Diagnostic Usefulness of Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration in a Case with Malignant Pleural Mesothelioma

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Abstract

A 74-year-old man was admitted to our hospital with right diffuse pleural thickening and effusion and with subcarinal lymph node swelling. The effusion obtained by thoracentesis showed no malignant cells, although positron emission tomography showed abnormal uptake in the right pleural thickening and subcarinal lymph node. Histopathological examination of the lymph node specimens obtained by endobronchial ultrasound-guided transbronchial needle aspiration showed a sheet of epithelioid-like large atypical cells. The tumor cells were immunohistochemically positive for calretinin and cytokeratin 5/6, and negative for CEA and TTF-1. Therefore, malignant pleural mesothelioma of epithelioid type was diagnosed.

Key words: endobronchial ultrasonography (EBUS), convex probe, mediastinal lymph node, mesothelioma

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Introduction

Malignant pleural mesothelioma (MPM) is related to asbestos exposure, and the risk of disease is assumed to become the maximum after 2010 (1). Due to the difficulty of diagnosis, a simple, accurate and less invasive diagnostic procedure is necessary.

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive biopsy procedure, visualizing the lesion surrounding the trachea and bronchi by convex probe. For the diagnosis of hilum and mediastinum lymph node metastasis in lung cancer, there is a report that the sensitivity is 94.6%, specificity is 100%, and it has a high diagnostic accuracy (2). In this report, we describe a first case of epithelioid MPM diagnosed by EBUS-TBNA.

Case Report

A 74-year-old man was admitted to our hospital because of low grade fever, cough and right pleural effusion. He had a history of asbestos exposure for 5 years (25 to 30 years old) and smoking 7.5 pack years. He was given a diagnosis of pleural asbestosis 6 years ago, and his chest CT has been examined once a year. His chest CT had not changed at 6 months before admission.

Physical examination on admission showed that his body temperature was 37.3°C, pulse rate 95 per minute and respiratory rate 22 per minute. Laboratory analysis revealed a C-reactive protein level of 5.8 mg/dL (normal range <0.3 mg/dL). Chest radiograph showed multiple nodular opacities and right pleural effusion. Pleural effusion was exudative and no malignant cell was observed. Hyaluronic acid in the effusion was 67,600 ng/mL, which was not high if the normal reference level selected is 100,000 ng/mL or less (3). Integrated positron emission tomography and CT (^18FDG-PET/CT) showed multiple regions of high uptake on the right pleura and subcarinal lymph node (Fig. 1A, 1B).

EBUS-TBNA was performed to evaluate the lymph node with a flexible ultrasonic puncture bronchoscope (BF-UC 260F-OL8; Olympus; Tokyo, Japan) under conscious seda-
Figure 1. ^18^FDG-PET scan showed multiple regions of high uptake on the right pleura and high uptake extending from the subcarinal lymph node to the caudal site (A). ^18^FDG-PET/CT showed the right pleural effusion as well as the high uptake of the subcarinal lymph node and right pleura nodules (B). EBUS-TBNA of the lymph node using a 22-gauge needle (arrow) for pathological diagnosis (C).

tion. The images were processed in a dedicated ultrasound scanner (EU-C2000; Olympus; Tokyo, Japan). The maximal diameter of the subcarinal lymph node was 3.5 cm. The internal echo was moderately heterogeneous (4). The power Doppler assessment revealed that the lymph node had the irregular winding vessels (5). However, these images could not definitely distinguish benign from malignant lymphadenopathy. The lymph node was sampled with a dedicated 22-gauge TBNA needle under direct EBUS guidance (Fig. 1C). The specimens obtained by EBUS-TBNA were examined cytologically, histologically and immunohistochemically.

The cytological smears were composed of scattered atypical cells and clusters arranged in sheet. These cells showed a high N/C ratio, various nuclear sizes and occasional prominent nucleoli. Neither keratinization nor formation of glandular structures was seen. These findings suggested that the cells were malignant but not likely primary lung cancer (Fig. 2A). Hematoxylin and eosin staining showed the cluster of epithelioid-like atypical cells (Fig. 2B). These atypical cells were positive for calretinin (Fig. 2C) and cytokeratin 5/6 (Fig. 2D), but negative for CEA (Fig. 2E) and TTF-1 (Fig. 2F). From these findings, the patient was diagnosed as epithelioid MPM and his stage was III based on the finding of metastasis of the subcarinal lymph node (N2 lymph node). Therefore, he received chemotherapy with cisplatin and pemetrexed.

Discussion

The diagnosis of MPM is difficult regarding the cytology of the pleural effusion. Boutin et al studied the diagnosis rate of various diagnostic procedures in 188 MPM patients, and they showed high diagnosis rates of 98% with the biopsy under thoracoscopy, although only 26% in cytology of pleural effusion, and 39% in pleural biopsy of the closed system (6). Therefore, it is important to obtain specimens under visible conditions in the diagnosis of MPM. In addition, the response for therapeutic drugs and the prognosis differ according to the histological type of MPM (7, 8). Thus, it is indispensable to diagnose MPM with its histological type. However, thoracoscopy for the purpose of biopsy is invasive for the patients, and Agarwal et al showed that the frequency of seeding of MPM after the biopsy was 16% (9).

In the present case, the histological specimens could be obtained from the subcarinal lymph node by EBUS-TBNA which is a minimally invasive procedure. Because the MPM shows various forms in the pathology, the differential diagnosis such as carcinoma and sarcoma is difficult. Immunohistochemical staining is valuable for the diagnosis of MPM, and two of the positive markers such as cytokeratin 5/6, calretinin, D2-40, and Wilms tumor protein-1 (WT-1) and two
of the negative markers such as CEA, MOC-31, and TTF-1 are useful (10, 11). In this case, two markers were positive for calretinin and cytokeratin 5/6, but two markers were negative for CEA and TTF-1. Here, we first showed that EBUS-TBNA is a useful procedure for the diagnosis and staging of MPM.

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a method of endoscopical needle biopsy by visualizing the mediastinal lymph node surrounding the esophagus. The utility of the diagnosis and staging has been reported in the example of the MPM with lymph node metastasis (12-14). In the case of suspected MPM, bronchoscopy is typically undertaken for the differential diagnosis of lung cancer. EBUS-TBNA is a more excellent procedure for observing the bronchial lumen and obtaining specimens from the mediastinal or lung lesions which are located adjacent to the trachea or bronchus than EUS-FNA (15). The lymph nodes that can be examined by EBUS-TBNA and EUS-FNA are situated in different regions, although some lymph nodes can be examined by both procedures. Therefore, the reasonable usage of these procedures is determined according to the target lymph node.

Seeding of MPM has never been reported in EUS-FNA that is the same method as EBUS-TBNA. In a retrospective study, 24% of the patients who underwent thoracotomy, 16% of the patients who underwent thoracoscopy and 5% of the patients who underwent core-needle biopsy had tumor seeding although no significant differences were seen among these procedures (9). Core needle biopsy was performed by using a thinner 17-gauge introducer needle than others. These results suggest that the skin incision size of each diagnostic procedure is associated with the frequency of tumor seeding. Alternatively, cutaneous metastasis or extension of malignant mesothelioma has been reported (16, 17), but endobronchial metastasis or extension has not. We speculate that the trachea and bronchi are organs where malignant mesothelioma invasion or metastasis rarely occur. Therefore EBUS-TBNA or EUS-FNA could be more safe than thoracoscopy in the diagnosis of MPM. Accumulation of cases will be necessary to confirm the risk of seeding in the EBUS-TBNA in the future.

In summary, EBUS-TBNA is a promising procedure to establish the diagnosis of MPM with lymph node metastasis as well as the lymph node stage of the disease. Furthermore, it is useful for the decision of the therapeutic plan.

References

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