Radiology Case Reports 16 (2021) 829–834

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Case Report

Primary undifferentiated pleomorphic cardiac sarcoma presenting as right heart failure

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ARTICLE INFO

Article history:
Received 6 November 2020
Revised 4 January 2021
Accepted 4 January 2021

Keywords:
Cardiac sarcoma
Undifferentiated sarcoma
Right heart failure

ABSTRACT

Right-sided heart failure is a common sequela of left heart failure and seldom presents as a primary disorder. The differential diagnosis of right heart failure includes a cardiac tumor. Cardiac malignancies are rare tumors with an overall poor prognosis. We evaluated a 69-year-old man who presented with a 3-week history of progressive lower extremity swelling, ascites, and scrotal swelling. Laboratory studies were significant only for mildly elevated liver function tests. CT scan of the abdomen and pelvis showed ascites, hepatic swelling, and a bland clot in the inferior vena cava extending from the level of the kidneys to the right atrium. A large mass originating from the right atrium was identified, and biopsy confirmed an undifferentiated pleomorphic cardiac sarcoma. Given the extensive tumor and clot burden, he was not an operative candidate. He developed portal hypertension with esophageal varices and expired due to variceal bleeding.

Background

Right-sided heart failure usually does not occur in isolation. Most often it presents as a manifestation of either left-sided heart failure or pulmonary pathology such as obstructive sleep apnea or pulmonary embolism. The potential for accumulation of significant amounts of fluid below the diaphragm may result in dramatic presentations of ascites, marked scrotal swelling, and lower extremity edema. Hepatic congestion from right heart failure leads to the complications of portal hypertension including esophageal varices and clotting disorders.

While the majority of right heart failure is caused by left heart failure, valvular disorders, and portal hypertension, it is incumbent on the medical team to ensure that other, less common conditions do not exist. Since the potential causes of right heart failure are extensive, primary right atrial malignancy is seldom considered. The current case was illustrative of the importance of a thorough differential diagnosis.

Case presentation

A 69-year-old male with a past medical history of diabetes mellitus type 2 presented to the emergency department with

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https://doi.org/10.1016/j.radcr.2021.01.016

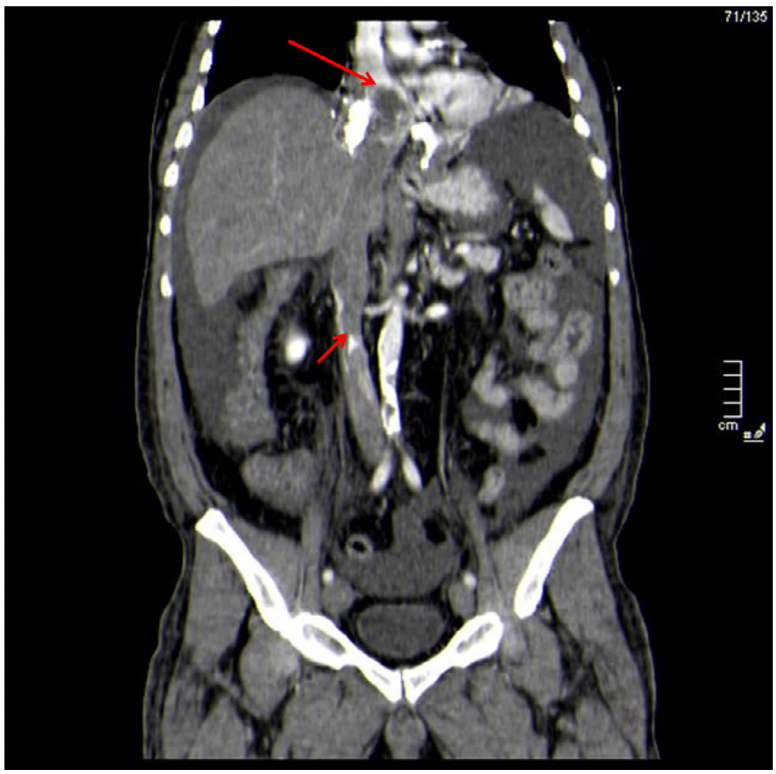

Fig. 1 – Abdomen/pelvis CT coronal reformat demonstrating thrombus extending from the right atrium (long red arrow) inferiorly to the level of the infra-renal inferior vena cava (short red arrow). Dense accumulation of intravenous contrast within the right atrium.

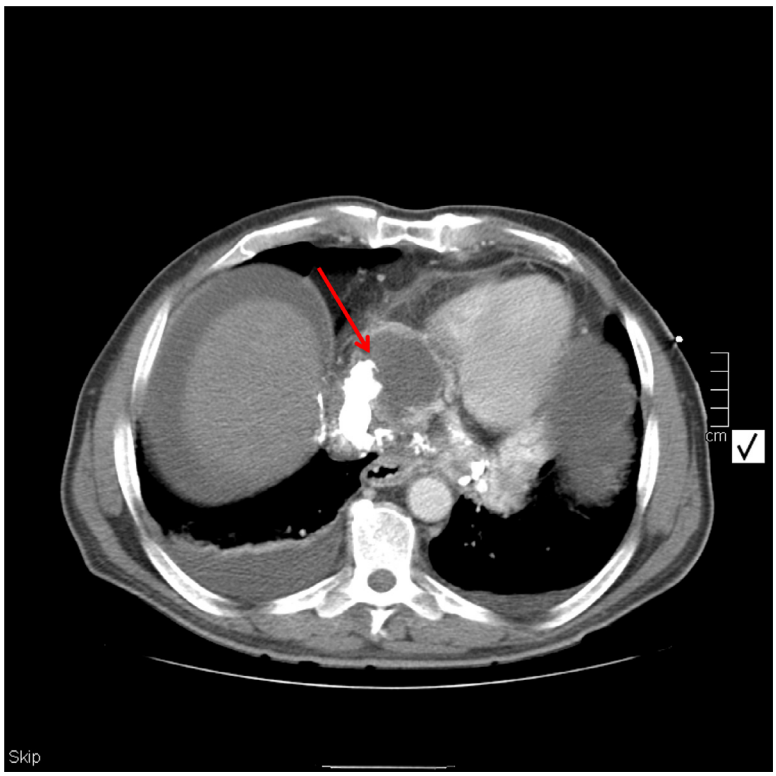

Fig. 2 – Abdomen/pelvis CT with contrast showing right atrial sarcoma extending into inferior vena cava (red arrow).

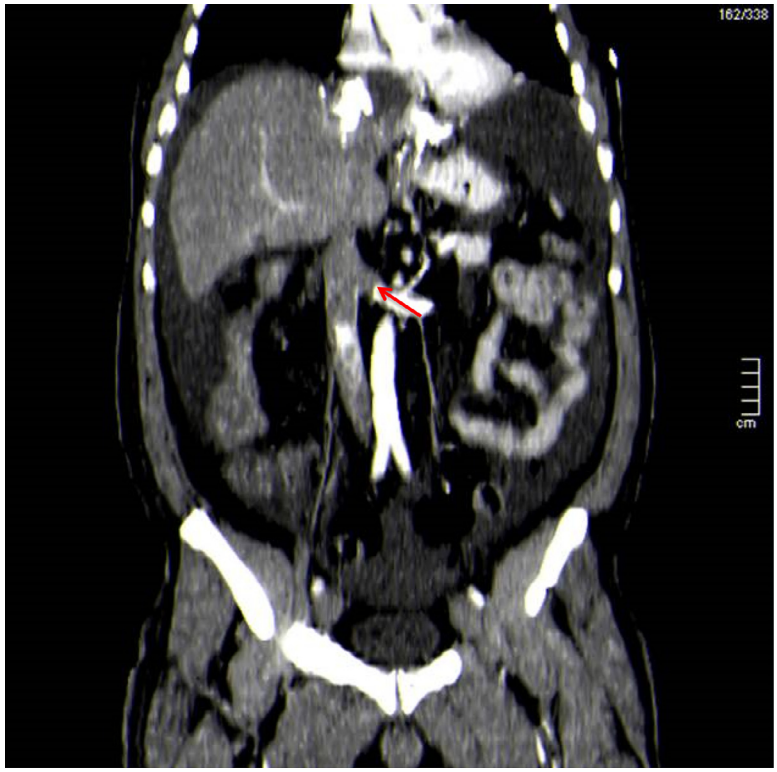

Fig. 3 – Abdomen/pelvis CT coronal MIPS reformat demonstrating thrombus at the origin of the left renal vein (red arrow), contiguous with the IVC thrombosis.

a 2-week history of progressively worsening bilateral lower extremity swelling and abdominal distention associated with mild weight loss and dyspnea on exertion. There was no previous history of cardiac, hepatic, or renal disease, and no history of hepatitis or alcohol abuse. He had recently been on a trip out of the country when his symptoms progressed to the point where he was no longer able to walk. He was evaluated at a local medical facility where he was started on several diuretics. Once his swelling receded, he returned back to the USA to be further evaluated. On initial clinical examination, he was found to be hypertensive (170/101) and tachycardic (104 beats per minute) with normal respirations and an oxygen saturation of 97% on room air. Physical examination was notable for bitemporal wasting, jugular venous distention, a tense distended abdomen, and 3+ pitting edema up to his bilateral hips.

Upon admission, a complete blood count was normal, and electrolytes were significant only for mildly decreased sodium at 131 millimoles (mmol) per liter. Creatinine clearance was normal and hemoglobin A1c was elevated at 7.3% (normal <5.7%). Alanine aminotransferase (ALT) was elevated at 174 International Units/liter (IU/L) (normal <55 IU/L), aspartate aminotransferase (AST) was high at 134 IU/L (normal 5-34 IU/L), and alkaline phosphatase was abnormal at 207 IU/L (normal 38-126 IU/L). Albumin was low at 3.2 grams/deciliter (g/dL) (normal 3.5-5.0 g/dL). Troponin I was negative. Prothrombin time (PT) was elevated at 20.9 seconds (normal ≤ 14.6 seconds) and International Normalized Ratio (INR) was 1.9 (normal 0.8-1.2). Hepatitis serologies were negative for hepatitis A, B, and C. HIV and tuberculosis testing were negative.

A computed tomographic (CT) study of the abdomen and pelvis revealed moderate ascites, liver congestion, and renal congestion. Bland thrombus was noted in the inferior vena cava (IVC) extending to the level of the renal veins. Evaluating more cephalad, the CT study showed bland thrombus filling the right atrium extending through the length of the superior vena cava (SVC), with the posterior aspect of the heart nearly encased by an irregular curvilinear mass. The mass was seen to extend along the left ventricular wall, along the posterior interventricular septum, and into the right atrium. This mass appeared to involve the medial diaphragmatic crus as well as adjacent mediastinal lymph nodes. The enhancing heterogeneous mass along the border of the left heart measured 7.0 × 3.0 cm (Fig. 1). Two 5-mm pulmonary nodules were noted to be suspicious for malignancy. A transthoracic echocardiogram showed a large, calcified, circular mass in the right atrium with an associated thickened pericardium (Fig. 2).

Subsequently, a CT-guided core biopsy was performed. Microscopic histopathology revealed the presence of medium-sized hypochromatic spindled nuclei without prominent nucleoli and moderate eosinophilic cytoplasm with indistinct cell borders and immunostaining positive for vimentin, supporting the diagnosis of an undifferentiated pleomorphic sarcoma (Fig. 3).

The patient arrived with a working diagnosis of congestive heart failure of uncertain etiology, presumed to be a sign

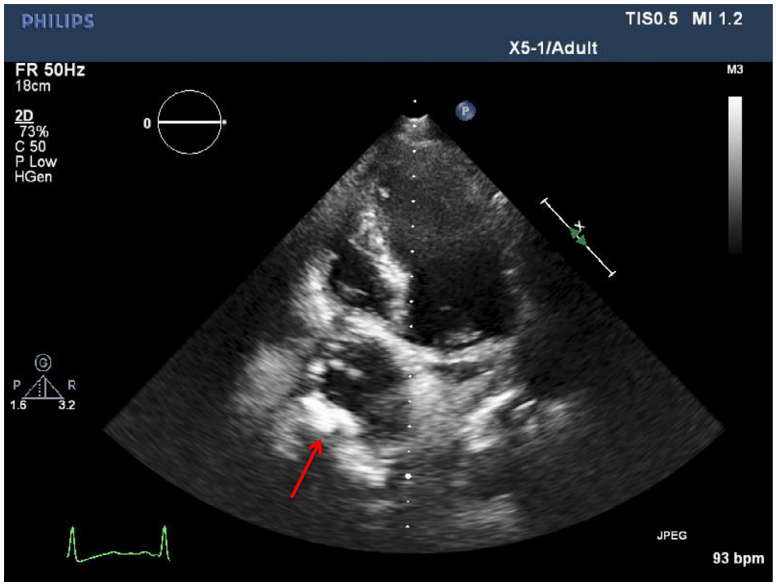

Fig. 4 – TTE showing a large, calcified, circular mass in the right atrium (red arrow) with an associated thickened pericardium.

of ischemia. However, given his negative cardiac history, unremarkable electrocardiogram and negative troponin I, imaging of the abdomen was ordered to determine the source and quantity of ascites. CT of the abdomen/pelvis showed moderate ascites, bilateral pleural effusions, and extensive clot formation in the IVC. The superior planes imaged included the heart, showing the massive extent of the clot throughout the length of the vena cava from the heart to the kidneys. Further inspection of the images revealed that mass as described as well as possible metastatic lesions in the lungs. A cardiac tumor, likely malignant, was diagnosed.

Transthoracic echocardiogram confirmed the presence of a right atrial mass of undetermined potential along with a constrictive epicardial mass as described. Percutaneous biopsy of the mass confirmed the core biopsy's aforementioned pathology.

Initial management included gentle diuresis and intravenous anticoagulation. Given the extensive nature of the clot, he was not deemed a candidate for thrombectomy. Thoracentesis and paracentesis combined with diuresis brought significant relief of symptoms. The patient developed esophageal varices along with portal hypertensive gastropathy, requiring several banding procedures for bleeding. The clot did extend into the renal veins, leading to acute kidney injury.

Discussions were held between hematology, oncology, hepatology, and cardiothoracic surgery. Given the extensive nature of both the tumor and the clot, he was not felt to be an operative candidate. The patient was not amenable initially to palliative care, hoping for a cure.

Due to his extensive mass and clot burden, he was unable to be offered an interventional procedure including resection and transitioned to compassionate use of pembrolizumab. He was readmitted 1.5 months later for hematemesis, melena, and anasarca along with have portal hypertension complications including bleeding 3+ esophageal varices requiring band ligation x4 and portal hypertensive gastropathy. Repeat TTE and CT showed the right atrial mass now extending external to the right heart chambers with a moderate pericardial effusion. He was medically stabilized with IV diuresis, paracentesis, and thoracentesis, and discharged with the plan to follow-up with GI for repeat upper endoscopy in 4-6 weeks. He was readmitted less than a month later for a hypervolemic exacerbation. Since the patient was unable to tolerate further immunotherapy, the multidisciplinary team and patient decided to focus on symptom management and strengthening at home. He expired 4 months after initial presentation during his fourth admission due to an esophageal variceal hemorrhage. A postmortem autopsy was not performed.

Discussion

Rapid onset of right-sided ventricular failure prompts the search for common cardiac etiologies including left-sided heart failure, mitral valve dysfunction, pulmonary hypertension, pulmonary emboli, myocarditis, pericardial fibrosis, or tricuspid valve dysfunction due to endocarditis or rheumatic myocarditis [1,2]. Despite a past medical history that was negative for the above conditions, this patient developed right-sided heart failure with rapid progression of expected stigmata including lower extremity edema, ascites, scrotal edema, liver engorgement, and portal hypertension with esophageal varices. While his initial presentation involved signs and symptoms below the diaphragm, further evaluation revealed that the source of his disease was a right atrial malignancy.

Primary cardiac malignancies are uncommon. Cardiac tumors have been noted in between 0.001% and 0.3% in autopsy series [3–5]. About 75% of cardiac tumors are benign [6]. Of all cardiac malignancies, about 75% are sarcomas [7,8]. Patients

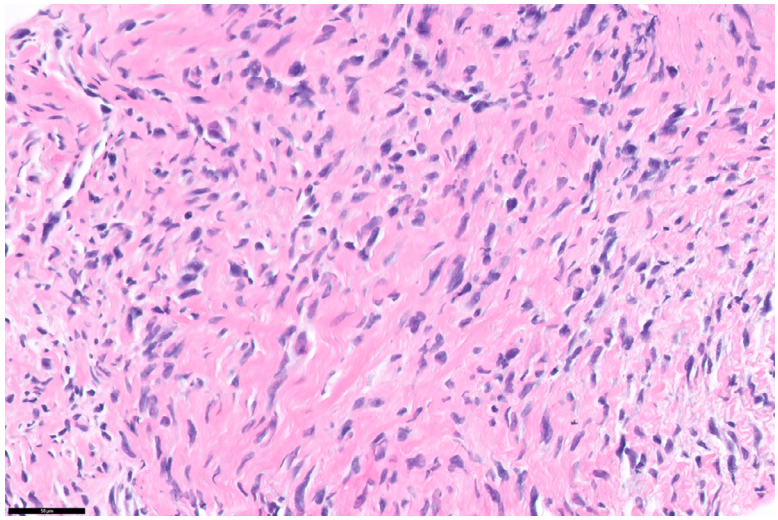

Fig. 5 – High magnification microscopic histopathology with H&E staining revealed the presence of medium-sized hypochromatic spindled nuclei without prominent nucleoli and moderate eosinophilic cytoplasm with indistinct cell borders.

tend to be middle-age (unlike the current case) and present with advanced disease [9,10]. Undifferentiated pleomorphic sarcomas are a rare subtype of cardiac sarcomas, representing one-third of all primary cardiac sarcomas [4,11]. While cardiac malignancies may affect any structure from the endothelium to the pericardium [12], most undifferentiated pleomorphic sarcomas develop in the left atrium.

Because of the distensibility of the atria, atrial tumors can become quite extensive and bulky before producing symptoms. The onset of symptoms is often insidious, and diagnostic imaging including transthoracic echocardiogram and computed tomography demonstrate an intracardiac mass that is typically located in the left atrium in 81% of undifferentiated pleomorphic sarcomas [12]. The current patient presented with a tumor that essentially filled the right atrium, and arguably the majority of his symptoms were related more to the subsequent development of an extensive bland clot extending from the heart to the kidneys. Diagnosis using ultrasound, contrast CT, and/or MRI is followed by biopsy confirmation [13,14].

Cardiac sarcomas are typically aggressive tumors [4,15]. Complete surgical resection combined with adjuvant chemotherapy and/or radiation is recommended for resectable disease, although there is a high risk of rapid recurrence [16,17]. While it is often technically difficult, R0 resection has shown significantly better outcomes than R1 resection. Therapeutic success is often challenging and unfeasible due to the highly aggressive and invasive nature of the sarcoma, with positive surgical margins being an independent predictor for poor survival [18,19]. More recent surgical approaches have included autotransplantation wherein the heart is removed, the lesion is excised, the heart is reconstructed, then reimplanted [7,20]. Cardiac transplantation is an emerging option in select patients.

Unfortunately due to the lack of prevalence of the disease and therapeutic data, evidence-based recommendations on choice or timing of chemotherapy and radiation are challenging [21]. In a series by Abu Salah, adding neoadjuvant chemotherapy to radical surgery was found to improve outcomes in right heart sarcomas, with overall survival increasing from 9.5 to 20 months [22]. Overall prognosis for undifferentiated pleomorphic sarcomas remains very poor with a median survival of less than 1 year [11,19,23,24]. Immunotherapy and tyrosine kinase angiogenesis inhibitors have shown some benefit [25] while a phase 2 trial of the programmed cell death 1 inhibitor pembrolizumab showed limited efficacy [26] in the treatment of cardiac sarcomas (Figs. 4 and 5).

Patient consent

Please check that all articles state that patient consent has been obtained. Please raise a query to the author if no such statement is present.

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