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ORIGINAL ARTICLE

Algorithmic approach by endobronchial ultrasound-guided transbronchial needle aspiration for isolated intrathoracic lymphadenopathy: A study in a tuberculosis-endemic country

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Background/Purpose: Isolated intrathoracic lymphadenopathy (IT-LAP) is clinically challenging because of the difficult anatomic location and wide range of associated diseases, including tuberculosis (TB). Although sampling via endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for histopathology is a major development, there is still room for improvement. This study aimed to investigate an algorithmic approach driven by EBUS-TBNA and conventional bronchoscopy to streamline the management of IT-LAP.
Methods: Eighty-three prospectively enrolled patients with IT-LAP were subjected to an EBUS-TBNA diagnostic panel test (histopathology, cytology, and microbiology) and underwent conventional bronchoscopy for bronchoalveolar lavage. The results were structured into an algorithmic approach to direct patient treatment, workup, or follow-up.
Results: The diagnostic yields of EBUS-TBNA based on histopathology were similar for each disease entity: 77.8% for malignancy, 70.0% for TB, 75.0% for sarcoidosis, 80.0% for anthracosis, and 70.0% for lymphoid hyperplasia ($p = 0.96$). The incidence of malignancy was 10.8% for

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total IT-LAP patients, and 12.0% and 33.7% for patients with TB and sarcoidosis, respectively. Thirty-five (42.2%) patients were symptomatic. The leading diagnosis was sarcoidosis (60%), followed by TB (20%), malignancy (11.4%), lymphoid hyperplasia (5.7%), and anthracosis (2.9%). By logistic regression analysis, granulomatous disease (odds ratio: 13.45; 95% confidence interval: 4.45—40.67, $p < 0.001$) was an independent predictor of symptoms. Seven (8.4%) and three (3.6%) IT-LAP patients diagnosed active TB and suggestive of TB with household contact history, respectively, were all placed on anti-TB treatment.

Conclusion: The algorithmic approach streamlines patient management. It enables early detection of malignancy, correctly places nonmalignant patients on an appropriate treatment regimen, and particularly identifies candidates at high risk of TB reactivation for anti-TB chemoprophylaxis.

Introduction

Lymphadenopathy (LAP) of the hilum or mediastinum may be an isolated presentation or may be associated with intra- or extrapulmonary lesions. In the latter case, diagnosis from intra- or extrapulmonary lesions may aid in the diagnosis and management of LAP.[1] However, without any other associated lesions, isolated intrathoracic LAP (IT-LAP) poses a clinically challenging condition.[2]

In tuberculosis (TB)-endemic countries, patients with asymptomatic IT-LAP due to previous TB exposure are not uncommon, thereby warranting close follow-up in clinical practice.[3,4] Routine sampling of LAP by surgical means is not generally due to cost,[5] which may be a minor expense when considering early detection of existing malignancy.[2,6] For IT-LAP patients with respiratory or systemic symptoms, lymph node examination is also frequently delayed because of the invasiveness of the surgical approach. Thus, diagnosis is usually based on clinical, radiologic, or conventional bronchoscopic profiles rather than histopathology. Therefore, patients remain at risk of delayed or inappropriate treatment.

The recent development of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has helped overcome this situation. Several studies, mostly based on cytology, have shown its usefulness for lymph node staging in lung cancer.[7—10] Its diagnostic performance is equivalent to that of mediastinoscopy, but with far less invasiveness.[11,12] However, unlike nodal staging, which can be qualified by cytology, specimens acquired by EBUS-TBNA for studying IT-LAP should be qualified by histology in order to obtain a specific diagnosis. The success rate for adequate tissue by EBUS-TBNA is reportedly 70—95%.[11,13—15] Furthermore, the amount of tissue may sometimes be considered insufficient for diagnosing certain diseases.[16] Not infrequently, bleeding and blood clots due to negative pressure aspiration can make adequate histopathologic yield even more challenging. Different reports focusing on TB,[6,17] sarcoidosis,[18,19] or lymphoma[14] in a clinical trial setting have shown diagnostic yields ranging from 75% to 95%.

In TB-endemic countries, the issue of IT-LAP is not prominent enough. Studies using merged diagnostic modalities of EBUS-TBNA and conventional bronchoscopy for bronchoalveolar lavage (BAL) are even less reported. This study examined the feasibility of an algorithmic approach driven by EBUS-TBNA and conventional bronchoscopy to streamline the diagnosis and management of IT-LAP.

Materials and methods

Study participants

Eighty-three patients of IT-LAP were consecutively included in a prospective manner, regardless of a presumptive diagnosis, from December 1, 2008, to December 1, 2011. The presence of hilar or mediastinal LAP with a short axis of >10 mm on chest computed tomography (CT) scan, without intrapulmonary lesions, was considered the inclusion criteria for IT-LAP. Individuals with respiratory symptoms caused by obstructive airway disease, gastroesophageal reflux disease, and rhinosinusitis were excluded. The Institutional Review Board of Chang Gung Memorial Hospital approved the study (No. 98-3639A3), and all study participants provided written informed consent.

Bronchoscopy and EBUS-TBNA

BAL was performed using a flexible fiberoptic bronchoscope (BF-P240 or BF-40, Olympus; Tokyo, Japan) for determination of the CD4/CD8 lymphocytic ratio. The TBNA was performed using a flexible ultrasound-guided bronchoscope with a convex probe at its tip (BF-UC206F-OL8, Olympus). Two experienced respiratory physicians conducted all the examinations. The obtained images were linked to an ultrasound scanner (EU-2000C, Olympus) with Doppler-flow imaging. Conscious sedation was induced using midazolam prior to inserting the bronchoscope.

Suspected lymph nodes directed by chest CT scan were selected for EBUS-TBNA with a 22-gauge needle (NA-201SX-4022, Olympus). The needle was passed a minimum of three times for each targeted lymph node,[13] to ensure a creamy rather than a watery or mucoid aspirate. The sample was immediately expressed onto four slides and fixed in 95% alcohol for later cytology evaluation. Whenever a tissue core was noted on the slide, the specimen was transferred by a 22-gauge injection needle into a container with formalin solution to prepare for subsequent histopathology. Rapid on-site examination was not performed. Normal saline needle washing was routinely sent for microbiology culture and smear (Ziehl—Neelsen stain and Grocott's methenamine silver stain) for TB and fungi.