Primary Cardiac Angiosarcoma
A Case Report and Review of the Literature

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Summary
In this study, we present the case of a 34-year-old man who was diagnosed with primary cardiac angiosarcoma 1 month after hospital admission. Cardiac angiosarcoma is a relatively rare disease that can be easily misdiagnosed as pneumonia or other diseases. Although surgery is the preferred treatment to prolong survival time, highly malignant tumors with local infiltration and systemic metastasis can lead to poor prognosis.

Key words: Cardiac tumor, Pericardial effusion, Pneumonia, Echocardiography

Primary cardiac angiosarcoma has been considered as a relatively rare tumor; however, it is the most common histologic subtype of primary cardiac malignant tumors in adults.1,2 Although advanced diagnostic technologies have been made available, such as tumor markers, echocardiography, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography/computed tomography (PET/CT), cardiac tumors can still easily be misdiagnosed at initial presentation. Thus, to optimize outcomes and improve survival of patients suffering from primary angiosarcoma, patients are treated with a combination of surgery and complementary treatments, such as chemotherapy and radiotherapy. However, due to the highly aggressive nature of this disease, patient outcomes are often poor.2,3 But with early diagnosis, more possibilities for treatment can be provided.

Case Report
A 34-year-old man was admitted to a hospital (which is affiliated with our hospital) after presenting with chest tightness, breathlessness, and a 10-second episode of syncope. As per his CT scan (Figure 1A), a large-volume pericardial effusion was observed with multiple bilateral patchy shadows in the lungs. His laboratory results revealed an elevated white blood cell count (11.5×10⁹/L), and the percentage of neutrophils was determined to be 79.6% and 14.2% for lymphocytes. Based on the radiological and laboratory features, the diagnosis was presumed to be pneumonia. The patient then underwent pericardiocentesis with the guidance of bedside echocardiography; however, at this time, instead of observing a space-occupying lesion, a pericardial effusion was noted, and imaging data could not be saved on the bedside ultrasound device. The patient’s symptoms of chest tightness and breathlessness reportedly improved after pericardiocentesis, and his condition then stabilized, with a heart rate of 80 beats per minute and respiratory rate of 18 beats per minute; meanwhile, his initial blood temperature, heart rate, blood pressure, and respiratory rate were 37.6°C, 123 beats per minutes, 106/58 mmHg, and 24 breaths/minute, respectively. Laboratory examination of the serosanguinous and cloudy pericardial effusion showed a red blood cell count of 3.78 × 10¹²/L, white blood cell count of 3.5 × 10⁹/L, and lymphocyte count of 1.3 × 10⁹/L, but tumor markers were not evaluated. As per examination, peripheral blood was found positive for anti-SmD1 and anti-Jo-1 antibodies; thus, the patient was initially diagnosed with viral pericarditis due to an underlying connective tissue disease and viral pneumonia. However, pneumonia persisted after adequate treatment with antibiotics (ganciclovir 6 mg/kg/day for 5 consecutive days and piperacillin 3.0 g with tazobactam 0.375 g, once every 6 hours, for 7 consecutive days). As the patient’s symptoms improved, he refused bronchoscopic alveolar lavage which would have allowed the treating physicians to obtain respiratory fluid for analysis using next-generation sequencing to confirm the underlying diagnosis; instead, he decided to leave the hospital to recuperate. Four weeks later, the patient represented to the emergency department of our hospital.

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with complaints of chest tightness, breathlessness, intermittent tingling of the right chest, severe cough, and one episode of hemoptysis. His laboratory tests revealed the following results: white blood cells, 11.8 × 10^9/L; neutrophils, 8.0 × 10^9/L; C-reactive protein, 15.6 mg/L; N-terminal pro-b-type natriuretic peptide, 66 pg/mL; and troponin T, 6 pg/mL. A repeated CT scan (Figure 1B) revealed a large amount of pericardial effusion and severe infiltrative shadows. Treatment was started with antibacterial (cefoperazone and sulbactam combined with moxifloxacin) and anti-viral agents (ganciclovir combined with arbidol). The pericardial puncture specimen was immediately sent to the laboratory for analysis, wherein results revealed increased levels of a fragment of cytokeratin 19 (CYFRA 21-1), ferritin, and cancer antigen 125 (CA125). The presence of elevated serum tumor markers with the pericardial effusion raised the suspicion of an alternative diagnosis. Echocardiography (Figure 2) and contrast-enhanced chest CT scan (Figure 3) showed a mass located at the right atrioventricular junction. Contrast-enhanced chest CT confirmed a filling defect in the right atrioventricular junction and bilateral pleural effusions. Fluorodeoxyglucose-18 combined with positron emission tomography/computed tomography (18F-FDG-PET/CT) (Figure 4) showed abnormal soft tissue lesions on the right anterior edge of the heart with increased focal glucose metabolism and increased focal radioactivity uptake with maximum standardized uptake values (SUVmax) of 11.9 and multiple patchy images of both lungs with uneven glucose metabolism.

In summary, laboratory analysis of the pericardial effusion and peripheral blood revealed abnormal tumor markers, and a space-occupying lesion of the right atrium was observed on echocardiography. Moreover, 18F-FDG-PET-CT showed a hypermetabolic lesion in the right atrium, so we considered the possibility of cardiac malignancy.

The patient consented to surgery, and the specimen was sent for pathological examination (Figure 5). Histology showed that the tumor was composed of atypical endothelial cells with pathological mitotic images. In addition, blood vessel channels composed of atypical endothelial cells with pathological mitotic images.
ellial cells were poorly formed and communicated with each other. Immunohistochemistry (Figure 6) was positive for vimentin, F11-1, CD31, and CD34, which are highly sensitive and specific to vascular tumors,4,5 so the diagnosis of primary cardiac angiosarcoma was confirmed. Pathological results also showed incomplete tumor resection with positive surgical margins, which is considered an adverse prognostic factor. The patient refused radiotherapy or chemotherapy and opted for treatment with traditional Chinese medicine including toads, notoginseng, senso, and astragalus. Four months after the operation, repeat echocardiography (Figure 7) showed a mass (4.4 × 2.5 × 2.0 cm) at the lower end of the anterior wall of the right atrium and the side wall of the right ventricle with an ejection fraction of 51%. The patient is still alive and independent at the time of writing of this manuscript.

**Discussion**

Primary cardiac angiosarcomas have been considered as rare tumors that are often misdiagnosed at initial presentation. Similar to previously reported cases, the patient described in this case presented with severe pericardial effusion and features of severe pneumonia.6 In this case, the patient first presented with severe diffuse bilateral pulmonary exudative infiltrates, and pericardial effusion was thought to be secondary to severe pneumonia in a young patient as opposed to a rarer underlying cardiac tumor. Cardiac angiosarcoma is very likely to be misdiagnosed as pneumonia, because of the rarity of the disease and its nonspecific clinical manifestations,7 including dyspnea, chest pain, and anemia, as well as due to the size of the tumor and its anatomical position.8 Breathlessness in this patient may have been due to cardiac tamponade caused by severe pericardial effusion and severe pneumonia. Patients with malignant tumors have been more likely to be relatively immunocompromised and therefore, prone to secondary infections. Besides, multiple plaque shadows in the lungs were observed on PET/CT; thus, small nodular metastases were not easily identified, and these could continue to stimulate the lungs, leading to continuous activation of lung inflammation. When the patient chose to leave the hospital to recuperate, various supportive treatments were stopped, and symptoms of pneumonia reportedly recurred 4 weeks later, leading to a second admis-

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**Figure 3.** A contrast-enhanced chest CT scan. A low-density mass measuring approximately 2.5 cm is noted in the right atrium with small bilateral pleural effusions. The filling defect of the right atrium is indicated by the arrow. LV indicates left ventricle; RA, right atrium; and RV, right ventricle.

**Figure 4.** A ¹⁸F-FDG-PET/CT scan. A, B: Hypermetabolism was seen in the cardiac mass of the right atrium; the maximum standardized uptake value was 11.9. C: Multiple plaque shadows in the lungs with uneven glucose metabolism.
Figure 5. Histological examination findings of the right atrium mass. A: The tumor cells were obviously hetero-
morphic, round, and pleomorphic (hematoxylin and eosin, 4 × ). B: The tumor was composed of atypical endothelial
cells with badly formed vascular channels (indicated as black arrow) (hematoxylin and eosin, 10 × ). C: Pathological
mitotic image indicated by a red arrow (hematoxylin and eosin, 40 × ).

Figure 6. Immunohistochemistry of the right atrium mass. A: Tumor cell cytoplasm vimentin (+). B: Tumor endothelial cell membrane CD31 (+). C: Tumor endothelial cell membrane CD34 (+).

Figure 7. Echocardiographic images of the patient 4 months after surgery. A mass (4.4 × 2.5 × 2.0 cm) at
the lower end of the anterior wall of the right atrium and the side wall of the right ventricle.

sion. However, an accurate diagnosis is deemed essential
as primary cardiac angiosarcoma is highly invasive, with
early systemic metastasis, and the lungs and pericardium
are common sites of invasion. This may lead to misdiag-
nosis of more common conditions. The main symptoms of this patient were cardiac tamponade and heart failure, which may be misattributed to severe pneumonia. Furthermore, cardiac tumors also need to be differentiated from other rare diseases to improve the accuracy of clinical diagnosis.9)

Angiosarcoma is the most common histologic subtype of primary cardiac malignant tumors among adults,1,2) and it usually occurs in men aged < 65 years, with a male-to-female ratio of around 2-3:1.5,7) The most vulnerable site is in the right atrium, with 74% of primary cardiac angiosarcomas occurring in the right atrium and often involving adjacent structures.2) We report the case of an angiosarcoma located at the right atrioventricular junction in a 34-year-old male patient.

Multiple technologies can be used to detect heart tumors, such as tumor markers, echocardiography, CT, MRI, and PET/CT. Echocardiography has been identified as the most effective diagnostic method, but heart tissue biopsy is considered the gold standard.2-5) In this case, the echocardiogram revealed the abnormal position of the heart. A subsequent biopsy was positive for CD34, CD31, and F11-1; thus, primary cardiac angiosarcoma was diagnosed.10,11)

Cardiac angiosarcomas are highly malignant tumors with high rates of local infiltration and systemic metastasis and are often associated with poor prognosis. The survival time of patients is estimated to be only 5 to 13 months.2,3) The rarity of this diagnosis makes it difficult to establish standardized treatments. Studies have shown that neoadjuvant chemotherapy, local radical resection, postoperative radiotherapy, and targeted therapy may prolong the survival rate.6,12,13) This case demonstrates the importance of considering a primary cardiac malignancy in the differential diagnosis of young patients presenting with unexplained refractory pneumonia. This is essential as early diagnosis can improve treatment planning.

Conclusion

Primary cardiac angiosarcoma is a relatively rare tumor, which can easily be misdiagnosed as pneumonia or other cardiorespiratory diseases. Prognosis has been deemed poor due to the highly aggressive and rapidly progressive nature of these tumors. Therefore, it is essential that clinicians have a high index of suspicion and formulate an appropriate diagnostic workup for primary cardiac angiosarcomas. Early diagnosis could prevent tumor progression and metastasis, even providing opportunities for further treatment.

Disclosure

Conflicts of interest: None.