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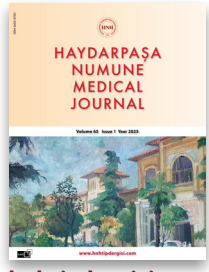

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ORIGINAL ARTICLE

Diagnostic Use of Endobronchial Ultrasound (EBUS) Guided Transbronchial Needle Aspiration (TBNA) in Intrathoracic Tuberculosis

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Abstract

Introduction: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is widely used for sampling mediastinal and intraparenchymal lymph nodes. This study aims to determine the diagnostic sensitivity of EBUS-TBNA in tuberculosis (TB) diagnosis and to establish the optimal number of punctures required for accurate sampling.

Methods: Patients who underwent EBUS-TBNA as the initial diagnostic procedure between August 2020 and October 2023 in the pulmonology clinic were retrospectively evaluated. The study included patients with pathological findings of granulomatous lymphadenitis and a confirmed TB diagnosis. Biopsy materials were analyzed for acid-fast bacilli (AFB), mycobacterial culture, PCR results, and pathology reports.

Results: Among 595 patients who underwent EBUS-TBNA as their initial diagnostic procedure, 101 (16.9%) were diagnosed with TB. Of these, 72 patients (71.28%) were diagnosed directly via EBUS-TBNA, whereas additional bronchoscopic procedures were required for 29 patients (28.72%). The mean size of the sampled lymph nodes was 1.9±0.4 cm, with an average of 5.46 aspirations performed per lymph node. The prevalence of TB among patients who underwent EBUS-TBNA was 16.9%, and the sensitivity of EBUS-TBNA in diagnosing TB was 71.28%.

Discussion and Conclusion: EBUS-TBNA is a safe and effective method for diagnosing intrathoracic tuberculous lymphadenitis. An average of five punctures per lymph node provided an optimal sample size for microbiological evaluation, thereby enhancing diagnostic performance.

Keywords: Diagnosis; endobronchial ultrasound; tuberculosis.

The definitive diagnosis of tuberculosis (TB) is traditionally achieved by detecting *Mycobacterium tuberculosis* in sputum through culture or molecular methods (e.g., PCR). However, obtaining sputum samples from the suspected patient population is not always feasible, often necessitating the use of bronchoscopic techniques. In the literature, approximately 25% of patients have negative acid-fast bacilli (AFB) evaluations in sputum, and 60% are unable to produce sputum samples[1].

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has become the preferred initial diagnostic method for evaluating intrathoracic lymphadenopathies. Owing to its minimally invasive nature, EBUS-TBNA has largely replaced more invasive diagnostic and sampling methods, such as mediastinoscopy. While it is commonly used for the diagnosis and staging of lung cancer, it is also a valuable tool in the differential diagnosis of granulomatous lymphadenitis. The cytopathological

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findings of granulomatous reactions are not exclusively indicative of TB, as other microorganisms may also cause granulomas. However, the presence of caseating granulomas, as opposed to noncaseating granulomas, is more specific for TB, provided that no other microorganisms are identified[2].

The causes of granulomatous lymphadenitis include infections (e.g., bacteria, TB, nontuberculous mycobacteria, viruses, fungi, and parasites), malignancies (e.g., Hodgkin's disease, non-Hodgkin's lymphoma, Langerhans cell histiocytosis, seminoma, and dysgerminoma), autoimmune diseases (e.g., granulomatosis with polyangiitis, Churg-Strauss syndrome, Crohn's disease, and adult-onset Still's disease), and idiopathic diseases (e.g., sarcoidosis and Kikuchi-Fujimoto disease)[3]. Among the benign causes, TB and sarcoidosis are more commonly observed in Türkiye[4].

Multiple factors influence the sensitivity of EBUS-TBNA, including the cytomorphological characteristics of granulomas (presence of caseating necrosis) and the detection of *Mycobacterium tuberculosis* (MTB) through culture or molecular methods. The reported culture positivity rate for intrathoracic TB lymphadenitis samples obtained via EBUS-TBNA ranges from 20% to 63%, which may be attributed to a low bacterial load within the lymph nodes, suboptimal sampling, or inadequate culture techniques[4,5].

Additionally, various polymerase chain reaction (PCR) tests have been developed for the rapid detection of MTB. These tests can identify target gene mutations, predict drug resistance patterns, and aid in guiding initial treatment strategies. Owing to their high specificity, TB-PCR can reliably diagnose cases that are culture negative and lack granulomatous findings[1,6].

Despite these advancements, data on the sensitivity of EBUS-TBNA in the diagnosis of TB lymphadenitis remain limited. Moreover, the literature lacks definitive guidance on the optimal number of biopsies required via EBUS-TBNA for suspected tuberculosis lymphadenitis.

Materials and Methods

Study Design and Settings

The study was conducted in the pulmonary disease clinic of a tertiary research and training hospital. The study design was planned as a retrospective cross-sectional analysis. (Local Ethics Committee Approval: 5.12.2024, 19/24). This study was performed in line with the principles of the Declaration of Helsinki.

Study Population

Patients aged 18–85 years who underwent EBUS-TBNA as the initial diagnostic procedure between 2020 and 2023 in our hospital's pulmonary disease clinic and had a final diagnosis of TB were included. Patients were excluded if they had pathological findings of metastasis, reactive lymphadenitis, nondiagnostic pathology or nonnecrotizing granulomatous lymphadenitis diagnosed as sarcoidosis through additional tests; incomplete medical records; or necrotizing granulomatous lymphadenitis without culture, AFB, or PCR evaluation (Fig. 1).

Data Collection

Patient files, bronchoscopy reports, pathology results, and microbiology laboratory results (mycobacterial culture, AFB, PCR), as well as thoracic computed tomography (CT) and PET-CT findings, were reviewed. For patients with a final diagnosis of TB, clinical characteristics (age, sex, comorbidities, smoking history), bronchoscopic techniques used, diagnostic methods (cytopathological, molecular, microbiological), sampled lymph node station and size, and the number of biopsies were recorded.

Definitions

EBUS-TBNA was performed in the presence of enlarged intrathoracic lymph nodes (≥1 enlarged mediastinal or hilar lymphadenopathy with a short axis ≥1 cm), intrapulmonary parenchymal lesions adjacent to the tracheobronchial wall detected on thoracic CT, or PET-CT-positive intrathoracic lymph nodes/lesions (defined by a standardized uptake value of >2.5 SUVmax) within the probe's reach. Lymph node classification was based on the international staging system[7]. On-site cytological evaluation was not performed. Informed consent forms were routinely obtained from all patients prior to EBUS-TBNA.

Standard evaluations included mycobacterial culture, AFB staining, and TB-PCR. Patients were considered to have TB lymphadenitis if they met one of the following criteria: positive mycobacterial culture or AFB staining;

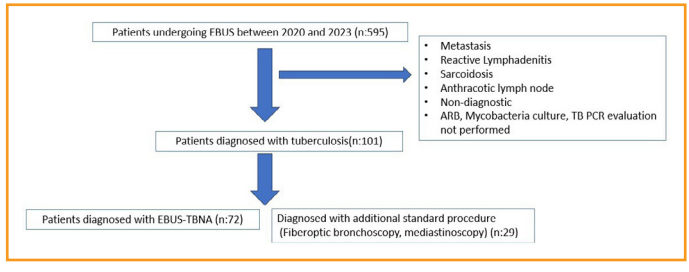

Figure 1. Flow Chart.

positive TB-PCR in the absence of culture or AFB positivity; or histopathological findings of necrotizing granulomatous inflammation, provided that other causes of the granulomatous reaction were excluded and that the clinical and radiological findings were consistent. Patients whose diagnosis remained unclear after EBUS-TBNA and without accompanying parenchymal lesions underwent mediastinoscopy with lymph node excision for TB lymphadenitis diagnosis. For patients with accompanying intraparenchymal lesions, endobronchial biopsy (EBB) via fiberoptic bronchoscopy and microbiological evaluations (mycobacterial culture, AFB staining, TB-PCR) were conducted to confirm TB.

All EBUS-TBNA procedures in our clinic were performed orally. Local anesthesia (lidocaine) and general anesthesia (midazolam) were used. A convex probe (CP) EBUS (Fujifilm-EB530US) was employed, and a 22-gauge cytology needle (NA201SX-4022; Olympus) was utilized. The samples were preserved in formalin and processed as cell blocks for histological examination. The needle contents were fixed on slides with 95% alcohol via a 20 mL syringe. Finally, the needle was flushed with 1 mL of sterile saline, and the samples were sent to the microbiology laboratory for Gram staining, AFB staining, mycobacterial culture, and TB-PCR. Microbiological specimens were analyzed microscopically via Ziehl–Neelsen staining.

Statistical Analysis

Descriptive statistics were used to evaluate the data in this study. Continuous variables were expressed as mean±standard deviation and minimum-maximum values, while categorical variables were presented as frequency (n) and percentage (%). The mean and standard deviation were calculated for lymph node size, age, and the number of samples obtained through EBUS. The distribution of diagnostic methods was reported as percentages.

Results

Among 595 patients who underwent EBUS-TBNA, 101 were diagnosed with tuberculosis (TB). The mean age of the TB-diagnosed patients was 67 years (range: 21–89), and 77.2% were male. Among the 101 patients with TB, 72 (71.28%) were diagnosed directly via EBUS-TBNA, whereas 29 patients (28.72%) required additional bronchoscopic interventions. The most frequently sampled lymph node via EBUS-TBNA was the subcarinal lymph node. The mean size of the sampled lymph nodes was 1.9±0.4 cm, and an average of five aspirations (5.46) were performed per lymph node (Table 1).

Among the patients diagnosed with TB via EBUS-TBNA, 53 (52.47%) were cytopathologically identified as having necrotizing granulomatous lymphadenitis. Additionally, 24 patients were TB-PCR positive, 6 patients were diagnosed through positive mycobacterial culture, and 4 patients were diagnosed via AFB positivity. Among the 29 patients for whom a definitive diagnosis could not be established via EBUS-TBNA, 23 underwent fiberoptic bronchoscopy and 6 underwent mediastinoscopy. Among the 23 patients who underwent bronchoscopy, 6 were diagnosed through endobronchial biopsy (EBB), 10 through AFB positivity in bronchial lavage, 16 through PCR positivity in bronchial lavage, and 10 through mycobacterial culture positivity in bronchial lavage. The prevalence of TB among the 595 patients who underwent EBUS-TBNA was 16.9%, and the sensitivity of EBUS-TBNA for TB diagnosis was calculated to be 71.28% (Table 1).

Table 1. Characteristics of the lymph nodes and results of additional interventional techniques

Variables	n=101
Gender (Male)	78 (77.2)
Age (mean)	67 (21-89)
Size of the sampled lymph node (cm- mean)	1.9±0.4
Sampled lymph node station, n (%)	
4R*	33 (26.6)
4 L*	7 (5.64)
7*	50 (40.3)
10R-L*	21 (16.9)
11R-L*	13 (10.4)
Total aspiration counts for each EBUS, n (%)	n=72
4	27 (37.5)
5	24 (33.3)
6	8 (11.1)
≥7	13 (18)
EBUS diagnostic method, n (%)	
Cytopathologic diagnosis	53 (73.6)
Mycobacterium Tuberculosis culture	6 (8.3)
AFB	4 (5.5)
Tuberculosis PCR	24 (33.3)
Diagnosis with additional mediastinoscopy	6 (5.9)
Diagnostic method with additional standard bronchoscopy, n (%)	n=23
EBB-cytopathological diagnosis	6 (26.0)
Bronchial lavage-AFB	10 (43.4)
Bronchial lavage-PCR	16 (69.5)
Bronchial lavage -Mycobacterium Tuberculosis culture	10 (43.4)

4R: Right paratracheal lymph node; 4L: Left paratracheal lymph node; 7: Subcarinal lymph node; 10R: Right hilar lymph node; 10L: Left hilar lymph node; acid-fast bacilli; EBUS: Endobronchial Ultrasound; AFB: Acid-Fast Bacilli; PCR: Polymerase Chain Reaction; EBB: Endobronchial Bioosy.

Discussion

To maintain the diagnostic value of EBUS-TBNA at an optimal level, performing at least three aspirations per lymph node and one additional aspiration for molecular testing is recommended[8]. While the literature suggests the use of additional samples for microbiological molecular analyses in patients with suspected granulomatous lymphadenopathy,[8] there is no clear consensus on the optimal number of aspirations. On the basis of the results of our limited patient population, EBUS-TBNA should be performed with at least five aspirations in patients with mediastinal lymphadenopathy suspected of TB.

Pathological and bacteriological evidence is considered the standard for diagnosing intrathoracic TB. Surgical approaches, such as mediastinoscopy and thoracoscopy, offer the highest diagnostic success rates but are more invasive and costly[9]. Less invasive techniques include endoscopic ultrasound-guided fine needle aspiration (EUS-FNA), conventional TBNA, and EBUS-TBNA. While the sensitivity of EUS-FNA for diagnosing TB has been reported to be 90%, it is limited in sampling common TB sites such as right paratracheal and hilar lymph nodes[10]. Conventional TBNA is used in the diagnosis of TB lymphadenitis (TBLA), but its use is limited because of its blind biopsy nature[5]. The combination of EBUS-TBNA with standard bronchoscopic techniques has been reported to be safe and significantly enhances diagnostic yield in patients with suspected pulmonary TB and lymphadenopathy[11]. In our study, a notable population (~30%) that could not be diagnosed with EBUS alone was successfully diagnosed via standard bronchoscopic techniques, highlighting the complementary diagnostic impact of combining these methods.

The sensitivity of EBUS-TBNA for TB diagnosis is reported to range between 74% and 85% in the literature, and our study similarly reported a sensitivity of 71.28%[12]. A retrospective study evaluating TBLA diagnosis reported a diagnostic yield of 64.6% for EBUS-TBNA,[11] whereas a prospective study on patients with intrathoracic TB reported a sensitivity of 85%[13]. Consistent with the literature, our study confirms that EBUS-TBNA is a safe and effective method for diagnosing TB[14].

Our study had several limitations due to its retrospective design. Patients with incomplete medical records and those with cytological findings of necrotizing caseating granuloma but without microbiological evaluation data were excluded. Another limitation was the lack of a universally accepted gold standard beyond culture and AFB staining, leading to debates on attributing TB in cases without positive cultures. Considering recent studies on the reliability of TB-PCR,[14-16] PCR positivity was deemed significant for TB diagnosis in our study.

Conclusion

In conclusion, EBUS-TBNA has high diagnostic sensitivity for investigating intrathoracic TB through aspiration of intrathoracic lymph nodes and pulmonary lesions adjacent to the tracheobronchial wall. The number of biopsy samples should be increased to improve the accuracy of microbiological and molecular tests.

Ethics Committee Approval: The study was approved by Antalya Training and Research Hospital Medical Research Scientific Ethics Committee (No: 19/24, Date: 05.12.2024).

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Conflict of Interest: The authors declare that there is no conflict of interest.

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