Primary Cardiac Angiosarcoma of the Right Auricle with Difficult-to-Treat Bilateral Pleural Effusion

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Abstract

A 70-year-old woman was admitted to our hospital with pleuritis and pericarditis. Cytological examination of pleural and pericardial effusion, and pleural biopsy specimens under thoracoscopy revealed no specific pathological findings. The pleural effusion was drained continuously; however, she died of circulatory insufficiency at day 45 from admission. At autopsy, a fragile hemorrhagic mass arising from the right auricle had invaded bilateral pleura and the pericardium directly without distant metastasis. Immunohistochemical staining showed that the tumor cells expressed endothelial markers such as CD31 and CD34 antibodies, and factor VIII-related protein. These findings supported the diagnosis of a poorly differentiated angiosarcoma.

Key words: primary cardiac angiosarcoma, pleural effusion, pericardial effusion, immunohistochemical staining

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Introduction

In some cases, it is difficult to diagnose the underlying disease that causes pleural effusion. The cause of pleural effusion is not evident in diagnostic thoracentesis in up to 25% of all cases, and false negatives occur in approximately 8%, even with thoroscopic biopsy (1).

Primary cardiac angiosarcoma is extremely rare. Most cases of cardiac angiosarcoma have metastasis to multiple organs at the time of diagnosis (2, 3); therefore, they have a poor prognosis. We present a rare case that had dyspnea on effort with difficult-to-treat bilateral pleural effusion, and we diagnosed the patient with primary cardiac angiosarcoma, which occurred from the right auricle that had invaded the bilateral pleura without distant metastasis at autopsy.

Case Report

A 70-year-old Japanese woman was admitted to the cardiology division at Jichi Medical University Hospital with a diagnosis of acute pericarditis with unidentified underlying disease. Her pericardial effusion was controlled after drainage. However, she was re-admitted to the pulmonary medicine division with dyspnea on effort 3 months later.

A physical examination upon admission revealed the following: height, 152 cm tall; weight, 44 kg; arterial blood pressure, 142/98 mmHg; pulse rate, 108/min; and temperature, 36.5°C. Respiratory sounds were remarkably diminished on the left side of the chest. Lymphadenopathy was absent. Laboratory findings revealed the following: white blood cell counts were 7,700/mm³ with 77.5% neutrophils; C-reactive protein levels were slightly elevated to 0.35 mg/dL; and brain natriuretic peptide levels were 92.1 ng/mL. A purified protein derivative skin test and QuantiFERON TB-2G were negative. Other tests, including antinuclear antibody, rheumatoid factor, human immunodeficiency virus antibody, and thyroid-stimulating hormone were negative. Tumor markers relevant to carcinoma were also negative: carcinoembryonic antigen (CEA) was 1.7 ng/mL, cytokeratin-19 fragment was 1.2 ng/mL, neuron-specific enolase was 16.6 ng/mL, and ProGRP was 45.8 pg/mL. An electrocar-

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diography showed normal sinus rhythm and it was within the normal limits including the ST-T changes. Chest X-ray on admission revealed left pleural effusion. The findings of the patient’s pleural effusion were as follows: bloody and exudative, pH, 8.0; protein, 4.9 g/dL (serum protein, 5.9 g/dL); glucose, 0.11 g/dL; lactate dehydrogenase (LDH), 295 IU/L (serum LDH, 292 IU/L); CEA, 0.9 ng/mL; adenosine deaminase, 11.6 IU/L; and a positive Rivalta reaction. Cytological examination of pleural effusion showed 88.0% lymphocytes and no malignant or abnormal cells. Cultures and PCR using AmpliCor Mycobacterium of the pleural effusion showed negative results.

To make a definitive diagnosis, we performed a biopsy from the left parietal pleura under thoracoscopy. Thoracoscopic findings of the visceral and parietal pleura included no abnormal findings, and there were no specific pathological findings without a reactive mesothelium. Chest computed tomography (CT) after left thoracic drainage revealed a lesion with irregular heterogeneous density with ill-defined margins, which was not identified on transthoracic echocardiography, in front of the right atrium (Fig. 1). A transthoracic echocardiogram only demonstrated normal left ventricular contraction, mild pericardial effusion, and right pleural effusion. Pericardial effusion revealed characteristics similar to those of the pleural effusion. Abdominal CT, upper gastrointestinal endoscopy, colonoscopy, cervical echography, and gynecological examination showed no specific findings.

Pleural effusion had to be drained continuously because it was produced at approximately 700 ml per day. At day 18 after admission, right pleural effusion, which had similar characteristics to those of left pleural effusion, was suddenly increased. The patient gradually weakened with hypoalbuminemia, and her blood pressure was not controlled with suddenly worsened respiratory failure at day 45 from admission. Unfortunately, the patient died of circulatory insufficiency without identification of the underlying disease.

At autopsy, hemorrhagic fibrinous adhesions were found over both lungs. On opening the pericardium, there was similar hemorrhagic fibrinous material. The hemorrhagic fibrinous material over the epicardium was considered to be fibrinous pericardium at a glance, but after sectioning, we observed that a fragile hemorrhagic mass approximately 5 cm in diameter arose outwardly from the muscle layer of the right auricle (Fig. 2A). This tumor proliferated to under the endocardium of the atrium without invasion to the inside. Microscopically, the tumor cells had oval to spindle-shaped nuclei and were diffusely proliferated (Fig. 2B, C). Although a vascular lake or hemorrhage was formed, there were no vascular structures lined by endothelial-like atypical cells. Immunohistochemical staining showed that the tumor cells expressed endothelial markers such as CD31 and CD34 antibodies, and factor VIII-related protein (Fig. 3). These findings supported the diagnosis of a poorly differentiated angiosarcoma.

**Discussion**

We report an autopsy case of primary cardiac angiosarcoma with bilateral pleural effusion that was difficult to treat. Primary cardiac tumors are rare with an incidence ranging from 0.0017% to 0.0033% in reported autopsy series, and the majority of them are benign (4). Although angiosarcoma is the most common primary cardiac malignant tumor, it is extremely rare. Approximately 80% of primary cardiac angiosarcomas occur from the right atrium and pericardium or another chamber around the right atrium (5). Clinical symptoms and signs include (a) a tumor mass that obstructs intracardiac blood flow or interferes with valve function, (b) arrhythmias or pericardial effusion with tamponade, (c) tumor embolism, and (d) systemic or constitutional symptoms (6). Most cases of cardiac angiosarcoma metastasize to multiple organs such as the lungs, liver, and bones; some cases are diagnosed by secondary symptoms derived from metastatic lesions. As a result, they have a poor prognosis of 2-24 months from the time of diagnosis (2, 3).

Meng et al reported that the sensitivities of transthoracic echocardiogram (TTE) and transesophageal echocardiogram to detect these primary masses are 93% and 97%, respectively (6). On the other hand, magnetic resonance imaging (MRI) currently appears to be the imaging modality of choice in the assessment of a patient with known cardiac angiosarcoma (7). Fluorine-18 fluorodeoxyglucose positron emission tomography imaging (FDG-PET) might also add additional information on the tumor and result in an early diagnosis (8). In the present case, the tumor, which arose from the right auricle and was not identified by TTE, invaded the pericardia, and therefore, she was found to have cardiac tamponade with pericarditis at the last hospitalization. In addition, while pericardial effusion did not increase, the left pleural effusion increased due to invasion of the left pleura. It then invaded the right pleura without invasion of the atrial endocardium or distant metastasis, and as a result, right pleural effusion was increased. This resulted in respiratory failure with no other symptoms of metastatic lesions, which
Figure 2. Macroscopic and microscopic features of the tumor. (A) Macroscopic features include a fragile hemorrhagic mass approximately 5 cm in diameter (arrow) arising from the right auricle. (B) Hematoxylin and Eosin staining, ×40. (C) Hematoxylin and Eosin staining, ×200. Microscopic features include tumor cells that have oval to spindle-shaped nuclei and are diffusely proliferated. Although a vascular lake or hemorrhage was formed, there were no vascular structures lined by endothelial-like atypical cells.

Figure 3. Immunohistochemical staining shows that the tumor cells express endothelial markers such as (A) CD34 and (B) CD31 antibodies, and (C) factor VIII-related protein (×400).
is a rare finding according to the literature. We did not take into consideration primary heart disease because pericardial effusion did not increase. In addition, we did not find distant metastasis with other systemic symptoms, and therefore, we did not perform MRI or FDG-PET.

In the pathological findings, typically, small clusters of anisocytic spindle-shaped tumor cells appear as vascular-like structures and hemosiderin-laden macrophages in many erythrocyte-rich environments (9). They vary from well-differentiated tumors that are composed of anastomosing vascular channels to undifferentiated tumors arranged as solid sheets of anaplastic cells. Histopathological variations of cardiac angiosarcoma make them difficult to recognize, and some lesions including metastasis may appear benign or may even be mistaken for “benign hemangioma” (5). Since the histopathology of angiosarcoma can show various findings, most cases of primary cardiac angiosarcoma are diagnosed by surgical biopsy. In the present case, it was difficult to diagnose from the biopsy specimens under thoracoscopy; therefore, primary cardiac angiosarcoma may be difficult to diagnose from tiny specimens. Immunohistochemical staining is recommended if possible, because factor VIII-related antigen, CD31, and CD34 are strongly positive throughout the cytoplasm for the tumor cells. In our case, we did not perform immunohistochemical staining in the biopsy specimens under thoracoscopy because we did not take into consideration angiosarcoma. Therefore, we consider that immunohistochemical staining should be performed, while taking into consideration primary cardiac angiosarcoma, which develops with this pattern.

The main treatment strategy in cardiac angiosarcoma is surgical resection with or without chemotherapy and radiation. However, Truong et al reported that patients treated with complete resection had improved overall survival compared with those with incompletely resected disease (25 months vs. 6 months, p=0.042) (10). The high rates of disease progression and mortality highlight the need for more effective local and systemic treatments that may be used in conjunction with surgery to improve patient outcomes. Chemotherapy for cardiac angiosarcoma with doxorubicin-based chemotherapy, paclitaxel, docetaxel, or cyclophosphamide has been reported (11-13). IL-2 therapy has been reported to be effective for angiosarcoma of the skin, and it has also been performed for cardiac angiosarcoma. The combination of chemotherapy and immunotherapy has been reported to be effective for cardiac angiosarcoma (14). Although the numbers of patients are too small to draw conclusions, the long-term benefits from systemic chemotherapy should be determined using a larger population. Data on the role of radiation in cardiac sarcoma management are also sparse. High doses of radiation to local tumors improve control, but they increase the chances of severe events such as pericarditis, cardiomyopathy, and vascular injury (15, 16). The most effective method to improve the outcome of cancer radiation therapy is to concentrate the dose of radiation only on the tumor. The present patient could not be treated with complete surgical resection and high doses of radiation, and therefore, she might have had a poor prognosis even if we had been able to diagnose her. In conclusion, it may be necessary to consider primary cardiac angiosarcoma in cases where it is difficult to treat pericarditis and pleuritis of unknown origin.

The authors state that they have no Conflict of Interest (COI).

References


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