cardiac MRI (T2 weighted images) showing heterogeneous hyperintense mass (arrows) in **A, B, C** - Left ventricle's outlet, four-chamber view, and short-axis view, respectively.



**Figure 5.** Photomicrography of the biopsy of the pulmonary nodule. **A** - Sinusoidal vascular channels lined by atypical endothelial cells and areas of necrosis (arrow) (H&E, 400X); **B** - Cytoplasmic staining positive to vascular marker: CD34 (x100).

mostly by atrial myxomas. The remaining cases are malignant neoplasias represented mostly by cardiac angiosarcomas with a specific type of differentiation, however undifferentiated pleomorphic sarcomas are more common.<sup>2-6</sup>

Angiosarcomas represent up to 30% of all cardiac malignancies.<sup>3</sup> Although they can arise from any heart chamber, in the majority of cases they are found in the right atrium.<sup>7</sup> Male and middle-aged patients, like the patient reported herein, are predominantly affected.<sup>3,8</sup>

The disease usually progresses without symptoms until the tumor burden compromises hemodynamic stability, and/or causes systemic derangement, or regional metastases arise.<sup>7</sup> Symptoms may be nonspecific, such as a mild increase in temperature, weight loss, exhaustion, muscle pain, night sweats, and cough.<sup>8</sup> Nonetheless, depending on the site of the tumor and its extension to the neighboring tissue infiltration, characteristic cardiac symptoms or signs will be present; such as angina, dyspnea, arrhythmias, stroke, and sudden cardiac arrest.<sup>7,9</sup> Pericardial effusion and cardiac tamponade are frequent.<sup>10</sup>

Because of the non-specific presenting symptoms, and the unfamiliarity of most physicians with this entity, the diagnosis is overlooked and consequently often delayed.<sup>11</sup> Besides the diagnostic delay, the aggressive behavior characterized by the early spreading of the tumor and rapid local infiltration contribute to the poor prognosis.<sup>12</sup> Most patients die within a few months after diagnosis.<sup>13</sup>

Some patients are incidentally diagnosed when submitted to thoracic imaging for other purpose. Non-invasive cardiac imaging greatly contributes to the radiologic evaluation of these tumors.

Intracardiac thrombus or vegetation constitute the main differential diagnoses; thus, the first step during diagnostic evaluation is ruling out these other diagnostic possibilities,<sup>7</sup> usually by echocardiography.<sup>14</sup> In this setting, transesophageal echocardiogram shows 97% of sensitivity in diagnosing cardiac masses.<sup>15</sup> In cases of an inconclusive cardiac tumor diagnosis by the former examination, CT or magnetic resonance imaging (MRI) can be utilized.<sup>7</sup>

MRI allows better overall soft-tissue characterization and is more versatile than the CT when it can provide some functional information, such as flow direction

and flow velocity in large vessels.<sup>16</sup> However, CT is more readily available in most centers, been then a modality of choice for evaluating abnormalities intrinsic to the myocardium.

Optimal images are important when preceding surgical resections, but in the present case performing both modalities in parallel did not alter the clinical reasoning.

There are two main morphologic types described in angiosarcoma. The first is a well-defined mass protruding into one of the cardiac chambers, usually the right atrium.<sup>17,18</sup> CT often shows a low-attenuating right atrium mass, which may be irregular or nodular. The contrast medium enhancement is heterogeneous.<sup>16</sup> The second morphologic type is a diffusely infiltrative mass extending along the pericardium that may appear on CT as pericardial effusion or thickening.<sup>16,18</sup>

Because of the tumor propensity to bleeding and the presence of necrosis, heterogeneous signal intensity on CT and MRI is typical. On T1-weighted fast spin-echo (FSE) sequences, tumors are typically low-signal, and T2-weighted FSE images typically show an increased signal. Areas of increased signal intensity on T1-weighted images (focal or peripheral) are thought to represent blood products and because of their high vascularity, strong signal enhancement is seen after gadolinium injection.<sup>18,19</sup>

18F-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG PET/CT) is another tool that can be helpful in the determination of the tumor's malignant potential as well as tumoral staging.<sup>20</sup> However, histological diagnosis still remains the diagnostic gold standard.<sup>21</sup>

Unfortunately, at the time of diagnosis, metastases are frequently present and are mostly disseminated to the lungs, although lymph nodes, bone, adrenal glands, liver, and spleen may also be involved.<sup>22</sup>

An interdisciplinary approach is crucial in the management of cardiac tumors. Considering the rarity of this malignancy, there is no recommended standard therapy and evidence is based on single case reports and retrospective series.

Surgical resection plays an important role, not only with a curative goal, but also to restore normal hemodynamics. Complete resection is the treatment

of choice, although many patients show progression of the disease even after resection.<sup>1</sup>

Adjuvant chemotherapy and radiotherapy have been described in case series, but no randomized trials have been conducted. Therefore, the benefit of these modalities in reducing local and distant recurrences after complete resection is uncertain.

Llobart-Cussac et al.<sup>23</sup> reported a series with 15 patients with localized cardiac sarcomas (6 of whom had angiosarcomas) who were treated with adjuvant doxorubicin-containing regimen within 6 weeks after a complete resection. The overall median time to recurrence was 10 months. For those patients with angiosarcoma, this median time was 3 months. Median survival time for angiosarcoma was 7 months.<sup>23</sup> However, combined modality and adjuvant therapy can provide long-term disease control.<sup>24-26</sup>

Heart transplantation has been considered as a final treatment option in individual cases, especially in young patients with no other treatment option,<sup>27</sup> but the reported outcomes are discouraging.<sup>28</sup>

In the metastatic scenario, chemotherapy may provide symptom relief, improve quality of life, and increase survival time. Prospective clinical trials on advanced soft tissue sarcoma researching clinical benefit with doxorubicin-based chemotherapy did not individualize outcomes of patients with angiosarcoma. However, many reports suggest a substantial rate of response with doxorubicin, doxorubicin plus ifosfamide, vincristine and taxanes.<sup>29-31</sup> Recent phase II trials, with target therapies sorafenib and bevacizumab in the treatment of advanced angiosarcoma, have yielded promising results on the efficacy of these agents.<sup>32</sup>

In the present case, diagnosis was not suspected on clinical grounds. The suspicion was raised after plain thoracic radiography and henceforth was enlightened with other imaging techniques. Angiosarcoma was confirmed with the immunohistochemical panel of a pulmonary nodule biopsy. Cardiac tumors, although rare, are somewhat easily diagnosed with the additional of imaging methods. Obtaining histological samples may be troublesome. When metastatic disease is the presenting form, pathological documentation may be more easily accessed. Awareness of the entity and the knowledge of its clinical features are the cornerstone to decreasing the delay in diagnosis.

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