INTERNAL MEDICINE

□ CASE REPORT □

Successful Diagnosis of a Thymoma by Endobronchial Ultrasound-guided Transbronchial Needle Aspiration: A Report of Two Cases

Yasushi Yoshida[1], Masato Singyoji[1], Hironori Ashinuma[1], Meiji Itakura[1], Toshihiko Iizasa[1] and Koichiro Tatsumi[2]

Abstract

We herein report two cases of thymomas diagnosed by endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). In both cases, the tumor was adjacent to the central airway. Therefore, we attempted to perform EBUS-TBNA in order to obtain specimens for a histopathological examination, which resulted in a diagnosis of thymoma. In one case, surgical resection was conducted and the histological evaluation of the resected specimen confirmed thymoma type AB, consistent with the histology from the EBUS-TBNA specimen. As a safe and minimally invasive procedure, EBUS-TBNA may be considered for the diagnosis of mediastinal tumors, including thymoma.

Key words: thymoma, subclassification, endobronchial ultrasound-guided transbronchial needle aspiration

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Introduction

Thymoma is the most common tumor type in the anterior mediastinal region due to the normal thymus position. However, to make a diagnosis of thymoma from fine needle biopsies, such as endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), is challenging due to the need to differentiate from many diseases. Moreover, a thymoma may be subclassified into six types according to the morphology of the epithelial cells and the ratio of lymphocytes and epithelial cells; these types are associated with specific clinical features and varying degrees of aggressiveness (1). Therefore, it is imperative to decide the subtype of a thymoma before planning the treatment strategy. However, fine needle aspiration does not provide a sufficient specimen for an adequate subclassification (2). Conversely, a recent report suggests that EBUS-TBNA allows the diagnosis and further subclassification of a thymoma (3). We herein present two cases of thymoma diagnosed by EBUS-TBNA. In one case, the diagnosis of thymoma and the subtype were confirmed by histology of the resected specimen.

Case Reports

Case 1

A 68-year-old woman with hypertension, bronchial asthma and hypothyroidism presented with an abnormal right mediastinal shadow on a chest X-ray taken during a regular health check-up. A contrast-enhanced computed tomography (CT) scan showed a massive tumor larger than 135 mm in the mediastinal region (Fig. 1a) and she was referred to the Thoracic Division of Chiba Cancer Center. A physical examination revealed no remarkable findings and laboratory data, including tumor markers, were within the normal ranges, except a slight elevation of thyroid stimulating hormone (TSH) to 5.97 μU/mL (normal range: 0.35 to 4.94) and free thyroxine (FT4) to 1.56 ng/dL (0.7 to 1.48) was observed. To further characterize this tumor, magnetic resonance imaging (MRI) of the chest was performed, which demonstrated a heterogeneous mediastinal tumor and an in-

[1]Division of Thoracic Disease, Chiba Cancer Center, Japan and [2]Department of Respirology, Graduate School of Medicine, Chiba University, Japan
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Correspondence to Dr. Yasushi Yoshida, pmdht627@yahoo.co.jp

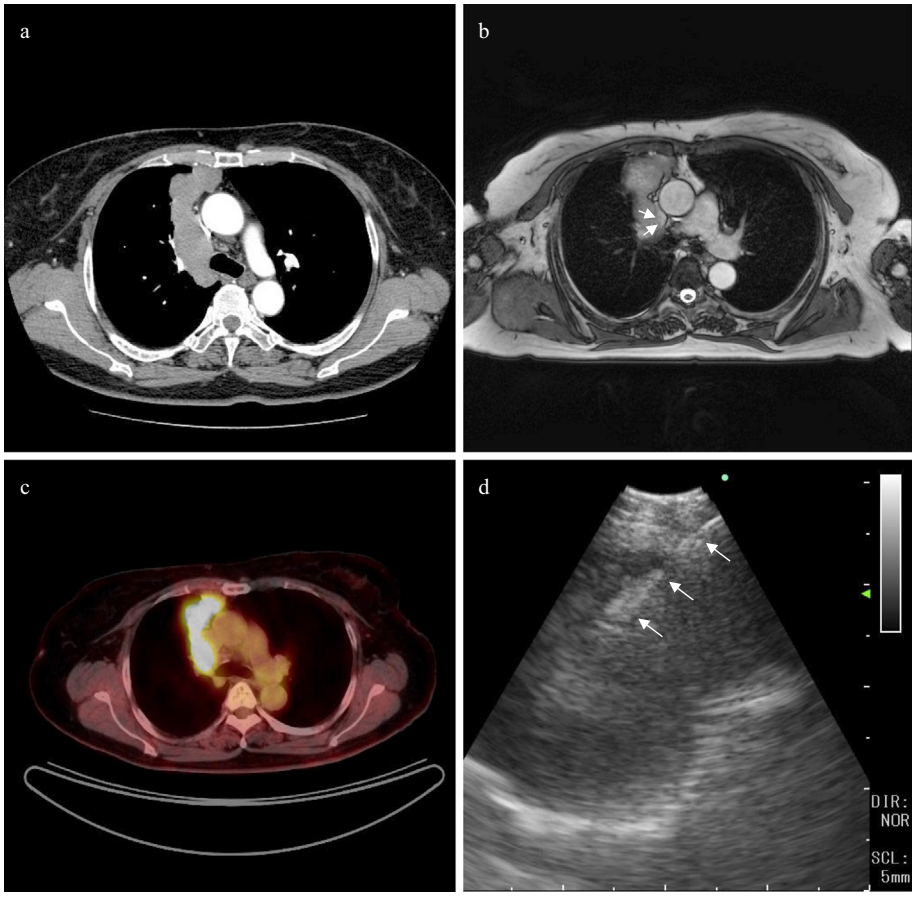

Figure 1. **Case 1. a: Contrast-enhanced chest CT showing a homogeneous mediastinal tumor adjacent to the trachea. b: An axial T2-weighted MR image of the chest showing a mediastinal tumor with irregular margin and heterogeneous intensity and invasion into the superior vena cava (arrows). c: A PET/CT scan showing the remarkable FDG uptake in the tumor. d: Endobronchial ultrasound showing needles (arrows) penetrated through a mediastinal tumor with heterogeneous echogenicity.**

vasion of the superior vena cava on the T2-weighted image (Fig. 1b). Whole body ^{18}F-2-deoxy-fluoro-D-glucose (FDG) positron emission tomography (PET) was additionally performed, which demonstrated a moderately elevated maximum standardized uptake value (SUVmax) of 8.35 to 9.08, suggesting malignancy (Fig. 1c). The tumor appeared to be in contiguity with the right main bronchus. Therefore, we proceeded to conduct EBUS-TBNA of the mediastinal tumor and endobronchial ultrasound indicated a heterogeneous pattern (Fig. 1d). A cytological examination of the biopsy showed epithelial cells and numerous small lymphocytes in Hematoxylin and Eosin (H&E) staining and a meshwork of epithelial cells in immunohistochemical staining of AE1/AE 3, thus leading to a diagnosis of thymoma (type B1 or B2) (Fig. 2). Due to the tumor size and the invasion to major vessels, surgery or radiotherapy were not indicated. The patient declined our recommendation of chemotherapy and instead selected palliative care.

Case 2

A 71-year-old woman who had been under treatment for hypertension was referred to the Thoracic Division of Chiba Cancer Center because a chest X-ray taken during a regular health check-up showed a right upper mediastinal tumor. A contrast-enhanced CT scan demonstrated a mediastinal tumor measuring 66.1×52.6 mm with heterogeneous hyperdensity located adjacent to the trachea (Fig. 3a). The physical examination revealed no abnormal findings and laboratory data showed a mild elevation of lactate dehydrogenase (LDH) to 230 IU/L (normal range: 80 to 200) and sialyl Lewis-X antigen (SLX) to 56 U/mL (up to 38). The subsequent FDG-PET scan disclosed a mildly elevated SUVmax of 3.59 only in the mediastinal tumor (Fig. 3b). We performed EBUS-TBNA and endobronchial ultrasound revealed homogeneous echogenity (Fig. 3c). The cytological examination showed polygonal cells and spindle cells aggregated and dispersed among the small lymphocytes in H&E staining and a network of epithelial cells and immunohistochemical staining of cytokeratin 19, suggestive of a thymoma, possibly type AB (Fig. 4). The patient underwent surgical excision of the tumor. The resected tumor measured 7.5×7.0 ×5.2 cm. The histological examination of the resected tumor confirmed a diagnosis of thymoma type AB, which was consistent with the diagnosis based on the EBUS-TBNA specimen (Fig. 5). The tumor was nearly completely encapsulated macroscopically and microscopically, but a partial transcap-

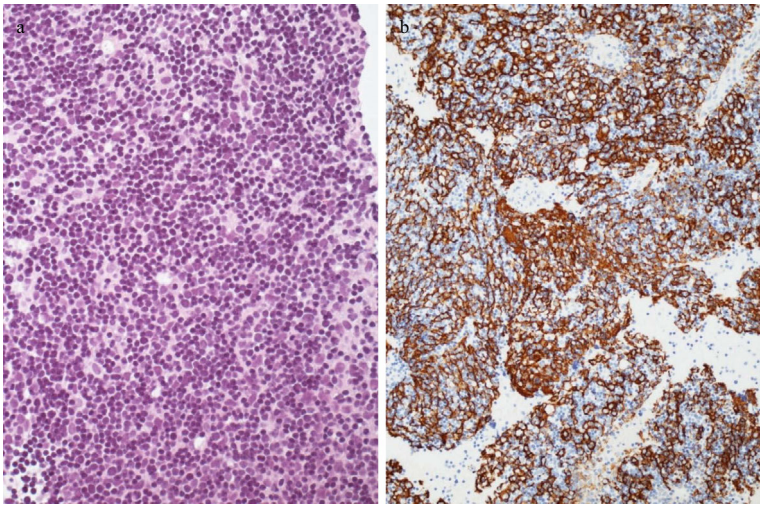

Figure 2. **Case 1. a: Cytological findings of a biopsy obtained by endobronchial ultrasound-guided transbronchial needle aspiration showing epithelial cells with clear nuclei larger than the lymphocytes and numerous small lymphocytes (Hematoxylin and Eosin staining, 40×). b: Immunocytochemical staining for cytokeratin AE 1/AE 3 showing a meshwork of epithelial cells (20×).**

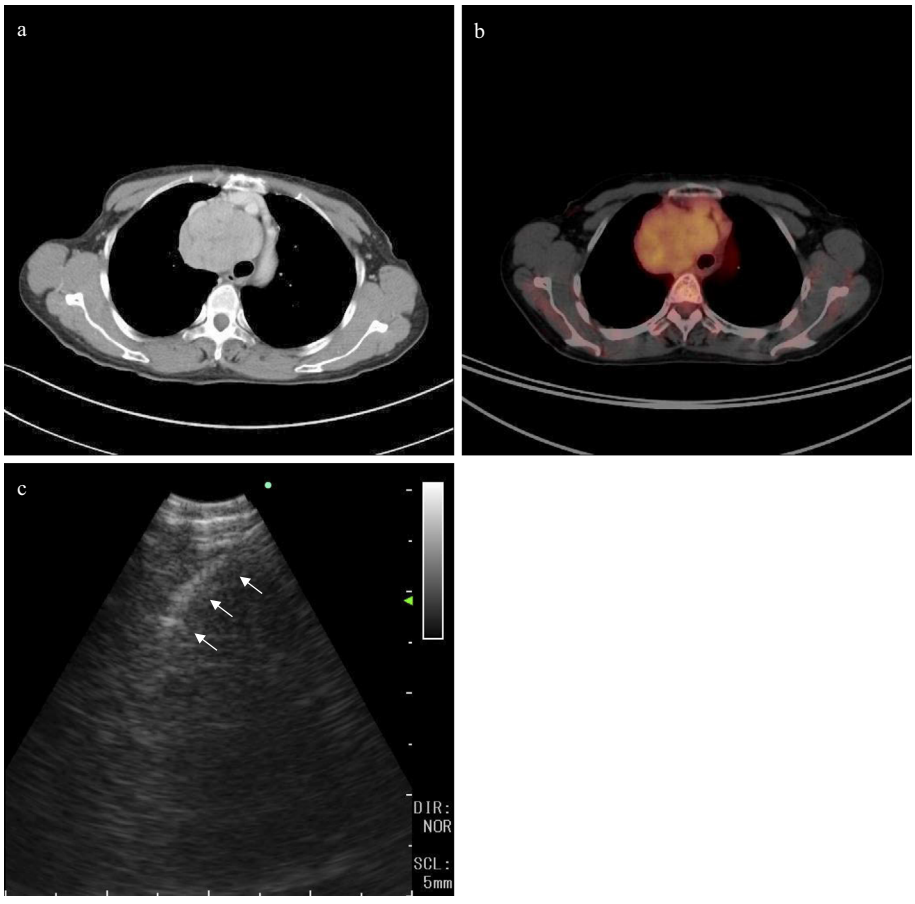

Figure 3. **Case 2. a: Contrast-enhanced chest CT showing a heterogeneous mediastinal tumor displacing the trachea greatly to the left. b: A PET/CT scan showing the insignificant uptake in the tumor. c: Endobronchial ultrasound showing needles (arrows) penetrated through a mediastinal tumor with a comparatively low echoic pattern.**

sular invasion was found (Masaoka stage II). The patient did not undergo additional irradiation or chemotherapy, as recommended by the guideline. She showed no sign of recurrence two and a half years after surgery.

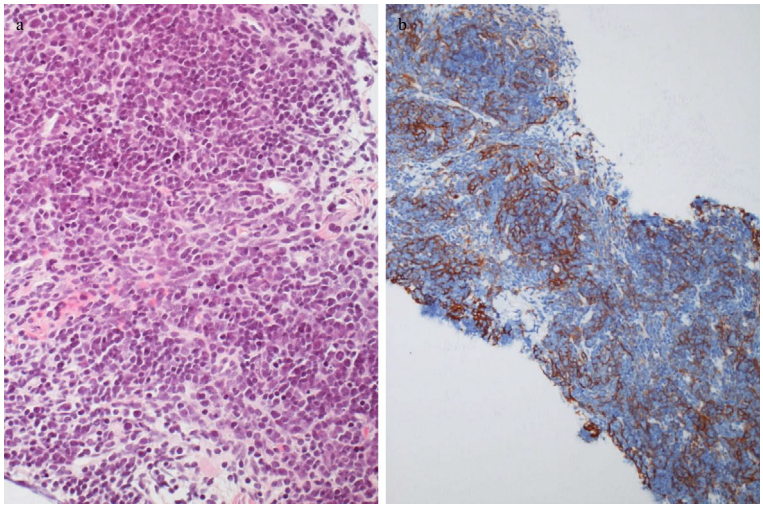

Figure 4. **Case 2. a: Cytological findings of a biopsy obtained by endobronchial ultrasound-guided transbronchial needle aspiration showing polygonal cells and spindle cells with pale chromatin and inconspicuous nuclei, aggregated (center of the figure) and dispersed among small lymphocytes (Hematoxylin and Eosin staining, 40×). b: Immunocytochemical staining for cytokeratin 19 showing a network of epithelial cells (20×).**

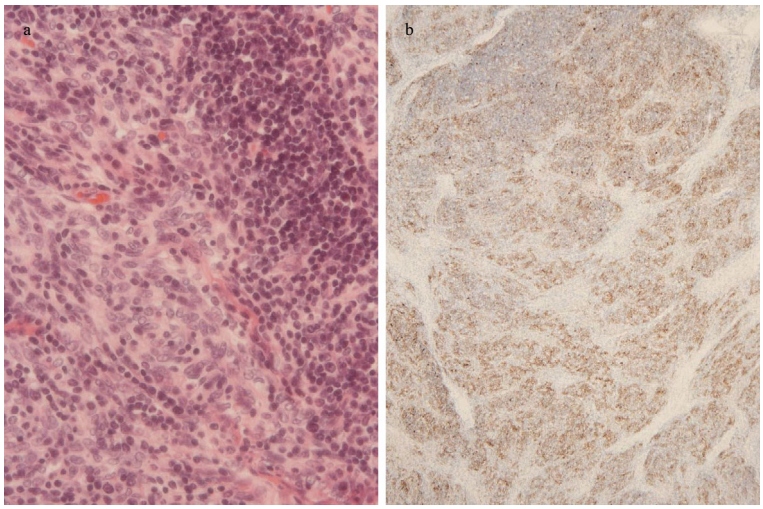

Figure 5. **Case 2. a: Microscopic findings showing aggregation of spindle cells having dispersed chromatin and inconspicuous nucleoli, with few lymphocytes in the left lower area and relatively larger number of small lymphocytes in right upper area (Hematoxylin and Eosin staining, × 40). b: Immunohistochemical staining for cytokeratin 19 showing reticular meshwork of epithelial cells (× 20).**

Discussion

The EBUS-TBNA method is utilized not only for the lymph node staging of lung cancer, but also for the diagnosis of other malignant (4) and benign diseases (5, 6). Compared to the conventional methods, including CT-guided fine needle aspiration, mediastinoscopy and video-assisted thoracoscopy (VATS), EBUS-TBNA provides a safer and less invasive approach for sampling tissues even in the mediastinal region (6). Only a limited number of cases have been reported in which a thymoma was successfully diagnosed by EBUS-TBNA (3, 6), because it has been considered challenging to diagnose thymoma by EBUS-TBNA (7, 8). The most critical disadvantage of EBUS-TBNA is that a very small volume of the entire tumor can be sampled. The tiny specimens obtained from EBUS-TBNA may preclude a precise diagnosis due to the heterogeneous nature of mediastinal tumors and may not allow subtyping of a thymoma, which is important for determining the prognosis (1) as well as the tumor stage (9). Another challenging reason is the fact that a thymoma is a relatively rare tumor with an incidence of 0.15 per 100,000 population, and a cytopathologist may not have sufficient experience to make an accurate di-

agnosis (8). Consequently, only hospitals that have skillful cytopathologists and pulmonologists, who can obtain an adequate amount of specimens by EBUS-TBNA are able to utilize EBUS-TBNA for making an accurate diagnosis of thymoma.

Moonim and colleagues (3) reported in detail the successful diagnosis and subclassification of three cases of thymoma using EBUS-TBNA. In two of the three cases, surgical resection was conducted and a histological examination of the resected tumor confirmed the results obtained from the EBUS-TBNA samples. Regarding the subclassification of a thymoma, these two cases were types B1 and B2. These subtypes are relatively simple to subclassify compared to the present case of type AB. Remarkably, we were able to detect the type A component despite the minute EBUS-TBNA sample, resulting in a diagnosis of type AB. In practice, however, an accurate subclassification is difficult using small partial samples collected by EBUS-TBNA. The EBUS-TBNA technique may allow the subclassification of a thymoma in cases of type B thymoma.

The conventional methods for investigating a mediastinal mass include CT-guided fine needle aspiration, mediastinoscopy, and VATS, which may lead to some complications. Mediastinoscopy and VATS are performed in the operating room under general anesthesia and are therefore more invasive than CT-guided fine needle aspiration. In general, the most common complications of CT-guided fine needle aspiration are pneumothorax and hemorrhage. In the mediastinal region, the procedure has to be conducted with special attention to avoid large vessels, including the internal thoracic artery, ascending aorta, and pulmonary artery, because of the possible life-threatening complications. Additionally, reports of needle track seeding after biopsy of a thymoma must be noted (10).

EBUS-TBNA is a novel and minimally invasive technique, and the complication rate is considered to be low. However, according to a recent nationwide survey of the complications associated with EBUS-TBNA in Japan, the incidence of infectious complications was higher than expected. Therefore, particular attention has to be given to the occurrence of mediastinitis that may lead to severe conditions necessitating treatment by broad-spectrum antibiotics and surgery (11). Conditions that require the use of prophylactic antibiotics should be considered, since no routine prophylactic antibiotic is currently recommended.

Sadohara et al. reported that MRI of a thymoma provides useful information in differentiating low-risk thymomas from high-risk thymomas and thymic carcinomas (12). In case 1, the findings of the mediastinal tumor on MRI were an irregular contour shape, incomplete capsule and great vessel invasion, suggestive of a high-risk thymoma or thymic carcinoma; therefore, the thymoma in case 1 was probably not due to type B1. Although the findings of heterogeneous and homogeneous echogenity of EBUS may also contribute to the differentiation of low-risk thymomas from high-risk thymomas and thymic carcinomas, future data must be accumulated to determine its usefulness.

In summary, we herein reported two cases of thymoma in which EBUS-TBNA successfully led to an accurate diagnosis with no complications. EBUS-TBNA is considered to be a less invasive method compared to conventional CT-guided fine needle aspiration, mediastinoscopy and VATS, especially when the tumor is adjacent to the trachea or main bronchus. EBUS-TBNA may be considered for the diagnosis of a mediastinal mass, and special care must be taken to prevent mediastinitis and other infectious complications.

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

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