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Metastatic Cardiac Angiosarcoma in a 26-Year-Old Male

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Background: Cardiac angiosarcomas are an extremely rare tumor with an incidence of only 0.056%. Diagnosing this rare tumor becomes even more difficult as the presentation of cardiac angiosarcomas varies based on anatomic location. Depending on the tumor's proximity to valves, symptoms may be more consistent with heart failure, while growth throughout the conduction system may produce arrhythmias**.**

Case Report: We present the case of a young male with a significant tumor burden of cardiac angiosarcoma in his lungs whose symptoms included pleuritic chest pain and hemoptysis. This patient did not have the classic finding of right-sided heart failure; instead, his presenting complaint was hemoptysis.

Conclusion: The diagnostician's differential diagnosis must be broad when encountering common chief complaints, such as hemoptysis and chest pain.

Keywords: *Angiosarcoma, coronary arteries, heart failure, heart neoplasm, hemoptysis*

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INTRODUCTION

Cardiac malignancies are rare, with primary cardiac tumors making up an extremely small subset. In one 20-year study, researchers performed 12,485 autopsies and found the incidence of cardiac tumors to be 0.056% for primary tumors and 1.23% for secondary tumors, a ratio of 1:22.[1] Of the primary tumors found in the study, none was an angiosarcoma; they were comprised of 2 myxomas, 2 rhabdomyomas, 2 hemangiomas, and 1 lipoma. Another study that evaluated the Surveillance, Epidemiology, and End Results (SEER-17) database from 1988-2005 found that of the small absolute number of primary cardiac tumors, one-fourth were malignant and most were sarcomas.[2] According to Vander Salm, approximately 75% of the primary cardiac tumors that arise are benign, most of which are myxomas.[3] Individuals with angiosarcoma were more likely to be younger than 65 years old. The likelihood of local vs metastatic disease in individuals with angiosarcoma was equal.[3] A review of 46 cases by Janigan et al found that cardiac angiosarcomas are at least partially in the right atrium 93% of the time, as determined by autopsy.[4] The majority of those tumors replaced the atrial wall; and, in one case, the tumor was mobile and attached to the atrial wall by a pedicle. In many cases, the exact origin of the tumor was difficult to determine given its significant local growth. Histologic evaluation of angiosarcomas is difficult as they can have the appearance of benign tumors. However, the sinusoidal pattern on histology is thought to be pathognomonic for angiosarcomas.[4]

Cardiac tumors increase morbidity and mortality via a variety of mechanisms.[3] One mechanism is that the tumor can impede blood flow or valve function and potentially cause tamponade. The tumor's impedance can decrease forward blood flow, causing symptoms of heart failure such as angina, syncope, and dyspnea. A second mechanism is that the tumor can grow into the pericardium, causing a constrictive pericarditis. Another mechanism of increased morbidity/mortality is that the tumor can interfere with the conduction system, leading to arrhythmias such as supraventricular tachycardia or heart block. Further, the tumor can embolize to the systemic circulation, an event that is more likely when the tumor is on the left side of the heart. The tumor's presence on the left side of the heart or metastasis from the right side of the heart can also lead to pulmonary hypertension. Finally, the tumor itself can lead to constitutional symptoms.[3] Despite these multiple potential mechanisms, many patients present with unrelated symptoms, or their cardiac tumors are found incidentally.

CASE REPORT

A 26-year-old African American male was admitted to an outside hospital with complaints of hemoptysis, left-sided pleuritic chest pain, and dyspnea on exertion for approximately 1 month prior to presentation. Other associated symptoms included an unquantified weight loss and night

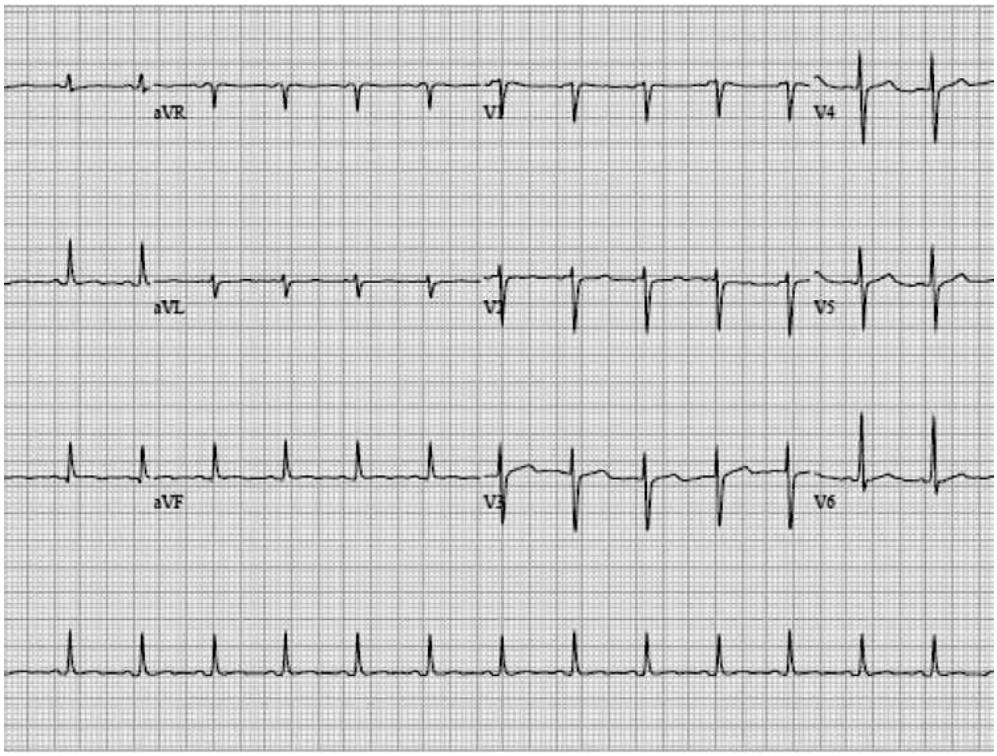

Figure 1. Electrocardiogram demonstrates sinus tachycardia with nonspecific T wave changes.

sweats. The patient's social history was positive for a 10-year smoking history, occasional alcohol use, and recent incarceration. On presentation, the patient's electrocardiogram (ECG) demonstrated sinus tachycardia with nonspecific T wave changes (Figure 1). Computerized axial tomography (CT) scan of his chest and abdomen revealed multiple pulmonary nodules, extensive mediastinal adenopathy, and a large hypervascular (6.0 × 6.2 cm) mediastinal mass abutting the right atrium and ventricle. The CT scan also showed bilateral pleural effusions, with the left effusion greater than the right; osteolytic lesions at L2 and L5; and a possible lesion in the liver. The CT scan showed no evidence of pulmonary embolism. Initial workup at the outside hospital included bronchoscopy with bronchoalveolar lavage. Follow-up cultures from the lavage, including acid-fast bacilli, were negative for infection.

The patient was transferred to our hospital on mechanical ventilation but with minimal oxygen requirements. His physical examination was positive for tachycardia, diminished lung sounds, and lower extremity edema. He had no sign of jugular venous distention, and no cardiac murmurs, rubs, or gallops were heard on auscultation. The patient was successfully weaned from the ventilator initially, but he required repeat intubation because of respiratory failure on the same day. Transthoracic echocardiogram demonstrated a 4.6 × 2.3 cm mass within the right atrium with 2 small mobile components. A repeat CT scan revealed enlargement of the mass, now measuring 7.0 × 6.4 × 4.4 cm in size. Part of the mass was within the heart, and part of the mass was abutting the right atrium from the exterior. The mass engulfed the right coronary artery. The superior vena cava was narrowed to 5 × 11 mm secondary to infiltration by the atrial component of the mass (Figure 2). The mass also extended inferiorly into the right ventricle. A large pericardial effusion was also noted. Pulmonary artery pressure was 28 mmHg.

Pulmonary infiltrates were more numerous and denser than on the prior CT scan (Figure 3). The patient received a thoracentesis; however, the pleural fluid was negative for malignant cells. The pleural fluid was only positive for reactive mesothelial cells, inflammatory cells, and blood. In a repeat thoracentesis, the pleural fluid was again nondiagnostic. A pleural drain was placed, and significant serosanguinous output occurred during hospitalization. Given the concern for atrial perforation, biopsy and resection of the cardiac mass were deferred by cardiothoracic surgery and interventional cardiology. The pleural mass was subsequently biopsied by interventional radiology. The biopsy demonstrated a high-grade malignant vascular neoplasm favoring metastatic angiosarcoma. Histologic examination demonstrated enlarged cells with marked nuclear pleomorphic, irregular hyperchromatic nuclei with increased mitosis, and scattered karyorrhectic bodies. The tissue biopsy was positive for vascular markers CD31 and CD34. CD99 showed blush positivity, while S100 was negative. The surrounding lung parenchyma showed plump reactive pneumocytes with adjacent intraalveolar hemorrhage.

The patient developed acute respiratory distress syndrome and required increased positive end-expiratory pressure and inspired oxygen fraction on day 5 of hospitalization. On day 10 of hospitalization, the patient

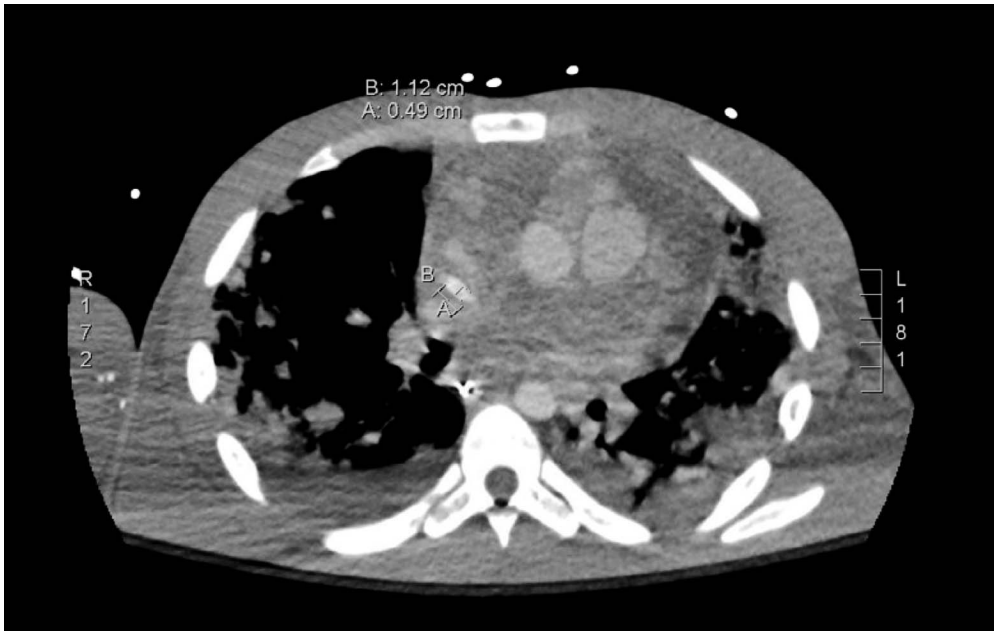

Figure 2. Computed tomography scan shows the large cardiac tumor narrows the superior vena cava via atrial infiltration.

developed hypotension and shock, requiring vasopressor support. Blood cultures were positive for methicillin-resistant *Staphylococcus aureus*. The patient's poor performance status and multiorgan failure made him a poor candidate for chemotherapy, and this treatment option was not pursued. On day 14 of hospitalization, the patient died of shock and sequelae of metastatic angiosarcoma.

DISCUSSION

A retrospective study by Odim et al of 29 patients with cardiac tumors found that on initial presentation, patients had heart failure, thromboembolism, or both approximately 50% of the time.[5] Our patient did not have those complaints but instead presented with complaints of hemoptysis and chest pain, thought to be attributable to his significant pulmonary tumor burden. Hemoptysis was

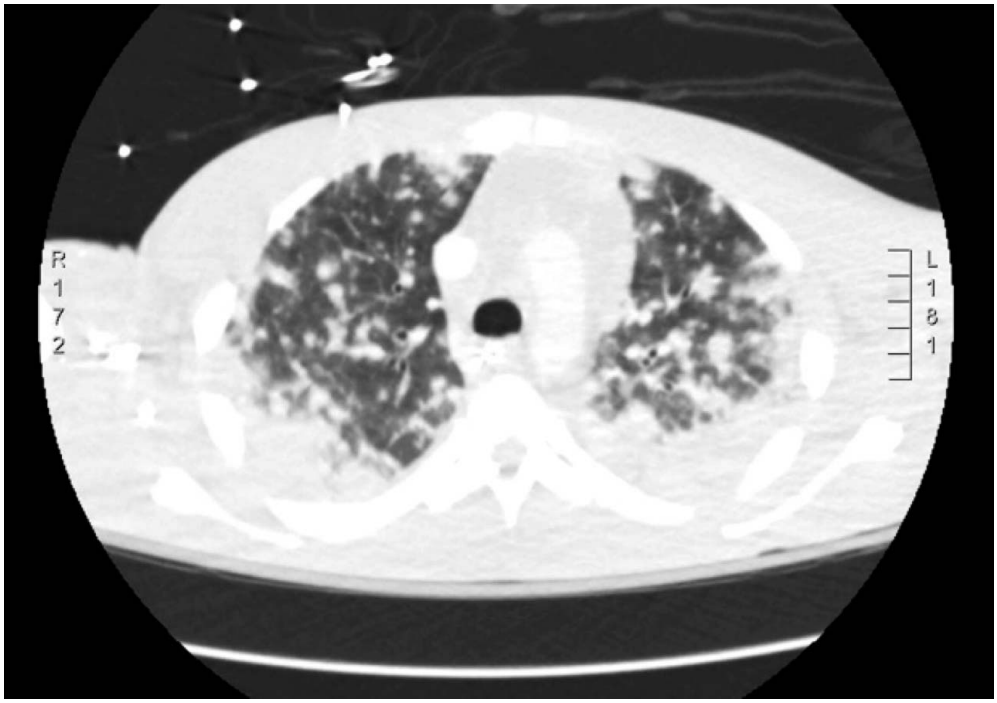

Figure 3. As shown by computed tomography, the patient presented with hemoptysis, likely secondary to the large tumor burden in his lungs.

likely secondary to the intrinsically vascular properties of the tumor, as well as the tumor's infiltration of the lobar and pulmonary arteries. Lack of right-sided heart failure symptoms on presentation may be from the tumor's initial distance to the right heart. As the tumor rapidly increased in size and compressed the superior vena cava, the patient went into shock; however, the patient was also septic at this time. The etiology of the patient's shock was thus multifactorial.

Chest pain was a nonspecific presenting finding in only 14% of patients in the Odim et al study.[5] Choi et al described a young man who initially presented with hemoptysis and was treated with antibiotics for presumed pneumonia.[6] The patient's status worsened until he developed symptoms of right heart failure including dyspnea, hypotension, tachycardia, and distended jugular veins.[6] Further workup revealed that the patient had metastatic angiosarcoma. Clinically presenting symptoms are largely determined by the location of the tumor, particularly its proximity to valves, and less so by the size of the tumor.[7]

Cardiac tumors have been described in reports as early as the 1700s, but the first antemortem diagnosis was made in 1934 with the use of an ECG.[7] Today, tumors are evaluated radiologically because of the higher sensitivity of imaging compared to ECG. Radiologic studies often consist of an echocardiogram and optimally of magnetic resonance imaging (MRI) if the patient is hemodynamically stable; however, CT scanning also provides some benefit. These modalities typically allow for the evaluation of the location and characteristics of a tumor.[3] Our patient received an echocardiogram but was not hemodynamically stable for an MRI; however, he was stable for a CT scan. ECG changes are found in 75% of patients with cardiac malignancies. Our patient's ECG demonstrated sinus tachycardia with nonspecific T wave changes.

As mentioned previously, primary cardiac sarcomas are often discovered after they have already metastasized, likely because of the location in the heart; the tumor is bathed in blood, leading to a high hematogenous metastasis rate.[8] Although a specimen is needed for a definitive diagnosis, location on the right side, and in particular the right atrium, can give the clinician a clue that a tumor is malignant.[9] Histologic analysis of the tissue demonstrates anastomosing vascular channels formed by malignant cells.[7] Metastasis is common. Our patient had evidence of distant metastasis to his liver as indicated by his first CT scan. As these right-sided cardiac tumors often metastasize to the lungs, biopsy from the lungs is sometimes necessary as in our patient. Caution must be used during biopsy as the rate of biopsy embolus is high. Elbardissi et al retrospectively studied more than 300 primary cardiac tumors and found the rate of embolus to be approximately 25%. This rate of embolus varies, depending on the structural characteristics of the tumor itself.[10]

All patients with angiosarcoma should be evaluated for resectability and heart transplant. Although surgical resection is the mainstay of therapy, it is often not possible in patients who present with advanced disease.[2] Malignant cardiac tumors also have a poor response to chemotherapy and radiation. The SEER-17 analysis showed that poor differentiation and surgical resection were prognostic factors, but stage, histology, and use of radiation therapy were not.[2] The median overall survival for cardiac sarcoma patients is only 6 months. This prognosis is dismal compared to the overall survival of noncardiac sarcoma patients of 93 months.[2] Survival time improved to 12 months if the mass could be resected and worsened to 1 month if it could not be resected.[3] Interestingly, even patients with metastatic disease underwent surgical debulking for palliation, as local disease is often the cause of death.[3]

Poor survival rates are multifactorial and are also attributable to limited treatment options. Although the SEER-17 analysis did not show that radiation therapy improved mortality, in one case report, radiation therapy provided benefit.[8] Radiation therapy was used for a 51-year-old man who was diagnosed with a high-grade unresectable cardiac sarcoma without evidence of metastasis, and the patient remained disease free 5 years after diagnosis. During the patient's 15-month course of radiation therapy, his tumor reduced in size from 7.5 cm to 4 cm. However, the patient suffered from recurrent pleural effusions requiring pleurodesis that subsequently developed into oxygen-dependent restrictive lung disease. The patient died 5.5 years after diagnosis because of respiratory failure. Autopsy demonstrated that the area corresponding with the initial tumor was filled with necrotic material, and the surrounding areas had microscopic changes secondary to radiation.[8]

CONCLUSION

Cardiac angiosarcomas are rare tumors with an even rarer patient survival rate. More research needs to be dedicated to improve the morbidity and mortality of these patients. Our patient's presenting chief complaint of hemoptysis and his lack of right-sided heart failure were an especially unique presentation for a rare tumor. This case should serve as a reminder for clinicians to broaden their differential diagnoses when encountering patients with textbook complaints.

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REFERENCES

1. Lam KY, Dickens P, Chan AC. Tumors of the heart. A 20 year experience with a review of 12,485 consecutive autopsies. *Arch Pathol Lab Med*. 1993 Oct;117(10):1027-1031.
2. Hamidi M, Moody JS, Weigel TL, Kozak KR. Primary cardiac sarcoma. *Ann Thorac Surg*. 2010 Jul;90(1):176-181. doi: 10.1016/j.athoracsur.2010.03.065.
3. Vander Salm TJ. Unusual primary tumors of the heart. *Semin Thorac Cardiovasc Surg*. 2000 Apr;12(2):89-100.
4. Janigan DT, Husain A, Robinson NA. Cardiac angiosarcomas. A review and case report. *Cancer*. 1986 Feb 15;57(4):852-859.
5. Odim J, Reehal V, Laks H, Mehta U, Fishbein MC. Surgical pathology of cardiac tumors. Two decades at an urban institution. *Cardiovasc Pathol*. 2003 Sep-Oct;12(5):267-270.
6. Choi CH, Konda S, Shake JG. Angiosarcoma of the right atrium presenting as hemoptysis. *Proc (Bayl Univ Med Cent)*. 2016 Jan; 29(1):79-80.

7. Salcedo EE, Cohen GI, White RD, Davison MB. Cardiac tumors: diagnosis and management. *Curr Probl Cardiol*. 1992 Feb;17(2): 73-137.
8. Movsas B, Teruya-Feldstein J, Smith J, Glatstein E, Epstein AH. Primary cardiac sarcomas: a novel treatment approach. *Chest*. 1998 Aug;114(2):648-652.
9. Afzal MN, Alguacil-Garcia A. Primary cardiac angiosarcoma: clinical and pathological diagnostic problems. *Can J Cardiol*. 1997 Mar;13(3):293-296.
10. Elbardissi AW, Dearani JA, Daly RC, et al. Embolic potential of cardiac tumors and outcome after resection: a case-control study. *Stroke*. 2009 Jan;40(1):156-162. doi: 10.1161/STROKEAHA.108.525709.

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