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Case Report

Cardiac angiosarcoma with metastatic to lung, brain, and bone ☆

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ABSTRACT

Cardiac angiosarcoma is a malignant tumor derived from vascular endothelium with a dismal prognosis. The imaging findings of cardiac angiosarcoma are nonspecific and endomyocardial and pericardial biopsies have insufficient accuracy. For these reasons, the diagnosis is sometimes difficult. Primary and metastatic tumors tend to bleed easily, causing hemoptysis and neurological symptoms. Brain metastases are not often known to be fatal when they cause hemorrhage. We report a 27-year-old man diagnosed with right atrium angiosarcoma, with metastases in the lung, brain, and bone. The patient had only respiratory symptoms at the first visit and did not show any symptoms derived from brain metastases yet died after 27 days due to hemorrhage from brain metastases. If brain metastasis from angiosarcoma is suspected based on imaging findings, urgent radiotherapy should be considered before histological examination for a definitive diagnosis.

Introduction

Cardiac angiosarcoma is a rare disease derived from vascular endothelial cells with a high rate of metastases and poor prognosis. The prevalence of malignant cardiac tumors is 0.08%. Angiosarcoma accounts for 30% of malignant cardiac tumors and is the most common type [1]. The mean survival time is 3.8 ± 2.5 months without surgery and more than 70% of cardiac angiosarcomas originate from the right atrium, and rarely from the right ventricle or left atrium [2–4]. On CT scans, angiosarcoma is identified as an enhanced mass and an MRI

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examination detects bleeding and evaluates heart function [5]. The imaging findings of the primary lesion are nonspecific and the final diagnosis is based on histopathological examination and immunohistochemical staining. Immunostaining shows positive expression of vascular endothelial markers including von Willebrand factor, vimentin, CD34, CD31, Ulex europaeus agglutinin 1, and vascular endothelial growth factor (VEGF) [6–8]. The frequent site of metastases is the lung, brain, liver, bone, spleen, skin and spine. Metastases in the lungs are most common and patients with metastases have a poor prognosis [9]. Primary and metastatic lesions occasionally represent hemorrhage and present with symptoms [10–12]. Although there is no standardized treatment, a combination of surgery, chemotherapy, and radiation therapy is often employed. Nevertheless, a significant extension of survival time is not anticipated [6,13]. We report a case of right atrium angiosarcoma with multiple metastases to the lung, brain, and bone, which had a rapid clinical course due to hemorrhage from the brain metastases.

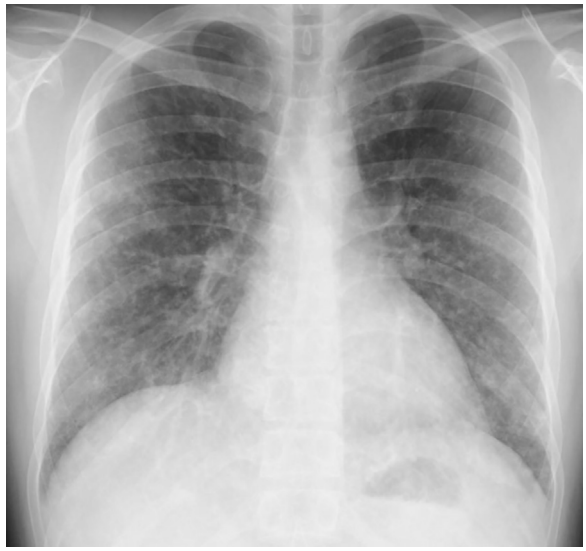

Fig. 1 – Chest X-rays showing reticular shadows in both lungs at the first visit.

Case presentation

The patient was a 27-year-old man who presented to the internal medicine department with chief complaints of cough, shortness of breath, and bloody sputum for 13 days. He had a history of surgery for Chiari malformation type 1. Chest X-rays showed reticular shadows in both lungs (Fig. 1). Computed tomography (CT) demonstrated multiple nodules with ground glass (Fig. 2A). A 13-day follow-up CT revealed deterioration of image findings (Fig. 2B).

After admission, a 5.9 × 3.4-cm tumor with heterogeneous enhancement in the right atrium was detected by contrast-enhanced CT (Fig. 3). Magnetic Resonance Imaging (MRI) examination was performed and multiple brain-occupying lesions showing heterogeneous signals on T2-weighted image were detected (Fig. 4A). Peritumoral edema was observed and multiple brain metastases were suspected. The brain lesions showed a partial high signal on the T1-weighted image and were suggested to be accompanied by hemorrhage (Fig. 4B). The right atrium and lung lesions showed [18F]-2-fluoro-2-deoxy-D-glucose (FDG) uptake on positron emission tomography/computed tomography (PET/CT) and bone metastasis was detected (Figs. 5A and B). The bone lesion was not detected by contrast-enhanced CT. For definitive diagnosis, bronchoalveolar lavage (BAL) and transbronchial biopsy were performed. BAL yielded only red blood cells and lymphocytes, with no specific diagnostic information. By transbronchial biopsy, 6 specimens were obtained. For one of the specimens, aggregations of atypical cells with hemorrhage and necrosis were seen and suggesting tumor tissue (Figs. 6A and B). The atypical cells were positive for Vimentin and CD31 (Fig. 6C). The other 5 specimens were nondiagnostic. We made a diagnosis of angiosarcoma and the right atrium mass was considered to be the primary tumor.

He was referred to another hospital for treatment on day 22. He showed deteriorating respiratory status, headache, and nausea, and was admitted on the same day. A treatment planning CT scan was attempted on the same day, but it could not be done due to severe headache and nausea. The scan was performed under sedation on day 25. First whole brain radiotherapy (WBRT) was performed under sedation on day 26. He had a small amount of hematemesis on the evening of the day. He exhibited a sudden drop in the level of consciousness on day 27 and died approximately 1 hour later. The cause of death was presumed to be hemorrhage from brain metastases.

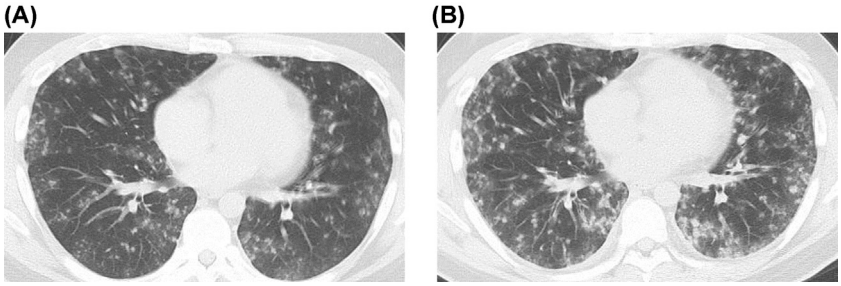

Fig. 2 – (A) Chest computed tomography image showing multiple nodules with ground glass in both lungs at the first visit. (B) CT scan 13 days later showing deterioration of chest radiograph findings.

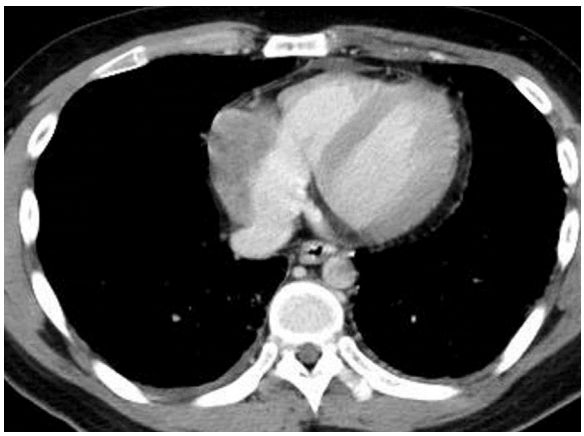

Fig. 3 – Axial contrast-enhanced computed tomography image showing a 5.9 × 3.4-cm mass in the right atrium with heterogeneous enhancement.

Discussion

Angiosarcoma is a rare malignant tumor originating from vascular endothelial cells, occupying 2% of soft tissue sarcoma [7]. Symptoms of angiosarcoma are nonspecific such as dyspnea, cough, heart failure, and arrhythmia. Sometimes cardiac tamponade is the first symptom. Diagnosis of cardiac angiosarcoma is often difficult due to these nonspecific symptoms. Echocardiography is a common examination for evaluating heart function and morphology. Transthoracic echocardiography (TTE) is useful for tumor delineation, visualizing 75% of cardiac angiosarcoma, and evaluating pericardial effusion and heart function [8,14,15]. Transesophageal echocardiography (TEE) can also assess primary tumors but is more accurate in detecting cardiac masses [16].

Imaging technique like CT, MRI, or PET/CT is examined to obtain tumor characteristics and detect metastasis. On unenhanced CT scans, a primary tumor is occasionally indistinguishable from right atrium and enhanced CT scans can detect the tumor as heterogeneously enhancing lesion [5]. MRI scans detect primary and metastatic bleeding. Tumor mobility, heart function and valve dysfunction are also evaluated. However, these imaging is often nonspecific and accurate diagnosis is difficult. Some cases misdiagnosed as intracardiac thrombus or myxoma have been reported [17,18]. PET/CT scans are useful for detecting distant metastases that may be missed by other imaging techniques. In our case, bone metastasis could not be detected by CT scans. Malignant lesions of the heart and the pericardium show higher SUVmax than benign ones [19].

Immunohistochemistry is important for the diagnosis of angiosarcoma. Angiosarcoma, derived from endothelial cells typically expresses endothelial markers (von Willebrand factor, cytokeratin, vimentin, CD31, CD34, and vascular endothelial growth factor (VEGF)). CD31 is highly sensitive and specific for vascular tumors. CD34 is less sensitive but still useful. Vimentin has high sensitivity but low specificity and cannot distinguish angiosarcoma from other soft tissue tumors. Cytokeratin, an intermediate filament, is positive in only one-third of cases. Von Willebrand factor is a highly specific but least sensitive marker.

Specimens for tissue diagnosis are obtained by excision of the tumor or tissue biopsy. Surgical resection of primary or metastatic tumors is definitive and easy when metastases are present in the skin but otherwise invasive. Endomyocardial biopsy is performed primarily when cardiomyopathy is suspected but can also be performed for tumors. For cardiac angiosarcoma, endomyocardial biopsy was diagnostic in 2 of 4 cases [20]. The major complication rate for right ventricular endomyocardial biopsy is 0.82% [21]. Pericardial biopsy was only successful in 0%∼23% [20,22]. Biopsy of lung nodules is

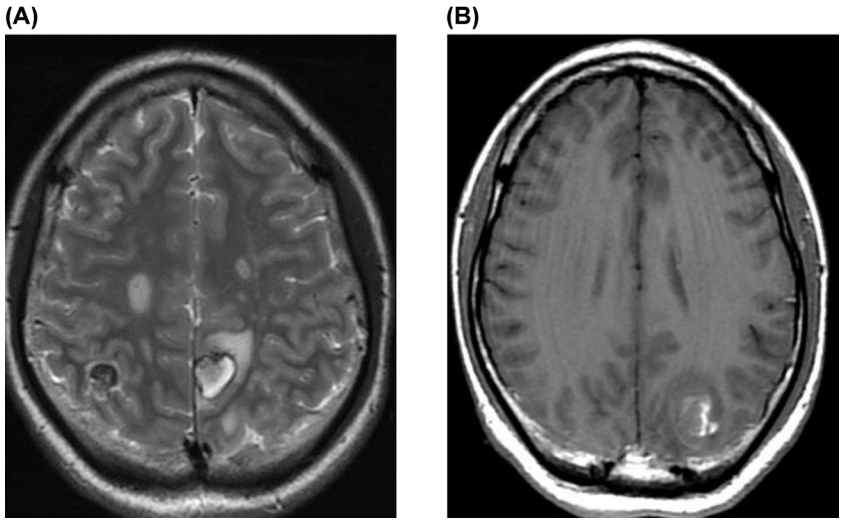

Fig. 4 – (A) T2-weighted imaging showing multiple high to low signal intensity space-occupying lesions in the brain parenchyma and peritumoral edema. (B) Some of the brain lesions were hyperintense on T1-weighted imaging and accompanied by hemorrhage.

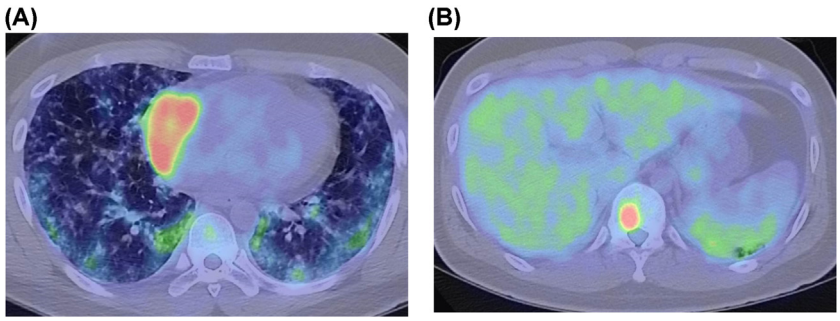

Fig. 5 – (A) Positron emission tomography/computed tomography showing FDG uptake in the right atrium and lung lesions, (B) bone metastasis that could not be detected by CT scan.

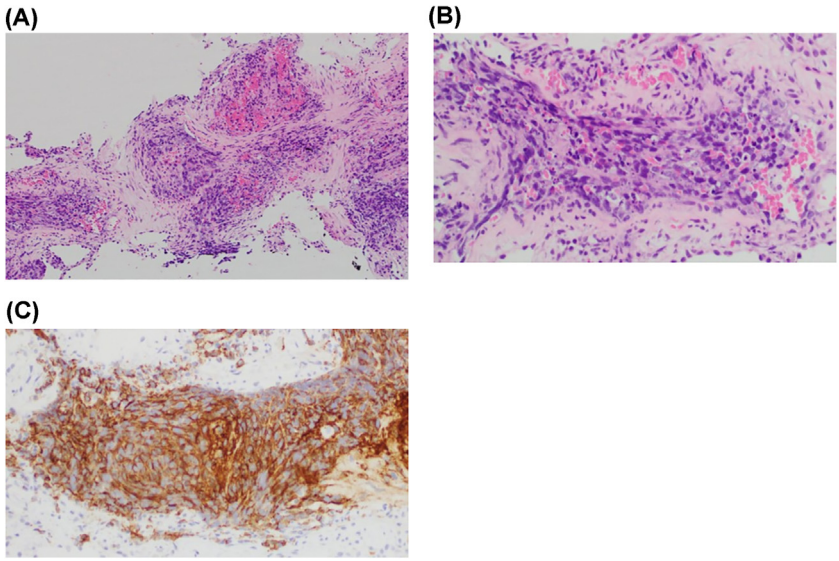

Fig. 6 – (A) The aggregations of atypical cells with hemorrhage and necrosis was observed in the fibrotic thickened alveolar tissue. (HE staining x100). (B) The tumor cell showed increased nuclear chromatin and nuclear debris. (HE staining x 200), (C) CD31 was positive, which indicated the cell derived from vascular endothelium. (x 200).

often attempted for the frequency of lung metastasis and multiple options for biopsy. Liu et al. [23] reported a case in which they were diagnosed with angiosarcoma by CT-guided fine-needle aspiration biopsy of pulmonary nodule. Transbronchial biopsy is less complicated and invasive but previous studies have often reported failure to diagnose [24,25]. There are a few reports of successful transbronchial biopsy [26]. Though our patient was diagnosed by transbronchial biopsy, 5 of 6 specimens did not lead to a diagnosis. It may be necessary to collect multiple specimens considering the high incidence of necrosis in the diagnosis of angiosarcoma.

More than half of the patients have metastases at diagnosis [4]. Lung is common metastatic site. Solitary or multiple solid nodule lesions are identified and ground-glass attenuation surrounding solid nodules is seen when accompanied by alveolar hemorrhage [27]. The patient may represent hemoptysis as a result of bleeding from lung metastases. Brain metastases are relatively rare but can be fatal. Most cases of brain metastases from cardiac angiosarcoma are associated with hemorrhage, according to previous reports [11,28–32]. Hemorrhage occurs in 14% of typical brain metastases, and the rate of bleeding from angiosarcoma is remarkable [33]. Previous reports have shown that patients with brain metastases presented with headache and other neurological symptoms. In our case, the patient had only respiratory symptoms at the first visit, but died within a month due to hemorrhage from brain metastases. This may reflect the lethality of brain metastasis of angiosarcoma. Patients diagnosed with brain metastasis in other reports have survived only for about a month [28,32].

Primary cardiac malignant tumors are mostly malignant lymphomas or sarcomas, including angiosarcomas [1]. Malignant lymphomas rarely cause bleeding and there are few reports of brain metastasis from sarcomas other than angiosarcomas [34,35]. Cerebral metastases of cardiac sarcoma are reported as hemorrhagic tumors, but we could not find any literature describing the radiological features of cerebral metastases of other sarcomas. Angiosarcoma may be a distinctive primary cardiac malignancy associated with hemorrhagic brain metastasis. This patient died the day after initiat-

ing radiotherapy, but Bishop et al. [28] reported that no deaths from cerebral hemorrhage due to brain metastasis occurred in patients who completed radiotherapy. Considering that the survival period of patients with cardiac angiosarcoma with brain metastasis is 1 month, it is important to diagnose as angiosarcoma by imaging alone. We propose that radiotherapy for brain metastasis should be considered before histological diagnosis if cerebral metastasis of cardiac angiosarcoma is suspected.

Conclusion

We experienced a case of cardiac angiosarcoma with metastases to the lungs, brain and bone. The patient died before adequate treatment could be performed due to hemorrhage from brain metastases.

Cardiac tumor with hemorrhagic brain metastases may be characteristic of angiosarcoma. Considering the poor survival time of patients with brain metastases, urgent radiotherapy may be considered based on imaging findings alone.

Patient consent

A written consent was obtained from the patient for publication of this case report and accompanying images.

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