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CASE REPORT

Large right atrial angiosarcoma with superior vena cava obstruction and cardiovascular collapse

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1. Background

Primary cardiac angiosarcoma is a rare disease. Atypical symptoms, the scarcity of incidence rates and the rapidly progressive nature of malignancy contribute to the delayed diagnosis in almost all reported cases. The initial presentation of right atrial angiosarcoma may occur in the late stage as a result of mechanical obstruction of venous return to the superior vena cava and tricuspid valve. The hemodynamic instability resulting from venous obstruction complicates the management of anesthesia and surgery in these patients. Due to the nature of the disease, the prognosis of cardiac angiosarcoma is usually dismal. A postoperative multidisciplinary approach is recommended.

2. Case Presentation

A 35-year-old Chinese man presented with a history of progressive cough, dyspnea, and swelling of the upper body for one week. He reported that he cannot lie fully flat due to orthopnea. He was otherwise healthy and had no past medical history or known allergies.

On examination, his blood pressure was corrected with continuous infusion of dobutamine via the femoral vein. There was visible jugular vein distension and swelling of the upper body. The heart rate was approximately 100/min and no murmur detected. The results of electrocardiography were normal, while a chest X-ray demonstrated right heart enlargement. Using a transthoracic echocardiograph, a mass (70×50 mm) was found to be occupying almost the entire right atrium with a moderate amount of pericardial effusion. Finally, a computed tomographic (CT) angiogram confirmed the presence of an atrial mass without metastasis in the lung or liver (Fig. 1).

An urgent operation was indicated. The patient was transferred to the theater in a compulsive position. Under

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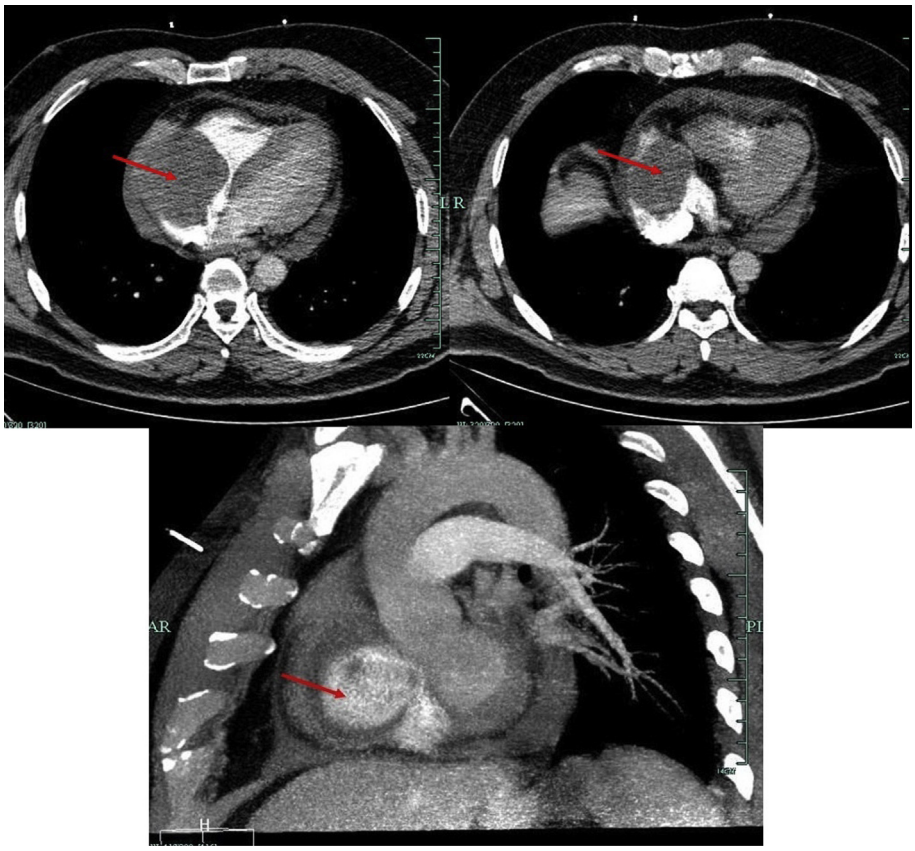

Figure 1 Computed tomographic (CT) angiogram showed the mass nearly occupied the entire right atrium.

anesthetic induction, non-responsive severe hypotension occurred at 53/30 mmHg although he was given intravenous fluid, vasoactive agents and position adjustment. The patient exhibited cyanosis and his oxygen saturation fell to 85%. Urgent endotracheal intubation was performed and cardiopulmonary bypass (CPB) was immediately established between the aorta and superior vena cava. After the initiation of CPB, the inferior vena cava was distally dissected for cannulation. With aortic occlusion and cardioplegia, the right atrium was opened. The mass was found to have infiltrated the lateral wall of right atrium and top of venous sinus septum (Fig. 2). The spherical solid tumor was 8×7×5 cm in size and had a relatively smooth surface. The tumor was removed with the attached atrial wall. The residual part of the tumor at the top of venous sinus septum was cauterized due to its proximity to the aortic valve before the right atrium was reconstructed with the pericardium. The patient was discharged 11 days after the operation and had relatively normal echocardiography results. Pathological examination indicated the mass was 7.5×5.5×4.5 cm in size. Cells were ovoid and fusiform. The mass had a rich blood supply and cell mitosis; also, necrotic tissue could be seen (Fig. 3a & 3b). Immunohistochemistry showed positivity for CD31, CD34 and Factor VIII-related antigen (Fig 3c &3d) with negative calponin and MyoD1. The diagnosis was concluded to be a right atrial mesenchymal tumor with a sarcomatous change (angiosarcoma).

The patient chose treatment by radiotherapy alone after being fully informed about the advantages and disadvantages of both radiotherapy and chemotherapy. Seven cycles of chest radiotherapy were prescribed after the operation. The dose was 300 cGy/Fr, 5 Fr/W. During radiotherapy, multiple metastases were detected in the bones, lungs and brain at 3, 6 and 6 months, respectively. Respiratory failure resulting from metastasis caused death at 10 months following the operation.

3. Discussion

Primary cardiac tumors are rare; they have a total incidence ranging from 0.0017% to 0.03%.[1,2] Most primary cardiac tumors are benign and more than 50% are myxomas. The second most common benign tumor is rhabdomyoma, which is also the most frequent neoplasm that occurs in childhood.[3] Malignant tumors account for approximately 7% of primary cardiac neoplasms[4] and sarcomas are the most common type of primary malignant tumor of the heart.[5]

Angiosarcoma is the most frequent type of sarcoma in the adult population, and it has a higher incidence in males.[6] Additionally, 75% of cardiac angiosarcomas occur in right side, especially in the right atrium.[7] Diagnosis is often delayed because the disease is rare and symptoms are nonspecific, such as obstruction of intracardiac blood flow, interference with valve function, arrhythmias, pericardial effusion with tamponade, tumor embolism and systemic symptoms.[8] Our patient's primary complaint was dyspnea induced by mechanical obstruction of the superior vena cava and tricuspid valve.

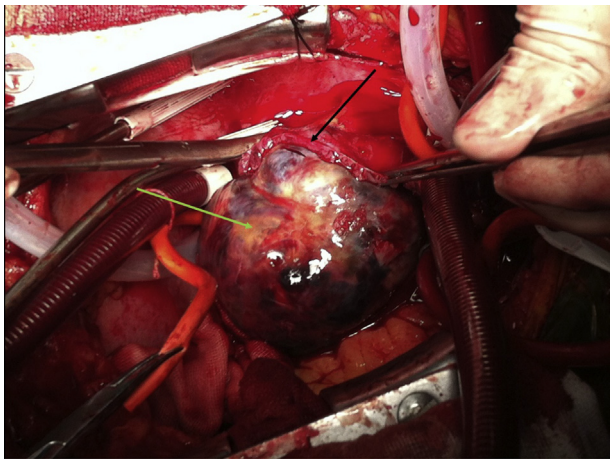

Figure 2 The large tumor had infiltrated the lateral wall of the right atrium. The black arrow shows the lateral wall of the right atrium. The red arrow shows the tumor.

CD31, CD34 and Factor VIII-related antigen are all well-accepted endothelial cell immunomarkers in human tissues.[9,10] CD31 is a transmembrane glycoprotein adhesion molecule that is expressed by platelets, megakaryocytes, and endothelial cells, and it is also known as platelet-endothelial cell adhesionmolecule-1 (PECAM-1). CD34 is a cell-surface marker that is expressed in endothelial cells and hematopoietic stem cells, as well as nerves, hair follicles, muscle bundles, and sweat glands. Factor VIII-related antigen is a protein found in endothelial cell Weibel-Palade bodies, and it is also expressed in megakaryocytes. The positive results of these biomarkers usually suggest the tumor may originate from endothelial tissue. On the other hand, calponin is an actin-, tropomyosin- and calmodulin-binding protein that is isolated from smooth-muscle cells. MyoD1 is known to be expressed in rhabdomyosarcoma.[11] The negative expression of calponin and MyoD1 suggests this tumor may not originate from the heart muscle.

The concerns for patients with right atrium tumors undergoing anesthesia include hypoxemia, a low cardiac output, possible right to left shunt, and potential pulmonary embolism. A large angiosarcoma may cause blood flow obstruction and unstable hemodynamic status, which makes emergent intubation and CPB necessary. It has been reported by Nath et al that a decrease in the blood pressure during anesthesia induction responds to aggressive fluid resuscitation.[12] In this particular case, circulatory failure during anesthesia induction did not respond to the combination of intravenous fluid, dobutamine and position adjustment. Emergent endotracheal intubation and cardiopulmonary bypass should be second-line for such a situation.

Cardiac angiosarcoma has a short clinical course and fatal outcome, ranging from one week to 36 months.[13] The mean survival time was only 3 to 9 months.[5,13] Multidisciplinary treatment was recommended. The removal of papillary muscles, valves, chordae tendineae, and damage to the conduction system causes a need for radical surgical resection, which is important for primary tumor resection, symptom relief and hemodynamic improvement.[14] During the operation, we found the tumor was encapsulated, and we completely resected the tumor from its pedicle.

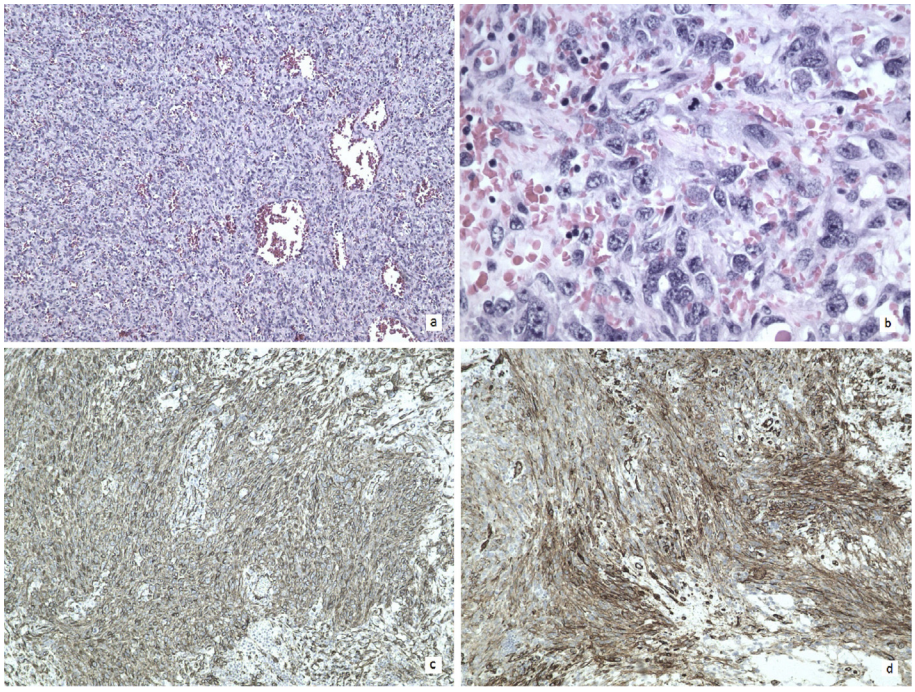

Figure 3 (A) Low-power photomicrograph demonstrating an admixture of tumor cells, necrotic tissue and blood vessels (H&E×40). (B) High-power photomicrograph demonstrating ovoid and fusiform tumor cells. Cell atypia and mitosis could be seen. (C) Immunohistochemistry demonstrating the tumor was CD31 positive. (D) Immunohistochemistry demonstrating the tumor was CD34 positive.

Although the resection was radical, metastases were still found 3 and 6 months later.

Due to the metastatic characteristics of such a tumor, complete surgical resection, followed by adjuvant chemotherapy and radiation, may extend survival. Doxorubicin is an effective chemotherapeutic agent used in angiosarcoma treatment,[16] and chemotherapy for cardiac angiosarcoma with methotrexate, cyclophosphamide, vincristine, and dacarbazine has been reported.[15] Two cases that had no recurrence at 36 and 34 months indicated the efficacy of combined therapy with docetaxel for cardiac angiosarcoma[17] and radiotherapy[18] in spite of incomplete resection. Because the patient in this case worried about the side effects of chemotherapy, he only underwent radiotherapy, which produced unsatisfactory outcomes compared to combined therapy.

Heart transplantation has also been performed for primary cardiac angiosarcoma,[18,19] but its effectiveness is uncertain. Immunotherapy using interleukin-2 can increase the survival of select patients,[20] as reported by Yamada et al for a case of angiosarcoma that was successfully treated with interleukin-2 and radiation.[21]

In summary, the atypical symptoms, scarcity and rapidly progressive nature of malignancy result in a poor prognosis. Multidisciplinary treatment is indicated and immunotherapy could prove to be an alternative approach in selected patient groups.

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