

# Primary Angiosarcoma—A Rare Cause of Right Ventricular Outflow Tract Obstruction: Case Report and Literature Review



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## INTRODUCTION

Primary cardiac neoplasms are extremely rare, with an incidence at autopsy of 0.0001% to 0.03%.<sup>1</sup> Most (75%) primary cardiac tumors are benign. The majority of malignant cardiac tumors are sarcomas, of which 30% are angiosarcomas.<sup>2</sup> Other subtypes include rhabdomyosarcoma, malignant fibrous histiocytoma, and fibrosarcoma.<sup>3</sup> Despite being the most common malignant cardiac tumor, cardiac angiosarcoma is often overlooked because of its rarity and nonspecific presentation.<sup>4</sup> As a result of its aggressive nature and late diagnosis, the prognosis remains poor. We describe a case of tumor in the right ventricular outflow tract (RVOT) and main pulmonary artery (MPA) that eluded preoperative diagnosis despite multimodality imaging.

## CASE PRESENTATION

A 77-year-old woman presented to the emergency department with rapidly progressive dyspnea on exertion and lethargy for the previous 2 months, to the point of being housebound by the time of presentation. She denied orthopnea and paroxysmal nocturnal dyspnea. There had been one episode of self-resolving chest discomfort lasting only a few seconds. She had been treated by her family physician with a course of oral antibiotics for possible respiratory tract infection. Other medical history included diabetes treated with oral hypoglycemic agents, hypercholesterolemia, and total thyroidectomy. Initial examination revealed a loud late peaking systolic murmur at the left sternal edge and clear lung fields, with no lower limb edema. Electrocardiography showed new widespread T-wave inversion. Chest radiography showed cardiomegaly and prominent proximal pulmonary arteries suggestive of pulmonary hypertension. The patient was admitted for further investigation. Transthoracic echocardiography showed restricted pulmonary valve leaflets with peak gradient 72 mm Hg (Figure 1, Video 1), right ventricular systolic dysfunction, and thickening of the RVOT free wall up to 1.3 cm, consistent with severe valvular pulmonary stenosis. Subsequent transesophageal echocardiography confirmed severely impaired right ven-

tricular function with marked RVOT hypertrophy. The pulmonary valve appeared thickened and restricted, with a possibility of filling defect in the RVOT (Figure 2, Videos 2 and 3). Computed tomography pulmonary angiography (Figure 3) and cardiac magnetic resonance imaging (MRI) (Figure 4) revealed a large, nonenhancing filling defect extending from the RVOT into the main, left, and right pulmonary arteries, adherent to the pulmonary valve. Lack of enhancement suggested pulmonary thromboembolism, with eccentricity and presentation suggesting chronic thromboembolus. Therapeutic anticoagulation with low-molecular weight heparin and warfarin was commenced, along with diuretic therapy. Computed tomography of the abdomen and pelvis showed no evidence of an underlying malignancy. Despite some early symptomatic alleviation with anticoagulation and diuretic therapy, the patient re-presented within 2 weeks with progressive dyspnea and signs of right ventricular dysfunction. She was referred for pulmonary endarterectomy. Preoperative positron emission tomography and repeat MRI were again suggestive of thrombus. At surgery, extensive tumor was resected from the right ventricle, RVOT, MPA, and branches. Although severe RVOT obstruction was relieved, the pulmonary pressures remained elevated secondary to persistent thrombus and tumor beyond the reach of surgical resection. Severe right ventricular dysfunction persisted, and the patient died 10 days postoperatively. Histopathologic examination of the specimen showed haphazardly arranged cells with high mitotic activity. The atypical cell population showed positive immunostaining to vimentin, smooth muscle actin, broad-spectrum cytokeratin, CD31 and CD34 (Figure 5).

## DISCUSSION

Cardiac angiosarcoma is the most common histologic subtype of primary malignant cardiac tumor. There is a high potential for local recurrence and systemic metastasis. The most common site is the right atrium (90%), with frequent involvement of surrounding structures, resulting in congestive heart failure, pericardial effusion, and tamponade.<sup>5</sup> The left side of the heart is involved in <5% of cases.<sup>2</sup>

Histologically, angiosarcoma is an endothelial cell tumour.<sup>5</sup> Metastases are present in up to 80% of cases at the time of diagnosis. The lungs are the most common site of metastases, followed by the liver, lymph nodes, adrenal glands, bones, and brain.<sup>6</sup> Men are 2 to 3 times more frequently affected than women.<sup>7</sup> A few cases of possible familial angiosarcoma have also been reported.<sup>8</sup> Primary cardiac angiosarcoma presents with nonspecific constitutional symptoms, with shortness of breath being the most common.<sup>9</sup> Other presentations include chest discomfort, weight loss, fatigue, and lethargy. Patients are often asymptomatic until more specific clinical findings manifest later in the course of disease as a result of infiltration into local structures and extent of metastases. The pericardium is frequently involved, resulting in pericardial effusion and tamponade. Other clinical complications include heart failure, valvular obstruction

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## VIDEO HIGHLIGHTS

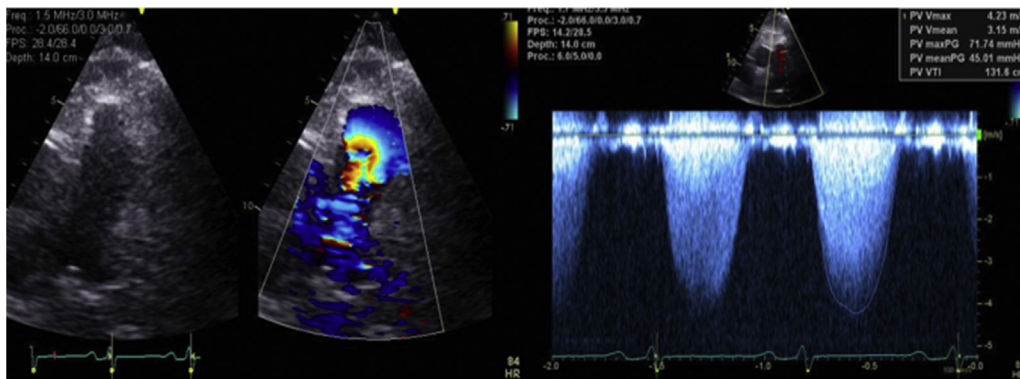
**Video 1:** Transthoracic echocardiogram with flow acceleration at the RVOT.

**Video 2:** Transesophageal echocardiogram of the short-axis views of the aortic valve and possible filling defect in the RVOT.

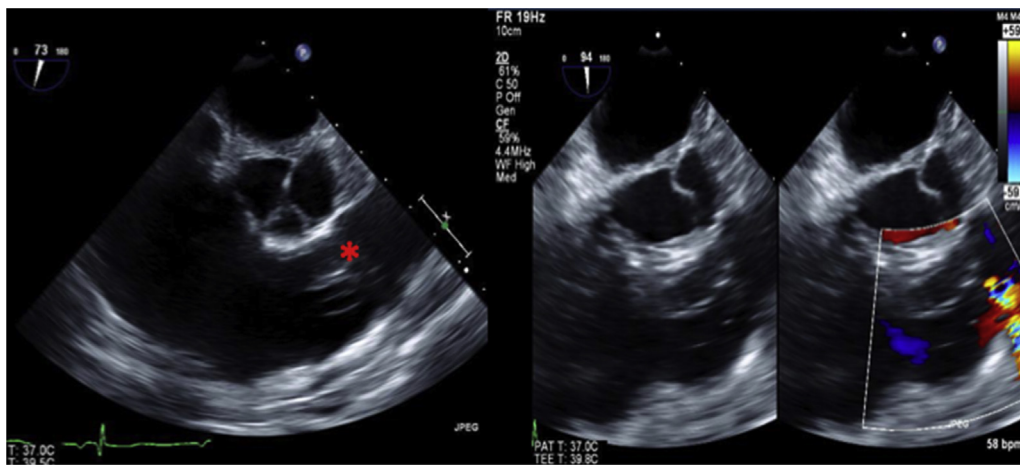
**Video 3:** Transesophageal echocardiogram with prominent filling defect in the RVOT and flow acceleration through it.

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in the detection of hemodynamic sequelae such as tamponade secondary to pericardial effusion and stenosis secondary to physical obstruction by the tumor mass. Transesophageal echocardiography may provide more detailed images of the mass and its relationship to surrounding cardiac structures, while computed tomography may assist in defining the mass and any extracardiac extension. Cardiac MRI is especially advantageous in defining tissue characteristics and, through the use of gadolinium-based contrast agents, differentiating between cardiac masses such as tumors, which display variable enhancement, and thrombi, which do not enhance at all.<sup>11</sup> In the case presented here, preoperative diagnosis remained challenging



**Figure 1** Transthoracic echocardiogram suggestive of flow acceleration through the RVOT.

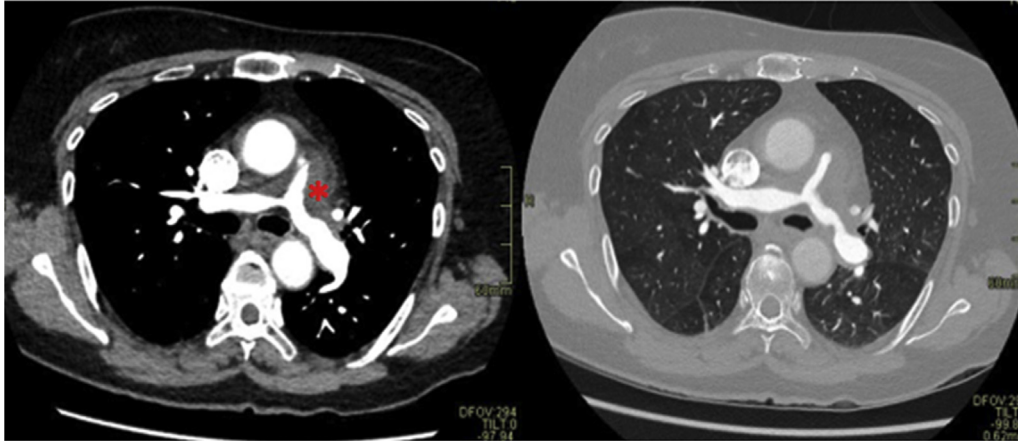


**Figure 2** Transesophageal echocardiogram showing filling defect (asterisk).

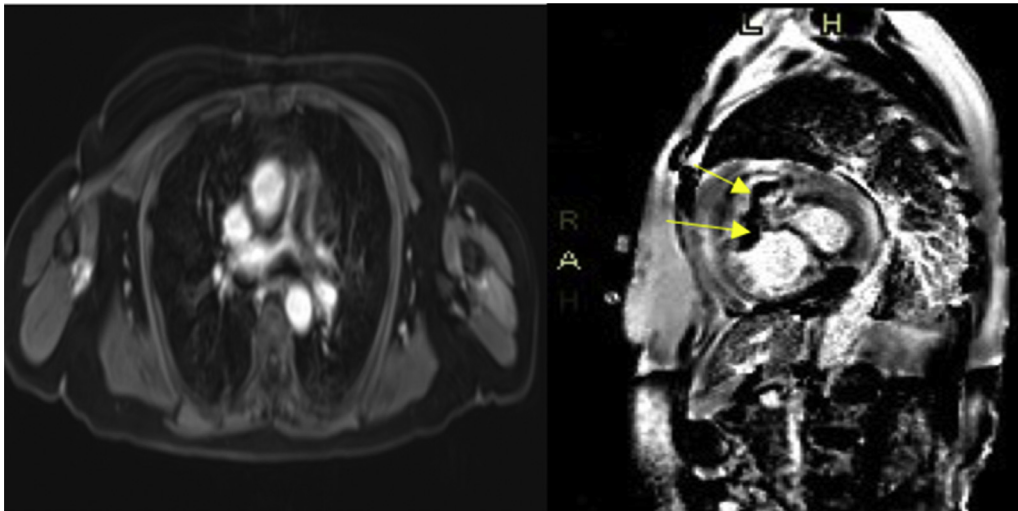
leading to stenosis, systemic or pulmonary emboli, and arrhythmias.<sup>10</sup> Our patient presented in the later stage of the disease and with initially generalized symptomatology. The location of the mass, lack of involvement of extracardiac tissue, and lack of enhancement on cardiac MRI led to the presumptive but erroneous diagnosis of pulmonary thromboembolism.

Because of its rarity and its nonspecific symptomatic presentation, the diagnosis of primary angiosarcoma is a challenge for clinicians, despite advances in multiple imaging modalities. Transthoracic echocardiography is usually the first-line investigation and has high sensitivity (97%) for the detection of cardiac masses.<sup>11</sup> It is helpful in assessment of the shape, size, and attachment of the mass, as well as

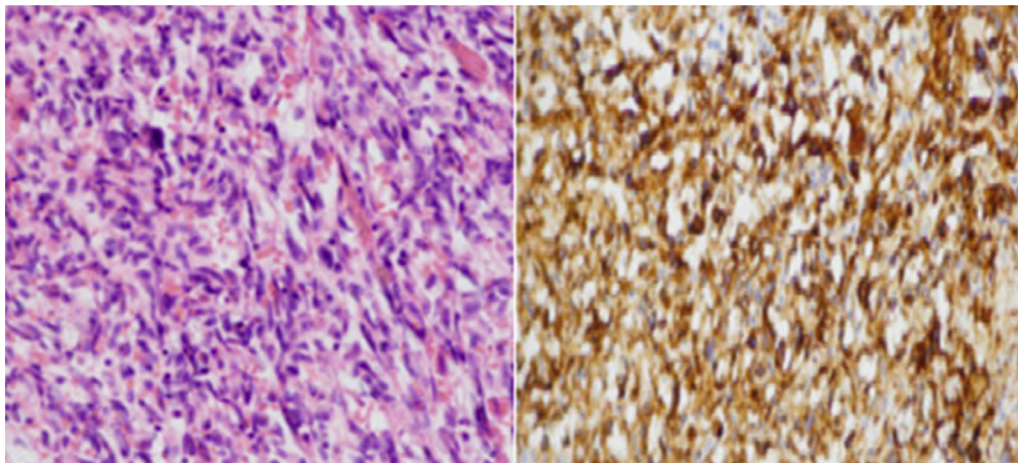
despite the use of multiple imaging modalities. This related to the enhancement characteristics and location of the mass, as well as relatively poor image quality due to patient dyspnea. Lack of enhancement with gadolinium chelate and location involving the MPA led to the incorrect presumptive diagnosis of an acute on chronic thromboembolus. Additional performance of long-inversion time late gadolinium-enhanced imaging, which is useful when thrombus is suspected, with an inversion time of approximately 600 msec, was not performed with a limited examination performed because of dyspnea. Long-inversion time imaging could have demonstrated some contrast enhancement that was not evident with conventional late gadolinium-enhanced imaging that aims to null myocardial signal.<sup>12</sup>



**Figure 3** Computed tomographic pulmonary angiogram with an eccentric filling defect (*asterisk*) within the pulmonary trunk, extending to the proximal left and right pulmonary arteries.



**Figure 4** Cardiac MRI. *Left*: Axial postcontrast T1-weighted fat-suppressed gradient-echo imaging demonstrating similar appearances to computed tomography. *Right*: Late gadolinium-enhanced imaging targeting the RVOT, showing no enhancement of the mass (*arrow*) that extends from the RVOT through the pulmonary valve and into the MPA.



**Figure 5** Hematoxylin and eosin staining displaying atypical spindle-shaped cell with high mitotic activity and positive immunostaining with CD34.

In retrospect, the involvement of the pulmonary valve and extension from the RVOT into the pulmonary arteries are atypical for pulmonary embolus, with infiltration and multichamber involvement characteristics typically seen with malignant neoplasms.

The prognosis of angiosarcoma remains poor, with mean survival of  $3.8 \pm 2.5$  months without intervention.<sup>13</sup> Radical surgical removal is the mainstay of treatment, with postoperative median survival of 14 months.<sup>7</sup> Adjuvant and neoadjuvant chemotherapy and radiotherapy have been used with limited improvement in survival.<sup>1</sup> There have also been a few case reports of orthotopic heart transplantation with poor outcomes.<sup>14</sup> In our case, surgical resection was attempted but the patient was at an advanced stage of the disease.

## CONCLUSION

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Primary cardiac angiosarcoma is rare but is the most common primary malignant cardiac tumor. Early diagnosis is important because of its aggressive nature. However, diagnosis remains challenging because of the nonspecific nature of the presenting symptoms and the rarity of the disease. A high index of suspicion is necessary to avoid delay in diagnosis and treatment.

## SUPPLEMENTARY DATA

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Supplementary data related to this article can be found at <https://doi.org/10.1016/j.case.2019.08.003>.

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