

Primary Malignant Sarcomatoid Mesothelioma in the Pericardium

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Abstract

Primary malignant pericardial mesothelioma is an exceptionally rare tumor, and making an antemortem diagnosis of this disease is notoriously difficult. We herein report the case of a 61-year-old woman with pericardial mesothelioma who presented with shortness of breath and peripheral edema of the lower limbs. Chest computed tomography (CT) showed an anterior mass and thickened pericardium with multiple pericardial nodules. A biopsy of the mediastinal mass was performed using right thoracotomy, and the histological findings indicated a sarcomatoid tumor. The patient was treated with chemotherapy; however, she but died three months after diagnosis. An autopsy confirmed a final diagnosis of sarcomatoid type primary malignant pericardial mesothelioma following extensive immunohistopathological examinations.

Key words: mediastinal tumor, asbestosis, cardiac tumor, pericardial tumor

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Introduction

Primary malignant pericardial mesothelioma (PMPM) is extremely rare and has a poor overall prognosis (1, 2). PMPM accounts for approximately 2-3% of all cardiac and pericardial primary tumors and approximately 1% of all mesotheliomas (3, 4). In an epidemiological survey, the incidence of PMPM was estimated to be 0.0022% (5). Making an antemortem diagnosis of PMPM is challenging and misdiagnosis is common (1-14). We encountered a case radiologically presenting with an anterior mediastinal mass and pericardial nodules, mimicking an anterior mediastinal tumor. A biopsy an antemortem histological specimen taken from the anterior mediastinal mass and a subsequent autopsy confirmed the diagnosis of sarcomatoid type PMPM. We herein report the clinical and histological features of this case and discuss PMPM.

Case Report

A 61-year-old woman was admitted to our hospital with a six-month history of dyspnea on exertion and lower extremity edema. She had a past history of diabetes and dyslipidemia. She had no history of occupational or incidental exposure to asbestos. On admission, her blood pressure was 122/86 mmHg, her pulse was 105 beats per minute, her temperature was 35.9°C, her respiratory rate was 18 breaths per minute, and her oxygen saturation was 96% on ambient air. Jugular overswelling was observed, which was increased in the decubitus position. On chest auscultation, the patient's cardiac and breath sounds were clear. Lower extremity edema was remarkable.

The laboratory findings showed slightly elevated levels of LDH (309 IU/L; normal: 115-245 IU/L) and soluble IL-2 receptor (538 IU/mL; normal: 145-519 IU/L), while others values, including the levels of tumor markers, were normal. The plasma brain natriuretic peptide level was 79.5 pg/mL.

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Chest radiography showed dilation of the right first arch, a right pleural effusion and elevation of the left diaphragm (Fig. 1). Chest computed tomography (CT) showed an anterior mass and thickened pericardium with multiple pericar-

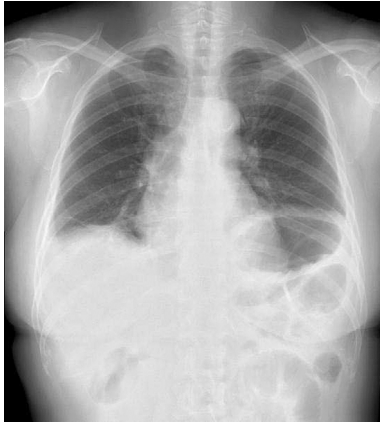


Figure 1. Chest radiography showed expansion of the right first arch, a right pleural effusion, and elevation of the left diaphragm.

dial nodules (Fig. 2A). ^{18}F -Fluorodeoxy glucose positron emission tomography (FDG-PET) revealed masses showing abnormal uptake in the anterior mediastinum (SUVmax: 19.5) and multiple pericardial lesions (Fig. 2B). Electrocardiogram demonstrated a sinus rhythm of 98 beats per minute, ST-segment depression in I, aVL and V3-4 and shade transformation of the T-waves in I, II, aVL, and aVF (Fig. 3). Transthoracic echocardiography (TTE) demonstrated a normal cardiac contractile force (ejection fraction: 78.25%) and a significant expansion disorder with a moderate pericardial effusion and thickened pericardium (Fig. 4). Cardiac catheterization demonstrated rapid rising of the early diastolic pressures and abrupt equalization in both ventricles, namely, the dip and plateau pattern. Biopsies of the mediastinal mass were performed using video-assisted thoracoscopic surgery (VATS) via the right side. A microscopic examination revealed round-to-spindle-shaped atypical cells with a clear nucleolus closely admixed on Hematoxylin and Eosin staining (Fig. 5). The reticulum was relatively rich and weakly acidophilic with mitosis, consistent with a diagnosis of sarcomatoid carcinoma.

Based on the results of FDG-PET and the microscopic

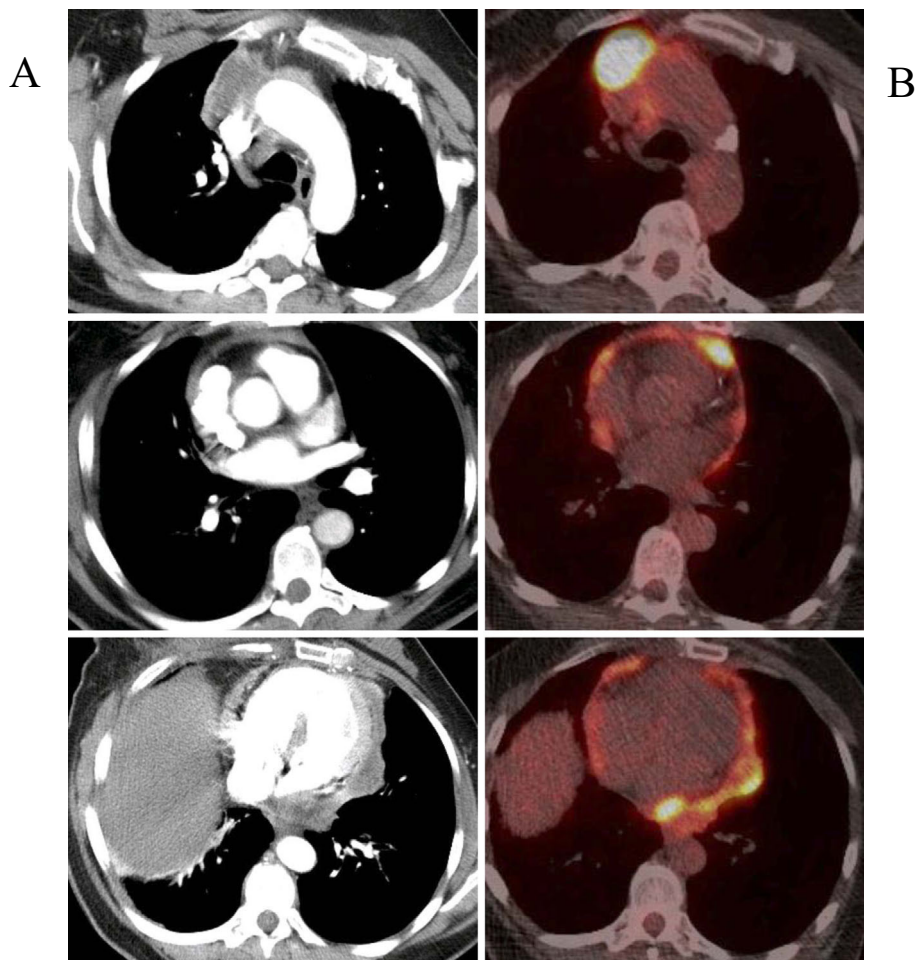


Figure 2. A: Chest computed tomography (CT) showed an anterior mass and thickened pericardium with focally pericardial nodules. B: ^{18}F -Fluorodeoxy glucose positron emission tomography (FDG-PET) revealed masses showing an abnormal uptake in the anterior mediastinum and multiple pericardial lesions.

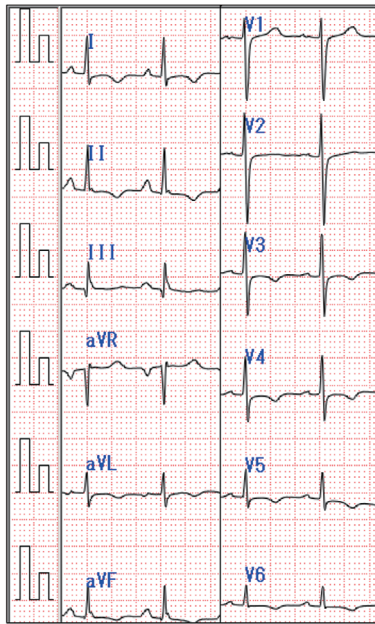


Figure 3. Electrocardiogram demonstrated a sinus rhythm of 98 beats per minute, ST-segment depression in I, aVL and V3-4 and shade transformation of the T-waves in I, II, aVL and aVF.

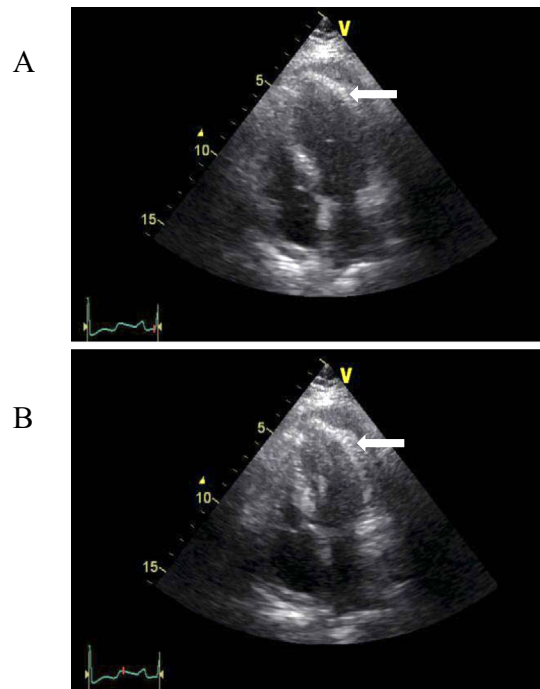


Figure 4. The diastolic and systolic phases on transthoracic echocardiography (TTE). TTE demonstrated a normal cardiac contractile force and a significant expansion disorder with a moderate pericardial effusion and thickened pericardium (arrow).

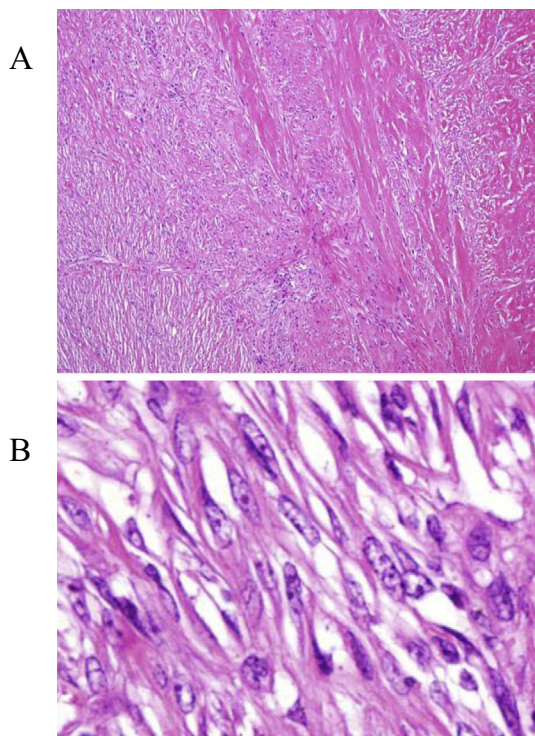


Figure 5. Histological findings of the pericardium on Hematoxylin and Eosin staining showed round-to-spindle-shaped atypical cells with proliferation of collagen fibers and proliferation of spindle-shaped cells with a storiform pattern.

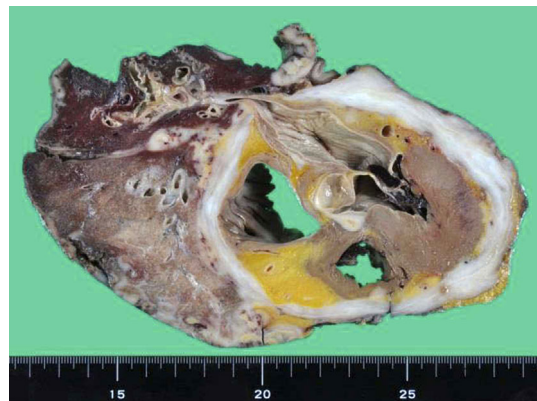


Figure 6. An autopsy revealed that the tumor had infiltrated and proliferated in the pericardium and myocardium and invaded the pericardial cavity.

examination, a diagnosis of sarcomatoid carcinoma of the thymus was made. Several combined chemotherapies with platinum compounds were administered; however, the pa-

tient showed no clinical improvement. She died three months after diagnosis and nine months after the onset of symptoms. An autopsy was performed, which indicated that the tumor had infiltrated and proliferated in the pericardium and myocardium and invaded the pericardial cavity (Fig. 6). The histological features were similar to those of the biopsy specimens. An immunohistochemical analysis indicated that the tumor cells were positive for cytokeratin AE1/AE3 and vimentin and negative for desmin (muscular marker), S-100 (nerve marker), CD34 (vascular marker), CD1a, CD21 (dendritic cells marker), Bcl-2 and CD99 (synovial marker). Calretinin and cytokeratin 5/6, a marker of mesothelioma, were

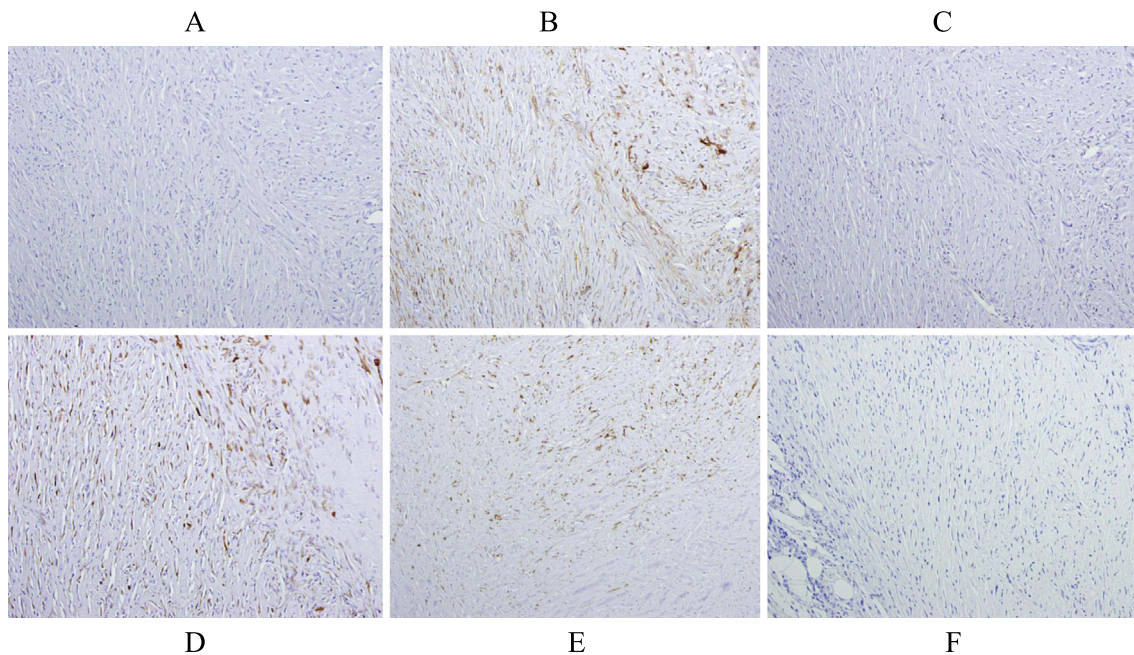


Figure 7. Results of the immunohistochemical analysis in the present case. A: Calretinin staining performed at autopsy was negative. B: Focal positivity for D2-40 was observed. C: WT1 staining performed at autopsy was negative. D: Cytokeratin CAM5.2 staining performed at autopsy was positive. E: Focal positivity for cytokeratin AE1/AE3 was observed. F: Cytokeratin 5/6 staining performed at autopsy was negative.

also negative. CD5 and thyroid transcription factor-1, specific markers of thymic squamous cell carcinoma and lung cancer, respectively, were also negative in the present case (Fig. 7). Based on these macroscopic and immunohistochemical findings, we made a diagnosis of sarcomatoid-type PMPM. We believe that the cause of death in this case was due to cardiac compression by the PMPM. No pleural or pericardial plaques or asbestos bodies were observed.

Discussion

PMPM is often discovered late during the clinical course or at autopsy (1-9). Therefore, making an antemortem diagnosis of PMPM is challenging and notoriously difficult. The clinical presentation of PMPM is nonspecific and radiological examinations are often noncontributory. The initial radiographic findings in the present case were instructive. The largest tumor mass was detected in the anterior mediastinum and showed the strongest positive accumulation on FDG-PET. These radiographic findings mimicked those of an anterior mediastinal tumor. Based on the histological findings obtained with VATS, we considered the thymus to be the primary origin, and a clinical diagnosis of thymic sarcoma with pericardial metastasis was made.

According to Karadzic et al. (6), metastases are present in approximately 25-45% of patients with PMPM and usually involve the regional lymph nodes, lungs, and kidneys. Nilsson et al. (2) summarized 16 case reports and reported that half of all cases had regional lymph node involvement. Therefore, regional lymph node metastasis is not uncommon

in patients with PMPM. Our case showed clinical signs of right heart failure from the initial presentation. The presence of pericardial neoplasms should be considered in the differential diagnosis even in patients without radiologically typical pericardial masses or effusions.

The histological pattern of PMPM is classified into three categories: predominantly epithelial, fibrous (or spindle cell as in our case), and biphasic (mixed) (14). Among these, the fibrous and sarcomatoid patterns are the least common (2). Obtaining immunohistochemical panels is essential for making a pathological diagnosis of mesothelioma. Calretinin, cytokeratin 5/6 (CK5/6) and D2-40 are positive markers for malignant mesothelioma (14, 15). In particular, calretinin and D2-40 are the two positive mesothelial markers most consistently expressed in sarcomatoid mesotheliomas (9, 15). Calretinin was negative in the present case, which is inconsistent with the findings of other case reports of sarcomatoid mesothelioma (7, 9, 15). The histological and clinical significances of negativity for calretinin remains unclear. However, the negative results of staining for CD21, CD31, CD34, CD5, desmin, myoglobin, S100, Ber-EP4 and thyroid transcription factor-1 excluded the diagnoses of pulmonary, synovial and muscular sarcoma and supported a diagnosis of PMPM. Therefore, conducting extensive immunohistological analyses can contribute to making an accurate diagnosis of specimens, even those taken from metastatic lesions.

There is some recent evidence that asbestos exposure is involved in the etiology of PMPM (11-13). However, the present patient had neither a history of asbestos exposure

nor the presence of asbestos bodies on histological analysis.

In summary, we described a rare case of sarcomatoid mesothelioma occurring in the pericardium. Albeit rare, the presence pericardial tumors should be considered in the diagnostic list in patients with clinical signs of right heart dysfunction, even in those showing radiographically atypical findings. Conducting immunohistological analyses is useful for making a final diagnosis of the disease, even the occurring in unusual sites.

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

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