Original Article

Access this article online

Quick Response Code:

Website: www.eurasianjpulmonol.com

DOI: 10.4103/ejop.ejop_5_18

Does anthracosis reported in endobronchial ultrasound-guided transbronchial needle aspiration exclude metastasis?

Serhat Erol, Ceyda Anar[1], Onur Fevzi Erer[1], Zekiye Aydogdu[2], Serir Aktogu[1]

Abstract:

OBJECTIVES: In some studies, it has been hypothesized that anthracotic pigmentation in mediastinal lymph nodes is a sign of benign conditions and excludes metastasis from thoracic and extrathoracic malignancies. The aim of this study was to evaluate the clinical significance of mediastinal lymph node anthracosis in cancer patients who underwent endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA).

MATERIALS AND METHODS: In this study, medical data of patients with lung cancer or extrathoracic cancer who underwent EBUS-TBNA for investigation of mediastinal lymph node metastasis were evaluated retrospectively. EBUS-TBNA cytology reported as anthracotic pigmentation was included in this study. Patients were excluded from the study if cytology of aspirated lymph nodes reported as "benign," "malignancy," or "granulomatous inflammation."

RESULTS: There were 50 eligible patients. Thirty-one (62%) patients underwent EBUS-TBNA for lung cancer staging and 19 (38%) for evaluation of extrathoracic metastasis. A total of 120 lymph nodes were sampled. The most sampled station was subcarinal. EBUS-TBNA was false negative in eight of 31 (25.8%) lung cancer patients and one of 19 (5.2%) extrathoracic malignancy patients.

CONCLUSIONS: Anthracotic pigmentation of lymph nodes in EBUS-TBNA cannot exclude metastasis in lung cancer patients and mediastinoscopy should be performed before surgery in this group. In patients with extrathoracic malignancy, anthracotic pigmentation is associated with benign conditions. However, further investigation with larger cohort is needed.

Keywords:

Anthracosis, endobronchial ultrasound-guided, interventional pulmonology, thoracic cancer

Introduction

Mediastinal lymph node metastasis is one of the most important determinants of treatment decision and prognosis in patients with pulmonary or extrathoracic malignancies (ETM). There may be other benign reasons such as tuberculosis (TB) or sarcoidosis for Mediastinal lymphadenopathy (MLA) in cancer patients.[1,2] Anthracosis which is one of these benign conditions can also cause false-positive positron emission computed tomography (PET/CT) mimicking malignancy.[3-6]

In cancer patients with MLA, it is mandatory to obtain lymph node samples before treatment decision. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has become standard diagnostic procedures in cases with MLA. It has been hypothesized that in nonsmall cell lung cancer patients, anthracotic particles in lymph nodes can prevent lymph nodes from metastasis.[7]

Department of Pulmonary Diseases, Ankara University, Ankara, Departments of [1]Pulmonary Diseases and [2]Pathology, Dr. Suat Seren Chest Diseases and Thoracic Surgery Teaching and Research Hospital, Izmir, Turkey

Address for correspondence:
Dr. Serhat Erol, Ankara University, Cebeci Hospital Pulmonary Diseases Department, Mamak, Ankara, 06112 Turkey.
E-mail: drserol@yahoo.com

How to cite this article: Erol S, Anar C, Erer OF, Aydogdu Z, Aktogu S. Does anthracosis reported in endobronchial ultrasound-guided transbronchial needle aspiration exclude metastasis?. Eurasian J Pulmonol 2018;20:12-6.

The aim of this study was to evaluate the clinical significance of mediastinal lymph node anthracosis in cancer patients who underwent EBUS-TBNA.

Materials and Methods

Study population

We retrospectively analyzed the medical data of patients with known lung cancer or ETM who underwent EBUS-TBNA for lung cancer staging or diagnosis of mediastinal metastasis of ETM. Patients with positive confirmation by mediastinoscopy or with at least 1-year follow-up after EBUS-TBNA were enrolled in this study.

All procedures were in accordance with the ethical standards of the institutional committee and with the 1964 Helsinki Declaration. Informed consent was obtained from all patients.

The work was approved by the Institutional Review Board.

Inclusion and exclusion criteria

Patients were included in the study if cytology of aspirated lymph nodes reported as anthracosis and excluded from the study if reported as "benign," "malignancy," or "granulomatous inflammation."

Definitions of false negative and true negative

EBUS-TBNA was accepted as "false negative" if mediastinoscopic pathology of lymph nodes was reported as malignancy or lymph node diameter on CT or metabolic activity on PET/CT increased during follow-up.

If mediastinoscopy confirmed anthracosis or during follow-up, CT or PET/CT did not reveal lymph nodes enlargement or increased metabolic activity EBUS-TBNA accepted as "true negative."

Endobronchial ultrasound-guided transbronchial needle aspiration procedure

All EBUS-TBNA procedures were performed by the same bronchoscopist. The EBUS-TBNA procedure was performed by an convex probe EBUS-guided TBNA bronchoscope (7.5 MHz, BF-UC160F; Olympus Optical Co, Tokyo, Japan) under conscious sedation. Vital signs patients were monitored during the procedure. Each target nodal station was punctured at least twice, and one or more tissue core specimens were obtained. The cytology specimens were smeared onto slides and air dried and stained and also cell blocks were prepared for every patient.

For the cell blocks, aspirated material was ejected into saline solution, embedded in paraffin, and thin sections were obtained.

The rapid on-site evaluation was not available at our institution.

Final diagnosis

LN accepted as 'malignancy' if microscopic examination revealed malignant cells, and as 'granulomatous inflammation' if granulomas have been demonstrated. If the microscopic examination of LN aspiration specimens revealed anthracotic pigments, the LN was accepted as anthracotic lymphadenitis. LN accepted as 'reactive adenitis' if microscopic examination showed none of the malignant cells, granulomatous inflammation or anthracotic pigmentation.

Results

A total of 191 patients – 125 for lung cancer stating and 66 for the diagnosis of ETM metastasis - underwent EBUS-TBNA. Of these, 50 patients were included according to the criteria explained above. There were 35 male and 15 female patients aged between 36 and 83. Forty-eight patients had PET/CT and standard uptake value (SUV) of lymph nodes were between 2 and 18. The characteristics of patients are shown in Table 1.

Thirty-one (62%) patients underwent EBUS-TBNA for lung cancer staging and 19 (38%) for the evaluation for mediastinal metastasis of ETM. A total of 120 lymph nodes with diameters between 8 mm and 34 mm were sampled. The most sampled stations were subcarinal[7]

Table 1: Clinical features of patients and number of sampled lymph nodes

	n (%)
Gender	
Male	35 (70)
Female	15 (30)
Patient groups	
Lung cancer	31 (62)
ETM metastasis	19 (38)
Number of sampled lymph nodes stations	
2	23 (46)
3	13 (26)
1	7 (14)
4	6 (12)
5	1 (2)
Lymph node stations	
7	41 (82)
4R	26 (52)
11R	19 (38)
11L	15 (30)
4L	14 (28)
2R	4 (8)
10L	1 (2)

ETM: Extrathoracic malignancy, 7: Subcarinal, 4R: Right lower paratracheal, 11R: Right interlobar, 11L: Left interlobar, 4L: Left lower paratracheal, 2R: Right upper paratracheal, 10L: Left hilar

and the right lower paratracheal (4R) lymph nodes. In nearly half of the patients, two lymph node stations were sampled [Table 1].

Of 31 lung cancer patients, 23 underwent mediastinoscopy for confirmation and eight had radiological follow-up. Lymph node metastasis was shown with mediastinoscopy in 6 (19.3%) patients. In two (6.5%) patients, lymph node diameters were increased during radiological follow-up [Table 2]. As a result, EBUS-TBNA was false negative in 8 of 31 (25.8%) lung cancer patients.

Eight of 19 ETM patients underwent mediastinoscopy for confirmation and all of them were negative for lymph node metastasis. The remaining 11 patients were radiologically followed up, and in one patient, progression of mediastinal lymph node enlargement was reported [Table 2]. EBUS-TBNA was false negative in 1 of 19 (5.2%) ETM [Figure 1].

As a result, EBUS-TBNA reported as anthracosis was false negative in 25.8% of lung cancer and 5.2% of EMT patients.

Discussion

In this retrospective study, we evaluated the clinical implication of anthracotic pigmentation reported in EBUS-TBNA. Anthracosis is black pigmentation which is not only caused by coal dust but also other occupational and environmental exposures such as air pollution, biomass fuels used for cooking, smoking, and previous TB.[8,9] Lymph node anthracosis can cause mediastinal lymph node enlargement on CT and can be false-positive mimicking lung cancer.[3-7] Possible explanation for false-positive PET/CT is increased cellular activity and ongoing inflammation.[9,10]

Table 2: Results of endobronchial ultrasound-guided transbronchial needle aspiration and follow-up according to groups

	EBUS-TBNA	
	True negative	False negative
Lung cancer staging group		
Radiological follow-up	6	2
Mediastinoscopy	17	6
ETM group		
Radiological follow-up	10	1
Mediastinoscopy	8	0

EBUS-TBNA: Endobronchial ultrasound-guided transbronchial needle aspiration, ETM: Extrathoracic malignancy

Kirchner *et al*.[4] and Yilmaz Demirci *et al*.[6] reported lymph node anthracosis diagnosed with EBUS. Both studies included patients with known pulmonary and extrapulmonary malignancies. All of these anthracotic lymph nodes were confirmed as benign with mediastinoscopy or radiological follow-up.

Park *et al*.[7] reported that only 4.9% of lymph nodes were malignant with mediastinoscopy in operable nonsmall cell lung cancer patients with microscopic anthracotic pigment in EBUS-TBNA specimens. They concluded that the accumulation of anthracotic particles could impair trapping malignant cells in lymph nodes.

In our study, anthracosis was not associated with benign conditions in lung cancer staging group. False-negative results in this group were higher contrary to the previous studies.[4,6,7] This might be due to number of sampled lymph node stations, number of passes for each lymph nodes or as Park *et al*.[7] mentioned, sampling of only PET/CT positive lymph nodes may be the reason for high false-negative results.

The European Society of Thoracic Surgeons (ESTS) guidelines recommend preoperative surgical staging in case of a negative endosonography because probability of having mediastinal nodal involvement for any individual patient with a negative endosonography result is 13%–15%.[11] Furthermore, meta-analysis revealed that mediastinoscopy has fewer false negatives.[12] For lung cancer staging, anthracosis does not exclude metastasis

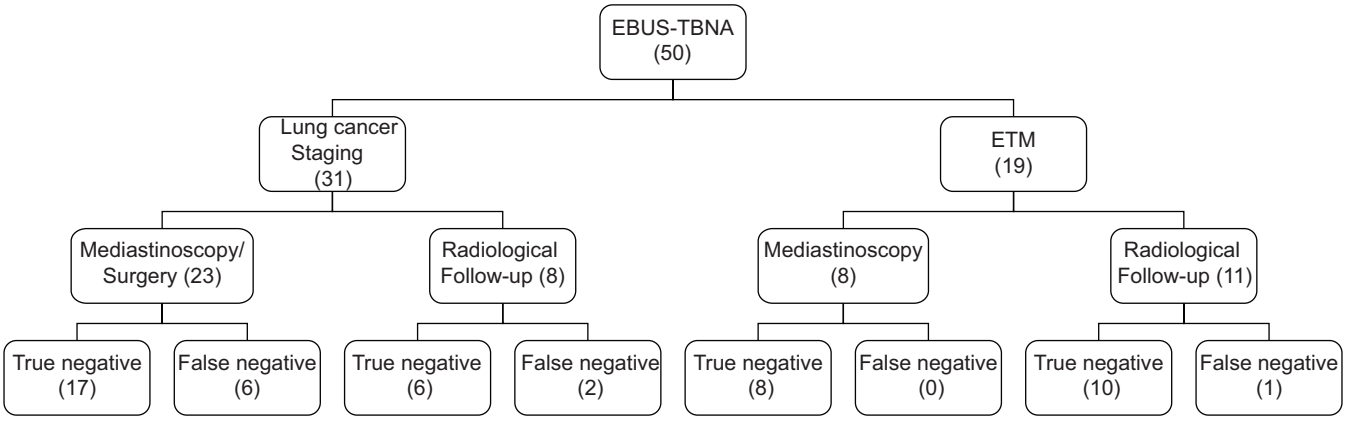

Figure 1: Diagnostic workup and follow-up results. EBUS-TBNA: Endobronchial ultrasound-guided transbronchial needle aspiration, ETM: Extrathoracic malignancy

and mediastinoscopy should be performed as ESTS recommended in cases with negative EBUS-TBNA.

In our study, we found false-negative rate as 5.2% in ETM group which was less than lung cancer group. The previous studies revealed the high specificity and sensitivity of EBUS-TBNA in detection of mediastinal lymph node metastasis of ETM.[2] In this group of patients, nearly half of the patients had benign conditions that cause mediastinal lymph node enlargement. Moreover, anthracosis is one of the frequently seen benign conditions. Although false-negative results can be seen with anthracosis, it is rare.[13-16] Thus, we think that it may be more appropriate to have occupational and environmental exposure history, CT images, and smoking history of the patient before further invasive diagnostic procedures in patients with ETM. Radiological follow-up may be more appropriate instead of surgical procedures in this group of patients.

CT findings can be used to differentiate enlarged anthracotic lymph nodes from malignant lymph node enlargement. Kirchner *et al*. found that the most common site of anthracotic lymph nodes was the subcarinal area.[17] In the same study, they reported that malignant lymph nodes had a higher frequency of ill-defined contours, nodal necrosis, and anthracotic lymph nodes showed calcification more often. Granulomatous inflammation shown to be a sign of benign conditions in patients with ETM.[18] Moreover, anthracosis may also be accepted as a sign of benign conditions in this group of patients.

In low- and middle-income countries, industrialization and related air pollution and exposure to indoor biomass fuel smoke, especially homemakers while cooking, cause higher incidence of anthracosis.[19] Furthermore, association between anthracosis and TB was shown in many studies.[20-25] Anthracosis also can cause pulmonary mass and mediastinal lymphadenopathy and false-positive PET results and may be erroneously diagnosed as lung cancer and/or lymph node metastasis.[3-10,23,26] Therefore, in patients with or without known malignancy, mediastinal lymphadenopathy with high SUV may be due to anthracosis, metastasis, MTLA, or coincidence of these conditions. Thus, clinicians have to make a proper differential diagnosis and rule out possible conditions with patient history, cytology, and microbiological examination.

Our study has some limitations. First, it is a retrospective study with a limited number of patients. Second, EBUS-TBNA was not confirmed with mediastinoscopy in all patients.

Conclusions

Anthracosis of lymph nodes in EBUS-TBNA cannot exclude metastasis in lung cancer patients and mediastinoscopy should be performed before surgery. In patients with extrathoracic malignancy, anthracotic pigmentation in EBUS-TBNA specimens is associated with benign conditions. However, larger confirmation studies are needed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Fernández-Bussy S, Labarca G, Canals S, Caviedes I, Folch E, Majid A, *et al*. Diagnostic yield of endobronchial ultrasound-guided transbronchial needle aspiration for mediastinal staging in lung cancer. J Bras Pneumol 2015;41:219-24.
2. Yang B, Li F, Shi W, Liu H, Sun S, Zhang G, *et al*. Endobronchial ultrasound-guided transbronchial needle biopsy for the diagnosis of intrathoracic lymph node metastases from extrathoracic malignancies: A meta-analysis and systematic review. Respirology 2014;19:834-41.
3. Mirsadraee M, Farshchi H. Endobronchial ultrasound in anthracosis. J Bronchology Interv Pulmonol 2010;17:188-9.
4. Kirchner J, Mueller P, Broll M, Kirchner EM, Pomjanski N, Liermann D, *et al*. Chest CT findings in EBUS-TBNA-proven anthracosis in enlarged mediastinal lymph nodes. Rofo 2014;186:1122-6.
5. Hewitt RJ, Wright C, Adeboyeku D, Ornadel D, Berry M, Wickremasinghe M, *et al*. Primary nodal anthracosis identified by EBUS-TBNA as a cause of FDG PET/CT positive mediastinal lymphadenopathy. Respir Med Case Rep 2013;10:48-52.
6. Yilmaz Demirci N, Alici IO, Yilmaz A, Demirağ F, Tatci E, Erdoğan Y, *et al*. Risk factors and maximum standardized uptake values within lymph nodes of anthracosis diagnosed by endobronchial ultrasound-guided transbronchial needle aspiration. Turk J Med Sci 2015;45:984-90.
7. Park YS, Lee J, Pang JC, Chung DH, Lee SM, Yim JJ, *et al*. Clinical implication of microscopic anthracotic pigment in mediastinal staging of non-small cell lung cancer by endobronchial ultrasound-guided transbronchial needle aspiration. J Korean Med Sci 2013;28:550-4.
8. Mirsadraee M. Anthracosis of the lungs: Etiology, clinical manifestations and diagnosis: A review. Tanaffos 2014;13:1-3.
9. Gupta A, Shah A. Bronchial anthracofibrosis: An emerging pulmonary disease due to biomass fuel exposure. Int J Tuberc Lung Dis 2011;15:602-12.
10. Onitilo AA, Engel JM, Tanimu SB, Nguyen TC. Anthracosis and large mediastinal mass in a patient with healed pulmonary tuberculosis. Clin Med Res 2010;8:99-103.
11. De Leyn P, Dooms C, Kuzdzal J, Lardinois D, Passlick B, Rami-Porta R, *et al*. Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. Eur J Cardiothorac Surg 2014;45:787-98.
12. Ge X, Guan W, Han F, Guo X, Jin Z. Comparison of endobronchial ultrasound-guided fine needle aspiration and video-assisted mediastinoscopy for mediastinal staging of lung cancer. Lung 2015;193:757-66.
13. Ozgül MA, Cetinkaya E, Tutar N, Ozgül G, Onaran H, Bilaceroglu S, *et al*. Endobronchial ultrasound-guided transbronchial needle aspiration for the diagnosis of intrathoracic lymphadenopathy in patients with extrathoracic malignancy: A study in a tuberculosis-endemic country. J Cancer Res Ther 2013;9:416-21.
14. Parmaksız ET, Caglayan B, Salepci B, Comert SS, Kiral N,

Fidan A, *et al.* The utility of endobronchial ultrasound-guided transbronchial needle aspiration in mediastinal or hilar lymph node evaluation in extrathoracic malignancy: Benign or malignant? Ann Thorac Med 2012;7:210-4.
15. Erer OF, Anar C, Erol S, Özkan S. The utility of EBUS-TBNA in mediastinal or hilar lymph node evaluation in extrapulmonary malignancy. Turk J Med Sci 2016;46:112-9.
16. Tertemiz KC, Alpaydin AO, Karacam V. The role of endobronchial ultrasonography for mediastinal lymphadenopathy in cases with extrathoracic malignancy. Surg Endosc 2017;31:2829-36.
17. Kirchner J, Broll M, Müller P, Pomjanski N, Biesterfeld S, Liermann D, *et al.* CT differentiation of enlarged mediastinal lymph node due to anthracosis from metastatic lymphadenopathy: A comparative study proven by endobronchial US-guided transbronchial needle aspiration. Diagn Interv Radiol 2015;21:128-33.
18. Bellinger CR, Sharma D, Ruiz J, Parks G, Dotson T, Haponik EF, *et al.* Negative predictive value of granulomas on EBUS-TBNA in suspected extrathoracic malignancy. Lung 2016;194:387-91.
19. Heidarnazhad H. Anthracosis in Iran, un-answered questions. Arch Iran Med 2012;15:124-7.
20. Mirsadraee M, Saffari A, Sarafraz Yazdi M, Meshkat M. Frequency of tuberculosis in anthracosis of the lung: A systematic review. Arch Iran Med 2013;16:661-4.
21. Bircan HA, Bircan S, Oztürk O, Ozyurt S, Sahin U, Akkaya A, *et al.* Mediastinal tuberculous lymphadenitis with anthracosis as a cause of vocal cord paralysis. Tuberk Toraks 2007;55:409-13.
22. Samet M, Ayatollahi J, Aboutorabi A, Rahimian M, Shahcheraghi SH, Mirjalili SA, *et al.* Comparison of samples obtained from bronchoscopy of patients with and without bronchial anthracosis for investigating the prevalence of mycobacterium tuberculosis. Germs 2015;5:78-82.
23. Pazoki M, Moazami Goodarzi H, Hashemi Taheri A, Seifirad S, Nematollahi N, Paknejad O, *et al.* Prevalence of tuberculosis in patients with anthracosis: Study on 150 subjects. Arch Iran Med 2012;15:128-30.
24. Mirsadraee M, Asna-Ashari A, Attaran D, Naghibi S, Mirsadraee S. Bronchial anthracosis: A new diagnosis for benign mass lesions of the lung. Tanaffos 2013;12:10-8.
25. Kunal S, Shah A. The concomitant occurrence of pulmonary tuberculosis with bronchial anthracofibrosis. Indian J Tuberc 2017;64:5-9.
26. Kim MA, Lee JC, Choi C. False-positive FDG-PET and bronchial anthracofibrosis. J Thorac Oncol 2012;7:1474.