Flex-rigid Pleuroscopy Under Local Anesthesia in Patients with Dry Pleural Dissemination on Radiography

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Objective: Medical thoracoscopy using a flex-rigid pleuroscope under local anesthesia is a recent diagnostic procedure for malignant pleural disease. Although most previous studies have reported its usefulness, especially in wet pleural dissemination, the feasibility of flex-rigid pleuroscopy in patients with dry pleural dissemination is not well established. We assessed the diagnostic performance of flex-rigid pleuroscopy under local anesthesia in patients suspected of dry pleural dissemination on radiography.

Methods: The pleuroscopic parameters of all patients (n = 56) who underwent flex-rigid pleuroscopy at the National Cancer Center Hospital from October 2011 to September 2013 were retrospectively reviewed. Those with computed tomography findings of asymmetric pleural thickening or pleural nodules without pleural effusion (dry group, n = 16) were compared with the remaining patients with pleural effusion (wet group).

Results: The dry group consisted of eight men and eight women, with a median age of 61 years (range, 48–79 years). The definitive diagnoses were adenocarcinoma (n = 10), mesothelioma (n = 2) and chronic inflammation (n = 3). The diagnostic accuracy was 93.8% (15/16). Only two minor complications were observed: mild chest pain (n = 1) and transient hypoxia (n = 1). No major complications such as pneumothorax were observed. The mean duration of post-operative chest tube drainage in the dry group was 2.31 ± 2.26 days. Complications, operation duration and diagnostic accuracy did not statistically differ between the two groups.

Conclusions: Flex-rigid pleuroscopy under local anesthesia can be a well-tolerated diagnostic procedure for radiographic dry pleural dissemination with respect to diagnostic yield and complications.

Key words: flex-rigid pleuroscopy – dry pleural dissemination – local anesthesia – pleural effusion

INTRODUCTION

Thoracoscopy has been established as an indispensable tool for the diagnosis and treatment of respiratory disease. Recently, flex-rigid pleuroscopy under local anesthesia had been used successfully for pleural diseases (1−7). The instrument is easy to manipulate and covers a wider endoscopic field because the handle is similar in design to a standard flexible bronchoscope. Although most previous studies have shown its efficacy, particularly in cases with pleural effusion, the feasibility of the procedure in patients without effusion is not known or has not been reported.

The British Thoracic Society (BTS) guidelines on pleural diseases recommended that local anesthesia should generally be undertaken only for patients with radiologically confirmed pleural effusion (8). Most patients suspected to have pleural dissemination with pleural effusion undergo thoracentesis for diagnosis, but pleural lesions without pleural effusion are sometimes encountered, and referred to as dry pleural dissemination (DPD) (9). In these patients, we cannot perform thoracentesis, and the diagnostic tool is limited to thoracoscopy.

The main treatment for patients with Stage IV non-small cell lung carcinoma (NSCLC) with good performance status...
is chemotherapy (10–12); for non-squamous NSCLC, choosing the optimal first line therapy necessitates molecular genetic analyses, including epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) (13–15). Obtaining an adequate tissue sample from the most accessible site (for example, the pleural lesion) is important for this purpose.

Herein, we assessed the diagnostic performance of flexible pleuroscopy under local anesthesia in patients suspected of DPD from radiological findings in comparison to its performance in patients with pleural dissemination with effusion.

PATIENTS AND METHODS

CASE SELECTION

This was a single-center retrospective study of 56 patients who underwent flex-rigid pleuroscopy at our institution from October 2011 to September 2013. All were suspected to have pleural dissemination and the indications for the procedure were either for diagnosis, staging or re-biopsy. Forty patients presented with pleural effusion (wet group), while 16 patients had asymmetric pleural thickening, pleural nodules or fissural nodules without pleural effusion on computed tomography (CT) (dry group). We used the information about Fluorine-18-fluorodeoxyglucose positron emission tomography (F-18 FDG PET/CT) as the selection of dry group. Fig. 1 shows a representative case of DPD in Dry group. This study was approved by the Institutional Review Board, and informed consent was obtained from all patients.

REVIEW OF CT AND F-18 FDG PET/CT IMAGING

All patients underwent a CT scan (Aquilion, X-Vigor, or TCT-900S; Toshiba, Tokyo, Japan) prior to the procedure, performed with 1.0 to 5.0 mm collimation from the level of the supraclavicular region to the diaphragm. Images were reviewed and analyzed by two doctors (Y.W. and S.S.) with standard mediastinal window and lung window settings. The variables noted were: location of the primary lesion, the presence of intrapulmonary nodules other than the primary lesion, uneven pleural thickening, fissural nodules, nodules abutting the pleura or the fissure of a primary lung lesion and lymph node swelling. F-18 FDG PET/CT was performed with a PET/CT scanner (Discovery 600M; General Electric Company, Schenectady, NY, USA). We analyzed the presence of FDG uptake on pleural, pleural or fissural nodules and hilar or mediastinal lymph node.

INSTRUMENTS

The instrument employed was a flex-rigid pleuroscope (LTF-260; Olympus, Tokyo, Japan) with an external diameter of 7 mm at the distal flexible portion and a 2.8 mm diameter working channel that accommodates biopsy forceps and other devices. The distal tip is bendable in one plane, with upward and downward angulations of 160°.

The insulated-tip diathermic knife 2 (IT-2: KD-611L; Olympus) was originally designed to minimize the risk of gastric wall perforation during endoscopic submucosal resection (16). It consists of conventional diathermic knife, three short blades and insulated ceramic tip; the outer diameter is 2.2 mm and the length of the needle knife is 4 mm. This device was used in 16 cases of our study population that had dense and thick pleura.

PRE-PROCEDURE

At our institution, cardiopulmonary dysfunction, a coagulation disorder, severe disturbance of respiratory function in the contralateral lung, severe hypoxemia and severe pleural adhesions were contraindications to flex-rigid pleuroscopy under local anesthesia. The pre-operative evaluation involved a detailed history and physical examination, and ancillary tests included a complete blood count, coagulation studies, electrocardiogram, arterial blood gas analysis, percutaneous oxymetry and a pulmonary function test.

In addition to decubitus chest radiographs and chest CT scans, linear-type ultrasonography was used to aid in the selection of an appropriate entry site. Particularly in the dry group, we identified mobility between the parietal and visceral pleura during breathing to ensure that there were no adhesions that could cause damage to the lung parenchyma during insertion of the trocar.

We used an intravenous drip of 15 mg pentazocine diluted in 50 ml saline as a pre-medication.

PROCEDURE

All procedures were performed in the operating room by one expert pulmonologist and two assistants. A single puncture technique was used. The patient was placed in the lateral decubitus position with the diseased side facing upward. After local anesthesia containing 1% lidocaine was administered, a 1–2 cm incision was performed, followed by blunt dissection through the muscle layers of the chest wall until the parietal pleura was exposed. During this procedure, we delivered anesthesia to the subcutaneous and muscle layers adequately. Upon reaching the parietal pleura, we gently stripped it off using a Kocher clamp to avoid injury to the closely apposed visceral pleura. After dissection of the parietal pleura and confirmation of collapse of the affected lung, a disposable flexible trocar (8 mm inner diameter) was inserted carefully, and inspection using the flex-rigid pleuroscope was commenced. Upon confirming the location of the pleural lesion, local anesthesia was administered by a subpleural injection (NM-9L-1 needle; Olympus) of saline containing 0.5% lidocaine and 0.005% epinephrine before taking a biopsy using standard flexible forceps (SFF: FB-55CR-1; Olympus).

We used the IT-2 for pleural tissues that were difficult to grasp using SFF. Local anesthesia was administered similarly
to the method described above; but this time, a pleural bulge was created. Following this, a pinhole was made through the bulge using coagulation forceps (FD-6C-1; Olympus). The tip of the IT-2 was inserted into the hole, and then a circular incision was performed through the full thickness of the affected pleura using ENDO-CUT mode electric current at 30–40 W (ICC200; ERBE, Tubingen, Germany). The incised pleura were carefully removed with SFF.

Pleuroscopic specimens obtained using SFF and the IT-2 were fixed in formalin. The pathological findings were independently obtained by two pathologists (K.T. and A.Y.). If the specimens revealed specific findings for a definitive diagnosis, we judged the procedure as successful.

After the examination, the flexible trocar was removed and the procedure was completed by inserting a 20- to 24-Fr double lumen chest tube for drainage.

**Figure 1.** (A) Pre-operative chest radiograph shows an abnormal shadow on left upper lung field without pleural effusion. (B) Chest computed tomography indicating solid nodule with spiculation in left upper lobe and multiple small nodules within major fissures on the left side. (C) Pleuroscopic image showing nodular lesions in the parietal pleura. (D) Biopsy specimen of pleura diagnosed as adenocarcinoma with irregular ductal formulation (H&E stain, ×20).

**STATISTICAL ANALYSIS**

The statistical analysis was performed using SPSS 12.0 for Windows (SPSS, Chicago, IL, USA). Student’s t-tests were used for continuous variables, and χ² tests or Fisher’s exact tests were used for dichotomous variables. Statistical significance was defined as P < 0.05.

**RESULTS**

**PATIENT CHARACTERISTICS**

The baseline characteristics of all the patients are shown in Table 1; further details of the characteristics of the dry group are shown in Table 2. The patients in the dry group (n = 16) had an equal gender distribution with a median age of
61 years (range, 48–79 years). None of the cases had a history of prior thoracentesis or thoracotomy. The majority of the pleuroscopy procedures were performed for both diagnostic and staging purposes. Minimal pleural adhesions were noted in three cases. The overall diagnostic accuracy was 93.8% (15/16). Eighty percent of dry group cases were malignant in etiology, and included adenocarcinoma from primary lung cancer (83%) and malignant pleural mesothelioma (MPM) (17%). The other one case which was diagnosed as suspected of MPM was subsequently performed pleural re-biopsy under general anesthesia and received a definitive diagnosis of MPM.

The mean operation duration was 55.3 ± 15.4 min. Only two cases had minor complications: transient hypoxia and mild chest pain. There were no major complications such as intrathoracic hemorrhage, re-expansion pulmonary edema or procedure-related death. Drainage by chest tube was continued for a mean duration of 2.31 ± 2.26 days, and in 69% (11/16) of the cases, the chest tube was removed on post-operative Day 1. The additional use of the IT-2 for biopsy was superior to SFF alone in 3 of 16 patients (MPM in 2 and chronic inflammation in 1).

In comparison to the wet group (Table 1), the dry group did not statistically differ in terms of diagnostic accuracy, operation duration, or complications.

CT AND FDG PET/CT FINDINGS

Among 16 Dry group cases, pre-operative PET-CT was performed in 13 cases. Among these 13 cases, FDG uptake of pleura or pleural nodules was detected in only 2 case and the other 11 cases had no findings of SUV uptake of pleura or pleural nodules. There were no Dry group cases with FDG uptake of fissural nodules and hilar or mediastinal lymph node.

The chest CT findings (Table 3) of patients with DPD from lung adenocarcinoma (n = 10) were as follows: presence of intrapulmonary nodule(s) other than the primary lesion in 6 (60%), uneven pleural thickening in 7 (70%), fissural nodules in 10 (100%), and a nodule abutting the pleura or the fissure of the primary lesion in 10 (100%). There was only one case of lymph node swelling located in the subclavian region, no other lymph node (including hilar or mediastinal lymph node) swelling was noted. Among these 10 DPD cases, 8 cases were performed pre-operative PET/CT, and FDG uptake of pleural lesion was detected in only one case (12.5%).

DISCUSSION

Flex-rigid pleuroscopy under local anesthesia has been reported to be a valuable and safe procedure for pleural diseases, with complication rates of only 1.5–10.5 percent (2). However, these results were from cases with pleural effusion, and there have been no reports on cases without pleural effusion. In this study, we assessed the diagnostic performance of
Carcinoma. The differential diagnoses for such findings are consistent with our cases in the dry group of lung adenocarcinoma (9, 18). To increase diagnostic accuracy of dry pleural nodules (18), histological pleuroscopic diagnosis remains mandatory before planning treatment for the cases suspected of DPD.

For MPM patients, pleural effusion is usually an early clinical sign; (27) however, tissue sampling by pleuroscopy could be performed at an even earlier stage when effusion is not yet present. In fact, MPM patients who underwent treatment with curative intent in the early stages of the disease had relatively better survival rates (28–30). Therefore, diagnosis in the early stages is important, especially in cases of suspected MPM without pleural effusion. In addition, a detailed history and meticulous assessment of CT and PET/CT findings are likewise necessary for suspected MPM cases.

In addition to the aforementioned advantages, the remaining issues include the diagnostic accuracy and safety of performing flex-rigid pleuroscopy under local anesthesia for DPD. Our results show that the overall diagnostic accuracy was 93.8% (15/16), and no significant difference was observed between the dry and wet groups. To increase diagnostic accuracy, we used the IT-2 in combination with SFF for cases that had severe pleural thickening (3, 31, 32). Furthermore, a recent report concluded that the diagnostic yield was similar between rigid and flex-rigid pleuroscopy if a pleural biopsy could be successfully performed (33). In our study, there were 3 cases undiagnosed by SFF alone that were successfully diagnosed by using the IT-2. Therefore, the combination of IT-2 and SFF use results in an effective procedure that increased the diagnostic yield in DPD cases.

The complication rate of the procedure was low, regardless of the presence of pleural effusion. To ensure a safe procedure, we paid attention to three points. The first was pre-operative case selection. Patients who were suspected to have dense pleural adhesions from a past history of thoracotomy or tuberculosis were excluded and instead referred for video-assisted pleuroscopy.

### Table 3. Chest CT findings before pleuroscopy of the lung adenocarcinoma cases with dry pleural dissemination (n = 10)

<table>
<thead>
<tr>
<th>Affected hemithorax</th>
<th>Number of cases (%)</th>
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<tr>
<td>Right</td>
<td>6 (60)</td>
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<tr>
<td>Left</td>
<td>4 (40)</td>
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<table>
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<tr>
<th>Affected lobar</th>
<th>Number of cases (%)</th>
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<tbody>
<tr>
<td>Upper</td>
<td>7 (70)</td>
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<tr>
<td>Lower</td>
<td>3 (30)</td>
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<table>
<thead>
<tr>
<th>Intrapulmonary nodule</th>
<th>Number of cases (%)</th>
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<tbody>
<tr>
<td>Present</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Absent</td>
<td>4 (40)</td>
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<table>
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<tr>
<th>Uneven pleural thickening</th>
<th>Number of cases (%)</th>
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<tbody>
<tr>
<td>Present</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Absent</td>
<td>3 (30)</td>
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<tr>
<th>Pleural or fissural nodules</th>
<th>Number of cases (%)</th>
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<tbody>
<tr>
<td>Present</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Absent</td>
<td>3 (30)</td>
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<table>
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<tr>
<th>Abutting the pleura or the fissure of primary lesion</th>
<th>Number of cases (%)</th>
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<tbody>
<tr>
<td>Pleural</td>
<td>6 (60)</td>
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<tr>
<td>Fissure</td>
<td>2 (20)</td>
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<tr>
<td>Pleural/ Fissure</td>
<td>2 (20)</td>
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<tr>
<th>Lymph node swelling</th>
<th>Number of cases (%)</th>
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<tr>
<td>Subclavian</td>
<td>1 (10)</td>
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<tr>
<th>Absent (hilar or mediastinal)</th>
<th>Number of cases (%)</th>
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<td></td>
<td>9 (90)</td>
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CT, computed tomography.

The procedure in patients who presented asymmetric pleural thickening or pleural nodules without pleural effusion on chest CT imaging. To our knowledge, this is the first report on flex-rigid pleuroscopy under local anesthesia for radiologically suspected DPD.

One of the indications for pleuroscopy is pleural malignancy. For primary lung cancer, accurate staging is important to prevent futile surgery (17). In some inoperable cases, like those in our study population, lymph node metastasis is not observed, and the only available site for diagnostic sampling is the pleura. Adenocarcinoma is the most common primary lung cancer metastasizing to the pleura, with or without effusion (9, 18, 19). Patients with DPD have a median survival of almost 2 years longer than patients with wet pleural dissemination (WPD) (9).

DPD is ideally evaluated on CT scan slices 1-2 mm in thickness, (19) but some reports noted that a 5-mm section thickness is sufficient (18) to look for signs of uneven pleural thickening, pleural or fissural nodules, and nodules abutting the pleura or fissure of the primary lesion (9, 18, 20, 21). These findings were consistent with our cases in the dry group of lung adenocarcinoma. The differential diagnoses for such findings are benign intrapulmonary lymph nodes, anthracotic or anthracofibrotic nodules and granulomas (18, 22, 23).

According to a FDG PET report on pleural abnormalities in NSCLC, positive findings on an FDG PET scan are sensitive for malignancy (24). Previous report also indicated the DPD cases of lung adenocarcinoma which were pre-operatively detected by PET/CT (18, 25). However, there are some limitations of FDG PET to be considered. First, non-malignant processes such as tuberculosis, fungal infections, sarcoidosis and pneumoconiosis can take up FDG and mimic the appearance of a malignant nodule on PET or PET/CT. In addition, in order to obtain a definite diagnosis, biopsy would be required because FDG PET cannot reliably help in distinguishing between benign and malignant pulmonary nodules. Secondly, false-negative scans of pleural dissemination can be seen due to a limited resolution of PET for 6–12mm lesions (26), as can a decreased maximum standardized uptake value (SUV) related to respiratory motion (18). Among DPD cases of lung adenocarcinoma, FDG uptake of pleura or pleural nodule was detected in only 12.5% cases regardless of the CT findings of uneven pleural thickening and multiple pleural or fissural nodules. Whereas integrated PET/CT helps improve the diagnostic accuracy of dry pleural nodules (18), histological pleuroscopic diagnosis remains mandatory before planning treatment for the cases suspected of DPD.

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pleuroscopic surgery under general anesthesia. Those who had severe co-morbid conditions including exacerbated obstructed airway disease, severe hypoxemia, cardiovascular dysfunction, coagulation disorders and so on were deemed unfit to undergo the procedure. Second, we used linear-type ultrasonography to detect mobility between the parietal and visceral pleura before selecting the optimal port site. This was performed to ascertain that there were no pleural adhesions that could preclude smooth trocar insertion and lead to lung damage. Lastly, we were careful in performing the blunt dissection through the muscle layers of the chest wall. Upon reaching the parietal pleura, we gently stripped it off using a Kocher clamp to avoid injury to the closely apposed visceral pleura. Because a Kocher clamp is blunt at the tip, it may be useful to peel off the parietal pleura while preventing lung injury in cases of DPD. Needless to say, adequate analgesia was ensured for a steady respiratory rhythm.

One advantage that we discovered in this study was a significantly shorter duration of post-operative chest tube drainage in the dry group. Nearly 70% of dry group patients had their chest tubes removed the day following the procedure. This could be explained by the fact that in cases without pleural effusion, it would require less time to drain the fluid and to perform pleurodesis. Regardless, a shorter duration of chest tube drainage translates to shorter hospitalizations, lesser risks of drain site infections, emphysema and improved performance of the activities of daily living.

Our study was limited by its retrospective design and by the small sample size. Further studies including a larger number of patients without pleural effusion are needed to provide additional evidence. Nevertheless, our study provides new information on performing pleuroscopy under local anesthesia for cases of suspected DPD.

CONCLUSION

Flex-rigid pleuroscopy under local anesthesia can be a well-tolerated diagnostic procedure for radiographically suspected DPD with respect to diagnostic yield and complication rates. A pre-operative assessment is important to help determine contraindications and to appropriately place the pleurosopic port to prevent injury to the lung parenchyma.

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Conflict of interest statement

None declared.

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