Case Report

Successful Diagnosis of a Combined Thymic Epithelial Tumor by Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration

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Introduction: Endobronchial ultrasound-guided tranbronchial needle aspiration (EBUS-TBNA) can be applied to not only the determination of the clinical stages of lung cancer, but also the diagnosis of lymphadenopathies such as lymphoma and sarcoidosis.

Case Report: We report the successful diagnosis of a combined thymic epithelial tumor in a 68-year-old female by EBUS-TBNA. The patient presented with a 6-month history of dysesthesia in bilateral legs. Chest computed tomography revealed a 5.5 cm-tumor with heterogeneous enhancement in the superior and anterior mediastinum. The serum levels of ProGRP and NSE were elevated and anti-Hu antibody was positive at the time of diagnosis. A biopsy by EBUS-TBNA revealed histological evidence of a combined thymic epithelial tumor consisting of small cell neuroendocrine carcinoma and thymic carcinoma. Chemo-radiotherapy reduced the tumor remarkably in size, but the patient's neurologic symptoms remained.

Conclusion: This case suggests that EBUS-TBNA is a safe and useful technique for the diagnosis of paratracheal mediastinal tumors.

Key words: Endobronchial ultrasound-guided transbronchial needle aspiration, Thymic carcinoma, Neuroendocrine tumor, Paraneoplastic syndrome
EBUS-TBNA. Histological studies revealed two different components in a single biopsied specimen, one with spindle-shaped cells and the other with dysplastic cells with enlarged nuclei. In immunohistochemistry, the spindle-shaped cells were positive for CD56 and negative for cytokeratin (Figure 2), the dysplastic cells were positive for CD5 and cytokeratin (Figure 3). On this basis, we diagnosed the tumor as a combined thymic epithelial tumor consisting of small cell neuroendocrine carcinoma and thymic carcinoma.

Chemotherapy with carboplatin (AUC = 4) and etopside (100mg/m²) with concurrent radiotherapy (40 Gy) brought about a complete response, but the patient's neurologic symptoms did not improve.

Discussion

Surgical biopsy, mediastinoscopy, CT-guided percutaneous cutting needle biopsy (PCNB), and conventional TBNA are standard methods for the
Combined thymic epithelial tumors are tumors that among histological types of thymoma, thymic carcinoma, and neuroendocrine carcinoma, two or more histological components reveal each clear region. Combined thymic epithelial carcinomas with thymic carcinomas and neuroendocrine carcinomas are extremely rare. In a survey of 1,320 patients with thymic epithelial tumors by Kondoh et al., only 2 of 186 cases were classified as combined thymic epithelial carcinomas. Diagnosis of mediastinal tumors. Surgical biopsy and mediastinoscopy require general anesthesia and entail a risk of complications. CT-guided PCNB is only minimally invasive, but it may lead to complications such as pneumothorax, hemorrhage, air embolism, or dissemination of malignant cells. If we had used CT-guided PCNB in our case, it would have involved a high risk of hemorrhage, as the tumor was very close to the major vasculatures. Because a conventional TBNA technique is a relatively blind technique without ultrasound, this procedure is unable to visualize target, and is hard to access smaller lymph nodes and nodes at some specific stations. EBUS-TBNA, on the other hand, is reported as a safe and low-invasive procedure with few life-threatening complications because an ultrasonic bronchofiberscope with a convex probe allows for real-time needle aspiration of mediastinal and hilar lymph nodes guided by ultrasound images. There were only a few case reports related with complications of EBUS-TBNA such as a mediastinal abscess and an endobronchial inflammatory polyp. In our patient we managed to obtain a specimen safely and surely with accurate visualization of the surrounding vasculatures under real-time endobronchial ultrasound guidance. This experience suggests that we should use EBUS-TBNA more actively before performing invasive procedures.

Compared to CT and positron emission tomography (PET), EBUS-TBNA has a high sensitivity and high specificity for mediastinal and hilar lymph node staging in patients with lung cancer, because EBUS-TBNA allows tissue diagnosis, which is extremely helpful and provides superior diagnostic accuracy compared to cytology, CT or PET. In an investigation of 105 patients with lung cancer and mediastinal lymph nodes by Yasufuku et al., EBUS-TBNA had a sensitivity of 94.6%, specificity of 100%, and diagnostic accuracy of 96.3%. As a consequence of the EBUS-TBNA, 29 mediastinoscopies, 8 thoracotomies, 4 thorascopies, and 9 CT-guided PCNB could be avoided. In a large study on 502 patients with lung cancers and mediastinal lymph node enlargement on CT, Herth et al. found that EBUS-TBNA had a sensitivity, specificity, and positive predictive value of 94%, 100%, and 100%, respectively. Similarly, EBUS-TBNA had a sensitivity of 90.9% and specificity of 100% in the diagnosis of lymphoma. In the diagnosis of sarcoidosis, EBUS-TBNA demonstrated noncaseating granulomas without necrosis in 82 to 85% of the patients ultimately diagnosed with sarcoidosis. These lines of evidence suggest that EBUS-TBNA may be suitable as the next diagnostic procedure to take following a nondiagnostic bronchoscopy.

**Figure 3**: (A) Another microscopic finding shows tumor cells with enlarged, irregular shaped nucleus and acidophilic cytoplasm (hematoxylin eosin stain, × 600). The tumor cells are positive for CD 5 (B) and cytokeratin (C) immunohistochemically (× 600).
Thymic carcinomas were with combined other histologic types (one combination of squamous cell carcinoma and small cell carcinoma, one combination of small cell carcinoma and thymoma). The etiology of these tumors remains unclear. There are two hypotheses on how combined thymic epithelial tumors arise: either by dedifferentiation of thymoma and thymic carcinoma or by biphasic differentiation of a multipotential thymic epithelial precursor. Thymic neuroendocrine tumors sometimes induce a variety of paraneoplastic syndromes such as myasthenia gravis, hearing loss, sleep disorder, central neuropathies, and peripheral neuropathies. Even if the treatment of thymic tumor is effective, the peripheral neuropathy usually shows no improvement. Improvement of the neurologic symptoms was also eluded in our case, though chemotherapy with concurrent radiotherapy brought about a complete response.

In conclusion, this case suggests that EBUS-TBNA is a safe and useful technique for the diagnosis of paratracheal mediastinal tumors.

References