Diagnostic Flexible Fiberoptic Pleuroscopy in Suspected Malignant Pleural Effusions*

George R. Robinson II, MD; and Kevin Gleeson, MD, FCCP

Up to 25% of malignant pleural effusions can remain undiagnosed following history, physical examination, thoracentesis, and percutaneous closed pleural biopsy. The next diagnostic procedure is often rigid thoracoscopy, an invasive procedure requiring an operating suite and usually a postprocedure chest tube. We performed flexible fiberoptic pleuroscopy using a fiberoptic bronchoscope in conjunction with a closed pleural biopsy on 12 patients with exudative pleural effusions that remained undiagnosed despite extensive clinical evaluation. A sterile 4.8-mm outside diameter flexible fiberoptic bronchoscope was placed into the pleural space during the course of a routine closed pleural biopsy. Pneumothorax was induced to allow visualization. Brush or forceps biopsy specimens of suspicious parietal pleural lesions were taken. Eight malignant pleural effusions had pleural biopsy if needed. The remaining 50,000 patients defy definitive diagnosis despite this thorough evaluation.

Of the approximately 200,000 malignant pleural effusions occurring annually in the United States, three fourths can be expected to be diagnosed on clinical grounds with pleural fluid analysis and closed pleural biopsy if needed. The remaining 50,000 patients defy definitive diagnosis despite this thorough evaluation. In our institution, the standard remaining options for treating these patients are observation without further diagnostic procedures, video-assisted rigid thoracoscopy with pleural biopsy, and open pleural biopsy.

Observation without a proved diagnosis is sometimes appropriate, yet is frequently unacceptable to patient and physician alike. Experience with video-assisted rigid thoracoscopy in our institution is growing, yet from the patient’s viewpoint, the risks and discomforts of this procedure are similar to open pleural biopsy: both are performed under general anesthesia and require several days of inpatient chest tube drainage and parenteral narcotics postoperatively. Because the prognosis for patients with malignant pleural effusions is poor, an alternative technique that could establish a diagnosis with a minimum of risk and discomfort would be highly desirable.

The use of a flexible fiberoptic instrument to examine the pleural space was reported in the 1970s in the United States and compared with rigid thoracoscopy as recently as 1988 in the United Kingdom. Although apparently allowing for limited pleural space visualization with a minimum of discomfort and risk, we are unaware of the routine use of the flexible instrument currently to attempt to establish a diagnosis in patients with exudative pleural effusions suspicious for malignancy that remain unexplained despite standard evaluation.

We hypothesized that a video-assisted flexible fiberoptic bronchoscope introduced into the pleural space in the course of a standard percutaneous closed pleural biopsy would allow adequate visualization and access to the pleural space and increase the diagnostic yield in malignant pleural effusions without adding substantially to patient discomfort or risk. Therefore, we performed diagnostic flexible fiberoptic pleuroscopy on 12 patients with exudative pleural effusions suspicious for malignancy that remained undiagnosed despite history, physical examination, diagnostic thoracentesis, and in 8 of 12 patients, closed pleural biopsy. These 12 patients represent a highly selected population of patients in...
whom conventional, comparatively inexpensive methods, usually including closed pleural biopsy, had failed to provide a diagnosis and the next step in the conventional diagnostic algorithm was rigid thoracoscopy or open pleural biopsy.

**Methods**

All procedures were performed in conjunction with routine percutaneous Abram's needle closed pleural biopsy between August 1991 and August 1993. To be considered for closed pleural biopsy with fiberoptic pleuroscopy, the following criteria needed to be met: (1) an exudative pleural effusion that remained undiagnosed despite history, physical examination, and pleural fluid analysis, including cytologic examination; (2) significant clinical suspicion of primary or secondary pleural malignancy; and (3) a desire of the patient or referring physician to proceed following a frank discussion of possible risks, benefits, and alternative approaches to their undiagnosed pleural effusions.

Flexible fiberoptic pleuroscopy was performed in our bronchoscopy suite using sterile technique in accordance with a protocol approved by the institutional review board. Following informed consent, all patients received supplemental oxygen by nasal cannula, standard chest leads to monitor cardiac rhythm, and were fitted with a finger pulse oximetry probe to monitor arterial hemoglobin oxygen saturation.

Patients were then either seated upright with the torso flexed and the forearms resting on a table or placed in a lateral decubitus position with the effusion dependent. The skin was sterilized with povidone-iodine solution and local anesthesia was induced with 4 to 5 mL of 1% lidocaine. A standard Abram's needle closed pleural biopsy was performed on all patients with three to six specimens taken. After the Abram's needle was removed, the needle tract was enlarged with a No. 15 scalpel blade with administration of additional 1% lidocaine as needed. A 6-mm internal diameter pediatric endotracheal tube, previously shortened to a length of approximately 10 cm, was then fitted over the Abram's needle and introduced into the pleural space through the incision (Fig 1). Once the pleural space was successfully entered as shown by return of pleural fluid, the Abram's needle was removed leaving the modified endotracheal tube as a conduit to the pleural space.

A sterile 4.8-mm outside diameter flexible fiberoptic bronchoscope was then fed through the endotracheal tube into the pleural space. The endotracheal tube was then removed over the bronchoscope leaving only the bronchoscope in the pleural space, with the chest wall producing a reasonably tight seal. Because visualization of the pleural surfaces was found to be impossible through pleural fluid, pneumothorax was induced by insufflation of 50-mL aliquots of room air through the working channel of the bronchoscope. Once visualization was adequate, the visceral and parietal pleura were examined by manipulation of the fiberoptic device. Cytologic brushing or biopsy using standard bronchoscopic instruments was then performed if indicated. On completion of these manipulations, the insufflated air was extracted through the suction channel, pleural fluid removed if desirable, the device removed from the chest, and the wound closed with two 1.0 silk sutures. The patient was then sent for standard posterior-anterior and lateral radiographs and observed in either the outpatient surgery recovery unit or returned to his hospital bed.

Patient follow-up was performed in several ways. Eight patients were seen at regular intervals by physician members of our pulmonary-critical care division. Three were followed up in the Congestive Heart Failure clinic at our institution. The final patient was followed up by the referring pulmonologist and subsequently by physicians in the Oncology Division at our institution.

**Results**

The patients' ages, indication for pleuroscopy, preprocedure pleural fluid characteristics, pleuroscopic findings, diagnoses obtained, and follow-up data are summarized in Table 1. Nine patients without clinical evidence of congestive heart failure were referred to help exclude pleural malignancy. Eight of nine had previous nondiagnostic percutaneous closed pleural biopsies. The remaining three patients were referred during routine evaluation for potential cardiac transplantation to help exclude malignancy or other pleural disease that might preclude further transplant consideration. All patients were afebrile, had normal blood pressure, heart rate, and arterial hemoglobin oxygen saturation in excess of 90% by pulse oximetry at the time of the procedure. Four patients were given 2 to 4 mg of intravenous midazolam sedation during the procedure.

The pleural space was entered and standard Abram's needle biopsy was performed on each patient without difficulty. The fiberoptic bronchoscope was introduced into the pleural space according to the technique outlined above. The visualized pleural spaces of eight patients were smooth and glistening without evidence of pleural studding (Fig 2). All eight had adhesions between the visceral and parietal pleura of varying degrees that were easily lysed with air insufflation.

The remaining four patients had pleural spaces with visually apparent pleural studding (Fig 3, Table 1). Through cytology brushing and forceps biopsy of parietal pleural lesions, adenocarcinoma was diagnosed in three of these patients with previously undiagnosed conditions. The fourth patient (patient 7) had a nondiagnostic brush biopsy specimen despite visually evident pleural studding. This patient subsequently underwent open pleural biopsy that revealed mesothelioma. Closed pleural biopsy specimens obtained immediately prior to pleuroscopic examination were nondiagnostic in 11 of 12 patients. Patient 5, who had a previously nondiagnostic closed pleural biopsy specimen, proved to have adenocarcinoma evident in this second closed pleural biopsy specimen. Overall, therefore, the diagnosis of malignancy was obtained solely by fiberoptic pleuroscopy.
### Table 1—Patient Data

<table>
<thead>
<tr>
<th>Patient/Age, yr</th>
<th>Pleuroscopy Indications</th>
<th>Protein, g/dL</th>
<th>LDH, U/L</th>
<th>RBC, cells/mm³</th>
<th>Lymphs, %</th>
<th>Findings</th>
<th>Diagnosis</th>
<th>Follow-up, mo</th>
</tr>
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<tbody>
<tr>
<td>1/79</td>
<td>Left pleural effusion; exposure to asbestos</td>
<td>3.1</td>
<td>1,386</td>
<td>&gt;10,000</td>
<td>67</td>
<td>Adhesions, otherwise normal</td>
<td>None</td>
<td>30 (alive)</td>
</tr>
<tr>
<td>2/52†</td>
<td>Right pleural effusion</td>
<td>3.7</td>
<td>2,477</td>
<td>14,123</td>
<td>22</td>
<td>Adhesions, otherwise normal</td>
<td>None</td>
<td>28 (alive)</td>
</tr>
<tr>
<td>3/57†</td>
<td>Right pleural effusion</td>
<td>4.5</td>
<td>428</td>
<td>2,811</td>
<td>92</td>
<td>Adhesions, otherwise normal</td>
<td>Died (postcardiac transplant, normal pleura at autopsy)</td>
<td></td>
</tr>
<tr>
<td>4/81</td>
<td>Bloody right pleural effusion</td>
<td>—</td>
<td>—</td>
<td>210,000</td>
<td>66</td>
<td>Studding</td>
<td>Adenocarcinoma from pleuroscopy</td>
<td>Died</td>
</tr>
<tr>
<td>5/58</td>
<td>Right pleural effusion</td>
<td>5.0</td>
<td>669</td>
<td>10,250</td>
<td>97</td>
<td>Extensive studding</td>
<td>Adenocarcinoma from pleuroscopy</td>
<td>Died</td>
</tr>
<tr>
<td>6/64†</td>
<td>Left pleural effusion</td>
<td>2.8</td>
<td>574</td>
<td>&gt;10,000</td>
<td>85</td>
<td>Adhesions, otherwise normal</td>
<td>None</td>
<td>26 (alive)</td>
</tr>
<tr>
<td>7/67</td>
<td>Left pleural effusion</td>
<td>5.3</td>
<td>751</td>
<td>11,235</td>
<td>45</td>
<td>Nodularity</td>
<td>Mesothelioma by open pleural biopsy</td>
<td>24 (in extremis)</td>
</tr>
<tr>
<td>8/85</td>
<td>Left pleural effusion; WBC &gt;100,000</td>
<td>2.9</td>
<td>213</td>
<td>5,320</td>
<td>45</td>
<td>Adhesions, otherwise normal</td>
<td>None</td>
<td>Died (sudden cardiac death)</td>
</tr>
<tr>
<td>9/61</td>
<td>Right pleural effusion; cavitary lung lesion</td>
<td>3.8</td>
<td>1,267</td>
<td>&gt;10,000</td>
<td>57</td>
<td>Adhesions, otherwise normal</td>
<td>? Parapneumonic</td>
<td>8 (alive)</td>
</tr>
<tr>
<td>10/67</td>
<td>Left pleural effusion</td>
<td>3.6</td>
<td>519</td>
<td>—</td>
<td>95</td>
<td>Adhesions, otherwise normal</td>
<td>None</td>
<td>8 (alive)</td>
</tr>
<tr>
<td>11/66</td>
<td>Right pleural effusion</td>
<td>5.0</td>
<td>1,563</td>
<td>—</td>
<td>60</td>
<td>Adhesions, otherwise normal</td>
<td>None</td>
<td>6 (alive)</td>
</tr>
<tr>
<td>12/66</td>
<td>Left pleural effusion</td>
<td>3.2</td>
<td>&gt;10,000</td>
<td>—</td>
<td>57</td>
<td>Nodularity</td>
<td>Adenocarcinoma from pleuroscopy</td>
<td>Died</td>
</tr>
</tbody>
</table>

*LDH= lactate dehydrogenase; RBC= red blood cells; lymphs= lymphocytes.
†Cardiac transplant candidate.

in two of four patients ultimately proved to have malignancy.

After the procedure, seven patients were transferred from the bronchoscopy suite to the outpatient surgery recovery area. After review of postprocedure radiographs, they were discharged from the hospital to home. The remaining five patients were hospitalized for reasons independent of this procedure and so were returned from the bronchoscopy suite directly to their rooms. One patient developed pleural fluid leakage out the chest wound for several days following the procedure. A second had subcutaneous emphysema noted in the neck 24 h following the procedure that prompted a chest radiograph that demonstrated a small pneumothorax. Each of these resolved without further intervention. No other complications were observed.

The three patients with fiberoptic pleuroscopy proved pleural adenocarcinoma died of their malignancies 8.0 ± 7.6 months after the procedure (Table 1). The patient with malignant mesothelioma is currently in extremis. Of the remaining eight patients, one died 4 months postfiberoptic pleuroscopy of complications following heart transplantation. On
autopsy, his pleural space had no evidence of malignancy or any other intrinsic pleural disease. A second patient died suddenly 14 months postprocedure of presumed myocardial infarction. No autopsy was performed, but no clinical evidence of metastatic malignancy was present. The remaining six patients remain alive and are seen regularly by their physicians (Table 1). All are in clinically stable condition with no evidence of malignancy or empyema during the mean follow-up period of 17.7 ± 11.4 months (Table 1). In summary, there is no available evidence that any of the eight patients with visually normal pleural spaces had occult pleural malignancy.

**DISCUSSION**

We performed video-assisted flexible fiberoptic pleuroscopy during the course of standard percutaneous pleural biopsy in 12 patients with exudative pleural effusions suspicious for malignancy that eluded diagnosis despite clinical evaluation, pleural fluid analysis and, in eight cases, needle biopsy of the pleura. In four patients, a pattern of diffuse studding of both pleural surfaces was seen. Three of these had a diagnosis of adenocarcinoma established by this procedure that eliminated the need for additional diagnostic procedures. The fourth had mesothelioma that required a thoracotomy for diagnosis.

The eight remaining patients who had pleural spaces that appeared to be free of diffuse disease during pleuroscopic examination have all remained apparently free of pleural disease on follow-up. Two patients have died: one had an autopsy-proved normal pleural space, and the second had no clinical evidence of metastatic malignancy. The remaining six have no evidence of infectious or malignant pleural disease a mean of 17.7 ± 11.4 months later. Three of these six have survived a minimum of 2 years with no evidence of disease. We therefore believe a false-negative diagnosis at flexible pleuroscopy to be unlikely.\(^5\) This procedure was well tolerated in an outpatient setting with no important complications observed.

The technique of thoracoscopy was first introduced by Jacobaeus\(^6\) in 1910 and was used to lyse adhesions prior to therapeutic pneumothorax. With the advent of antituberculous antibiotics, the use of thoracoscopy waned. The addition of a cold light source and technical improvements in the rigid thoracoscope allowed for resurgence of this technique in the early 1970s for the diagnosis of pleural space disorders. With the advent of fiberoptic technology, the flexible bronchoscope became available also in the early 1970s and was first reported for examination of the pleural space by Senno et al\(^5\) in 1974. In 1975, Ben-Isaac and Simmons\(^7\) reported the use of a fiberoptic instrument to examine the pleural space in dogs and Gwin et al\(^8\) reported the examination of pleural spaces in nine human patients. They found that metastatic disease to the pleura was diagnosed by
flexible pleuroscopy with biopsy in all five patients with visibly evident pleural "nodules," thus obviating the need for any further diagnostic procedures. Subsequent studies showed improved diagnostic yield when a rigid thoracoscope was compared with a flexible fiberoptic instrument, an impression that appeared to result from technical difficulty in taking biopsy specimens from obvious pleural metastasis on one hand, and an 80% prevalence of mesothelioma, a tumor well known to defy diagnosis with small biopsy specimens, on the other. A report by Sarkar et al suggested that flexible pleuroscopy obtained adequate biopsy material in 37 of 40 cases when the etiology of the pleural effusion was infectious (tuberculosis). They also reported minimal morbidity with the procedure in a population somewhat different from our study. Very little work using the flexible instrument has been subsequently published.

Flexible fiberoptic bronchoscopy for diagnosis of pleural malignancy showed initial promise as a method for establishing a tissue diagnosis when traditional methods failed, but it appeared to fall out of favor when rigid pleuroscopy with biopsy was shown to be superior in establishing a tissue diagnosis of malignant mesothelioma. As is evident from the previous reports described above and from our own experience, the pleural space in malignant mesothelioma is abnormal with visible studding. In most cases, the pathologic confirmation requires tissue samples larger than our procedure, a closed pleural biopsy, or frequently video-assisted rigid thorascopic pleural biopsy can provide. In our experience, malignant mesothelioma is rare compared with metastatic pleural malignancy. We do not believe that the insensitivity of flexible fiberoptic pleuroscopy for diagnosing malignant mesothelioma invalidates our attempts to diagnose other malignant pleural diseases as noninvasively as possible using this technique. It is likely that a rigid instrument in combination with a flexible bronchoscope or a hybrid instrument with both rigid and flexible components would provide improved visualization and biopsy material. However, our experience indicates that when pleural malignancy is present to the point where significant pleural effusions are present, the pleura is diffusely involved and therefore amenable to evaluation using the fiberoptic instrument usually employed for bronchoscopy. We are unaware of other centers routinely using flexible fiberoptic methods to diagnose pleural malignancies currently.

We acknowledge several potential problems with this technique. The relatively small working channel in the flexible fiberoptic bronchoscope definitely limits the size of biopsy specimens obtained, similar to the limitations of a transbronchoscopic lung biopsy, and the capacity to control potential bleeding complications. Meticulous care during the procedure in patients with a normal coagulation profile should make the risk of bleeding remote. In the unlikely event of a bleeding complication, it is imperative to have chest surgeons available in the facility. In addition, the flexibility of the scope may actually reduce maneuverability and control of the working end, thereby reducing the amount of pleura visualized. This could be a major limitation if it were necessary to locate and evaluate a localized pleural process. However, because malignant pleural disease is almost always diffuse, this may not be of practical importance. It is unclear that any of these shortcomings are prohibitive when this procedure is contemplated to determine if malignant pleural disease is present in a patient in whom the physician wishes to avoid invasive procedures.

We believe a role exists for video-assisted flexible fiberoptic pleuroscopy in the diagnosis of exudative pleural effusions in the selected group of patients in whom the clinical suspicion of pleural carcinoma is high and desire to be invasive is low for several reasons. First, the procedure is simple and easy to learn as an extension of the commonly used closed needle biopsy of the pleura. Second, it can be performed using resources already available to clinical pulmonary physicians. Some academic pulmonary divisions and pulmonologists may have access to, and experience with, the rigid thoracoscope; however, this is not the case in our region where it is used only by surgeons. Third, it may well provide a diagnosis when less invasive measures have failed to do so, reducing the need for the more invasive and much more expensive rigid thoracoscopy or thoracotomy. Finally, and perhaps most importantly, this procedure in our experience is well tolerated and adds little or nothing to the discomfort or confinement associated with a standard closed pleural biopsy. In our practice, flexible fiberoptic pleuroscopy has become the preferred procedure when an exudative pleural effusion is highly suspicious for pleural malignancy has eluded definitive diagnosis despite thoracentesis and closed pleural biopsy.

In summary, video-assisted flexible fiberoptic pleuroscopy may be a well-tolerated, minimal risk procedure with definite potential to provide a diagnosis of pleural malignancy when standard evaluation of exudative pleural effusions fails to do so. We do not believe that this technique is appropriate for the evaluation of pleural disease unlikely to be malignancy. Furthermore, it is unlikely that the number of procedures likely to be necessary justifies the use of this technique by all physicians skilled in fiberoptic bronchoscopy. Its role in the evolving clinical science of pleural disease diagnosis remains to be determined.
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