











Multiple hepatic metastases of cardiac angiosarcoma

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ABSTRACT

The differential diagnosis of hepatic focal lesions is challenging because the etiology can be inflammatory, infectious, and even neoplastic. A rare cause of metastatic liver nodules is cardiac angiosarcoma. We report a case of this tumor, which was diagnosed only after autopsy. A 26-year-old Caucasian man was admitted for progressive dyspnea and cough over the past 3 weeks. Physical examination showed only hypophonetic heart sounds. Laboratory analysis demonstrated anemia and elevated inflammatory markers, despite normal biochemical parameters and liver function. Transthoracic echocardiography revealed massive pericardial effusion. Abdomen computed tomography (CT) showed multiple hepatic nodules, the largest of which measured 3 cm, but the percutaneous biopsy revealed only lobular necrosis and perisinusoidal fibrosis without granulomas or neoplastic cells. During hospitalization, the patient had fever and night sweats with weight loss, and empiric treatment for extrapulmonary tuberculosis associated with corticosteroids was initiated. The outpatient follow-up revealed complete improvement of the pericardial effusion, but maintenance of the liver lesions. After 2 months of hospital discharge, the patient was readmitted with hemorrhagic shock due to bleeding liver lesions, which were evidenced by CT. Embolization of the right hepatic artery was performed, but the patient soon died. The autopsy revealed a primary cardiac angiosarcoma with multiple hepatic metastases, rupture of the Glisson's capsule and laceration of the liver. The case shows how important and difficult the diagnosis of focal liver lesions is, since it may result in an unexpected fatal outcome.

Keywords

Sarcoma; Neoplasm Metastasis; Heart Neoplasms.

INTRODUCTION

The diagnosis of hepatic focal lesions is challenging because the etiology can be inflammatory, infectious, and even neoplastic. The liver is an important site of metastasis, occurring in 30%–40% of the necropsies in patients who die from cancer. Diverse mechanisms

explain this predilection, especially the great blood flow that converges to this organ, and the large lymphatic drainage.^{1,2}

Angiosarcoma is a rare, aggressive primary cardiac tumor with large invasiveness and high metastatic

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capacity. The liver is one of its main dissemination sites.³⁻⁵ The diagnosis is difficult, but echocardiography and tomography are the most useful methods. We describe a case of cardiac angiosarcoma with multiple hepatic metastases diagnosed only after autopsy.

CASE REPORT

A 26-year-old previously healthy Caucasian man complained of dry cough and progressive dyspnea over the past 3 weeks. He had dizziness, retrosternal pain, and one episode of fever. The physical examination was normal, except for hypophonetic heart sounds.

His chest x-ray showed a large cardiac area (Figure 1A), and transthoracic echocardiography (Figure 1B) revealed a massive pericardial effusion (PE) without signs of cardiac tamponade. Computed tomography (CT) identified multiple rounded hepatic focal lesions less than 1 cm, all hypodense and hypovascular. The largest one measured 3 cm in the segment IVa. Laboratory analysis showed anemia, elevation of inflammatory markers, an erythrocyte sedimentation rate of 95 mmHg and C-reactive protein of 92 mg/L (normal value <3 mg/L), but biochemistry, liver, and thyroid function were normal. Viral markers for hepatitis B, C, HIV, rheumatoid factor, and antinuclear antibody were negative.

Ultrasound-guided percutaneous biopsy was performed with technical difficulties in accessing

the largest lesion and revealed lobular necrosis and perisinusoidal fibrosis without granulomas or neoplasms. During hospitalization, the patient had fever and night sweats with weight loss, so empiric treatment for extrapulmonary tuberculosis was started in association with corticosteroids, considering the high prevalence of this pathology in our country.

The outpatient follow-up revealed complete improvement of the PE, but maintenance of the liver lesions after 2 months. Days later, the patient was admitted as an emergency with hemorrhagic shock due to bleeding liver lesions, which were revealed in the new abdominal CT (Figures 2A and 2B), and was further submitted to embolization of the right hepatic artery, without response, and soon died. At this time, the thoracic CT (Figure 3C) revealed a right atrial hypodensity, which was not evidenced in the initial echocardiography and abdominal tomography.

AUTOPSY FINDINGS

The autopsy revealed a primary right atrium angiosarcoma (Figure 3A) with multiple hepatic metastases, rupture of the Glisson's capsule, and laceration of the liver (Figure 3B). Figure 3C shows the microscopic analysis of the liver tumor and Figure 3D shows the positive immunohistochemistry for CD34. The tumor was negative for HHV8.

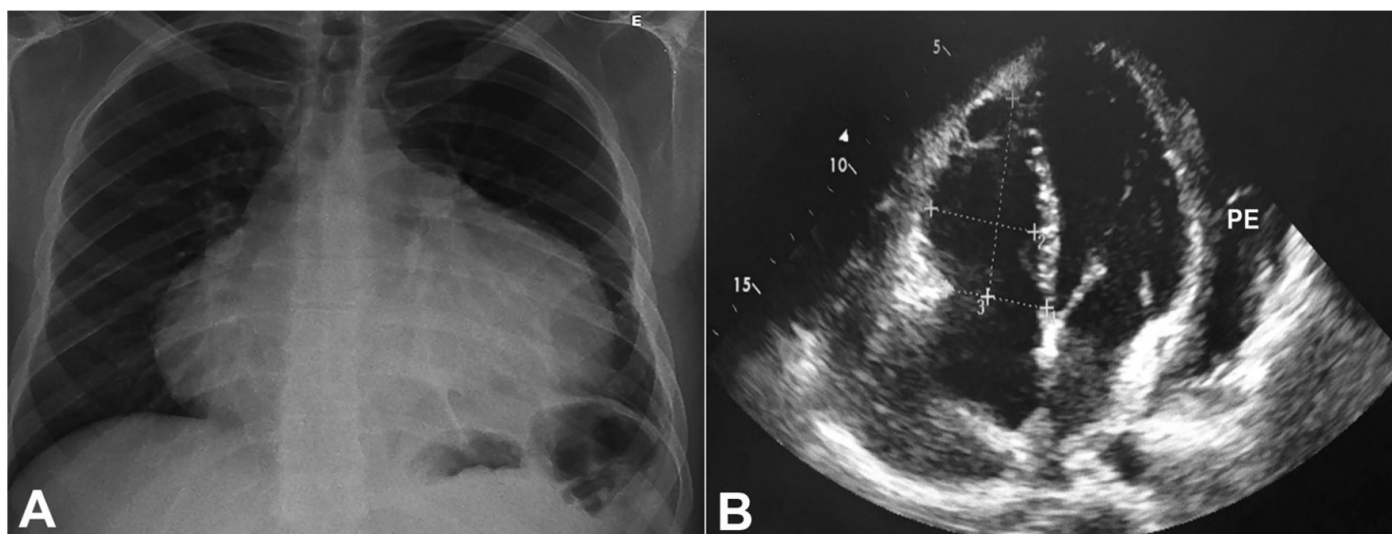


Figure 1. A – Increased cardiac area on chest X-ray. **B** – Transthoracic echocardiography revealing pericardial effusion but not showing the tumor.

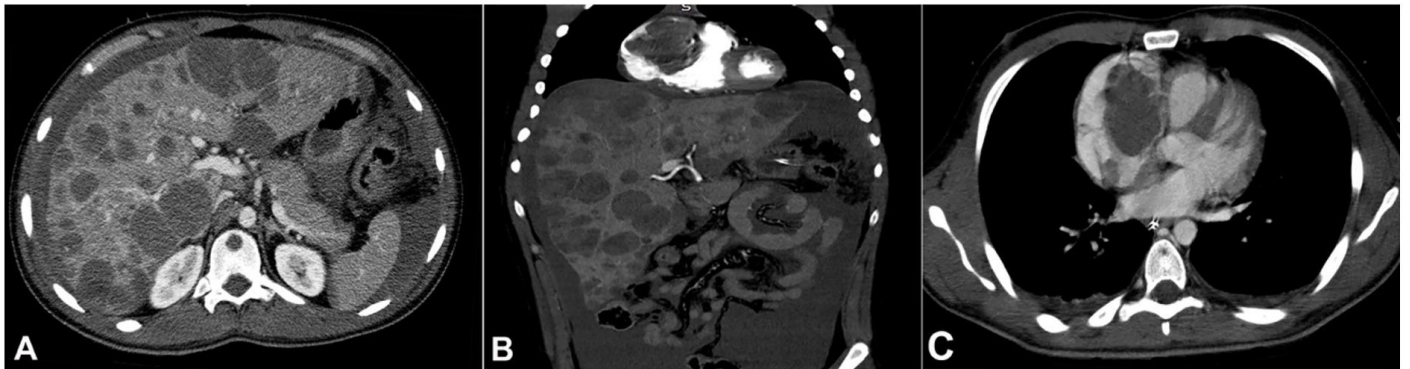


Figure 2. Abdominal CT. **A** – Axial plane: multiple hypodense hepatic lesions and hemorrhagic ascites. **B** – Coronal plane: evidence of the right atrial mass. **C** – Thoracic CT, axial plane: reveals right atrial hypodensity. CT = computed tomography.

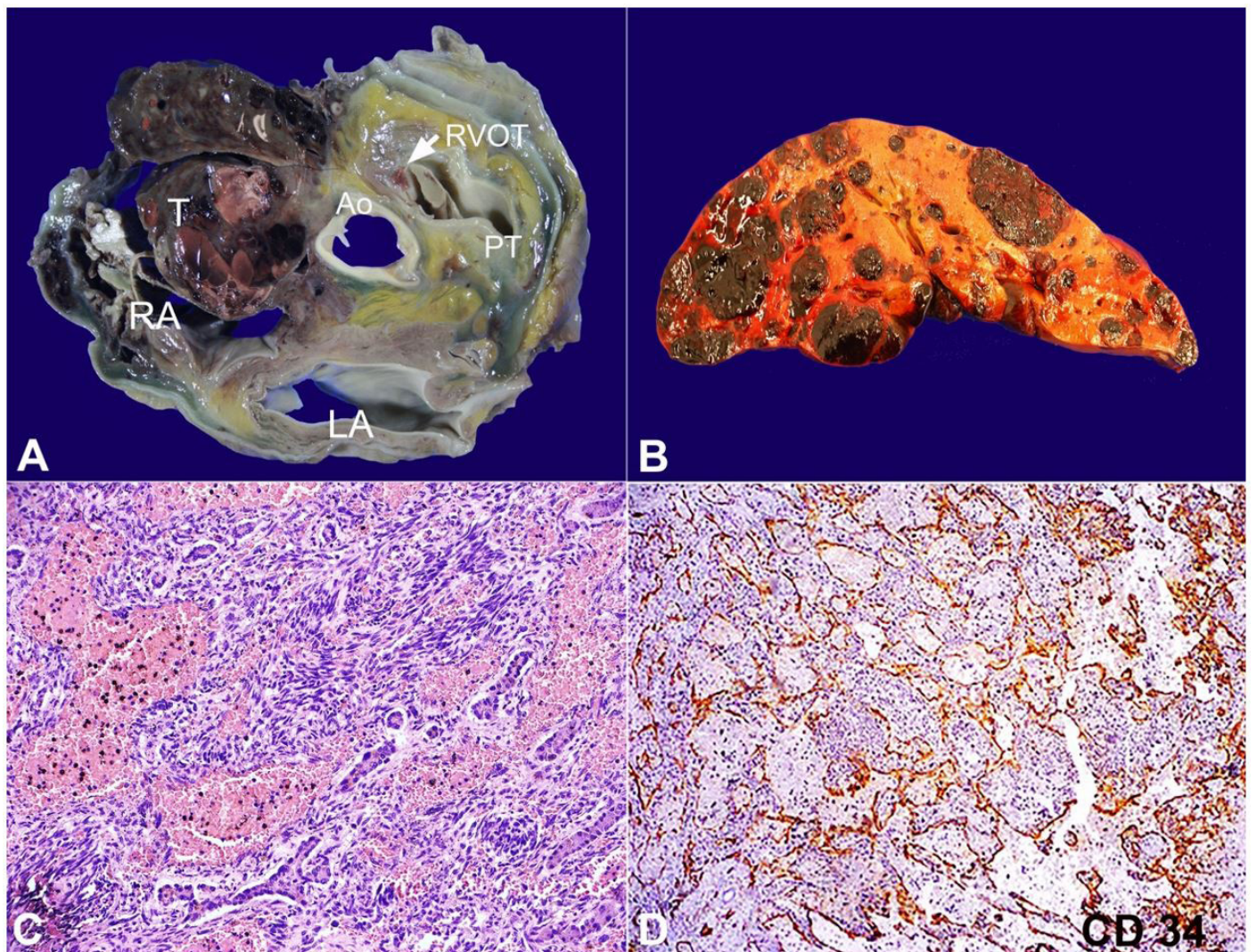


Figure 3. **A** – Gross view of the right atrial angiosarcoma. **B** – Macroscopic appearance of the hepatic cut surface showing multiple and scattered metastases of the angiosarcoma. **C** – Photomicrograph of the hepatic fragment with spindle cells delimiting poorly-formed vascular structures, characteristic of angiosarcoma (H&E, 100X). **D** – Immunohistochemistry: strong and diffuse positivity for CD34 (40X). Ao = aorta; LA = left atrium, PT = pulmonary trunk, RVOT = right ventricle outflow tract, RA = right atrium, T = tumor.

DISCUSSION

Primary cardiac neoplasms are extremely rare, and the diagnosis is often established through autopsies. It is found in less than 0.05% of autopsies.^{6,7} The majority of cardiac tumors are benign (75%), and the myxoma is the most common. Among malignant cardiac tumors, sarcomas are the most frequent.^{7,8} Cardiac angiosarcomas are very aggressive neoplasms, with a high rate of local recurrence and systemic metastasis.⁷⁻⁹ Males are two to three times more affected than females, and most patients are young. The main site is in the right atrium (70%-90%) and the tumor can invade the vena cava and tricuspid valve, resulting in congestive heart failure, PE, and cardiac tamponade.¹⁰⁻¹²

Patients are usually asymptomatic, although dyspnea, weight loss, anemia-related fatigue, and malaise can occur.⁶ Butany and Yu¹³ reported that 46% of subjects present with chest pain as the chief complaint. Our patient's tumor was in the right atrium; there was PE, and he had dyspnea, chest pain, and weight loss, as described.

Histologically, an angiosarcoma is an infiltrative vascular tumor with a broad histologic profile ranging from a well-differentiated neoplasm with frank vascular differentiation to a poorly differentiated lesion. The neoplasia is formed in infiltrating, free anastomosed cells coated by epithelioid endothelial cells with variable atypia, and may have the appearance of multiple layers. It can have free-floating intraluminal endothelial cells ("fish in the creek"). This tumor may mimic poorly differentiated carcinoma, an inflammatory process, lymphoma, or melanoma.¹⁴ Immunohistochemistry has shown that the most reliable markers are CD31 (positive in 90%) and CD34 (positive in 50%–74%).^{6,7,14} Rarely, it is positive for cytokeratins, EMA, and CD30 (usually in the epithelioid angiosarcoma variant). The tumor is negative for HHV8, SMA, and desmin.¹⁴ In our case, CD34 was positive, and HHV8 was negative. This last information excludes the possibility of Kaposi sarcoma, another differential diagnosis.

At autopsy, it was initially doubtful whether the primary neoplastic lesion was in the heart or liver. The factors that suggested a primary cardiac tumor with liver metastasis were: 1) our patient's younger age, since hepatic angiosarcomas are more frequent in

subjects older than 60 years, sometimes with exposure to agents such as thorium oxide, vinyl chloride, arsenic, and anabolic steroids;¹⁵ 2) single heart lesion X multiple hepatic lesions; 3) the location in the right atrium is a mark of cardiac angiosarcomas;^{6,7} 4) the most common sites of metastatic dissemination of liver angiosarcoma are lungs and spleen, when intra-cardiac involvement is rare,^{15,16} and 5) the liver is commonly involved in the metastatic spread of cardiac angiosarcomas.³⁻⁶

Some barriers prevented us from diagnosing the tumor before our patient's fatal evolution. Evidence of the cardiac mass on transthoracic echocardiography was difficult to see because of the presence of PE. In a series of 33 cases published by Kupsky et al.,¹⁷ the echocardiography had 75% of sensitivity. In patients which this exam failed to detect the cardiac mass, there was PE. It also happened in the subjects reported by Riles et al.¹⁸ and Choi et al.³ The transesophageal method has 97% sensitivity in detecting these masses.⁶ Fine-needle liver biopsy may not reach the tumor or may only access necrosis,¹⁹ and this led us to initially postulate that the lesions were only inflammatory. However, in this case, even if an earlier diagnosis had been made during the first admission, it is unlikely that the poor prognosis would have changed due to the presence of metastasis. Most reported cases of cardiac angiosarcoma with metastatic involvement had an ominous outcome, where the patients died within a few months.^{6,7} In our case, the initial improvement after treatment for tuberculosis actually may have occurred because of the corticosteroid, which was another confounding factor.

This case shows how important and difficult the diagnosis of focal liver lesions is, since it may result in an unexpected fatal outcome. In addition, the presence of PE may be an obstacle to the usefulness of transthoracic echocardiography.

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The authors retain an informed consent signed by the deceased's relatives, and the manuscript is in accordance with the Institutional Ethics Committee.

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