GUEST EDITORIAL

A Needle through Time: Celebrating 21 Years of Endobronchial Ultrasound-guided Transbronchial Needle Aspiration in Pulmonary Medicine!

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Traditional metsshods with limited diagnostic yield and invasive surgical techniques prompted the development of minimally invasive, real-time, image-guided sampling of mediastinal and hilar lymph nodes *via* endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA).[1,2] Since its inception, EBUS-TBNA has grown exponentially and is now established as the standard of care in mediastinal sampling.[3] EBUS-TBNA is a safe, minimally invasive outpatient procedure that can be completed under moderate sedation with minimal patient discomfort and achieves diagnostic accuracy exceeding 90% for both benign and malignant etiologies.[3,4] It has significantly impacted treatment decisions in thoracic and extrathoracic malignancies, as well as in various inflammatory processes and infections.

Prior to the advent of EBUS-TBNA, mediastinal sampling was performed using conventional transbronchial needle aspiration (TBNA) and mediastinoscopy.[5–7] Mediastinoscopy, a surgical procedure, was traditionally regarded as the gold standard for mediastinal sampling. By 2011, studies had reported the noninferiority of EBUS-TBNA to mediastinoscopy and its superiority to conventional TBNA.[4,8,9] EBUS-TBNA can additionally sample N1 to N3 nodes, making it superior to mediastinoscopy for accurate lung cancer staging.[10,11] When combined with endoscopic ultrasound with a bronchoscope-guided fine-needle aspiration (EUS-B-FNA) using the same bronchoscope, EBUS-TBNA allows for comprehensive mediastinal sampling. It is now considered the first-line modality of choice for sampling mediastinal or hilar lymphadenopathy. The feasibility of EBUS-TBNA is also reported in the pediatric population.[12]

Over the past 2 decades, the lung cancer treatment landscape has evolved significantly, especially with improved survival in advanced cases due to targeted and molecular therapies. Despite this advancement, EBUS-TBNA remains an indispensable diagnostic tool. It can upstage a radiologically normal mediastinum and downstage lesions that are positron emission tomography (PET)-positive with high diagnostic accuracy.[10,11] It is currently the only modality capable of simultaneously diagnosing and staging lung cancer in a single procedure.[4] Subcentimeter lymph nodes, often non-FDG-avid on PET-computed tomography (PET-CT), can be safely and precisely sampled using EBUS-TBNA. EBUS-TBNA has also been reported as a safe modality in elderly patients and those with superior vena cava syndrome. Postsurgical mediastinal sampling, which remains challenging due to anatomical distortion, can be safely and accurately performed with EBUS-TBNA, facilitating restaging of lung cancer.[4]

Despite the emergence of screening programs, most lung cancers are diagnosed at an advanced and unresectable stage.[13] The exponential evolution of medical oncology has increased the demand for high-quality cytological, histological, and molecular material from tissue samples. Consequently, these patients rely on minimally invasive diagnostic modalities expected to yield tissue suitable for molecular profiling. The emergence of molecular profiling and next-generation sequencing (NGS) in lung cancer has marked a pivotal shift toward precision oncology. NGS requires higher quantities of deoxyribonucleic acid (DNA) compared with conventional molecular testing, as it involves testing for hundreds of mutations. These mutations include both actionable alterations and those currently under investigation in clinical trials. International oncological guidelines now recommend concurrent diagnosis, staging, and acquisition of adequate material for genetic testing. Often, tissue samples from EBUS-TBNA are the only samples available at the time of diagnosis. These samples have been reported to have excellent adequacy and quality for these advanced tests.[14–16] EBUS-TBNA is also referred to as endobronchial ultrasound-guided transbronchial needle biopsy (EBUS-TBNB) when core biopsies are obtained.[17,18] There have been advances in EBUS-TBNA needles to obtain core biopsies; however, they can be obtained with 21-gauge needles as well.[17] Its diagnostic yield further improves when core tissue biopsies are obtained using fine-gauge needles.[17,19] Optimal processing of EBUS-TBNA cytological specimens also enhances diagnostic yield for lymphoma.[20]

EBUS-TBNA maintains a high diagnostic yield in benign diseases as well. As with other interventional pulmonology techniques, bronchoscopic modalities discovered for lung cancer have led to a paradigm shift in nonmalignant diseases as well. An additional diagnostic dilemma that physicians often encounter, especially in tuberculosis (TB)-endemic regions like India, is fever and mediastinal lymphadenopathy. More often than not, these individuals are treated empirically without microbiological or pathological subtyping. The dilemma takes a turn for the worse when they do not respond to empiric treatment. The emergence of drug-resistant tuberculosis, from multidrug-resistant to extensively drug-resistant tuberculosis, makes it extremely difficult to achieve an accurate diagnosis in people with tuberculous mediastinal lymphadenopathy. Fortunately, microbiological tests such as BACTEC-MGIT techniques of acid-fast bacilli (AFB) culture and cartridge-based nucleic acid amplification tests (CB-NAATs) like GeneXpert have facilitated rapid diagnosis and management of drug-resistant tuberculosis. The feasibility of performing these tests on samples obtained by EBUS-TBNA has

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significantly helped in accurately diagnosing and microbiologically subtyping these lethal infections.[21,22] It enables timely therapy modification and individualized treatment regimens in patients with tuberculous mediastinal lymphadenopathy.[22] Noninfective granulomatous inflammation confounds the clinical picture in both malignancy and tuberculosis. It becomes extremely challenging to differentiate sarcoidosis from active tuberculosis, especially in TB-endemic regions like India. EBUS-TBNA becomes crucial in these situations as well. EBUS-TBNA has demonstrated the highest diagnostic accuracy for sarcoidosis among available modalities.[23,24] Owing to its high diagnostic yield, EBUS-TBNA is effective in diagnosing mediastinal lymphadenopathy in people living with human immunodeficiency virus (HIV).[25] The bronchoscopic ultrasound also aids in characterizing lymph nodes as malignant, granulomatous, or tuberculous in nature.[26,27] However, while not definitive, this feature assists in targeting specific regions within the lymph node for sampling.

EBUS-TBNA is also evolving as a platform to facilitate cryobiopsy of mediastinal lymph nodes. EBUS-guided cryobiopsy improves its diagnostic yield for lymphoma to 91% while not increasing the rate of complications.[20,28,29] Studies have also reported the feasibility of therapeutic interventions *via* EBUS-TBNA, such as intranodal cisplatin injections.[30,31] EBUS-TBNA has also been used successfully to sample lymph nodes *via* transvascular approaches, including transaortic access.[32,33] The role of EBUS-TBNA is expected to expand further with the increasing implementation of lung cancer screening programs and global initiatives like STOP TB. Its unmatched combination of diagnostic accuracy and safety continues to establish EBUS-TBNA as a cornerstone in pulmonary diagnostics.

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