



## Case report

# Combined pleuroscopy and endobronchial ultrasound for diagnosis and staging of suspected lung cancer

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## ABSTRACT

The standard approach to staging of lung cancer in patients with pleural effusion (clinical M1a) is thoracentesis followed by pleural biopsies if the cytologic analysis is negative. If pleural biopsy findings are negative, endobronchial ultrasound-guided transbronchial needle aspiration is used to complete the staging process and, in some cases, obtain diagnosis. In this case series we report 7 patients in which a combined procedure was performed for staging of known or suspected lung cancer. We found that the combined approach was both feasible and safe in this case series.

## 1. Introduction

The major determinant of prognosis and treatment in patients with non-small cell lung cancer (NSCLC) is disease stage, as defined by the International Association for the Study of Lung Cancer (IASLC) [1]. Therefore, when lung cancer is suspected, both tissue diagnosis and staging information are required for treatment decisions. To minimize the risks and costs of multiple procedures, the most appropriate site from which to obtain the initial biopsy should be one that will determine the highest disease stage, as long as it carries an acceptable risk.

In a patient with suspected or confirmed NSCLC and a pleural effusion, confirming the presence of malignant cells in the pleural space critical since this represents the highest disease stage (M1a, stage IV). Unfortunately, cytology findings obtained with thoracentesis are diagnostic for malignancy in only about 40% to 60% of cases, and a second sample only slightly increases this yield [2]. Hence, when pleural fluid cytology is not diagnostic, pleuroscopic pleural biopsies can be very useful, with an estimated sensitivity of 95% for pleural malignancies [3]. If pleural biopsies confirm metastasis, further mediastinal staging is obviated. However, if pleural metastases are not confirmed, and the patient has an indication for mediastinal staging, usually a minimally invasive needle technique such as endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) or combined

EBUS–endoscopic ultrasound-guided–TBNA, are recommended by most guidelines [4,5].

Both EBUS-TBNA and pleuroscopy are well-tolerated procedures with low risk of complications [6]. Performing a pleuroscopy with rapid on-site evaluation (ROSE) of pleural biopsy specimens, may provide useful information for the proceduralist in patients with suspected NSCLC and suspected malignant pleural effusions (stage M1a). If ROSE does not confirm malignancy, mediastinal staging with EBUS-TBNA can be performed in the same setting, potentially expediting patient care. Performing pleuroscopy followed by EBUS-TBNA in a single procedure setting has clear logistical advantages, but reports of consecutive pleuroscopy and EBUS-TBNA in the same setting are not available. The main objective of this case series was to investigate the feasibility of combining pleuroscopy and EBUS-TBNA for diagnosing and staging of lung cancer. Institutional review board approval was obtained from the Institutional Review Board with protocol number PA17-0705.

## 2. Case reports

With the exception of one patient, all underwent at least one thoracentesis, with findings of exudative pleural effusion negative for malignancy. In all cases pleuroscopy was performed first and revealed no tumor studding on visual assessment. ROSE of touch preparations were negative for malignancy. Once pleuroscopy was completed, EBUS-

Abbreviations: EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; NSCLC, non-small cell lung cancer; ROSE, rapid on-site evaluation

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**Table 1**  
Summary of patients that underwent combined pleuroscopy with EBUS-TBNA.

Patient	Age/gender	Pre-procedure diagnosis	Pre-procedure stage	Tumor studding	Post-procedure diagnosis	Post-procedure stage
1	74/M	NSCLC	T2aN1M1a	No	NSCLC	T2aN1M0
2	76/F	NSCLC	T2bN0M1a	No	NSCLC	T2bN0M0
3	71/M	NSCLC	T3N2M1a	No	NSCLC	T3N2M0
4	60/M	SCLC	Limited SCLC	No	Recurrent SCLC	Limited SCLC
5	60/M	NSCLC	T3N0M1a	No	Sarcoma on EBUS-TBNA	Sarcoma no pleural involvement
6	53/F	Suspected NSCLC	T2bN1M1a	No	Lymphoma on EBUS-TBNA	Lymphoma no pleural involvement
7	58/M	NSCLC recurrence	T2aN2M1a	No	Recurrence on EBUS-TBNA	Recurrence, no pleural involvement

TBNA was performed to assess the mediastinum. The final stage is based on final histopathology results of pleuroscopy and EBUS-TBNA. Table 1 provides a summary of the findings.

### 2.1. Case 1

A 74-year-old male with newly diagnosed left lung mass (T2a), left hilar adenopathy (N1), and left-sided pleural effusion (M1a) had clinical stage IV disease. The final stage was T2aN1M0 (IIa).

### 2.2. Case 2

A 76-year-old female with newly diagnosed right lower lobe adenocarcinoma (T2b), no hilar or mediastinal lymphadenopathy (N0), and pleural effusion (M1a) had clinical stage IV disease. The final stage was T2bN0M0 (IIa).

### 2.3. Case 3

A 71-year-old male with newly diagnosed left upper lobe squamous cell carcinoma (T3), left paratracheal and hilar lymphadenopathy (N2), and pleural effusion (M1a) had clinical stage IV disease. The patient refused thoracentesis and requested the highest sensitivity procedure. The final stage was T3N2M0 (IIIa).

### 2.4. Case 4

A 60-year-old male had limited small cell lung cancer that developed pleural effusion and progression of mediastinal lymphadenopathy while on chemotherapy. Patient underwent the procedures for determination of radiation field. The final diagnosis was consistent with progression of small cell lung cancer, and the final pathological findings from pleuroscopy were negative for malignancy.

### 2.5. Case 5

A 60-year-old male with newly diagnosed large right lung mass suggestive of primary lung cancer (T3), no hilar or mediastinal lymphadenopathy (N0), and new pleural effusion (M1a) had clinical stage IV disease. The patient was diagnosed as having sarcoma on EBUS-TBNA of the mass.

### 2.6. Case 6

A 53-year-old female with newly diagnosed right pleural effusion and a right hilar mass suggestive of primary lung cancer (T2b) had clinical stage IV lung cancer. The patient was found to have B-cell lymphoma on EBUS-TBNA of the mass.

### 2.7. Case 7

A 58-year-old male with a history of stage IIB adenocarcinoma, who had undergone neoadjuvant chemoradiotherapy with plan for surgery, developed new pleural effusion and new subcarinal lymphadenopathy

and was referred for restaging. The patient was found to have recurrence of lymphadenopathy in a subcarinal lymph node.

The pleuroscopy was performed first under monitored anesthesia care (MAC) sedation with propofol infusion. Oxygenation was maintained with a non-rebreather facemask. The sedation was then deepened and muscle relaxation was provided as per anesthesia practice at our institution. A laryngeal mask airway was then inserted under general anesthesia for the duration of EBUS. The mean anesthesia period for both procedures was  $127 \pm 46.6$  minutes (range, 66–234 minutes). There were no procedure or anesthesia-related complications, and all patients except one were discharged home on the same day in stable condition.

## 3. Discussion

To our knowledge, this is the first case series to demonstrate the feasibility of combining pleuroscopy with EBUS-TBNA for diagnosis and staging of known or suspected lung cancer. We had no procedure or anesthesia-related complications.

Pleuroscopy is the procedure of choice for patients with known or suspected lung cancer and pleural effusion suggestive of malignancy, particularly when thoracentesis is not diagnostic. If pleuroscopic biopsies rule out malignancy, EBUS-TBNA can be performed in the same session for mediastinal staging. Based on our findings, the combined approach is well tolerated and appears to be highly accurate in providing complete diagnostic and staging information required for choosing optimal treatment which in select patients may expedite the time to treatment.

The availability of ROSE touch preparations is key to the successful implementation of this strategy of combined staging (pleuroscopy with EBUS-TBNA). Combined staging does appear to be associated with a longer sedation time since it includes a combination of procedures, but it did not seem to be associated with any adverse outcomes in this small series. From the patient's perspective, combining procedures may alleviate some of the anxiety associated with waiting for a final diagnosis from separate procedures and the associated delay in starting definitive cancer treatment. However, the reliability of visual assessment of the pleura and intraoperatively obtained ROSE touch preparations to exclude malignant pleural involvement is unclear since there is not enough evidence to show how well either one performs in this setting. Visual assessment of the pleura at the time of pleuroscopy is not that effective in discriminating between benign and malignant pleural abnormalities. In a survey of 16 centers that performed up to 10 pleuroscopies per month, direct visual assessment correctly diagnosed malignant or benign disease in 12 (59.3%, SD 2.5) out of 20 patients [7]. ROSE of pleural biopsy samples performs better in this setting, with a recent study by Porfyrides et al., concluding that ROSE during pleuroscopy had a sensitivity of 79%, a specificity of 94%, a diagnostic accuracy of 88%, a positive predictive value of 90%, and a negative predictive value of 87% [8]. A limitation of this study is that suspicious findings and inadequate findings were collapsed into just two categories, malignant and benign, resulting in a loss of information with decreased discriminatory function. Given these caveats, although diagnostic accuracy seems high with ROSE touch preparations and the

pleuroscopy significantly increases the probability of detecting malignancy, it probably should not be used to make definitive treatment decisions prior to final pathologic confirmation. Our findings however suggest that a negative pleuroscopy with ROSE touch preparation analysis does provide enough reassurance to proceed with a low risk procedure like EBUS-TBNA for mediastinal staging.

One of the main limitations of this study in addition to small sample size, is that the retrospective nature of this series meant that those patients who underwent pleuroscopy and were positive for malignancy on touch preparations never underwent EBUS and as such were not included. As such, possible false positives on touch preparation analysis might have been systematically missed.

In conclusion, a combined staging approach with pleuroscopy followed by EBUS-TBNA is feasible and should be considered in patients with suspected M1a lung cancer. Further studies are needed to assess the negative predictive value of pleuroscopic visual assessment and ROSE of biopsy samples since performing EBUS in these patients is predicated on those findings.

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#### Conflict of interest

The authors have no conflict of interest to disclose.

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