Use of Endobronchial Ultrasound Guided Mediastinal Cryobiopsy in Addition to Endobronchial Ultrasound Guided Transbronchial Needle Aspiration and Rapid on Site Evaluation for Evaluation of Enlarged Mediastinal Nodes (Case series)

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Abstract

Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) with rapid on site evaluation (ROSE) has been used worldwide in the diagnosis of enlarged mediastinal nodes, with minimally invasive techniques, for many years. With recent advances in the genetic study of cancer, in order to determine the appropriate chemotherapy for cancer, more tissue samples need to be studied, and the amount of tissue obtained via EBUS-TBNA may not be adequate in patients with cancer, lymphoma and sarcoidosis. Recently it has been found that the technique of EBUS-guided mediastinal cryobiopsy (EBUS-MCB) may provide an adequate tissue amount for study with minimal invasiveness and performed safely. We reported 3 cases of enlarged mediastinal nodes, using EBUS-TBNA, and ROSE, and EBUS-MCB in an additional 2 cases. EBUS-MCB provided additional information in 1 case, and confirmation in 1 case. EBUS-MCB is a useful tool to supplement EBUS-TBNA and ROSE in the investigation of enlarged mediastinal nodes.

Keywords: endobronchial ultrasound, rapid on site evaluation, cryobiopsy

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EBUS-TBNA, is a minimally invasive technique adopted for the diagnosis of hilar and mediastinal lymphadenopathies, the gold standard for mediastinal staging of non-small cell lung cancer (NSCLC).[1] But very small cytological samples are collected, which may be not adequate to describe the histopathology of lymphoproliferative disorders and to assess molecular patterns in patients with advanced lung cancer.[2] Mediastinal cryobiopsy has emerged as a promising technology to improve the diagnostic yield of mediastinal lymphadenopathy.[3] So, we used EBUS-MCB in addition to EBUS-TBNA and ROSE in the evaluation of patients with enlarged mediastinal nodes.

Material and Methods

Three patients with enlarged mediastinal nodes were recruited.

Inclusion criteria for EBUS TBNA and ROSE were enlarged mediastinal nodes. Exclusion criteria were 1) bleeding disorder, 2) dyspnea, and 3) desaturation of oxygen

Inclusion criteria for EBUS MCB were inconclusive via EBUS TBNS and ROSE, insufficient tissue for further immunohistoloic study of malignancy. Exclusion criteria for EBUS MCB were: 1) adequate results from EBUS TBNA and ROSE, 2) ROSE revealed caseous necrosis, granuloma suggesting tuberculosis

All patients were informed of the risks and benefits of EBUS TBNA, ROSE and EBUS MCB. Informed consent were signed.

The first patient was a 60 year old man, presented with a history of lymphoma-treated completely with chemotherapy 10 years ago;

then at the follow up, the chest computer scan revealed enlarged mediastinal nodes 1.5 cm at subcarina. The initial differential diagnosis was recurrent lymphoma, or another cancer such as a second primary lung cancer or infection; positron emission tomography with computed tomography (PET/CT) was performed and revealed hypermetabolic activity, other organs were normal.

The second patient was a 68 year old man, a heavy smoker, developed left upper lobe nodule 1 centimeter. Tissue pathology via transthoracic needle biopsy revealed adenocarcinoma. His PET/CT revealed hypermetabolic nodule at left upper lobe, as well as left mediastinal nodes (L11) and subcarina node (C7). So sequential mediastinal nodes needle aspiration was considered to stage the lung cancer for operability.

The third patient was a 70 year old woman, at a check up for heart via CT calcium score; incidental finding of subcarinal mass 4.3 centimeters.

EBUS procedures were performed under general intravenous anesthesia with secured airway through laryngeal mask. After identifying the appropriate lymph node using an EBUS bronchoscope (BF-UC190F), a conventional EBUS-TBNA was performed using 22-gauge needle (NA-U401SX; OLYMPUS Medical Systems).

Three times EBUS TBNA were performed for each station of the mediastinal nodes.

Rapid on-site pathology (ROSE) was conducted immediately to provide the solutions in the operating theater. In case of undiagnosed /inadequate tissue pathology, cryobiopsy will be considered.

To enable sequential cryobiopsy, a second puncture was made immediately after the initial TBNA, targeting the proximal border of the lymph node. The goal was to rupture the lymph node capsule and create a tunnel for seamless introduction of the 1.1 mm cryoprobe (Erbecryo 20402-401, Germany). Before inserting the cryoprobe, the echogenic needle trace, typically seen as a hyperschoic line within the lymph node on ultrasound was used as a reference point to guide the cryoprobe placement. After the introduction of the 1.1 mm cryoprobe, a freeze cycle of 6 seconds was applied. Samples were subsequently retrieved en-block with the EBUS bronchoscope and were then thawed in saline and fixed in formalin. Cryobiopsy was performed three times.

All participants were admitted as in-patients for 24 hours after the procedure for observation.

Results

For the first patient, ROSE revealed only a few lymphocytes; but EBUS-MCB revealed granuloma; and special stain for acid fast bacilli and Giemsa stain were negative, compatible with sarcoidosis.

ROSE in the second patient revealed only lymphocytes in both L11 and C7, confirmed by EBUS-MCB. The patient underwent a lobectomy.

For the third patient, ROSE revealed histiocytes, lymphocytes, multinucleated giant cells and caseous necrosis compatible with granulomatous disease, particularly tuberculosis, so EBUS-MCB was not performed in order to diminish contagious timing in the operating room.

No complications were detected.

Discussion

EBUS-TBNA with ROSE is very useful as a minimally invasive technique to identify etiology among patients with enlarged mediastinal nodes. In case of undiagnosed or inadequate tissue by EBUS-TBNA and ROSE, EBUS-MCB can be an additional procedure to provide bigger tissue pathology safely without having to undergo mediastinoscopy, such as in our case #1.

In case #2, EBUS-MCB helped confirm that there was no cancer in contralateral side of the mediastinal lymph nodes; so the patient was considered to be stage I, which was an operable case.

In case #3, diagnosis was made via EBUS-TBNA and ROSE, so EBUS-MCB was not performed, especially as a case of tuberculosis, to shorten the contagious time in the operating room. There were no complications in any of the 3 cases.

Maturu et al[4] in 2024 conducted a prospective study of patients who underwent EBUS-TBNA for undiagnosed mediastinal lymphadenopathy. Patients in whom ROSE did not yield a diagnosis (non-diagnostic ROSE) or ROSE revealed scanty atypical cells (inadequate ROSE) were subjected to EBUS-MCB. Of the 196 patients undergoing EBUS-TBNA, 32 patients underwent EBUS-MCB. The additional diagnostic yield of EBUS-MCB over EBUS-TBNA was 43.7% (14/32 cases). The material obtained by EBUS-MCB was adequate for ancillary studies. The most common complication observed was a minor bleed in 13 cases.

Poletti V., et al[5] in 2024 reported a retrospective study conducted on 48 patients who underwent both EBUS-TBNA and EBUS-MCB. The overall diagnostic yield of EBUS-MCB surpassed that of EBUS-TBNA (95.8% vs 54%), notably excelling in the diagnosis of sarcoidosis (92.8% vs 78.5%), hyperplastic lymphadenopathy (100% vs 0%), lymphoproliferative disease (100% vs 0%).

No significant differences were observed in the diagnosis of NSCLC and SCLC. Sample obtained through EBUS-MCB facilitated the acquisition of next generation sequencing (NGS) and immunohistochemical analyses more readily, thereby reducing the number of non-diagnostic procedures.

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Chalhoub M, et al6 in 2024; systematic review of EBUS-TBNA and cryobiopsy, proposed that addition of cryobiopsy to EBUS-TBNA offers higher diagnostic yields in both malignant and nonmalignant mediastinal lesions. The procedures can be added to EBUS-TBNA for less than 10 minutes in general and with low complications.

Conclusion

EBUS-MCB is a useful method to provide a minimally invasive evaluation in addition to EBUS-TBNA and ROSE in patients with enlarged mediastinal nodes, with minimal complications in less time. Also this can avoid further investigations such as mediastinoscopy.

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