Commentary

Endobronchial ultrasound-guided transbronchial needle aspiration: unraveling myths of mass in the chest

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Lung cancer is one of the most common neoplasms worldwide and a major cause of cancer death. Rapid diagnosis and accurate staging for patients with suspected lung cancer are essential to appropriate treatment. However, many of submucosal or parabronchial intrapulmonary lesions are invisible by bronchoscopy despite their adjacency to the central airway. Classical approaches in these cases, such as conventional bronchoscopy, transbronchial needle aspiration (TBNA) and computed tomography-guided transthoracic needle aspiration (TTNA), are of limited use in a sense of definitive diagnosis (1-3). With the advance in bronchoscopic diagnostics during the recent years, endobronchial ultrasound-guided TBNA (EBUS-TBNA) emerges as a novel technique for bronchoscopic sampling under ultrasound guidance. EBUS-TBNA enables real-time aspiration of lesions adjacent to the trachea or large bronchi (4). EBUS-TBNA circumvents the limitations of classical TBNA, making the technique safer and more precise in the diagnosis of lung cancer (5). Radial EBUS with a guide sheath and miniature ultrasound probe, or combined with electromagnetic navigation bronchoscopy, provides high diagnostic yield of peripheral pulmonary lesions (5,6). In a study by Zhao and colleagues, among 66 cases of intrapulmonary lesions unconfirmed by conventional bronchoscopy, 59 were finally confirmed by EBUS-TBNA (89.4%), with the sensitivity, specificity and accuracy being 93.7%, 100.0% and 93.9%, respectively (7). However, the low negative predictive value of this procedure render an indispensable need for further examination by other modalities in patients with no malignancy detected by EBUS-TBNA alone (7).

Since imaging alone is not adequately sensitive or specific for evaluation of lymph node metastases, mediastinal nodes are generally sampled when enlarged on CT (short axis >1 cm) and/or metabolically active on PET. Tissue sampling performed with invasive or minimally invasive techniques is crucial for the staging of lung cancer. Until recently, mediastinoscopy was considered as the gold standard for detection of mediastinal lymph node with a sensitivity of 80% and a specificity of 100% (8). However, mediastinoscopy can only access lymph node stations 1-4 and 7, while those at lower subcarinal regions can become a nightmare for this procedure. The compulsory need for mediastinoscopy to be performed under general anesthesia gives rise to significant rates of procedure-related morbidity (2%) and mortality (0.08%) (9). Furthermore, repeated mediastinoscopy by no means can be easy and acceptable in a same patient. By using EBUS-TBNA, sampling mediastinal nodes can be far less invasive with a satisfactory sensitivity of 85% to 95% and a specificity of 100% (8,10). During the procedure, certain ultrasonic features of the lymph nodes, such as circular appearance, distinct margin, heterogeneous echogenicity and signs of necrosis, can be of clinical use to predict metastasis of lung cancer (11). Compared with mediastinoscopy, EBUS-TBNA offers several advantages, such as lower risk of morbidity and mortality, wider accessible regions which include the hilar and interlobar lymph nodes (12). However, stations 5, 6, 8 and 9 are not accessible by this technique. On the other hand, endoscopic ultrasound fine needle aspiration (EUS-FNA) is useful for accessing the posterior mediastinal lesions but incompetent for evaluating lesions anterior to

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the trachea (13-16). Therefore, combined use of EBUS-TBNA and EUS-FNA may result in highly accurate staging of lung cancer compared with either method used alone (17). Presently, needles for EBUS-TBNA are available in two sizes, 22-guage (22G) and 21G. The differences between 22G and 21G needles in sample adequacy and diagnostic yield were not statistically significant, according to a retrospective study of 1,299 patients by Yarmus and coworkers (18). Mini-forceps offer a higher diagnostic yield than needle aspiration in EBUS guided sampling, especially when the histological samples are decisive for making diagnosis (19). Randomized controlled trials on this aspect are needed for validation. Rapid on-site evaluation (ROSE) handled by experienced cytologists plays an important role in ensuring the diagnostic yield of sampling procedure (20). Oki *et al*. reported that ROSE during EBUS-TBNA is associated with a lower need for additional puncture number other than diagnostic yield (21). More studies on the role of ROSE during EBUS-TBNA should be worthwhile. For patients who have received neoadjuvant chemo-radiotherapy, EBUS-TBNA can be an alternative in mediastinal restaging. Subsequent determination by surgical staging is recommended in cases of negative EBUS-TBNA sampling (22). However, another study looking at a consecutive group of 61 patients with non-small cell lung cancer (N2) showed a negative predictive value of 67% and concluded that it is not necessary to re-stage the mediastinal nodes following a negative EBUS-TBNA (23). Further studies are required to address the debate and to improve the negative predictive value of EBUS-TBNA.

EBUS-TBNA can also be useful for definitive diagnosis and classification of malignant lymphoma and non-neoplastic lesions in patients with mediastinal lymphadenopathy. Differential diagnosis sometimes relies much on EBUS-TBNA in certain thoracic disease entities that may be mimickers of tumors [such as sarcoidosis, ground glass opacity pulmonary lesions (24)] or rarely encountered (such as histoplasmosis). With advances in technology, endoscopic ultrasound is becoming an important tool in natural orifice transluminal endoscopic surgery (25-27), and has evolved from a purely diagnostic imaging modality to an interventional procedure.

In conclusion, EBUS-TBNA has been increasingly popular as a widely adopted procedure for evaluating a variety of chest diseases, in particular, for the diagnosis and staging of lung cancers. Despite more studies pending to improve the clinical performance of EBUS-TBNA, encouraging outcomes in diagnostics and therapeutics with this procedure mark a milestone and have lightened up a hope for the patients. A beam of sunlight is visible at the horizon of tomorrow, when the darkness of malignancy in the chest is fully unraveled with on-going refinement of this technique.

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