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ORIGINAL ARTICLE

Endobronchial ultrasound in mediastinal lymphadenopathy approach and use of ancillary techniques: experience in ABC Medical Center

Ultrasonido endobronquial en el abordaje de la adenopatía mediastinal y uso de técnicas auxiliares: experiencia del Centro Médico ABC

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Abstract

Introduction: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has emerged as an innovative technique for diagnosis and staging of lung cancer, allows lymph node staging, mediastinal and hilar structures, detection and correct diagnosis of mediastinal and hilar tumors, metastatic lesions and the study of infectious diseases and non-infectious lesions. **Objective:** To describe the cytological features of specimens obtained by EBUS-TBNA and the use of ancillary techniques for cytological diagnosis of mediastinal lymphadenopathies. **Method:** Transversal, descriptive, observational and retrospective study using databases of our surgical pathology department at ABC Medical Center. **Results:** We evaluated 12 patients, of whom prevalence was higher in male, the mean age was 60 years. The final diagnosis was positive for lung adenocarcinoma metastases in 58% and for non-pulmonary site metastases in 8%, and granulomatous lymphadenitis was observed in 2 patients. **Conclusions:** EBUS-TBNA is a safe procedure that assess mediastinal and hiliar lymphadenopathies and allows lymph nodes to be sampled and obtain alternative diagnosis rather than metastatic lesions.

Keywords: Endobronchial ultrasound. Mediastinal lymphadenopathy. Ancillary techniques.

Resumen

Introducción: El ultrasonido endobronquial con aspiración transbronquial con aguja fina (EBUS-TBNA) es una herramienta innovadora para el diagnóstico y la etapificación del cáncer pulmonar, que permite la estadificación de linfadenopatías mediastinales e hiliares así como la detección y el diagnóstico correcto de tumores mediastinales e hiliares, lesiones metastásicas, enfermedades infecciosas y lesiones no infecciosas. Objetivo: Describir las características citológicas de los especímenes obtenidos mediante EBUS y el uso de técnicas auxiliares para el diagnóstico citológico de adenopatía mediastinal. **Método:** Estudio descriptivo, transversal, observacional y retrospectivo, utilizando la base de datos del departamento de patología quirúrgica del Centro Médico ABC. **Resultados:** Se estudiaron 12 pacientes, mostrando mayor prevalencia en hombres y una edad promedio de 60 años. El diagnóstico final fue positivo para metástasis de adenocarcinoma pulmonar en el 58% y para metástasis de sitio no pulmonar en el 8%, y se observó linfadenitis granulomatosa en 2 pacientes. **Conclusiones:** El EBUS-TBNA es un procedimiento seguro para la evaluación de adenopatías mediastinales e hiliares que permitie obtener hallazgos distintos de metástasis de neoplasias en estas biopsias.

Palabras clave: Ultrasonido endobronquial. Abordaje mediastinal. Técnicas auxiliares.

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Introduction

Real-time endobronchial ultrasound-guided transbronchial fine-needle aspiration (EBUS-TBNA) is a minimally invasive diagnostic technique that complements flexible videobronchoscopy and allows the bronchoscopist to evaluate beyond the inner surface of the airway. The most widely used ultrasound system is the linear probe, as it provides images of lymph nodes, blood vessels, the heart, and possible tumor masses adjacent to the airway, in addition to visualizing the needle inside the studied structure¹.

EBUS-TBNA consists of a probe with a convex transducer operating at a frequency of 7.5 MHz and a penetration depth of 5 cm at its tip, which scans parallel to the direction of bronchoscope insertion². Images are obtained through direct contact of the probe with the lesion.

Using this technique, all high paratracheal mediastinal lymph node stations (2R, 2L), low paratracheal (4R, 4L), and subcarinal (7) are accessible, except for the subaortic and paraesophageal lymph nodes (5, 6, 8, and 9)³. Hilar and interlobar lymph nodes (10 and 11) are also accessible^{3,4}. Mediastinal adenopathies that should be studied via puncture are those that on the computed tomography (CT) have an enlarged short axis (>1 cm) or that on fluorodeoxyglucose positron emission tomography (FDG-PET) show significant metabolic activity⁵.

Imaging modalities - primarily CT and FDG-PETfrequently used as initial staging methods, show in Yasufuku's study⁶, lower sensitivity and specificity than EBUS-TBNA. Unlike modalities, EBUS-TBNA can approach lymph nodes \leq 10 mm in size and identify neoplastic infiltration in them.

Mediastinoscopy allows for detailed examination of lymph node stations 1, 2R, 2L, 4R, 4L, and 3, and the anterior subcarinal lymph nodes⁷. However, it is not possible to access lymph nodes located in lymph node stations 5, 6, 8, and 9⁷. The mean sensitivity rate of mediastinoscopy in published studies is approximately 80%, and the mean false-negative rate is around 10%. Mediastinoscopy is a highly invasive technique, requires general anesthesia, is costly, and has a rate of complications of approximately 2% up to 3%⁸.

The main indication for EBUS-TBNA is the mediastinal staging of lymph nodes in patients with suspected or previously diagnosed primary or metastatic lung cancer. It allows for cytological and histological evaluation of these lymph nodes, making it a minimally invasive technique for the cytodiagnosis of mediastinal lesions⁹.

Other clinical applications, besides the diagnosis and staging of lung cancer, include re-staging of the posterior

mediastinum after neoadjuvant chemotherapy and the diagnosis of extrathoracic metastatic malignancy, mediastinal and hilar lymphadenopathy, sarcoidosis, lymphoma, tuberculosis, endemic mycoses, and mediastinal tumors¹⁰.

The prognosis of lung neoplasms is determined, among other aspects, by the stage of the disease at the time of diagnosis. Therefore, having an accurate staging diagnosis is crucial to determine the best therapeutic option for each patient.

The sensitivity rate of EBUS-TBNA in the diagnosis and staging of lymph nodes ranges goes from 85% up to 100%, and its negative predictive value from 11% up to 97.4%; specificity and positive predictive value are 100% in all cases^{10,11}.

In appropriate patients, it is a minimally invasive procedure without risk when performed by trained personnel. Potential complications include hemomediastinum, pneumothorax, pneumomediastinum, and abscess at this level. Overall, it is a safe and well-tolerated technique. Coagulation defects related to the use of anticoagulants or antiplatelet agents should be corrected (withdrawn 5-7 days before the procedure) and a platelet count > 50,000,000 should be ensured due to the risk of bleeding. It should be delayed for, at least, 6 weeks after an acute myocardial infarction and is contraindicated in cases of unstable ischemic heart disease, arrhythmias, and severe hypoxemia¹².

The objective of our study was to describe the cytological characteristics of specimens obtained via EBUS and the use of auxiliary techniques for the cytological diagnosis of mediastinal adenopathy.

Method

We conducted a descriptive, cross-sectional, observational, and retrospective study using the database of the surgical pathology department of Centro Médico ABC. The search included all patients with mediastinal adenopathy under study who were evaluated by EUS-EBUS from January 1st, 2016 through August 31st, 2018. The study included all patients with EUS-EBUSguided aspiration biposies and excluded those with biopsies obtained via transesophageal endoscopic ultrasound. Clinical data were obtained from each patient's electronic health record, including age, sex, previous diagnosis, and prior treatment. In all cases, a rapid evaluation of Hematoxylin and Eosin-stained smears was performed, as well as an evaluation of the cell block. In patients with a previous diagnosis of lung cancer, immunohistochemical staining with TTF1 and napsin A was performed.



Figure 1. A: cluster of epithelial cells with ample cytoplasm. B: lymphoid nodules forming granulomas. C: necrotizing granuloma with multinucleated giant cells. D: at higher magnification, the presence of yeast consistent with *Histoplasma capsulatum* (GMS stain) is notable. E: the smear shows a hypercellular population with overlapping clusters of atypical cells. They exhibit atypical features, including ample cytoplasm, irregular nuclear contours, nucleomegaly, irregularity, and hyperchromasia. F: immunohistochemical reaction on the cell block shows nuclear positivity for TTF1 and napsin A (inset). G: panoramic micrograph with clusters of neoplastic cells, chronic inflammation, and necrotic tissue. H: at higher magnification, the atypical characteristics of the cells are apparent.

Results

The study included a total of 12 patients (8 men and 4 women), with a mean age of 60 years. Among these, 6 (50%) had a previous diagnosis of pulmonary adenocarcinoma and 6 (50%) were previously healthy or had a history of another neoplasm: 1 (8%) had a previous diagnosis of malignant melanoma, 1 (8%) of esophageal adenocarcinoma, and 1 (8%) of breast cancer. Clinical data obtained are summarized in Table 1.

The final diagnosis was positive for metastasis of pulmonary adenocarcinoma in 7 (58%) patients and positive for metastasis of a non-pulmonary site in 1 (8%). In 2 patients (16.6%), immunohistochemistry

was not contributory, and they presented with granulomatous lymphadenitis. One out of these 2 patients (16.6%) had an association with yeast-like structures (Fig. 1).

Discussion

EUS-EBUS has become the initial diagnostic modality for the study of mediastinal and pulmonary adenopathies. This technique represents a rapid and minimally invasive method for the staging of lung cancer. Its sensitivity rate ranges from 36% up to 96%, and specificity rate from 88% up to 100%. The advent of targeted therapy has revolutionized the treatment of lung cancer. Currently, pathologists must classify non-small cell lung carcinoma

Table 1. General characteristics of patients

Clinical data	n = 12
Males, n	8
Females, n	4
Age in years, mean (range)	60 (28-77)
Final diagnosis, n Malignant Benign Insufficient	10 2 0

and perform molecular biology studies where possible. Using EBUS, material can be obtained in up to 98% of cases for immunohistochemical studies. There are other findings in EBUS-guided aspiration biopsies, besides neoplastic cells, including granulomas. Granulomas have been detected in 2% up to 22% of EBUS-guided biopsies. Some studies have shown that up to 5% of patients with a history of lung cancer may develop a sarcoid-like granulomatous reaction after treatment. Sarcoid-like reactions in patients with non-pulmonary neoplasms have been well documented in cases of lymphoma, gastric carcinoma, and breast cancer. Although their pathogenesis is poorly understood, it has been suggested that they represent an uncontrolled immune response to neoplasm.

Conclusions

The use of EBUS for the evaluation of mediastinal adenopathy has increased worldwide, allowing for findings other than metastases of neoplasms in these biopsies, such as granulomas. The use of histochemistry and immunohistochemical panels is of great help for a precise final diagnosis, and molecular biology studies can even be conducted in cases that warrant them.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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