Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of paraesophageal lung tumors – diagnostic yield and added value

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Abstract

Aims: There are few data on the use of endoscopic ultrasound (EUS) for the biopsy of suspected malignant lesions of the lung. The main objective of this study was to evaluate the performance of transesophageal EUS fine needle aspiration (EUS-FNA) for the diagnosis of paraesophageal lung tumors and also for the confirmation of metastatic sites of lung cancer during the same procedure. **Material and methods**: We performed a retrospective study in a tertiary care unit including 19 patients with paraesophageal lung tumors referred to our department for a lung biopsy. Transesophageal EUS-FNA was performed using a linear echoendoscope and 22G needles. **Results:** In all 19 patients with suspected lung tumors the confirmation of the malignant disease was achieved. Pathological examination revealed 16 cases of non-small cell lung cancers, 2 small cell lung cancers and one case of lung metastases. Diagnostic yield of lung EUS-FNA was 1, with no post-procedural complications. In 7 cases, we performed also biopsies of suspected metastasis and all biopsies revealed the same histopathological type as the primary tumor. **Conclusions**: Our study supports the use of this minimally invasive technique for paraesophageally located lung tumors and demonstrates that EUS-FNA is safe and has an excellent diagnostic yield.

Keywords: endoscopic ultrasound-fine needle aspiration (EUS-FNA); lung; cancer; biopsy

Introduction

Lung cancer represents an important health problem worldwide, causing the most frequent malignancy related death [1]. Diagnosis of lung cancer is frequently suggested by radiological techniques, especially computed tomography (CT), but a personalized management needs precise pathological diagnosis. This can be obtained through tissue biopsy via either transluminal, percutaneous or surgical approach. When tumors are in contact or near to the major airways, endobronchial ultrasound (EBUS) can provide a histological diagnosis. For centrally located lung tumors, without endobronchial abnormalities or in close relation to the airways, endobronchial techniques are rarely efficient and fail to establish the diagnosis [2].

Centrally located lung tumors can be biopsied under CT guidance, but the sensitivity is lower than for

the peripheral tumors and the complication rate is much higher than for endoscopic ultrasound (EUS) fine needle aspiration (EUS-FNA) [3-5]. The pneumothorax incidence after CT guided biopsy was reported to be 9-54% [3,6,7]. The small diameter of the paramediastinal lung tumors (less than 2 cm) also decreases the sensitivity of CT guided biopsy [8]. These issues brought EUS to the forefront, in order to provide a minimally invasive diagnosis in these cases. The procedure is indicated when the lung tumor has a close relation with the esophagus or suspicious mediastinal lymph nodes can be visualized and punctured through a transesophageal approach [4,9,10].

The importance of EUS for mediastinal lymph nodes evaluation and lung cancer staging is recognized and supported by European guidelines [4]. But the literature concerning the transesophageal biopsy of the lung cancer is still sparse, and in many medical centers this procedure is not performed [11,12]. There are very few studies including patients with previous non-diagnostic bronchoscopy that underwent EUS-FNA addressed to paraesophageal lung tumors [9,10] and few lung EUS-FNA studies included patients having either a negative bronchoscopy or a negative CT-guided biopsy [13-16]. A recent study supports the added value of EUS-FNA after a non-diagnostic bronchoscopy, showing an increase of the diagnostic yield from 51 to 91% [17].

Another issue concerning the added value of EUS-FNA in lung cancer staging is the possibility to procure samples also from extra thoracic suspected metastatic lesions - from the liver, adrenal glands, retroperitoneal lymph nodes etc [18,19].

We conducted this study in order to assess the sensitivity and diagnostic yield of EUS-FNA in paraesophageal lung tumors in patients with negative bronchoscopy and to evaluate the feasibility of the method to confirm the metastatic sites of the lung cancer at the same session.

Material and methods

Study design and patients

This was a monocentric retrospective study of the chart files, undertaken at the Emergency County Clinical Hospital Cluj-Napoca, Department of Gastroenterology and the Iuliu Hatieganu University of Medicine and Pharmacy of Cluj-Napoca, between 1 July 2016 and 1 July 2019. The study was approved by the Ethics Committee of the University of Medicine and Pharmacy.

We selected for inclusion consecutive patients who had underwent a EUS-FNA in order to obtain a tissue specimen from an intrapulmonary lesion suspected to be lung cancer, patients in which the routinely performed bronchoscopy was non-diagnostic. All the patients se-

lected had lung tumors located paraesophageally. The patients with thoracic CT scans showing thoracic aorta interposition between the tumor and the esophagus and those diagnosed by surgical biopsy were excluded. All CT and PET-CT imaging, bronchoscopy, EBUS and EUS reports, histopathological and follow-up data were collected.

Patients were followed up for complications during admission for at least 24 h and as outpatients for 30 days.

The primary endpoint of the study was to assess the diagnostic yield of EUS-FNA after a negative bronchoscopy in paraesophageal lung tumors. We also evaluated the results EUS-FNA addressed to possible metastatic sites of these tumors (performed in the same session) and the EUS FNA related complications. The duration of the procedure and of the passage was measured.

The EUS-FNA procedure

All procedures were performed under anesthetic propofol deep sedation. A flexible EUS endoscope (Olympus GF-UCT180, Olympus® Medical Systems Europe, Ltd., Hamburg, Germany) was used. The echoendoscope was advanced into the duodenum and the patients were examined according to a validated and systematic published method for lung cancer patients, analyzing the 6 landmarks (liver, left adrenal gland, aorta, lymph stations 7, 4R, 4L) [20]. After the lung tumor evaluation in gray scale, color Doppler examination was performed in order to assess the vascularization of the tumor, and the vessels found to be interposed between the esophagus and the tumor. We performed also strain elastography in order to analyze the rigidity of the tumors compared to the surrounding tissues. FNAs were performed using 22G needles (Olympus EZ Shot 3+®, Olympus Medical Systems Europe, Ltd., Hamburg, Germany, or Boston Scientific Expect®needle) under ultrasonic guidance; the stylet was removed using the slow pull technique or suction method. After each FNA passage, we analyzed the aspirated specimens macroscopically, deciding if the samples were satisfactory (at least 20mm length), or if another passage was needed. In cases with suspected metastatic lesions in other EUS-FNA accessible sites, we performed the biopsies in the same sessions.

Rapid on-site evaluation (ROSE) was not available. All procedures were performed by a single operator (RC), with more than 20 years of experience in endoscopy and more than 15 years in lung cancer percutaneous US-guided biopsy.

Statistical analysis

Nonparametric data are presented by mean and range. The diagnostic yield was calculated as the number of biopsies that resulted in a diagnosis divided by the total number of biopsies performed.

Results

The analysis included 19 patients (15 males, mean age 65.1 years, range 45-80 years). Demographic data of the patients, tumor localization and dimension, number of passages and histological results are detailed in Table I.

The median tumors diameter was 6.7 cm (range 3.1-11 cm) and a mean 2.1 passages/patient (1-3 passages) were performed.

In the same sessions, supplementary FNA was realized from the left adrenal glands in 2 patients (no. 4, 15),

mediastinal lymph nodes in 3 patients (no. 4,10,19) and suspected liver metastasis in 2 patients (no.10, 18). The results revealed the same type of tumor as in the primary biopsied sites, confirming the metastatic lesions.

In all cases, lung EUS-FNA was diagnostic (19/19, 100%).

No early or late complications following the EUS-FNA procedures were registered.

The mean duration of the EUS-FNA procedure was 15 minutes and 13 seconds, and the mean passage time was 55 seconds.

In figure 1 we illustrate 2 cases included in the study.

Table I. Demographic data, tumor characteristics and pathology results

No.	Sex	Age	Localization	Dimension – cm (EUS)	No. of passages	Pathology results
1	M	74	URL	4.5	3	Squamous cell carcinoma
2	M	67	URL	7	3	Adenocarcinoma
3	M	61	URL	11	1	Adenocarcinoma
4	M	76	ULL	6.2	3	Adenocarcinoma
5	M	71	LLL	4	3	Adenocarcinoma
6	M	78	URL	8	2	Squamous cell carcinoma
7	F	57	URL	6	3	Small cell neuroendocrine carcinoma
8	M	73	ULL	11	2	Squamous cell carcinoma
9	F	57	LRL	8.2	2	Adenocarcinoma
10	M	80	URL	7.4	3	Squamous cell carcinoma
11	M	60	LLL	8	2	Adenocarcinoma
12	F	73	ULL	5.4	2	Small cell neuroendocrine carcinoma
13	M	62	ULL	6.2	2	NSCLC
14	F	59	URL	3.5	2	Breast carcinoma metastases
15	M	62	ULL	4.2	2	Adenocarcinoma
16	M	67	LRL	3.1	2	NSCLC
17	M	57	ULL	7.3	1	Squamous cell carcinoma
18	M	58	LLL	7	1	Squamous cell carcinoma
19	M	45	ULL	9.1	2	Adenocarcinoma

URL = upper right lobe; ULL = upper left lobe; LRL = lower right lobe; LLL = lower left lobe; NSCLC = non-small cell lung carcinoma.
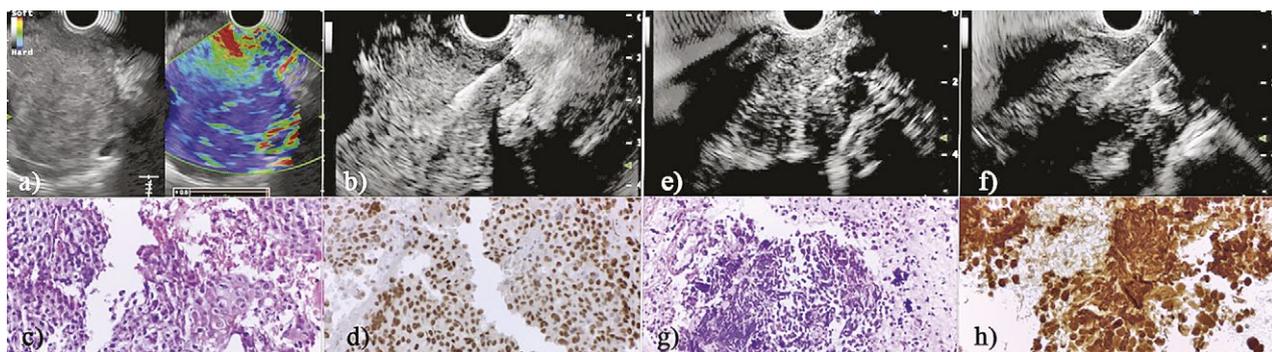
Fig 1. Case 1: a) EUS image of squamous cell lung cancer as a hypoechoic mass with an irregular contour, hard in comparison to the surrounding tissue in the elastography mode; b) EUS FNA of the squamous cell lung cancer – with the needle inside the tumor; c) Histopathological aspect of squamous cell carcinoma, HE stain (x 40); d). Squamous cell carcinoma – immunohistochemistry. Tumor cells are positive for p63 (x40). Case 2: e) Paraesophageally located small cell lung cancer – hypoechoic, irregular tumor, contiguous with mediastinal lymph nodes metastasis; f) EUS FNA of small cell lung cancer – 22G needle puncturing the tumor; g) Histopathology of small cell neuroendocrine carcinoma, HE stain (x 20); h) Small cell neuroendocrine carcinoma – immunohistochemistry. Tumor cells are positive for TTF-1 (x 40).

Discussion

We analyzed the diagnostic yield of EUS-FNA of the paraesophageally located lung tumors and obtained an excellent rate, without complications. Also, we were able to diagnose, in the same EUS session, suspected metastatic lesions from other sites. The average duration of one passage was less than one minute and the duration of the whole procedure was 15 minutes.

The good sensitivity of the EUS-FNA for lung cancer staging, as well as mediastinal lymph nodes metastasis and the diagnosis of paraesophageally located lung tumors has already been reported [21]. EUS should be used along EBUS for the mediastinal staging in lung cancer, according to the latest guideline of the European Society of Gastrointestinal Endoscopy (ESGE), the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS) [4]. By using both techniques, mediastinal staging accuracy increases in cases shown as normal by a CT examination.

In this study we evaluated a series of patients with paraesophageal lung tumors that could not be histologically diagnosed throughout bronchoscopy or percutaneous US guided biopsy. The approach and puncture of the tumor by transesophageal route were considered feasible after the analysis of the CT images. There are few reported series of patients who have underwent EUS-FNA for this less common indication [21].

We obtained 100% sensitivity and diagnostic yield for the diagnosis of paraesophageally located lung cancers by EUS-FNA. Our data are concordant with the results of other studies supporting the importance of using EUS in these cases. A study involving pneumologists showed a very good diagnostic yield (26 of 27 patients) for EUS performed with an echobronhoscope [12]. A relatively recent systematic review and meta-analysis [21] which included 11 studies, with a total of 313 patients [9,13,22-24], showed an average diagnostic yield of 0.90 and an average sensitivity of 0.92 for diagnosing intrapulmonary lung tumors by EUS using the gastrointestinal echoendoscope. The complications rate found was less than 2% [21]. In our study, we had no complications either. Therefore, we consider that a proper indication for lung EUS-FNA is essential for a higher accuracy in this delicate area of lung pathology.

In our study, among the primary lung tumors, the proportion of the patients with non-small cell lung carcinoma (NSCLC) was 88.88%, the other being small cell lung carcinoma, similar to the known statistical rates. We were also able to characterize the NSCLC as squamous and adenocarcinomas types, except for two cases in which the histological differentiation between the 2 types of NSCLC could not be done.

Another potential advantage of EUS in lung cancer is represented by the possibility to evaluate and procure samples from metastatic lesions - from liver, adrenal glands (mostly left side) abdominal lymph nodes or other sites, during the same session. We performed supplementary biopsies in 7 cases, all lesions being confirmed as metastasis. This feature increases the added value of EUS-FNA in the diagnosis and staging of paraesophageal lung cancer, particularly in cases where metastases are suspected and/or their imaging aspect is non-specific.

A limit of our study is represented by the relatively small number of patients included. Also, we did not include patients with lung tumors without contact to paraesophageal mediastinal pleura.

Despite the multiple advantages over other radiation techniques, EUS-FNA is still an underused technique for paraesophageally located lung tumors and for accessible metastatic sites. Efforts should be taken to extend knowledge concerning EUS-FNA.

Conclusions

EUS-FNA of the paraesophageally located lung tumors represents a very accurate and minimally invasive diagnostic method. The complication rate of this procedure is also very low.

Conflicts of interest: none.

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