Case Report

Tract creation with a 25-gauge needle for convex endobronchial ultrasound-guided core biopsy in intrapulmonary lesions adjacent to bronchi: three case reports

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Background: The use of endobronchial ultrasound-guided core biopsy (EBUS-CB) using forceps or cryoprobes to obtain true histological samples has improved the diagnostic yield for mediastinal and hilar lymphadenopathy. Tract creation in the bronchial wall of the central airway is primarily performed using electrocautery devices in EBUS-CB; however, their poor maneuverability and the risk of vascular injury and damage to the tip of the bronchoscope have prevented the application of EBUS-CB for diagnosing intrapulmonary lesions beyond the central locations. This report presents three cases wherein a 25-gauge transbronchial needle aspiration (TBNA) needle with high flexibility and safety was used to create a tract in the bronchial wall for EBUS-CB of the intrapulmonary lesions adjacent to the bronchi.

Case Description: In all cases, EBUS-TBNA using a 25-gauge TBNA needle was performed on the intrapulmonary lesions adjacent to the bronchi, followed by EBUS-CB with 1.9-mm forceps in two cases and also with a 1.1-mm cryoprobe in one case. The EBUS-TBNA specimens revealed no abnormality or only a small number of tumor cells. However, subsequent EBUS-CB, through the tract created by EBUS-TBNA, enabled the collection of a sufficient amount of histological samples with well-preserved histoarchitecture. The histological diagnosis was made via immunostaining, and multigene mutation testing was also successfully analyzed.

Conclusions: The use of a 25-gauge needle for creating a tract allows EBUS-CB for the intrapulmonary lesions and may allow for the collection of sufficient histological samples for biomarker analysis and tissue diagnosis.

Keywords: Case report; endobronchial ultrasound-guided core biopsy (EBUS-CB); endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA); pulmonary lesions; 25-gauge needle

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Introduction

Bronchoscopy is a safe and established modality used for the diagnosis of intrapulmonary lesions with suspected malignancy (1,2). However, obtaining sufficient histological samples from intrapulmonary lesions adjacent to, but not invading, the bronchi is challenging as it requires the collection of tumor cells located beyond the thick bronchial wall (3,4). Endobronchial ultrasound-guided core biopsy (EBUS-CB) performed using forceps or cryoprobes has improved the diagnostic yield for mediastinal and hilar

lymphadenopathy by enabling the collection of adequate histological samples (5-7). An important aspect of EBUS-CB is the creation of a tract that facilitates the biopsy devices to reach the target lesion. Electrocautery devices were used to create a tract in the bronchial wall of the central airway in patients with lymphadenopathy in previous studies (7-9). However, their poor maneuverability and the risk of vascular injury and damage to the tip of the bronchoscope have made the creation of tracts for EBUS-CB in patients with intrapulmonary lesions beyond the central locations challenging (9). The use of EBUS-CB in patients with intrapulmonary lesions beyond the central locations would enable the safe and reliable collection of sufficient histological samples of thoracic malignancies that are suitable for immunohistochemistry and multigene mutation testing using next-generation sequencing (NGS).

This report describes three cases of intrapulmonary lesions adjacent to the bronchi wherein tracts for EBUS-CB were created in the bronchial wall using a 25-gauge transbronchial needle aspiration (TBNA) needle. We present the these in accordance with the CARE reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-23-556/rc).

Case presentation

Case 1

A 73-year-old female was referred to our hospital for the diagnosis of two lesions, one in each of the bilateral lower lobes, observed on computed tomography (CT) images (shown in *Figure 1A*). Bronchoscopy revealed an endobronchial tumor of 29.4-mm occupying and invading the lower lobe of the bronchus in the left lung. Cryobiopsy performed under direct vision led to the histological diagnosis of small cell lung cancer (SCLC). Bronchoscopy was repeated to clarify whether the 20.3-mm intrapulmonary lesion adjacent to the right B8a bronchus had metastasized from SCLC. The convex probe-EBUS (CP-EBUS) scope (BF-UC290F; Olympus, Tokyo, Japan) was inserted into the right B8a bronchus and the lesion adjacent to the bronchus could be detected under EBUS guidance. Tumor invasion into the bronchus was endoscopically not shown (shown in *Figure 1B*). The CP-EBUS scope could barely be inserted into the bronchus; therefore, EBUS-TBNA using a 25-gauge needle (Vizishot2; Olympus, Tokyo, Japan) was performed three times at the same site using endoscopic and EBUS images as reference. The needle tip was retracted just above the bronchial mucosa during EBUS-TBNA puncture, and the puncture site was widened using a combination of angulation and rotation maneuvers. The EBUS-TBNA specimen was confirmed as positive through rapid on-site evaluation (ROSE). Subsequently, EBUS-CB was performed three times via the tract created during EBUS-TBNA using 1.9-mm forceps (FB-211D, Olympus, Tokyo, Japan) (shown in *Figure 1C*). EBUS-TBNA and EBUS-CB caused minimal or no bleeding. The patient was diagnosed with non-small cell lung cancer (NSCLC) in the EBUS-TBNA and EBUS-CB (shown in *Figure 1D*,*1E*, bar: 100 μm) specimens, with partial squamous cell carcinoma features suspicious. The EBUS-TBNA specimens showed only a small amount of tumor cells, while the EBUS-CB specimens showed a sufficient amount of tumor cells. Immunostaining of the EBUS-CB specimen was negative for thyroid transcription factor-1, Napsin A, cytokeratin 5/6, p40, chromogranin A, synaptophysin, and cluster of differentiation 56, the patient was diagnosed with NSCLC not otherwise specified. The patient was diagnosed with double primary cancer, SCLC, and NSCLC, and chemotherapy was initiated for SCLC.

Case 2

Follow-up CT of a 55-year-old male patient who had undergone total thyroidectomy and cervical lymph node dissection for papillary thyroid cancer 15 years previously revealed the presence of multiple bilateral intrapulmonary

Highlight box

Key findings

- We present three cases wherein a 25-gauge transbronchial needle aspiration (TBNA) needle was used to create a tract in the bronchial wall for endobronchial ultrasound-guided core biopsy (EBUS-CB) of the intrapulmonary lesions adjacent to the bronchi.

What is known and what is new?

- EBUS-CB using forceps or cryoprobes for intrapulmonary lesions adjacent to the bronchi remains challenging owing to the difficulty in creating tracts in the bronchial wall using electrocautery devices.
- A 25-gauge needle was used to create a tract for EBUS-CB in the bronchial wall to enable the collection of histological samples from the intrapulmonary lesions adjacent to the bronchi.

What is the implication, and what should change now?

- The use of a 25-gauge needle for EBUS-TBNA to create a tract in the bronchial wall would enable the application of EBUS-CB for the diagnosis of intrapulmonary lesions beyond central locations.

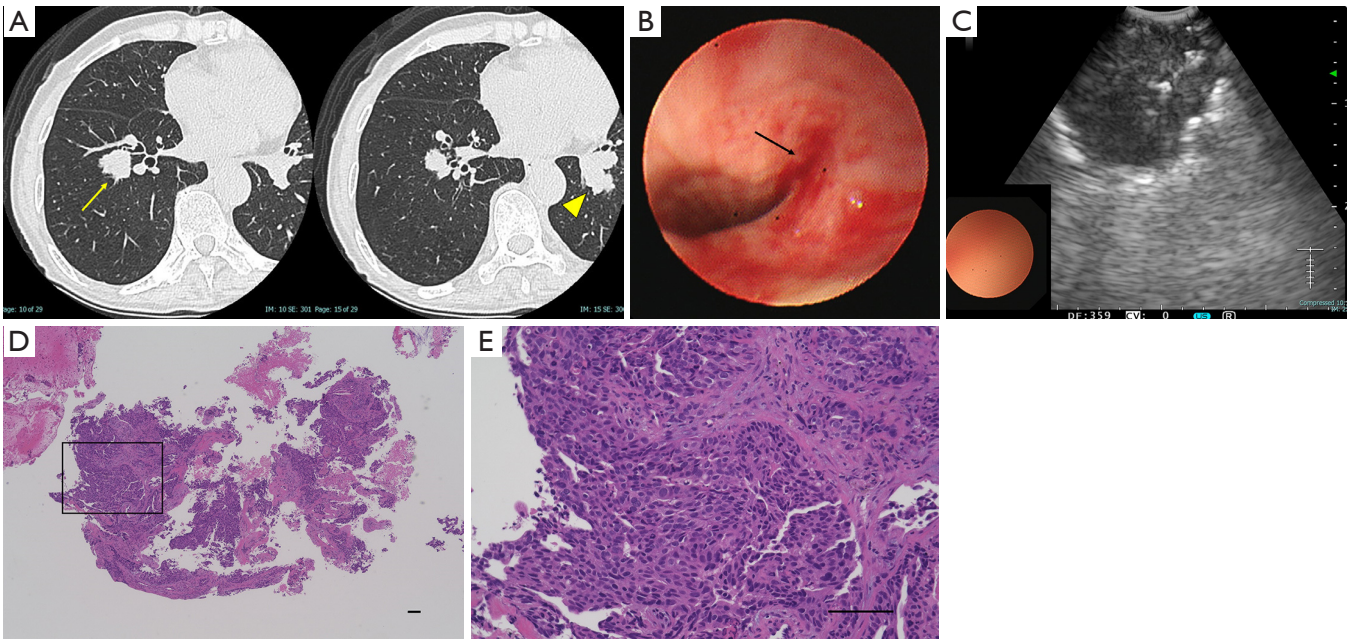

Figure 1 Images of a 73-year-old female with two lesions, one in each of the bilateral lower lobes. (A) Chest CT shows bilateral intrapulmonary lesions. A direct visual biopsy of the left lung lesion (yellow arrowhead) led to the diagnosis of small cell lung cancer. The right lung lesion (yellow arrow) underwent EBUS-TBNA using a 25-gauge needle and EBUS-CB performed using 1.9-mm forceps. (B) Puncture site of EBUS-TBNA and EBUS-CB (arrow) in the right B8a bronchus; tumor invasion into the bronchus was endoscopically not shown. (C) EBUS image acquired during EBUS-CB of the right intrapulmonary lesion. (D,E) Hematoxylin and eosin-staining of the EBUS-CB specimen (bar: 100 μm). A sufficient amount of tumor tissue was collected. Atypical cells with enlarged, irregular but not naked nuclei can be observed, leading to the diagnosis of non-small cell lung cancer. CT, computed tomography; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; CB, core biopsy.

lesions (shown in *Figure 2A*). Pulmonary metastasis of thyroid cancer was suspected. Bronchoscopy with radial EBUS was performed to evaluate the indication of molecular-targeted agents for thyroid cancer at the previous hospital; however, tumor tissue specimens could not be obtained, and the patient was referred to our hospital. Among the multiple lesions, EBUS-CB combined with EBUS-TBNA was performed for a 44.6-mm intrapulmonary lesion adjacent to B8b in the right lower lobe. The CP-EBUS scope (BF-UC290F) was inserted into the right B8b (shown in *Figure 2B*), and the lesion was delineated using EBUS images. The target lesion was adjacent to the third-generation bronchus; therefore, a 25-guage TBNA needle (Vizishot2) was chosen for its flexibility. EBUS-TBNA was performed four times at the same site by manipulating the needle and bronchoscope to widen the puncture site using the endoscopic and EBUS images. Subsequently, EBUS-CB was performed five times via the created tract in the bronchial wall using 1.9-mm forceps (FB-211D) (shown in *Figure 2C*). Both EBUS-TBNA and EBUS-CB specimens were positive in the ROSE. Although the EBUS-TBNA samples revealed a small number of tumor cells with blood contamination and crush artifacts, the tumor tissue volume was insufficient for multigene mutation testing. In contrast, less damaged papillary growth of tumor cells with enlarged nuclei was observed in the EBUS-CB samples (shown in *Figure 2D,2E*, bar: 100 μm). Immunostaining was positive for paired box gene 8, and the patient was diagnosed with pulmonary metastasis of papillary thyroid cancer. NGS analysis performed using the Oncomine Dx Target Test Multi-CDx system (Thermo Fisher Scientific) was successfully assessed and revealed positivity in *BRAF* V600E mutation.

Case 3

Contrast-enhanced CT revealed the fusion of the primary tumor and hilar lymph nodes and the formation of a necrotic

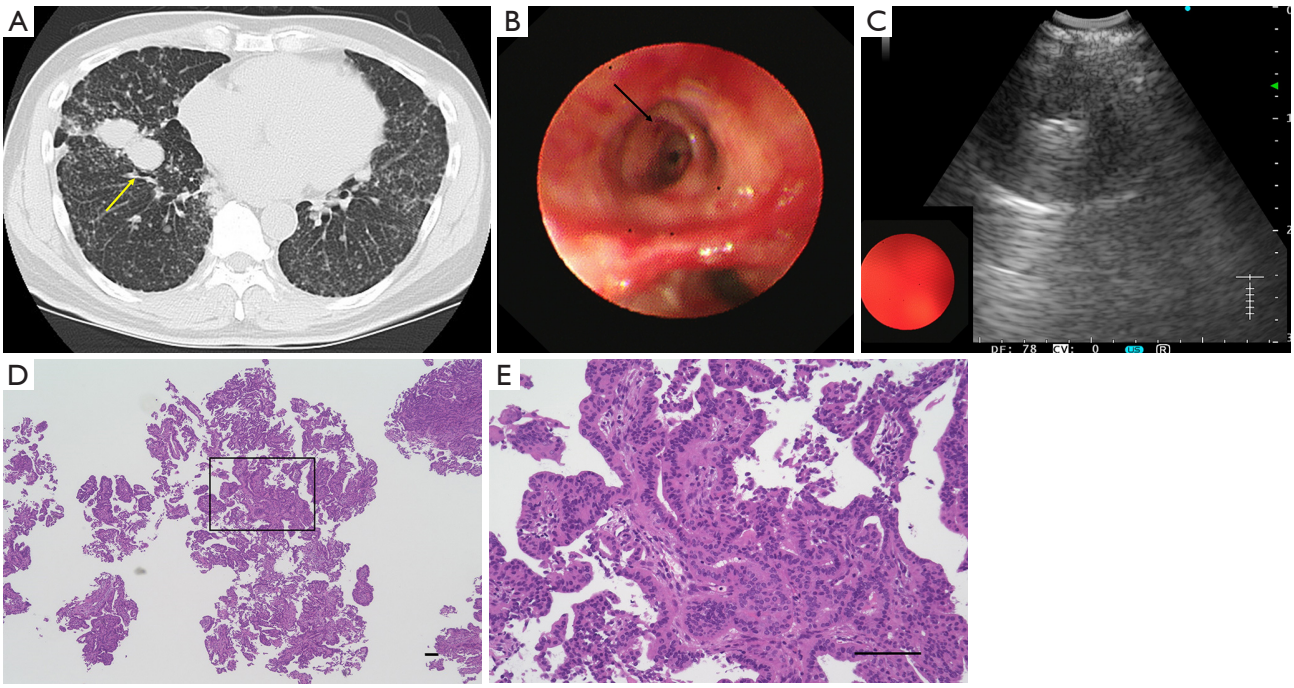

Figure 2 Images of a 55-year-old male patient who had undergone total thyroidectomy and cervical lymph node dissection for thyroid cancer. (A) Chest CT shows intrapulmonary lesion adjacent to the bronchus in the right lower lobe (yellow arrow) and multiple intrapulmonary lesions. (B) The small puncture site of EBUS-TBNA performed using a 25-gauge needle and EBUS-CB (arrow) can be observed in the right B8b bronchus. (C) EBUS image reveal a 1.9-mm forceps tip within the right intrapulmonary lesion during EBUS-CB. (D,E) Hematoxylin and eosin-staining of EBUS-CB specimen (bar: 100 μm). Atypical cells with enlarged nuclei can be observed in the papillary growth, leading to the diagnosis of lung metastasis of thyroid cancer via immunostaining. CT, computed tomography; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; CB, core biopsy.

mass in a 72-year-old male undergoing chemotherapy for advanced-stage lung adenocarcinoma of the right lower lobe (shown in *Figure 3A*). Bronchoscopy was performed using a CP-EBUS scope (BF-UC290F) to collect tumor tissue specimens for NGS analysis. The entrance of the basal bronchus was narrowed due to the enlarged tumor and lymphadenopathy; however, no obvious invasion of the tumor into the bronchial mucosa was observed. The primary tumor and #11Ri were visualized as a single necrotic lesion on EBUS images. The bronchial artery was also detected in the immediate vicinity of the lesion on EBUS power/color Doppler mode imaging. EBUS-TBNA was performed three times with a 25-gauge needle to avoid puncturing the bronchial artery while creating the tract (shown in *Figure 3B*). The EBUS-TBNA specimens tested positive for ROSE. EBUS-CB was performed three times using a 1.1-mm cryoprobe (Erbe Elektromedizin GmbH, Tuebingen, Germany), and the freezing time was set to 5–7 s (shown in *Figure 3C*). Mild bleeding, which was stopped via endoscopic suction, was observed. The size of the entrance of the tract into the lesion was set to the minimal pinhole size (shown in *Figure 3D*). A diagnosis could not be made using the EBUS-TBNA specimens owing to their limited size, the presence of necrosis, and poorly preserved histoarchitecture. In contrast, the EBUS-CB specimens led to the diagnosis of adenocarcinoma (shown in *Figure 3E,3F*, bar: 100 μm). The EBUS-CB specimens contained necrotic and inflammatory material; however, a size of at least 4.0 mm^2, well-preserved tissue architecture, and a tumor content of approximately 30% led to successful NGS analysis using the Oncomine Dx Target Test Multi-CDx system analysis. However, no genetic mutations were found.

No serious complications occurred in any of the cases, and the patients were discharged the day after the examination, allowing prompt introduction of treatment. Furthermore, the scope tip was not damaged in any of the cases.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study

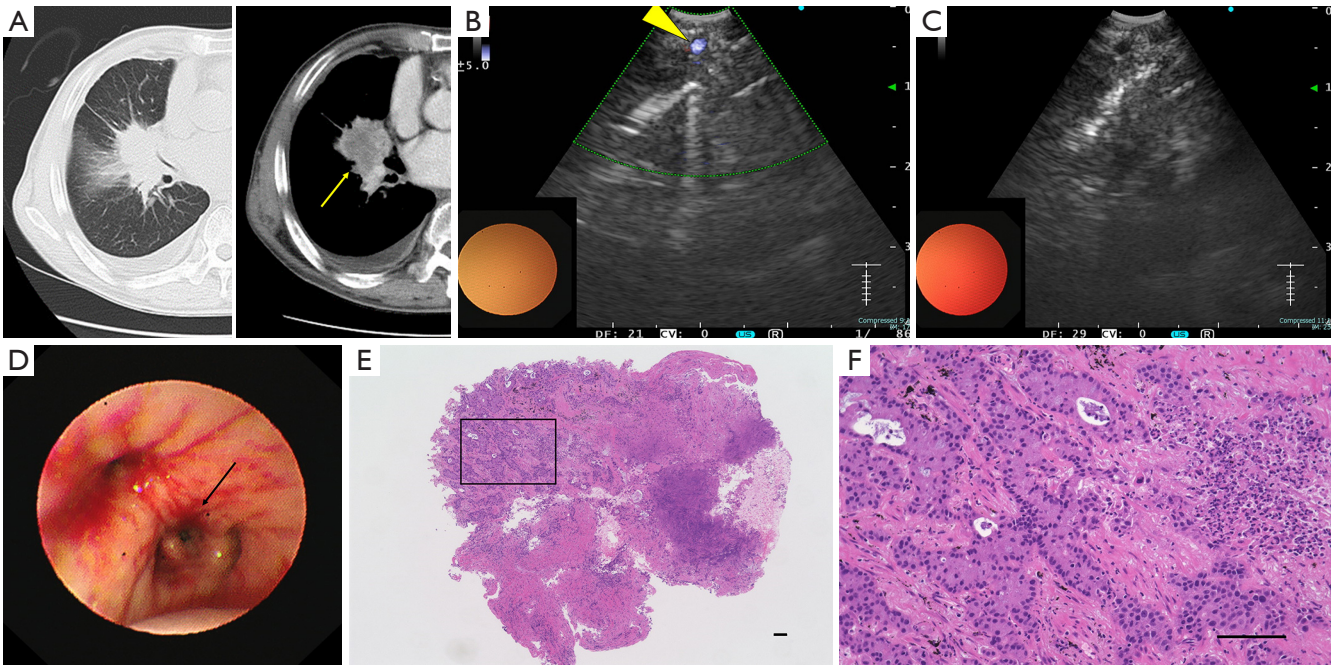

Figure 3 Images of a 72-year-old male undergoing chemotherapy for advanced-stage lung adenocarcinoma of the right lower lobe. (A) The tumor in the right lower lobe and #11Ri lymph nodes can be observed as one necrotic mass on chest CT (yellow arrow). (B,C) EBUS images during EBUS-TBNA with a 25-gauge needle and EBUS-CB with a 1.1-mm cryoprobe. The bronchial artery (yellow arrow) is shown on the EBUS power/color Doppler-mode image, and the puncture is made to avoid it in both EBUS-TBNA and EBUS-CB. (D) Minute puncture site (arrow) is seen in the bronchi of the middle and lower lobes. There is no obvious invasion of the tumor into the bronchial mucosa. (E,F) Hematoxylin and eosin-staining of EBUS-CB specimen (bar: 100 μm). A poorly differentiated adenocarcinoma with necrosis and inflammatory cell infiltration can be observed. CT, computed tomography; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; CB, core biopsy.

was approved by the Ethical Committee of Osaka City University Graduate School of Medicine (approval No. 4364). Written informed consent was obtained from the patients for the publication of this case report and the accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

EBUS-TBNA was performed with a 25-gauge needle to create a tract for EBUS-CB in three patients with intrapulmonary lesions adjacent to the bronchi in the present report. EBUS-CB have performed using forceps or cryoprobes in the histological diagnosis and NGS analysis in patients with mediastinal and hilar lymphadenopathy. However, it is difficult to perform in patients with intrapulmonary lesions owing to the inability to create tracts in the bronchial wall in the narrow and limited peripheral bronchial area during electrocautery incisions. There have been reports of tract creation for EBUS-CB using 19- to 22-gauge needles (10,11). However, the 25-gauge EBUS-TBNA needle with high flexibility and safety than 22 gauge or thicker needles (12) allows for safe tracking in the peripheral bronchial area, and may allow for the addition of EBUS-CB in diagnosing intrapulmonary lesions that have not invaded the bronchi or airway. Specifically, although the 25-gauge needle yields a smaller specimen volume than the 22-gauge needle (13), EBUS-TBNA with a 25-gauge needle allows safer tract creation in more peripheral intrapulmonary lesions for EBUS-CB.

EBUS-CB, which was developed for the diagnosis of mediastinal and hilar lymphadenopathy, was used to diagnose intrapulmonary lesions in the present three cases. The diagnostic yield of conventional bronchoscopy performed using forceps, aspiration needles, and cryoprobes has been limited for diagnosing

intrapulmonary lesions adjacent to the segmental and subsegmental bronchi owing to the requirement for collecting tumor cells beyond the bronchial wall and the absence of real-time echo guidance (14-17). On the other hand, performing EBUS-CB for intrapulmonary lesions, which requires the tract creation into the lesion, is difficult due to the low maneuverability of electrocautery devices under the limited endoscopic field of view in second-generation or subsequent bronchi. A tract leading to the intrapulmonary lesion was created using a 25-gauge needle in addition to performing a combination of angulation and rotation maneuvers during the needle stroke to widen the puncture site of EBUS-TBNA, called the "spiral digging technique", in the present study (18). The spiral digging technique did not result in the incidence of TBNA needle breakage or other complications in any of the cases. In all of the present cases, forceps or cryoprobe could be smoothly inserted after EBUS-TBNA; however, difficult insertion can be mitigated by additional EBUS-TBNA, biting the insertion site with forceps, or a second surgeon pushing the scope during insertion could facilitate forceps or cryoprobe insertion. The flexible 25-gauge EBUS-TBNA needle, as a tract-creation device for EBUS-CB, could overcome the weaknesses of electrocautery incisions, such as low maneuverability and the risk of vascular injury and damage to the CP-EBUS scope tip (as in case 3). In addition, this technique can be easily introduced and used as an extension of the conventional EBUS-TBNA procedure, even by clinicians who are not experts in the field of bronchoscopy, unlike previous techniques that used an electrocautery device to incise the bronchial wall.

Adequate tissue specimens must be obtained to estimate the histological type of thoracic malignancies, assess programmed death ligand 1 expression, and perform multigene mutation testing (19). The specimens obtained via EBUS-TBNA using a 25-gauge needle were small and showed considerable contamination in all three cases in the present report. In contrast, specimens obtained via the subsequent EBUS-CB contained sufficient tumor tissue for immunostaining and NGS analysis. EBUS-TBNA for peripheral intrapulmonary lesions has been shown to have a higher diagnostic yield than EBUS-guided transbronchial biopsy (20). However, previous studies have reported that samples obtained from lymphadenopathy using EBUS-CB are of higher quality than those obtained using EBUS-TBNA (21). Furthermore, compared with EBUS-TBNA alone, EBUS-CB has been shown to improve the suitability of tissue samples for molecular and immunological analysis of NSCLC (22). Creating a tract with a 25-gauge needle during EBUS-TBNA and performing EBUS-CB subsequently would enable a sufficient amount of high-quality tumor samples to be obtained, and the biopsy site can be adjusted to be within the lesion to avoid large vessels and necrotic components and collect tissue specimens from areas with more active tumor cells based on intraoperative ultrasound appearance and rapid on-site cytological evaluation results. Thus, the combination of a 25-gauge needle for EBUS-TBNA and subsequent EBUS-CB may be one of the preferred biopsy techniques that aid in treatment decision-making for thoracic malignancies located adjacent to the bronchi.

The recently launched CP-EBUS scope has a smaller probe tip (6.6-mm) and greater upward angulation range compared with that of the conventional scope. The thin CP-EBUS scope can be inserted into the upper and lower subsegmental bronchi, which is difficult to perform using a conventional CP-EBUS scope (23). In our cases, a thin CP-EBUS scope was used to perform EBUS-TBNA and EBUS-CB on intrapulmonary lesions. Additionally, in combination with a flexible 25-gauge needle, the scope maintained good maneuverability even in narrow and restricted bronchial areas and enabled tract creation for EBUS-CB. Notably, a thinner CP-EBUS scope with a 5.9-mm tip is currently under development (24), which can be inserted up to the fourth-generation bronchus, but can only fit up to a 25-gauge needle given the small 1.7-mm working channel of the scope. However, by performing EBUS-TBNA with a 25-gauge needle for tract creation, as in the present case report, the thinner CP-EBUS scope may enable clinicians to perform subsequent EBUS-CB with a 1.1-mm cryoprobe of more peripheral peribronchial lesions and overcome the inability to use a 22-gauge needle. Compared with forceps biopsy, cryobiopsy has been shown to have better diagnostic results without major complications (25). Accordingly, EBUS-CB using a 1.1 mm cryoprobe with a thinner CP-EBUS scope that has a narrow 5.9 mm tip may facilitate the diagnosis of more peripheral intrapulmonary lesions.

Finally, a limitation of this case report is that it is based on only three reported cases, and it is uncertain whether the findings can be applied to all cases.

Conclusions

The use of a 25-gauge needle for EBUS-TBNA to create a tract in the bronchial wall would enable the application of EBUS-CB for the diagnosis of intrapulmonary lesions

beyond central locations.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-23-556/rc

Peer Review File: Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-23-556/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-23-556/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethical Committee of Osaka City University Graduate School of Medicine (Approval No. 4364). Written informed consent was obtained from the patients for the publication of this case report and the accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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