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Original Article

The Contribution of Cell Blocks in the Diagnosis of Mediastinal Masses and Hilar Adenopathy Samples From Echobronchoscopy *



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ABSTRACT

Background: Cell block material from puncture can be obtained with endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in many cases. The aim of this study was to analyze the value of additional information from cell blocks obtained with EBUS-TBNA samples from mediastinal and hilar lymph nodes and masses.

Methods: Review of pathology reports with a specific diagnosis obtained from EBUS-TBNA samples of mediastinal or hilar lesions, prospectively obtained over a two-year period. The generation of cell blocks from cytology needle samples, the contribution to morphological diagnosis, and the possible use of samples for immunohistochemistry were analyzed.

Results: One hundred and twenty-nine samples corresponding to 110 patients were reviewed. The diagnosis was lung cancer in 81% of cases, extrapulmonary carcinoma in 10%, sarcoidosis in 4%, lymphoma in 2.7%, and tuberculosis in 0.9%. Cell blocks could be obtained in 72% of cases. Immunohistochemistry studies on the cell blocks were significantly easier to perform than on conventional smears (52.6% vs 14%, P<.0001). In 4 cases, the cell block provided an exclusive morphological diagnosis (3 sarcoidosis and one metastasis from prostatic carcinoma) and in 3 carcinomas, subtype and origin could be identified. Exclusive diagnoses from the cell block were significantly more frequent in benign disease than in malignant disease (25% vs 0.9%, P=.002).

Conclusions: Cell blocks were obtained from 72% of EBUS-TBNA diagnostic procedures. The main contributions of cell blocks to pathology examinations were the possibility of carrying out immunohistochemical staining for the better classification of neoplasms, especially extrapulmonary metastatic tumors, and the improved diagnosis of benign lesions.

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Aportación del bloque celular en el diagnóstico de adenopatías y masas mediastínicas o hiliares realizado por ecobroncoscopia

RESUMEN

Introducción: La punción transbronquial guiada por ecoendoscopia permite obtener bloques celulares a partir del material de punción. Nuestro objetivo fue analizar su contribución al diagnóstico citológico convencional.

Metodología: Revisión retrospectiva de las punciones por ecobroncoscopia realizadas de forma consecutiva durante 2 años con diagnóstico específico. Se analizó la capacidad de generar bloques celulares, su contribución al diagnóstico y a la realización de técnicas de inmunohistoquímica.

Resultados: Se revisaron 129 muestras de lesiones correspondientes a 110 pacientes. En el 91% el diagnóstico fue de malignidad. Las lesiones puncionadas más frecuentemente fueron las adenopatías 4R (28%) y subcarinal (21%). El 72% de las muestras se procesaron como bloque celular, siendo su capacidad para realizar técnicas de inmunohistoquímica significativamente mayor a la de las muestras citológicas (52,6% vs. 14%, p < 0,0001). En 4 casos el bloque permitió un diagnóstico morfológico exclusivo (3 sarcoidosis y

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una metástasis de adenocarcinoma prostático) y en 3 carcinomas definir el subtipo y origen. El diagnóstico exclusivo mediante bloque celular fue significativamente más frecuente en la patología benigna que en la maligna (25% vs. 0.9%, p=0,002).

Conclusiones: La obtención de bloque celular a partir de muestras de punción por ecobroncoscopia fue del 72%. Sus principales aportaciones fueron la mejora del diagnóstico de lesiones benignas y la capacidad para realizar técnicas de inmunohistoquímica cuya contribución es esencial para la tipificación de neoplasias. © 2013 SEPAR. Publicado por Elsevier España, S.L. Todos los derechos reservados.

Introduction

The recent introduction and generalized use of new diagnostic and staging tools, particularly positron emission tomography combined with computed tomography (PET-CT) and endoscopic ultrasound (EUS), have improved efficiency in the diagnosis of mediastinal node involvement, sidelining the use of more aggressive and costly tests such as surgical examination of the mediastinum.¹

The incorporation of real-time endobronchial ultrasoundguided transbronchial needle aspiration (EBUS-TBNA) has led to a considerable improvement in the validity and the safety of this relatively non-invasive diagnostic test, while maintaining an excellent cost-effectiveness ratio.^{2,3} Although all these technological advances have improved the diagnostic yield of cytohistological samples, insofar as the sampling of adequate material for diagnosis is concerned, the rate of false negatives is as high as 20% in most published series.^{4,5} Preparation of a cell block with the cytological sample may provide additional morphological information and allow both immunohistochemical and molecular techniques to be performed, thus helping improve histological subtyping and even targeted therapies.^{6–11} It may also help identify benign diseases that normally need larger specimens for diagnosis.^{6–10}

On this basis, the aim of this study was to analyze the contribution made by cell blocks to conventional cytological smear obtained by EBUS-TBNA in the diagnosis of lymphadenopathies and mediastinal and hilar masses.

Methodology

Design

This was a retrospective observational study of a prospectively collected series in which the capacity to generate cell blocks from cytological specimens obtained by EBUS-TBNA from hilar and mediastinal lymphadenopathies and/or pulmonary lesions and their additional diagnostic value were analyzed.

Patients

The pathology reports from the EBUS-TBNA performed in patients with hilar and/or mediastinal lymphadenopathies with a short axis >1 cm on CT or 5 mm in the case of pathological uptake on PET-CT or with accessible lung lesions, in whom an etiological diagnosis was determined, were reviewed. All procedures were performed consecutively between September 2009 and December 2011 in the Complexo Hospitalario de Vigo, a tertiary level hospital with a referral area of 350 000 inhabitants, and 800 000 inhabitants specifically for this technique, since neighboring towns with secondary level referral hospitals are also included. EBUS-TBNA was indicated for staging or diagnosis of lung cancer or extrathoracic lesions, and the study of mediastinal or hilar masses/lymphadenopathies of undetermined etiology. Specific informed consent for participation in the study was obtained in writing from all patients. The study was approved by the ethics committee of the region (Research Ethics Committee of Galicia).

EBUS-TBNA and Evaluation of Specimens

All procedures were performed in an outpatient setting in the conventional bronchoscopy room, with echocardiographic, pressure and pulse oximeter monitoring, under conscious sedation with midazolam and fentanyl. All procedures were performed by a team of 3 pulmonologists, a nurse and a nursing assistant with wide experience in the technique.¹² A BF-UC180F-OL8 bronchoscope (Olympus, Japan) and an Aloka Prosound alpha 5 endoscope (Aloka, Japan) were used. After endoscopic examination, the lesion was measured and aspirated using NA2015X-4022 needles (Olympus, Japan). Between 1 and 3 passes through the lymphadenopathy, depending on the immediate results. An expert pathologist was present during all procedures to perform rapid on-site evaluation (ROSE) on all specimens after drying and Diff-Quick staining. Another part of the specimen was fixed in alcohol, and if clots or abundant hematic material or tissue microfragments were obtained, these were fixed with formaldehyde and placed in paraffin to make a cell block. Cytological specimens were systematically stained according to the Papanicolaou method, and histological specimens were stained with hematoxylin and eosin.¹³ Specimens were considered acceptable when they contained abundant lymphocytes or lymphoid tissue indicative of lymph node, malignant cells or findings suitable for the determination of another specific diagnosis (diagnostic specimens). The specimens were analyzed by the same pathologists who carried out the ROSE. Suspicious and inconclusive specimens were not included, nor were those with a diagnosis of anthracosis. In addition to the etiological diagnoses, sociodemographic variables, type, site and size of the aspirated lesion, the feasibility of preparing cell blocks and their contribution to the morphological diagnosis and their utility for performing immunohistochemical studies were recorded.

Statistical Analysis

Overall results were expressed in percentages and absolute frequencies for qualitative variables and as mean and standard deviation (SD) for quantitative variables. The diagnostic value of the procedures was analyzed with McMemar's exact test, using a twotailed level of significance of 0.05. The data were analyzed using the *Statistical Package for Social Sciences* software, version 15.0 (SPSS, Chicago, IL, USA). For the descriptive study, both lymphadenopathy and patient were taken as an analysis unit. For the purposes of the comparative study, each lymphadenopathy was used as an analysis unit.

Results

A total of 129 EBUS-TBNA specimens from 110 patients, retrieved from various node stations and corresponding masses, were included in the study. Patient characteristics and the aspirated lymphadenopathies and masses (9 pulmonary and one esophageal) are summarized in Table 1. In 81% of the patients, the diagnosis was lung cancer, in 10% extrapulmonary cancer, in 5.4% sarcoidosis, in 2.7% lymphomas and in 0.9% tuberculosis. The most frequently aspirated lesions were 4R (28%) and subcarinal (21%)

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