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Mediastinitis as a complication of transbronchial lymph node biopsy: a case report

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Abstract: Introduction: Bronchofiberoscopy, particularly when combined with real-time endobronchial ultrasound-guided transbronchial needle aspiration (RT-EBUS–TBNA), is a widely available, long-established, and safe diagnostic modality for respiratory diseases, with particular relevance to the evaluation of primary and secondary lung neoplasms.
The aim of this study is to present a case of purulent mediastinitis as a complication of RT-EBUS–TBNA, which highlights the increased likelihood of infectious complications in patients with additional risk factors such as diabetes mellitus and immunosuppression, in this instance related to chronic systemic corticosteroid therapy. Furthermore, this report reviews the available literature on the incidence of complications, including infectious events, following EBUS-guided transbronchial biopsy.
Conclusions: Complications following EBUS-guided transbronchial biopsy are rare; therefore, the procedure should be regarded as a safe and recommended diagnostic method.

Keywords: EBUS-guided transbronchial biopsy, EBUS bronchoscopy complications, EBUS complications.

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Introduction

Bronchofiberoscopy, particularly when combined with real-time endobronchial ultrasound-guided transbronchial needle aspiration (RT-EBUS–TBNA), is a widely available, long-established, and safe diagnostic modality for respiratory diseases. The use of endobronchial ultrasound enables visualization of proliferative lesions adjacent to the bronchial wall [1] and plays a crucial role in the evaluation of primary and secondary lung neoplasms worldwide [2–4].

Endobronchial ultrasound is also an important modality for diagnosing other causes of lymphadenopathy, including lymphoproliferative disorders and granulomatous diseases such as sarcoidosis and tuberculosis [5–8].

The introduction RT-EBUS–TBNA into standard clinical practice has revolutionized lung cancer staging by significantly reducing the need for more time-consuming and invasive surgical procedures (mainly mediastinoscopy). Moreover, samples obtained through this method facilitate patient selection for targeted advanced oncologic therapies [9, 10].

Due to the high demand, widespread availability, and proven efficacy, the global number of EBUS procedures is rising annually. Consequently, the incidence of procedure-related complications is also increasing [11].

Case presentation

A 69-year-old non-smoking female patient, maintained on long-term 8 mg methylprednisolone for polymyalgia rheumatica, with a history of arterial hypertension, hypothyroidism, and type 2 diabetes, was admitted to the Rheumatology Department of the University Hospital to assess for the presence of a potential neoplastic process.

At admission, the patient denied any respiratory symptoms. She reported frontal headache and postnasal drip. Two months before admission, she had been treated for paranasal sinusitis.

Laboratory tests revealed low inflammatory markers (CRP <0.60 mg/L) with a mildly elevated erythrocyte sedimentation rate (ESR 21 mm/h). Peripheral blood morphology showed leukocytosis with neutrophilia (WBC 12.5 × 10^3/μL, neutrophils 9.3 × 10^3/μL). Mildly elevated creatinine levels were noted (96.5 μmol/L) with an MDRD-estimated GFR of 53 mL/min/1.73 m^2; coagulation parameters were within normal limits.

During hospitalization, a contrast-enhanced chest CT scan was performed and revealed enlarged subcarinal lymph nodes (23 × 40 mm) without any accompanying focal pulmonary lesions (Fig. 1). Subsequent flexible bronchoscopy showed a normal endobronchial tree. Bronchial washings were obtained for cytological, bacteriological, mycological, and BACTEC testing. Culture results revealed growth of *Serratia marcescens* (ESBL-negative), while other findings were within normal limits. An RT-EBUS–TBNA of station 7 lymph nodes yielded a non-diagnostic result (Fig. 2).

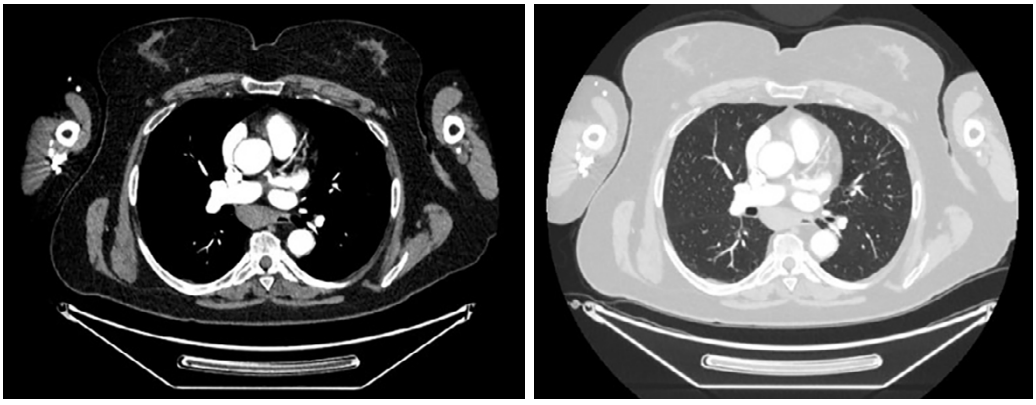

Fig. 1. Enlarged station 7 lymph nodes (before biopsy).

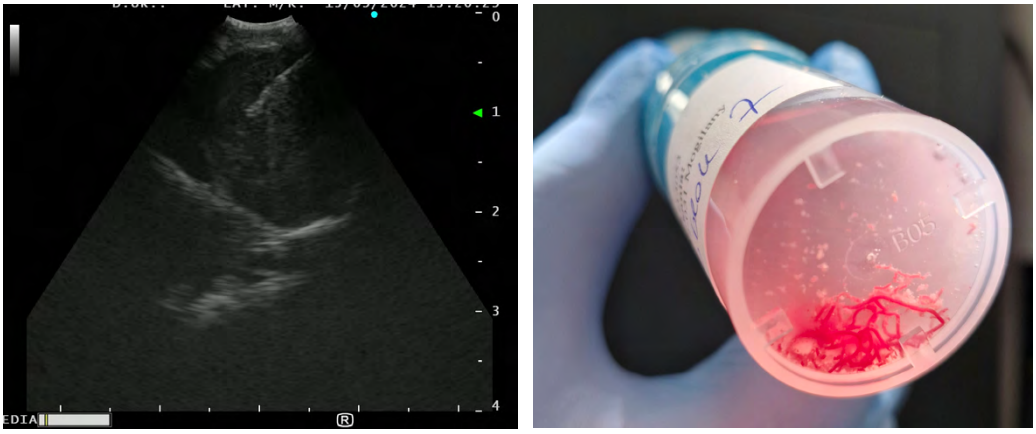

Fig. 2. RT-EBUS-TBNA of a station 7 lymph node (left). Specimen obtained via transbronchial needle aspiration – cell block (right).

Less than three weeks later, the patient presented to her primary care physician with symptoms of persistent dry cough, migratory chest pain of a stabbing nature, general weakness, and increased sweating. The patient denied fever. A chest X-ray performed in the outpatient setting did not reveal any abnormalities. No laboratory tests were conducted. The patient was treated with moxifloxacin for 7 days, with clinical improvement.

Two months after the initial endoscopic examination, due to the previously non-diagnostic lymph node biopsy, the patient was re-admitted to the hospital. Upon admission, her general condition was good. She reported nonspecific chest pain but denied infection-related symptoms such as cough, fever, or dyspnea. Laboratory tests showed mild leukocytosis (similar to previous results), a slightly elevated CRP (7.14 mg/L), and a normal procalcitonin level.

During hospitalization, a repeat fiberoptic bronchoscopy was performed, revealing a widened carina and edematous, hyperemic bronchial mucosa. During RT-EBUS–TBNA of station 7 lymph

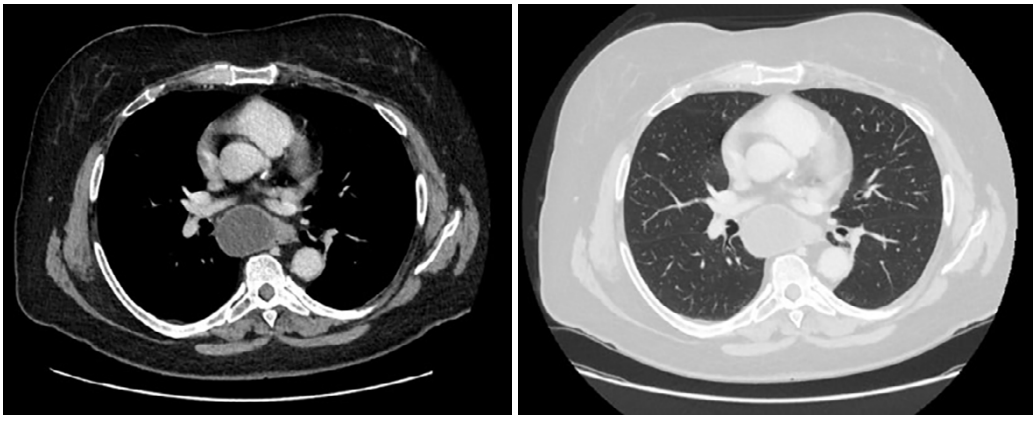

Fig. 3. CT image showing enlarged station 7 lymph nodes with fluid attenuation and features of necrosis (post-biopsy).

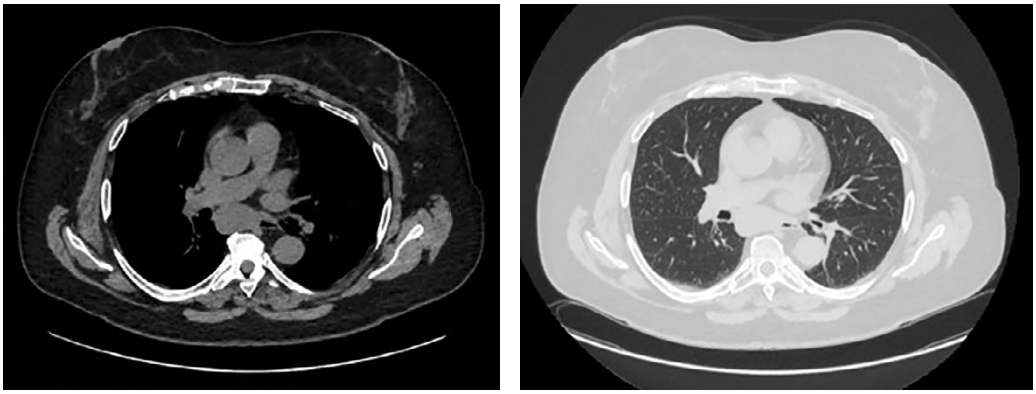

Fig. 4. Follow-up imaging of station 7 lymph nodes after treatment demonstrating partial regression of lesions.

nodes, purulent material was aspirated. Chest CT imaging revealed further enlargement of the subcarinal lymph node conglomerate (now measuring 60 × 41 mm), with a large central fluid component and features of necrosis (Fig. 3).

Due to suspected mediastinitis, broad-spectrum empirical antibiotic therapy was introduced immediately and continued for 10 days during hospitalization. Culture of bronchoscopic specimens yielded only normal respiratory tract flora. Results for tuberculosis and blood cultures were negative. Cytological analysis of the lymph node once again yielded a non-diagnostic result. The patient was evaluated twice by thoracic surgeons, who gave no indications for surgical intervention. Following discharge, the patient received broad-spectrum antibiotic treatment in the outpatient setting for approximately 2 months.

As a result of the administered treatment, all symptoms were fully resolved. The patient remains under radiological surveillance, which shows gradual regression of mediastinal lymphadenopathy (reduction in size and resolution of necrosis, Fig. 4).

Discussion

Ultrasound-guided mediastinal biopsy, whether performed via the transbronchial or transesophageal approach, provides diagnostic accuracy comparable to that of mediastinoscopy. However, endoscopic techniques are significantly less invasive, resulting in a markedly lower complication rate [12].

The EBUS–TBNA procedure is considered a safe and effective diagnostic modality, recommended by the European Respiratory Society (ERS), though not without potential risks [13]. These include infections of the respiratory tract and mediastinum, bleeding, pneumothorax or pneumomediastinum, and respiratory failure [14]. Infectious complications are more frequently observed in patients with comorbidities, particularly diabetes mellitus [14, 15].

Fever is the most common and generally benign adverse symptom following bronchoscopy with transbronchial lymph node biopsy. According to Moon *et al.*, who retrospectively studied a cohort of over 6,000 patients undergoing EBUS-guided mediastinal biopsy, post-procedural fever occurred in 10% cases. It was more common in patients who underwent more than four lymph node punctures, those who had multiple endoscopic procedures (e.g., bronchial washings,

endobronchial and transbronchial biopsies), and in patients with diagnosed tuberculosis. Further risk factors included older age, low hemoglobin levels, and elevated pre-procedural CRP. The authors suggest that fever may result from transient bacteremia caused by contamination of endoscopic instruments with oropharyngeal flora [16].

An alternative theory was proposed by Minami *et al.*, who compared the post-procedural outcomes in intubated and non-intubated patients before EBUS–TBNA. In both groups, biopsy needles were washed and analyzed for microbial cultures. Positive needle wash cultures were observed in only 3.3% of intubated patients. In contrast, in non-intubated ones, they were found in 100% patients, despite both groups showing the same incidence of post-procedural fever (10%). The authors suggested that the fever may result from a non-infectious inflammatory response [17]. This observation was further supported by Kim *et al.*, who studied two groups of patients, one of which performed pre-procedural oral antiseptic rinses. No differences were observed between the groups in terms of fever incidence, infectious complications, or positive bronchoscopic cultures [18].

Kim *et al.*'s study of nearly 700 EBUS–TBNA patients reported fever within the first 24 hours in 20% of cases. However, only three patients developed more serious complications: two cases of pneumonia and one case of mediastinal abscess. All patients who developed mediastinitis had a pre-existing diagnosis of diabetes mellitus. No other patient-related or procedural factors were associated with increased risk of infection beyond diabetes [19].

We further reviewed other multicenter studies, which revealed an incidence of no more than 0.5% (from 0.19% to 0.48%) of infectious complications, comprising mediastinal infections, pneumonia, or mediastinal cyst infection. The presence of necrotic areas within the target lesions revealed on chest CT, as well as the use of transesophageal biopsy (EUS, EUS-B), were associated with a higher risk of infection.

Other studies identified immunosuppression and the presence of cavitation or low-dose attenuation within target lesions on CT scans as independent risk factors for infectious complications [20–22].

There are also reports suggesting a higher risk of complications during transesophageal mediastinal biopsy in patients with sarcoidosis, in whom ultrasound imaging shows edematous, inhomogeneous, hyperechoic lesions in the biopsy area. In such cases, a transbronchial approach or antibiotic prophylaxis should be considered as a first-line strategy [23].

However, it cannot be denied that the combined use of EBUS and EUS-B is a recommended and safe diagnostic approach [20, 24].

A highly possible mechanism of infection following mediastinal biopsy is contamination of the instruments by oral and esophageal bacteria or bronchial secretions. The bronchoscope's working channel becomes contaminated during insertion or aspiration, and the needle may be contaminated during its passage through the channel [25].

Other authors suggest that bacteremia may result from mucosal injury caused by the endoscope, allowing oropharyngeal flora to enter the bloodstream. Studies show that contamination of instruments with saprophytic flora is common (up to 35% of cases) [26]. However, infectious complications following mediastinal biopsy remain rare, affecting no more than 1% of patients. Moreover, in all reported cases, patients responded well to antibiotic therapy, with favorable prognoses.

The evidence from both retrospective and prospective studies supports the conclusion that ultrasound-guided mediastinal biopsy is a safe procedure with a very low rate of infectious complications. Most authors do not recommend routine prophylactic antibiotic use. However, the question remains whether biochemical or imaging markers could help identify a subgroup of

increased-risk patients who might benefit from prophylaxis or early therapeutic intervention. Some researchers suggest an early assessment of biomarkers such as procalcitonin (PCT), interleukin-6 (IL-6), and CRP.

Procalcitonin levels rise within 4–12 hours in bacterial infections and may be useful in diagnosis, as well as in monitoring the efficacy and duration of antibiotic therapy [27]. In contrast, the role of C-reactive protein in detecting inflammatory processes, including sepsis, may appear questionable due to its delayed production and low specificity. It, however, remains a good indicator of response to antibiotic therapy [28]. Interleukin-6 levels, which may rise as early as two hours after tissue injury and inflammation, appear to be a promising prognostic biomarker.

Conclusions

Although EBUS–TBNA is generally considered a safe procedure, complications may occur. The presented case of purulent mediastinitis following RT-EBUS–TBNA highlights the increased risk of infectious sequelae in patients with additional risk factors, such as diabetes and immunosuppression, in this case resulting from systemic corticosteroid therapy. Our observation aligns with findings from previous studies. It is crucial to emphasize that immunocompromised states are not contraindications to the use of RT-EBUS–TBNA, which remains an effective and valuable diagnostic tool. However, patients in the risk group require careful monitoring, and antibiotic prophylaxis may be considered in selected cases.

Attention should also be paid to the technical aspects of EBUS, particularly in avoiding contamination of the channel with respiratory flora.

Conflict of interest

None declared.

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