Endobronchial Ultrasound-guided Transbronchial Needle Aspiration in a Patient with Pericardial Mesothelioma

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Abstract

Pericardial mesothelioma is a very rare pericardial tumor. Diagnosing pericardial disease can be challenging, and obtaining an antemortem diagnosis of pericardial mesothelioma is particularly difficult. We herein report the case of a 60-year-old man with pericardial mesothelioma diagnosed on endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). Chest computed tomography showed a mass surrounding the pericardium, and EBUS-TBNA of the right inferior paratracheal and subcarinal stations was consequently performed. No uptake was noted on 18F-fluorodeoxy glucose positron emission tomography, other than in the pericardial mass. The results of histological and immunohistochemical examinations indicated the features of malignant mesothelioma. We therefore diagnosed the patient with pericardial mesothelioma, which was subsequently confirmed at autopsy.

Key words: endobronchial ultrasonography, mesothelioma, pericardium


Introduction

Malignant mesothelioma is an aggressive tumor that originates from the mesothelial cells of the pleura, peritoneum, pericardium and/or testicular vaginalis. According to the surveillance program conducted by the Japanese Ministry of Health, Labour and Welfare, the distribution of the malignant origin is as follows: the pleura (85.5%), peritoneum (13.2%), pericardium (0.8%) and testicular vaginalis (0.5%) (1). Pericardial mesothelioma is a very rare pericardial tumor, and diagnosing pericardial disease can be challenging, with an antemortem diagnosis of pericardial mesothelioma obtained in only 10-20% of cases (2). We herein report a case of pericardial mesothelioma diagnosed on endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) that was subsequently confirmed at autopsy.

Case Report

A 60-year-old man was admitted to our hospital with symptoms of dyspnea on exertion and lower extremity edema. Five months prior to admission, enlargement of the cardiac silhouette was noted on a chest radiograph during a routine health examination. Because he exhibited no symptoms at that time, the patient did not undergo further tests. However, one month before the current admission, he developed dyspnea on exertion and lower extremity edema and was admitted to another hospital. Chest computed tomography showed a mass surrounding the epicardium that was enhanced diffusely and reached the sternal notch, so as to surround the ascending aorta, in addition to the presence of bilateral pleural effusion (Fig. 1). The patient was therefore transferred to our hospital for a further evaluation. He had no history of occupational or incidental exposure to asbestos. Chest radiography showed an enlarged heart shadow.
and bilateral pleural effusion (Fig. 2). An electrocardiogram demonstrated a sinus rhythm of 89 beats per minutes with multiple supraventricular premature beats, ST-segment depression in V4-6 and shade transformation of the T-waves in I and V3-6. Transthoracic echocardiography showed a pericardial mass with significant expansion disorder and little pericardial effusion. 18F-fluorodeoxy glucose positron emission tomography (FDG-PET) revealed a mass with an abnormal uptake around the heart; however, no sites of abnormal uptake were noted in the pleura or other organs (Fig. 3).

For the differential diagnosis, we considered the possibility of pericardial mesothelioma, sarcoma, malignant lymphoma and a mediastinal tumor. EBUS was thus performed in order to determine the nature of the mass. The EBUS images showed several heterogeneous masses with a distinct margin at the right inferior paratracheal station (#4R) and subcarinal station (#7) (Fig. 4). A cytological examination disclosed poorly differentiated malignant cells, while a histological evaluation demonstrated malignant cells with increased chromatin, enlarged nuclei and eosinophilic cytoplasm. An immunohistochemical analysis of the tissue specimens was also performed, which showed positive staining for antibodies against pan-cytokeratin (clone: AE/AE3), calretinin and Wilms tumor-1 (WT-1). However, the tissues were negative for thyroid transcription factor-1 (TTF-1) and surfactant protein A (clone: PE-10) (Fig. 5). These findings suggested a diagnosis of pericardial mesothelioma.

Because the patient’s dyspnea resulting from heart failure rapidly worsened, chemotherapy was not administered. He subsequently died two weeks after admission to our hospital due to obstructive shock. At autopsy, a macroscopic examination showed a white solid tumor in the pericardium around the heart. The pericardial cavity was completely occupied by the tumor; however, no pericardial effusion was observed (Fig. 6). A histological examination revealed that the tumor consisted of two parts, including a region of proliferating malignant cells with enlarged nuclei and eosinophilic cytoplasm in the tubulopapillary, alveolar and trabecular structures and a region of proliferating spindle-shaped malignant cells in fibrous stroma. The immunohistochemical analysis of the autopsy specimens showed positive staining...
Figure 3. $^{18}$F-fluorodeoxyglucose positron emission tomography revealed a mass with an abnormal uptake around the heart. No sites of abnormal uptake were noted in the pleura or other organs.

Figure 4. Endobronchial ultrasound images of the right inferior paratracheal station (A) and sub-carinal station (B).

For pan-cytokeratin AE/AE3 and calretinin (Fig. 7), with no findings of pleural or peritoneal involvement. These results confirmed the diagnosis of epithelial pericardial mesothelioma. There were no asbestos bodies.

Discussion

Based on the data for 22 large autopsy series, the frequency of primary cardiac tumors is approximately 0.02%, with three-quarters of primary cardiac tumors being benign and one-quarter being malignant (3). Malignant mesothelioma is the most common primary malignancy of the pericardium, although only approximately 350 cases of pericardial mesothelioma have been reported in the literature. Asbestos exposure is associated with pericardial mesothelioma less frequently than pleural mesothelioma. Several factors...
are considered to be causes of pericardial mesothelioma, including a genetic predisposition, immune impairment, infection, radiation, diet and recurrent serosal inflammation (4). The present patient had no history of asbestos exposure or these factors.

While CT, FDG-PET and MRI are useful for diagnosing ...

**Figure 5.** Tissue specimens obtained via endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) stained with Hematoxylin and Eosin staining (A: original magnification, ×400). Tissue specimens obtained via EBUS-TBNA immunostained with antibodies against calretinin (B: original magnification, ×200), AE/AE3 (C: original magnification, ×100) and Wilms tumor-1 (D: original magnification, ×200).

**Figure 6.** The autopsy revealed a white solid tumor (arrows) in the pericardium around the heart. The pericardial cavity was completely occupied by the tumor.
pericardial mesothelioma, cytological and/or histological examinations are required to obtain a definitive diagnosis. Cytological analyses of the pericardial fluid often yield negative results; therefore, the diagnosis usually requires the histologic evaluations of tissues obtained during surgery or at autopsy.

EBUS-TBNA is highly effective for determining the lymph node stage of lung cancer (5) and is often used to stage malignant pleural mesotheliomas (6). Although the EBUS-TBNA instruments can only access some parts of the mediastinum, this technique is less invasive than other diagnostic procedures and may be used to acquire both cytological and histological samples. Immunohistochemical analyses are frequently employed to confirm the diagnosis of malignant mesothelioma. Therefore, EBUS-TBNA has an advantage with respect to its ability to be used to obtain histological samples. In the present case, while the cytological examination showed poorly differentiated malignant cells, the histological evaluation revealed malignant mesothelioma with the aid of an immunohistochemical analysis. In 1974, Andersen and Hansen established the following criteria for diagnosing primary pericardial mesothelioma: 1. the tumor is strictly localized to the pericardium without penetration of the parietal pericardium; 2. there are only metastases to the lymph nodes; 3. no other primary tumors are detected, either during the clinical course or at autopsy; and 4. a complete autopsy is performed in cases of death (7). Our case meets these criteria and is the first reported case of pericardial mesothelioma diagnosed using EBUS-TBNA.

Pericardial mesothelioma carries a poor prognosis due to its late presentation and limited treatment options. In addition, symptoms are nonspecific, such as orthopnea, coughing and substernal chest pain (8). However, some patients experience long-term survival following chemotherapy and radiotherapy (9). Therefore, some primary pericardial mesothelioma patients appear to receive a survival benefit from chemotherapy, including primary pleural mesothelioma patients. It is thus necessary to develop a useful diagnostic approach for determining the optimal treatment strategy in such patients. Nilsson and Rasmuson reported that, among their cases with information regarding metastases, one-half of the patients had regional lymph node involvement (10). Hence, we suggest that EBUS-TBNA may become a useful tool for diagnosing primary pericardial mesothelioma.

In summary, this is the first case report of pericardial mesothelioma diagnosed on EBUS-TBNA. Making the ante-mortem diagnosis of pericardial mesothelioma is challenging, and surgery is often required to obtain a definitive diagnosis. As some cases spread to the paratracheal region and/or involve the regional lymph nodes, EBUS-TBNA is a less invasive diagnostic tool for detecting pericardial mesothelioma.

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