EBUS-TBNA-related Complications in a Patient with Tuberculous Lymphadenopathy

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Abstract

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is becoming more common for diagnosing intrathoracic lymphadenopathy, including tuberculous lymphadenopathy. We herein report two cases of complications possibly related to EBUS-TBNA for tuberculous lymphadenopathy. The first patient was a 26-year-old woman who developed intrabronchial polypoid granulomas exclusively at puncture sites two months after undergoing EBUS-TBNA. Although endobronchial extension may occur, the risk of aggravation caused by puncture should be considered. The second patient was a 39-year-old woman with transient smear-positive bloody sputum that developed immediately after EBUS-TBNA and persisted for three days. Temporary isolation following EBUS-TBNA should be considered for possible tuberculous lymphadenopathy.

Key words: endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), tuberculous lymphadenopathy, endobronchial tuberculosis, brain tuberculosis


Introduction

The diagnosis of mediastinal and hilar tuberculous lymphadenopathy is usually challenging owing to its nonspecific clinical and X-ray findings and the low diagnostic yield of sputum examinations. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has recently become more common for the diagnosis of mediastinal and hilar lymphadenopathy, including tuberculous lymphadenopathy (1, 2). Navani and colleagues (1) reported excellent results using EBUS-TBNA in patients with intrathoracic tuberculous lymphadenopathy; the procedure was diagnostic in 94% of cases, with a positive smear in 17% of the patients, positive cultures in 47% of the patients and pathological findings consistent with tuberculosis in 86% of the patients. Whereas the diagnostic success rate is very similar to that achieved with mediastinoscopy or conventional TBNA (3-8), EBUS guidance allows for the safe aspiration of the hilar nodes and nodes measuring <10 mm in size (1) and increases the proportion of patients that can be diagnosed using this technique. EBUS-TBNA has been concluded to be safe and effective, with just one complication in 156 consecutive patients. Nevertheless, as we document here, it is necessary to be aware of other types of probable EBUS-TBNA-related complications peculiar to patients with tuberculous lymphadenopathy.

Case Reports

Case 1

A 26-year-old woman presented with mediastinal and hilar lymphadenopathy (Fig. 1A). She had suffered a transient
low-grade fever and persistent nonproductive cough lasting for two months. Chest computed tomography (CT) demonstrated mediastinal and hilar lymphadenopathy (Fig. 1B). Positron-emission tomography with F-18-fluorodeoxyglucose (FDG-PET) showed abnormal accumulation in the lymph nodes, with a standardized uptake value of 3.3 - 5.5. Brain magnetic resonance imaging (MRI) revealed multiple nodular lesions exhibiting high intensity on T2-weighted images and fluid-attenuated inversion recovery (FLAIR) images that increased in number over a period of three weeks. Lung cancer with brain metastases was suspected, and EBUS-TBNA of the hilar and subcarinal lymph nodes was performed. The EBUS images showed round, distinct and heterogeneous subcarinal and hilar lymph nodes without central hilar structures or signs of coagulation necrosis (9 (Fig. 2)).

The vascular image patterns of the lymph nodes were not recorded (10). A dedicated 22-gauge needle was used to perform TBNA. A rapid on-site cytologic evaluation was not available, and the frozen sections suggested caseous necrosis without malignant cells. The smear of the EBUS-guided aspirate was negative for acid-fast bacilli. Polymerase chain reaction (PCR) assays were negative for Mycobacterium tuberculosis and Mycobacterium avium complex (MAC). A subsequent scalene lymph node biopsy revealed tuberculous lymphadenopathy, which was diagnosed histologically and confirmed by a positive culture one month later. Antitubercular chemotherapy with daily isoniazid, rifampicin, pyrazinamide and ethambutol (HRZE therapy) was initiated two days after the EBUS-TBNA procedure. An interferon γ release assay was performed one day before EBUS-TBNA; however, we received the results, which were positive, after the EBUS-TBNA procedure had already been carried out.

Two months after the initiation of antitubercular chemotherapy, chest CT showed intrabronchial polypoid lesions exclusively at the puncture sites (Fig. 3A). A bronchoscopic examination demonstrated intrabronchial polyps with irregular surfaces (Fig. 3B). A transbronchial biopsy revealed granulomas with foreign body macrophages, compatible
with a diagnosis of bronchial tuberculosis (Fig. 4). In order to prevent bronchial stenosis, steroid inhalation was initiated. The initial HRZE therapy was extended for six months due to brain tuberculosis. The patient recovered completely, without stenosis (Fig. 3C). Her intracranial tuberculomas also disappeared. Maintenance chemotherapy was continued with daily isoniazid, rifampicin and ethambutol for an additional four months (10 months in total). A bronchoscopic examination performed 15 months after EBUS-TBNA showed normal bronchial walls with anthracosis, suggesting pigmentation derived from the lymph nodes (Fig. 3D). The sputum remained smear-negative throughout the patient’s clinical course, both before and after EBUS-TBNA. The patient is now well, with no bronchial stenosis 28 months after the EBUS-TBNA procedure.

**Case 2**

A 39-year-old woman with a history of untreated mixed connective tissue disease presented with a fever and intrathoracic lymphadenopathy with small nodules in the right lung field (Fig. 5A-C). She had been taking oral steroids for three weeks for a drug-induced skin rash possibly caused by antibiotics. Repeated microbiological examinations of the sputum, gastric secretions and bronchoscopic alveolar lavage
Figure 5. A: Chest radiograph obtained on admission (Case 2) showing right hilar lymphadenopathy, B: Contrast-enhanced chest CT image showing mediastinal and hilar lymphadenopathy, C: Chest CT image showing right hilar lymphadenopathy and small nodules in the right lung field, D: Chest CT image obtained three weeks later showing an infiltrative shadow and multiple nodules. Although a diagnosis of miliary tuberculosis could not be excluded, repeated microbiological examinations showed negative results, leading to the suspicion of malignant lymphoma associated with pulmonary infection.

fluid did not indicate tuberculosis. FDG-PET showed abnormal accumulation in the cervical, mediastinal, hilar and abdominal lymph nodes and the right lower lung lobe. Possible slight accumulation was recognized in the liver, spleen and bone marrow, suggesting malignant lymphoma. Her serum-soluble interleukin-2 receptor level was elevated to 16,000 U/mL. The interferon γ release assay was not informative due to the patient’s low response to mitogen control. The patient’s fever, which was above 38°C, persisted for three weeks, and chest CT images showed pulmonary nodules and infiltrative shadows increasing in size despite the administration of antibiotic treatment (Fig. 5D). Although a diagnosis of miliary tuberculosis could not be excluded, repeated microbiological examinations consistently yielded negative results, reinforcing the possibility of malignant lymphoma associated with a pulmonary infection. Because large specimens were required for the immunophenotypic and cytogenetic analyses, mediastinoscopy of the paratracheal nodes was performed. At the same time, EBUS-TBNA was performed in the hilar nodes, which were thought to be most informative for diagnosis but not accessible via mediastinoscopy. The EBUS images showed round, distinct and heterogeneous hilar lymph nodes without central hilar structures but with signs of coagulation necrosis (Fig. 6). The EBUS-TBNA aspirate was smear-positive, and PCR assays identified Mycobacterium tuberculosis. The biopsied mediastinal node exhibited caseous necrosis with many acid-fast mycobacteria (Fig. 7).

The patient was isolated, and antitubercular HRZE therapy was initiated the next day. She developed smear-positive bloody sputum immediately after the EBUS-TBNA procedure that persisted for another two days but reverted to smear-negativity three days later. The patient was then transferred to an isolation ward in another hospital for two months of initial HRZE therapy, followed by a seven-month consolidation phase with daily isoniazid and rifampicin administered on an outpatient basis. Although she suffered from bacterial meningitis during the initial HRZE treatment, the patient is now well following the completion of nine months of chemotherapy.
Figure 6. EBUS images (Case 2) showing round, distinct and heterogeneous hilar lymph nodes with signs of coagulation necrosis. TBA performed with a 22-gauge needle revealed smear-positive aspirates, resulting in the development of transient smear-positive bloody sputum over the following three days.

Figure 7. The biopsied mediastinal node (Case 2) showing many acid-fast mycobacteria (Ziehl-Neelsen stain; original magnification ×400).

Discussion

Although an association between EBUS-TBNA and the contiguous endobronchial extension of tuberculous lymphadenitis inflammation is controversial, the possibility for aggravation caused by puncturing the bronchial mucosa remains. Gupta et al. (11) reported a patient with tuberculous lymphadenitis in whom an endobronchial polyp developed following EBUS-TBNA. Consequently, they recommended that the number of lymph node passes should be minimized to prevent excessive puncturing of the bronchial mucosa. Von Bartheld et al. (12) reported the occurrence of multiple mediastinal-esophageal fistulae following transesophageal endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) for mediastinal tuberculous lymphadenitis. Bilacıeroğlu et al. (4) reported that intrabronchial lesions subsequently appeared in 34 of 63 patients with tuberculous lymphadenitis diagnosed on conventional TBNA. Of these cases, fistulae developed in 12 patients in the bronchus, while a further six patients had positive sputum or bronchial aspirate smears and positive cultures. Local complications, such as fistula formation or non-healing wounds at the biopsy site, have long been a concern after surgical approaches for tuberculous lymphadenopathy (13). Geldmacher et al. (14) reported that ulceration and/or fistula or abscess formation occurred in 10% of patients who underwent a biopsy or fine needle aspiration for cervical, mediastinal or axillary tuberculous lymphadenitis.

On the other hand, Steinfort et al. (15) reported an HIV-positive patient who exhibited contiguous endobronchial extension of tuberculous lymphadenitic inflammation before undergoing TBNA. The authors noted that while common in young children in endemic TB regions, this type of presentation is uncommon in adults. In the present Case 1 and the case reported by Gupta et al. (11), endobronchial granulomas developed two months after the initiation of antitubercular therapy. Although the development of endobronchial extensions may be a natural course during the initial enlargement period (14), the possibility for aggravation caused by puncturing the bronchial mucosa remains. Excessive puncturing should therefore be avoided. Whereas Gupta et al. did not mention the actual number of passes, Yasufuku et al. (16) reported that the median number of passes was two (range, one to five) for each site. Nakajima et al. (17) recommended two or three aspirations per lymph node station, if without rapid on-site cytology, and 10 to 15 strokes of the needle over 30 to 60 seconds for each puncture.

The sonographic EBUS features of the lymph nodes in the present cases did not distinguish these nodes from metastatic lymph nodes. Fujiwara et al. (9) classified the different sonographic features of mediastinal lymph nodes and reported that a round shape, distinct margin, heterogeneous echogenicity and signs of coagulation necrosis were independent predictive factors for metastatic lymph nodes, with hazard ratios of 3.1, 3.1, 2.0 and 5.6, respectively. Although the characteristic sonographic EBUS features of tuberculous lymphadenitis have not yet been reported, they are likely to be hard to differentiate from those of metastatic lymph
nodes, in the same way that the CT findings of tuberculous lymphadenitis are sometimes indistinguishable from those of metastatic lymph nodes. Recently, Nakajima et al. (18) reported that capturing the vascular image patterns of lymph nodes using the Power/Color Doppler mode is helpful for identifying metastatic lymph nodes during EBUS-TBNA. Vascular imaging of tuberculous lymph adenopathy may therefore represent an informative tool in the future as a potential method of distinguishing tuberculous from metastatic lymph nodes.

In Case 2, transient smear-positive bloody sputum was observed immediately after EBUS-TBNA but disappeared three days later. Its immediate emergence and rapid disappearance suggest that acid-fast mycobacteria and blood had escaped from the lymph nodes and been aspirated into the peripheral airway for a couple of days. Usually, tuberculous lymph nodes do not contain a large amount of acid-fast mycobacteria, resulting in the low positive rate of microbiological examinations, which has been reported to be approximately 20-30% of positive smears and 40-50% of positive cultures (3-8). The sputum smears were negative throughout the patient’s clinical course in Case 1, both before and after EBUS-TBNA. In Case 2, the patient’s immunocompromised status due to steroid use and diagnostic delay explains the large amount of acid-fast mycobacteria in the lymph nodes. Caution must be exercised to detect immediate transient smear-positive bloody sputum caused by puncturing mycobacteria-rich lymph nodes, especially in severely infected or immunocompromised patients. Temporary isolation until smear-negative sputum results are confirmed is an appropriate option.

Regarding the non-disease specific complications associated with EBUS-TBNA, the rate at which such complications occur has been reported to be only 1.23% among 7,345 cases in Japan, including hemorrhage in 0.68% of cases and mediastinitis in 0.10% of cases (19). Infectious complications sometimes result in severe conditions requiring antibiotic treatment or surgical drainage. It is recommended that puncturing necrotic lymph nodes or cystic areas be avoided due to the high risk for infectious complications. Although the development of infectious mediastinitis after EBUS-TBNA for tuberculous lymphadenitis has not yet been reported, caution should be exercised regarding puncturing lesions of necrotic enlarging tuberculous lymphadenopathy, sometimes with signs of coagulation necrosis.

The indications for performing EBUS-TBNA for probable tuberculous lymphadenopathy should be considered carefully. In the type of cases presented here, obtaining a clinical diagnosis without microbiological confirmation may be considered to be sufficient to initiate antituberculous therapy if the possibility of tuberculous lymphadenopathy is considered. Although diagnosing this disease is challenging due to its nonspecific clinical, radiological and sonographic findings [and in Case 1, the radiological findings of intracranial tuberculosis were also nonspecific and heterogeneous (20, 21)], awareness of these problems may help in managing such difficult clinical decision making.

Although performing EBUS-TBNA is useful in probable tuberculous lymphadenopathy patients in order to exclude malignancy or obtain drug sensitivity results, potential complications peculiar to tuberculosis should be considered, such as progression to bronchial tuberculosis or the development of smear-positive bloody sputum immediately after the procedure. The indications for performing EBUS-TBNA in patients with tuberculous lymphadenopathy should be considered carefully.

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

References


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