

THE VALUE OF ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION FOR THE DIAGNOSIS OF PULMONARY SARCOIDOSIS REAL-LIFE SETTINGS

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ABSTRACT. *Background:* Endobronchial ultrasonography-assist transbronchial needle aspiration is a minimally invasive technique which is used to hilar and mediastinal lymphadenopathy. The purpose of this study was to investigate the value of EBUS-TBNA diagnosis of sarcoidosis. *Methods:* The study included 42 patients who underwent EBUS-TBNA because of a suspicion of sarcoidosis (stage I and II) on pulmonary radiography and thorax tomography. A total of 104 lymph node stations were sampled from 42 patients. *Results:* A diagnosis of sarcoidosis was made histologically in 38 of the 42 patients from whom lymph node sampling was performed with EBUS-TBNA. *Conclusion:* EBUS-TBNA is a successful method in the histopathologic diagnosis of grade I and grade II sarcoidosis. Therefore, EBUS-TBNA should be considered first in the diagnosis of stage I and stage II sarcoidosis.

KEY WORDS: sarcoidosis, EBUS, EBUS-TBNA, real-life settings, diagnosis, endobronchial ultrasound, value

INTRODUCTION

Sarcoidosis disease is a systemic inflammatory disease of unknown etiology that is seen worldwide and affects people of every age and race (1). Sarcoidosis develops in a clinical spectrum varying from an asymptomatic condition to advanced or recurrent conditions (2). The diagnosis of sarcoidosis is established on the basis of pathological evidence of non-calcified granuloma in the absence of other infectious causes, and clinical findings and radiological images supporting the diagnosis by discounting other reasons such as malignancy and tuberculosis (3). Although non-calcified granuloma can be seen in any organ system at varying rates, it occurs most

often in the lungs, and thoracic lymphadenopathy is determined in up to 85% of cases (4). Pulmonary sarcoidosis is one of the most common forms of sarcoidosis, and bronchoscopy is recommended with tissue sampling as the step in obtaining a tissue diagnosis and other potential diagnoses. Endobronchial ultrasonography-assisted transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive procedure that is used for diagnostic purposes (5). The diagnostic value of EBUS-TBNA can show differences in diseases other than lung cancer. In previous studies, the diagnostic success rates of EBUS-TBNA in mediastinal and hilar lymph nodes may vary according to the study methodology, the level of specialization of the center, and the methods used in the selection of patients for EBUS (6). Diagnostic success in prospective studies with strict protocols may differ from real-life studies. The first studies confirming the success of EBUS came from a small group of authors in specialized centers, the majority of whom were interventional pulmonologists. These studies reported high diagnostic sensitivity (85%-92%) of EBUS-TBNA in sarcoidosis diagnosis (7-9).

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The purpose of this study was to evaluate the usefulness of EBUS-TBNA in the diagnosis of sarcoidosis in real-life settings.

METHODS

This retrospective study included 42 patients who underwent EBUS-TBNA because of clinical and radiological suspicion of Stage I and Stage II lung sarcoidosis in Afyonkarahisar Health Sciences University Medical Faculty Hospital between January 2020 and June 2024. Lymph nodes stations were determined with reference to the lymph node map recommended by the International Lung Cancer Society (10). All the patients underwent EBUS-TBNA. The study protocol was approved by the Ethics Committee Directorate of Afyonkarahisar Health Sciences University (2011-KAEK-2/2023/12).

EBUS-TBNA procedure

The EBUS-TBNA procedure is carried out under local anesthesia with mild conscious sedation. Patients underwent the procedure after fasting for at least 4 h. Topical anesthesia was achieved using xylocaine (maximum 8 mg/kg). Sedation was achieved by either deep sedation with propofol or mild sedation with low-dose midazolam with or without opioids. Endobronchial ultrasonography was performed with a fiberoptic ultrasound bronchoscope (CP-EBUS; BF-UC 180F-Olympus Medical Systems, Tokyo, Japan) and dedicated 22-gauge needles. The EUS-B-FNA procedure was not performed. Other sampling techniques that could be used concomitantly (endobronchial biopsy, transbronchial biopsy, and bronchoalveolar lavage) were not applied. After fixation of the histology samples in 10% buffered formalin and staining with hematoxylin and eosin, the aspirated materials were sent to the laboratory for histopathological examination, as there was no facility for rapid cytopathological examination on-site. Any patients who were diagnosed with benign lymphadenopathy using EBUS-TBNA were then followed up clinically and radiologically for at least 6 months.

Statistical analysis

Diagnostic success was calculated for each patient. Diagnostic accuracy and sensitivity were

calculated for each patient using standard formulae. Data analyses were performed using IBM SPSS software. Results were stated as mean \pm standard deviation values or number(n) and percentage(%).

RESULTS

The data were evaluated for 42 patients who underwent EBUS-TBNA because of suspected sarcoidosis. The patient group comprised 29 females and 13 males with a mean age of 49.16 years (range, 20-77 years). Over half of the patients were non-smokers (n=24, 57%). The lung function tests were determined to be normal in the majority of the patients (n=32, 76%), obstructive in 7, and restrictive in 3. The demographic and clinical characteristics of the patients are shown in Table 1.

A total of 104 lymph nodes were sampled from the 42 patients. Localization of the enlarged lymph nodes was determined to be 64 (61.5%) in the mediastinum, and the remaining 40 were hilar and interlobe. The most frequently sampled region was the subcarinal lymph node (station 7) (38/104, 36.5%). Sampling was made of a mean of 2.4 lymph nodes (min-max, 1-5) per patient. The short axis diameter of the lymph nodes was measured as a mean of 16 mm (min-max, 10-32 mm). Non-calcified granulomas were determined in 79 (75.96%) of the total 104 lymph nodes, in 38 (90%) of the 42 patients. The features of the sampled lymph nodes are summarized in Table 2. The diagnostic success of EBUS-TBNA

Table 1. Demographic and Clinical Characteristics of the Cases (n=42)

	n (%) or mean \pm SD
Age (mean years)	49.16
Male	29
Female	13
RFT	
Normal	32 (76%)
Obstructive	7
Restrictive	3
Smoking Status	
Never	24 (57%)
Current	11
Former	7

Abbreviation: RFT: respiratory function test

Table 2. Characteristics of Lymph Nodes Sampled with EBUS-TBNA (n:104)

Sampled lymph node area	n (%)
2R	1(0,9)
4R	18(17)
4L	7(6)
7	38(36)
10R	15(14)
11R	16(15)
11L	9(8)

was determined to be 90% for non-caseating granulomas. In the microbiological results performed on pathology samples, acid-fast bacilli positivity on Ziehl-Neelsen staining and/or microbiological culture positivity were not found. Four patients whose EBUS-TBNA samples were negative for sarcoidosis were followed clinically and radiologically for a median of 10 months (6-12 months). No procedure-related adverse events were recorded.

DISCUSSION

The study results confirmed that EBUS-TBNA sampling of mediastinal and hilar lymph nodes in patients with suspected sarcoidosis had high diagnostic value in the determination of non-calcified granuloma. The success rate of EBUS-TBNA for Stage I and Stage II sarcoidosis was determined to be 90% in this study. For the pathological diagnosis of sarcoidosis disease, it is recommended that tissue samples are taken from the most easily accessible organ using the least invasive method (11). Lung sarcoidosis is the most frequently seen form of sarcoidosis. In previous studies, the diagnostic value of bronchoscopic transbronchial lung biopsy (TBLB) taken to confirm the histological diagnosis has been reported to be 40%-90% (12-14). In a study by Hong et al., the diagnostic success of TBLB was found to be 33% in Grade I sarcoidosis patients and 36% in Grade II (4). Pneumothorax and pulmonary hemorrhage may be seen after transbronchial biopsy. It was reported in a previous study that pneumothorax and pulmonary hemorrhage are seen in 5% of patients after TBLB (15). Although a biopsy taken from bronchial mucosa with a normal bronchoscopic appearance can provide additional benefit in patients with suspected sarcoidosis, the diagnostic success is low. Cho et al.

determined 8% success of endobronchial biopsy in being able to show granulomatous disease (16). Tsunada et al. evaluated 46 patients and reported success in showing granulomatous disease with endobronchial biopsy at the rate of 24% (17). Bronchoalveolar lavage (BAL) fluid analysis can also be performed to determine sarcoidosis. In 90% of sarcoidosis patients, an increase in lymphocyte count can be determined in BAL fluid, and the CD4/CD8 ratio can also be examined in BAL fluid. However, it has low sensitivity, as a CD4/CD8 ratio ≥ 3.5 can be determined in 55% (53-59%) (18). The main drawback of BAL fluid is that a pathological diagnosis cannot be provided. Sarcoidosis is most often seen as mediastinal or hilar lymphadenopathy. EBUS-TBNA has emerged as a minimally invasive procedure for the evaluation of mediastinal lymphadenopathy. In a study by Jiang et al., the success rate of EBUS-TBNA in 62 patients with suspected sarcoidosis was determined to be 93% (19). Wong et al. evaluated 65 patients with suspected sarcoidosis mediastinal lymphadenopathy and determined the EBUS-TBNA success rate of 92% (7). In another study of 37 patients, Cho et al. reported 92% diagnostic success of EBUS-TBNA (16). The results of the current study showed the diagnostic success of EBUS-TBNA to be 90%. In the study conducted by Dhooria et al., in which 150 patients were evaluated, no significant difference was found in the sensitivity of diagnostics with the 19G needle and the 22G needle (respectively 75.0% vs. 69.6%) (20). In our study, a 22g needle was used during the EBUS procedure in all cases. Therefore, affected sarcoid lymph nodes can be sampled from both the esophagus and the airways. Endoscopic ultrasound (with bronchoscope)-guided fine needle aspiration (EUS-B-FNA) is an introduced procedure consisting of a transesophageal needle aspiration using an ultrasound bronchoscope. It allows for performing both transbronchial and transesophageal needle sampling with the same instrument, in the same session, and by one operator (21). Crombach et al. have compared endobronchial (EBUS-TBNA) and transoesophageal EUS-B-fine-needle aspiration (FNA) approaches for indications such as undiagnosed mediastinal lymphadenopathy (22). In this study, the granuloma detection rate of mediastinal/hilar nodes by endosonography in patients with suspected sarcoidosis stage I/II is high and similar for EBUS and EUS-B-FNA. In the Mondoni et al. review, they emphasized when

clinical conditions would discourage the transbronchial route. EUS-B-FNA should be considered the technique of choice. In our study, EUS-B-FNA was not applied to the patients (21). Oki et al. investigated how many passes are needed for endobronchial ultrasound-guided transbronchial needle aspiration for sarcoidosis in a prospective multicenter study (23). In this study, they recommend, if rapid on-site cytological evaluation is not available, at least 4 passes per patient for either single or multiple lesions with EBUS-TBNA for pathological diagnosis of stage I/II sarcoidosis. Since our study was retrospective, these data could not be obtained and not be evaluated from this perspective.

Limitations of this study could be said to be the retrospective, single-center design, with the inclusion of a relatively low number of patients, and this could have caused potential selection bias.

In conclusion, the results of this study demonstrated that EBUS-TBNA was an extremely successful method in the diagnosis of Stage I and Stage II sarcoidosis. Therefore, EBUS-TBNA should be kept in mind in the histopathological diagnosis of Stage I and Stage II sarcoidosis.

Conflict of Interest: Each author declares that he has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement, etc.) that might pose a conflict of interest in connection with the submitted article.

REFERENCES

- Spagnolo P, Rossi G, Trisolini R, Sverzellati N, Baughman RP, Wells AU. Pulmonary sarcoidosis. *Lancet Respir Med*. 2018;6(5):389-402.
- Baughman RP, Wells A. Advanced sarcoidosis. *Curr Opin Pulm Med*. 2019;25(5):497-504.
- Spagnolo P, Bernardinello N. Sarcoidosis. *Immunol Allergy Clin North Am*. 2023;43(2):259-72.
- Hong G, Lee KJ, Jeon K, et al. Usefulness of endobronchial ultrasound-guided transbronchial needle aspiration for diagnosis of sarcoidosis. *Yonsei Med J*. 2013;54(6):1416-21.
- Eckardt J, Olsen K, Jørgensen O. Minimally invasive diagnosis of sarcoidosis by EBUS when conventional diagnosis fail. *Sarcoidosis Vasc Diffuse Lung Dis*. 2010;27(1):43-8.
- Murthi M, Donna E, Arias S, et al. Diagnostic accuracy of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in real life. *Front Med (Lausanne)*. 2020;7:118.
- Wong M, Yasufuku K, Nakajima T, et al. Endobronchial ultrasound: new insight for the diagnosis of sarcoidosis. *Eur Respir J*. 2007;29:1182-6.
- Garwood S, Judson MA, Silvestri G, Hoda R, Fraig M, Doelken P. Endobronchial ultrasound for the diagnosis of pulmonary sarcoidosis. *Chest*. 2007;132:1298-1300.
- Oki M, Saka H, Kitagawa C, Tanaka S, et al. Real-time endobronchial ultrasound-guided transbronchial needle aspiration is useful for diagnosing sarcoidosis. *Respirology*. 2007;12:863-8.
- Rusch VW, Asamura H, Watanabe H, et al. The IASLC lung cancer staging project: a proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2009;4:568-77.
- Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. *N Engl J Med*. 2007;357:2153-65.
- Gilman MJ, Wang KP. Transbronchial lung biopsy in sarcoidosis. An approach to determine the optimal number of biopsies. *Am Rev Respir Dis*. 1980;122:721-4.
- Koonitz CH, Joyner LR, Nelson RA. Transbronchial lung biopsy via the fiberoptic bronchoscope in sarcoidosis. *Ann Intern Med*. 1976;85:64-6.
- de Boer S, Milne DG, Zeng I, Wilsher ML. Does CT scanning predict the likelihood of a positive transbronchial biopsy in sarcoidosis? *Thorax*. 2009;64:436-9.
- Bilaçeroğlu S, Perim K, Günel O, Çağırıcı U, Büyüksirin M. Combining transbronchial aspiration with endobronchial and transbronchial biopsy in sarcoidosis. *Monaldi Arch Chest Dis*. 1999;54:217-23.
- Cho R, Pandey V, Wong J, Keenan J, et al. The role for endobronchial biopsy in the era of endobronchial ultrasound guided transbronchial needle aspiration for the diagnosis of sarcoidosis: a single center experience: Role for EBUS in the diagnosis of sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis*. 2024;41(2):e2024029.
- Tsunoda T, Oyama Y. Utility of additional endobronchial biopsy for the diagnosis of sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis*. 2024;42(2).
- Tanrıverdi H, Uygur F, Örnek T, et al. Comparison of the diagnostic value of different lymphocyte subpopulations in bronchoalveolar lavage fluid in patients with biopsy proven sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis*. 2016;32(4):305-12.
- Li K, Jiang S. A randomized controlled study of conventional TBNA versus EBUS-TBNA for diagnosis of suspected stage I and II sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis*. 2014;31(3):211-8.
- Dhooria S, Sehgal IS, Prasad KT, et al. Diagnostic yield and safety of the 19-gauge versus 22-gauge endobronchial ultrasound-guided transbronchial needle aspiration needle in subjects with sarcoidosis (GUESS). *Respiration*. 2024;103(6):336-43.
- Mondoni M, D'Adda A, Terraneo S, et al. Choose the best route: ultrasound-guided transbronchial and transesophageal needle aspiration with echobronchoscope in the diagnosis of mediastinal and pulmonary lesions. *Minerva Med*. 2015;106(5 Suppl 1):13-9.
- Crombag LMM, Mooij-Kalverda K, Szlubowski A, et al. EBUS versus EUS-B for diagnosing sarcoidosis: the International Sarcoidosis Assessment (ISA) randomized clinical trial. *Respirology*. 2022;27(2):152-60.
- Oki M, Saka H, Ando M, et al. How many passes are needed for endobronchial ultrasound-guided transbronchial needle aspiration for sarcoidosis? A prospective multicenter study. *Respiration*. 2018;95(4):251-7.