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Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration in the Diagnosis of Mediastinal Lymphnode Metastases from Extrathoracic Malignancies

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Abstract

Introduction: Mediastinal Lymphadenopathy (LAP) in patients with an extra thoracic malignancy is an important clinical condition that needs to be resolved. Endobronchial Ultrasound-Guided Needle Aspiration (EBUS-TBNA) is a minimally invasive procedure that can be used for diagnosing mediastinal LAP. The diagnostic utility of EBUS-TBNA in determining the nature of intra thoracic LAP in patients with extra thoracic malignancy was evaluated.

Material and Method: In present study, 38 consecutive patients' extra thoracic malignancy and mediastinal LAP according to computed tomography or fluorine 18-labelled deoxyglucose positron emission tomography who underwent EBUS-TBNA between January 1st, 2018, and December 1st, 2018, were retrospectively analyzed.

Results: EBUS was performed in 38 patients with extra thoracic malignancy with suspected mediastinal Lymphnode (LN) metastasis. EBUS-TBNA biopsy was achieved only in 26 patients (68.5%) but it failed in totally 12 patients (31.5%). Mediastinal LN metastases were detected in 30.8% of 26 patients who achieved biopsy. Granuloma was detected in 11.5% of patients. Most frequent LN metastasis was revealed in larynx cancer (66.7%).

Conclusion: Mediastinal lymphnode metastasis was proved highest rate in larynx cancer by EBUS-TBNA. Biopsy failure is still important problem in EBUS performed in patients with extra thoracic malignancy with suspected mediastinal LN metastasis.

Keywords: Endobronchial ultrasound; Mediastinal lymphnode; Extra thoracic malignancies

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Introduction

Mediastinal Lymphadenopathy (LAP) is a common finding in patients with extra thoracic malignancies. Mediastinal Lymphnode (LN) metastases may significantly change treatment and prognosis when they are discovered at the time of initial staging. If mediastinal LAP is discovered after treatment and pathological evaluation is needed to exclude or confirm disease recurrence.

Before the advent of Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration (EBUS-TBNA), sampling of intrathoracic LAP was most commonly performed by mediastinoscopy or Endoscopic Ultrasound-Guided fine Needle Aspiration (EUS-FNA). However, mediastinoscopy is associated with a 1% complication rate [1] and requirement for general anesthesia, whereas EUS-FNA does not allow access to the right paratracheal and hilar LN [2]. EBUS-TBNA allows sampling of paratracheal, subcarinal, and hilar LAP under sedation in the outpatient setting. The technique has an established role in the diagnosis and staging of lung cancer with a sensitivity of more than 90%, even early in the learning process [3]. Limited data, however, exist on the role of EBUS-TBNA in the diagnosis of extra thoracic malignancies [4].

In present study, we describe the diagnostic utility of EBUS-TBNA in determining the nature of intra thoracic LAP in patients with extra thoracic malignancy.

Material and Methods

In this study, 38 consecutive patients with an active or previous diagnosis of extra thoracic malignancy and a suspected mediastinal metastasis according to Computed Tomography (CT) (short axis >1 cm) or Fluorine 18-Labelled Deoxyglucose Positron Emission Tomography (F-18 FDG PET) who underwent EBUS-TBNA between January 1st, 2018, and December 1st, 2018, were

Table 1: Cancer types with suspected mediastinal lymph node metastasis.

Cancer Type	n (%)
Breast	11 (29)
Larynx	8 (21.1)
GIS	6 (15.8)
Over & Endometrial	5 (13.1)
Skin	2 (5.2)
Tyroid	2 (5.2)
Prostat	2 (5.2)
Renal Cell	1 (2.6)
Myelodysplastic Syndrome	1 (2.6)
Total	38

retrospectively analyzed.

EBUS-TBNA was performed under mild sedation with intravenous midazolam alone. Vascular structures were avoided using the Doppler function; the LN was aspirated using either a 21-gaugeneedle. Samples were expelled both onto glass slides where air-dried smears were made for cytology and also into liquid fixative suitable for cell block preparations.

Results

EBUS was performed in 38 patients with extra thoracic malignancy with suspected mediastinal LN metastasis. Of 38 patients 19 (50%) was males, 19 was females. The median age at diagnosis was 64, 8 years (ages ranged 44 to 80). These malignities were breast, larynx, Gastrointestinal System (GIS), over & endometrium, skin, tyroid, prostate, renal cell, myelodysplastic syndrome. Breast (29%), larynx (21.1%), GIS (15.8%) and over & endometrium (13.1%) malignities were the most frequently sent tumors to be done EBUS-TBNA procedure (Table 1). Interestingly all 8 patients with larynx cancer and all 6 patients with GIS malignities were males.

EBUS-TBNA biopsy was achieved only in 26 patients (68.5%) of 38 patients but it failed in totally 12 patients (31.5%) (Table 1). It failed in 8 patients (21%) because size of LNs were too small to get biopsy (<5 mm) (Table 2). And also it failed in 4 patients (10.5%) in whom there were LNs larger than 5 mm but patients could not adapt to the EBUS procedure or LN were so near the vessels that biopsy procedure could not be achieved (Table 2).

Mediastinal LN metastases were detected in 8 (30.8%) of 26 patients who achieved biopsy.

In this study, cancer types according to the incidence of LN metastasis proven by EBUS-TBNA biopsy were as larynx, skin, prostate, breast, 4 (66.7%), 1 (50%), 1 (50%), 2 (33.3%), in descending order (Table 3). Granuloma was detected in 3 patients (11.5%).

Discussion

Although mediastinoscopy and open thoracic surgery are standard methods for mediastinal lymphnode staging, they are invasive and costly. Endoscopic ultrasound-guided fine needle aspiration is less invasive but is limited in terms of access to some nodes and the amount of tissue that can be sampled [5-7]. Endobronchial ultrasound-guided needle aspiration and biopsy is a minimally invasive procedure that can be used for diagnosing mediastinal lymphadenopathy [8].

In this study high rate (31.5%) of EBUS biopsy failure was found.

Table 2: Rate of failed EBUS-TBNA biopsy.

Cancer Type	**Failed Biopsy** LAP <0.5 mm	LAP >0.5 mm	Total
Breast	2 (18%)	3 (27.2%)	5
Larynx	2 (25%)	-	2
GIS	2 (33.3%)	1 (16.7%)	3
Over & Endometrial	2 (40%)	-	2
Skin	-	-	-
Tyroid	-	-	-
Prostate	-	-	-
Renal Cell	-	-	-
Myelodysplastic Syndrome	-	-	-
Total	8 (21%)	4 (10.5%)	12 (31.5%)

Table 3: Nature of lymphadenopathy according to the cancer types.

Cancer Type	Metastasis	Bening	Granuloma	Total
Breast	2 (33.3%)	3 (50%)	1 (16.7%)	6
Larynx	4 (66.7%)	2 (33.3%)	-	6
GIS	-	3 (100%)	-	3
Over & Endometrial	-	2 (66.7%)	1 (33.3%)	3
Skin	1 (50%)	1 (50%)	-	2
Tyroid	-	1 (50%)	1 (50%)	2
Prostate	1 (50%)	1 (50%)	-	2
Renal Cell	-	1 (100%)	-	1
Myelodysplastic Syndrome	-	1 (100%)	-	1
Total	8 (30.8%)	15 (57.7%)	3 (11.5%)	26

Most important reason for failure of biopsy was presence of too small LNs to get biopsy (<5 mm) (21%) although those LNs were found 1 cm or more in size on Thorax CT or PET-CT. This result suggests that radiologists should evaluate radiological findings more carefully to avoid unnecessary interference. We think that difficulty in adapting to procedure was related with mild sedation. Proximity of lymphnodes to the vessels were the other reason for failure of biopsy. We think that experiences of physicians performing biopsy was also important factor in success of it.

In present study mediastinal LN metastases were detected in about one third of patients with extra thoracic malignancies (30.8%). This ratio was 57.6% in a study by Park et al. [9] and 43.6% in a study by Sanz-Santos et al. [10], 31.2% in a study by Parmaksız et al. [11] and 30.7% in a study by Mehta et al. [12]. Most frequent LN metastasis proven by EBUS-TBNA biopsy was revealed in larynx cancer (66.7%) (Table 3). The incidence of LN metastasis in breast cancer was only 33.3%. Although the number of cases were low, lymphnode metastasis could not be proved in GIS, over & endometrial renal cell, thyroid cancers, and, myelodysplastic syndrome.

Granuloma was detected in 11.5% of patients. This was 3.4% in study by Sanz-Santos et al. [10], 20.8% in a study by Parmaksız et al. [11] (12.5% tuberculosis, 3.3% sarcoidosis), 46.1% in a study by Mehta et al. [12], 9% in a study by Navani et al. [13] (all of them was sarcoidosis). The statement that the presence of granulomas may reliably exclude malignancy is questionable. The coexistence of granulomas and malignant cells in metastatic lymphnodes has been described [14]. So some authors recommend further investigation when granulomas only are observed in EBUS-TBNA and the

suspicion of malignancy remains [13].

In conclusion, lymphnode metastasis was proved highest rate in larynx cancer by EBUS-TBNA. Biopsy failure is still important problem in EBUS performed in patients with extra thoracic malignancy with suspected mediastinal LN metastasis. What to do when granulation is detected is controversial.

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