Fiberoptic Bronchoscopy and Pleural Effusion of Unknown Origin*

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We reviewed our experience with fiberoptic bronchoscopy (FOB) in patients with pleural effusion of unknown origin. Seventy patients underwent FOB for the investigation of pleural effusion between 1978 and 1983. Those with a second reason for FOB, a mass on chest roentgenogram, or lobar atelectasis were excluded. Forty five patients remained: 28 patients with unexplained pleural effusion after pleural fluid analysis and pleural biopsy (UPE), and 17 patients with malignant pleural fluid cytology and/or pleural biopsy but no known primary tumor (MPE). In the UPE group, only one FOB demonstrated malignancy, despite a final diagnosis of tumor in seven. No other specific diagnoses were made by FOB in this group. In the MPE group, FOB demonstrated bronchogenic carcinoma in two; ultimately, five patients were found to have a bronchogenic neoplasm. Although pleural effusion of unknown origin is frequently caused by bronchogenic carcinoma, FOB in the absence of other indications for this procedure is rarely diagnostic and should not be routinely employed.

Fiberoptic bronchoscopy (FOB) is widely used to investigate abnormalities of the tracheobronchial tree. The number of indications for this procedure has grown considerably since its introduction, but recent literature has demonstrated its limitations, as in the diagnostic evaluation of cough and the treatment of acute atelectasis. While review articles on FOB do not list pleural effusion as an indication, several clinical studies and a recent textbook have recommended FOB as part of the evaluation of pleural effusion of unknown origin. This practice seems justified since neoplasm is frequently the cause of a pleural effusion that remains undiagnosed after analysis of pleural fluid and biopsy.

While FOB has been used at our institutions to evaluate pleural effusions of unknown origin, our impression was that the procedure was not often helpful, contrary to the conclusion of one previous study. Although the procedure is generally safe, it is associated with discomfort and anxiety to the patient, and if not indicated, contributes unnecessarily to health care costs. We therefore evaluated our experience with FOB to determine its usefulness in evaluating pleural effusions of unknown origin in patients who had no other indication for this procedure. In our study, the yield of FOB for this group was too small to recommend its routine use.

METHODS

Records of all patients who underwent FOB from 1978 to 1983 by the Brown University Pulmonary Service at the Rhode Island Hospital (RIH) and the Providence VA Medical Center (PVAMC) were reviewed. During the study period, a total of 2,136 procedures was performed at the two hospitals. Pleural effusion was given as an indication in 70 patients. Hospital records and chest roentgenograms were reviewed for these patients. Patients who had an indication for FOB, in addition to pleural effusion such as hemothysis, parenchymal lesion, or lobar atelectasis were excluded. Forty five patients remained in the study group.

In these patients with pleural effusion of unknown origin, we identified two subgroups. Twenty-eight patients (19 from RIH, nine from PVAMC) had an unexplained pleural effusion (UPE) defined as an effusion of unknown cause after pleural fluid analysis, and in all but three cases, biopsy of the pleura. A second group of 17 patients (14 RIH, three PVAMC) had a malignant pleural effusion (MPE) diagnosed by malignant cytology and/or pleural biopsy, but without a known primary tumor.

Findings on examination of the tracheobronchial tree and laboratory results were tabulated. All patients had bronchial washings for cytology; bronchial brushing and biopsies were done as indicated. Final diagnoses were determined by chart review and follow-up with the patient's physician. Effusions due to infection, asbestos, or systemic lupus erythematosus were diagnosed by clinical criteria such as positive bacterial cultures, history of occupational exposure, and serologic studies. Patients in whom no diagnosis was made were labelled as having "idiopathic" pleural effusions.

RESULTS

Clinical characteristics of the 28 patients with UPE and 17 patients with MPE are summarized in Table 1. In the UPE group, all effusions but one were exudates as defined by established criteria. The one patient with a transudative effusion was found to have malignant mesothelioma. No patient in this group had a massive pleural effusion, defined as filling more than three quarters of the hemithorax. One effusion was bilateral. Four patients had pleural fluid glucose less

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than 60 mg/dl. Nondiagnostic closed pleural biopsies had been performed in 22 patients prior to FOB. Three additional patients had an open pleural biopsy subsequent to FOB; one yielded a diagnosis of carcinoma and two were nondiagnostic. The three patients who did not have pleural biopsies were felt to have parapneumonic effusions based on clinical presentation, bacteriology, and subsequent followup.

All 17 patients with MPE had pleural fluid cytology or pleural biopsy positive for malignancy. Six effusions were described as bloody. Effusions were massive in two patients. No effusions were bilateral. Glucose was less than 60 mg/dl in three. Eighty-eight percent of this group had malignant fluid cytology; 47 percent had a pleural biopsy showing malignancy.

Results of FOB are summarized in Table 2. Only one FOB in 28 patients with UPE proved diagnostic. This patient had abnormal bronchial mucosa on the side of the effusion; the bronchial washing was positive for adenocarcinoma. This diagnosis was confirmed by mediastinoscopic lymph node biopsy. Bronchoscopic findings in all other cases of UPE revealed only normal mucosa, compression of the bronchial anatomy presumed due to effusion or bronchitis. In patients with MPE, there were two patients with FOB diagnostic for tumor. One patient had visual bronchoscopic findings of neoplasm, and a biopsy confirmed the diagnosis of adenocarcinoma. A second had bronchial washings revealing adenocarcinoma.

The final diagnoses in the UPE group was infection in four patients; benign asbestos effusion, two; and systemic lupus erythematosus, one. Six of seven patients with bronchogenic neoplasms had negative findings on bronchoscopy. The final diagnosis in these cases was made by thoracotomy (two), mediastinoscopy (two), needle aspiration biopsy (one), and subsequent sputum cytology (one). Thirteen patients were considered to have idiopathic pleural effusions. All had a nondiagnostic pleural biopsy. Follow-up for this group ranged from six months to six years (mean 21 months). Four had a positive PPD skin test, but none was felt clinically to have tuberculous pleuritis. One 22-year-old patient was treated with isoniazid for one year; and another patient had previously been treated with isoniazid. No instances of postprimary tuberculosis have developed in these patients. In eight patients of the idiopathic group, the effusions have been followed to resolution.

In the MPE group, nine patients (53 percent) were found to have adenocarcinoma. Three of these were bronchogenic; in six the origin remained uncertain. Two patients (12 percent) had bronchogenic carcinoma of other cell types. One patient (6 percent) had metastatic laryngeal carcinoma. This patient had had a laryngectomy 16 months prior to developing malignant effusion. There was no evidence of local recurrence at the time of bronchoscopy. Five patients (29 percent) were found to have malignant mesothelioma.

**Discussion**

The cause of a pleural effusion can generally be determined by an orderly sequence of clinical and laboratory examinations. In the absence of an obvious explanation such as congestive heart failure, a thoracentesis should be the initial diagnostic procedure. However, a significant number of patients have no diagnosis after pleural fluid analysis. A closed pleural biopsy may then yield additional information leading to a diagnosis. For example, the presence of granulomas on pleural biopsy is highly predictive for tuberculosis but present in only 60 to 80 percent of patients with tuberculous pleuritis. In patients with malignancy, cytologic examination of the pleural fluid is positive in 50 to 70 percent of patients, and pleural biopsy is positive in up to 65 percent of patients. In 19 to 25 percent of patients, the cause of pleural effusion remains unexplained after pleural fluid analysis and pleural biopsy. There is no uniform approach to the management of these patients. Occasionally, empiric antituberculosis therapy is given to the patient with a positive tuberculin skin test. In other patients, a variety of different diagnostic techniques may be employed including FOB, pleuroscopy, and open thoracotomy.

Williams and Thomas evaluated the role of FOB in 28 patients with pleural effusion of undetermined etiology. In this group, four patients had a diagnostic
FOB, three for malignancy and one for tuberculosis. The authors concluded that FOB was of value in the evaluation of patients with undiagnosed pleural effusion. In their group, all three patients with malignancy presented with hemoptysis. We do not believe that the results would have justified the authors' conclusion had patients with hemoptysis, an accepted indication for bronchoscopy, been excluded.

We have reviewed our experience with FOB for pleural effusions that remained undiagnosed after pleural fluid analysis and pleural biopsy. Our final diagnoses of malignancy in 29 percent of cases and idiopathic pleural effusion in 46 percent are similar to other reports.6,14 We found only one of 28 patients had FOB diagnostic for malignancy. No other useful information was found with this procedure. Based on our findings, we feel that when undiagnosed pleural effusion is the sole pulmonary abnormality, FOB is not indicated.

Six patients (22 percent) in our group with UPE and negative FOB had a final diagnosis of bronchogenic carcinoma made by another procedure. This finding is not surprising since a diagnosis of bronchogenic neoplasm often cannot be made by FOB if the lesion is in the periphery of the lung. Although none of our patients with bronchogenic carcinoma and UPE had resectable disease, an ipsilateral pleural effusion in association with bronchogenic carcinoma may, in rare cases, be curatively resected. In a study by Decker and associates,41 four of 70 patients with lung cancer and pleural effusion with negative cytology were resectable. The authors concluded that although pleural fluid in a patient with bronchogenic carcinoma is a poor prognostic sign, surgical exploration should not be ruled out. It remains unclear, therefore, the extent to which the search for bronchogenic carcinoma should be pursued in a patient with pleural effusion.

Other diagnostic procedures may be employed in the undiagnosed pleural effusion. Boutin and associates42 evaluated the utility of rigid tube pleuroscopy in 215 patients with undiagnosed pleural effusion. Seventy percent of these patients were found to have malignancy; in 89 percent, the tumor was found by pleuroscopy. Since this study was done in a cancer referral hospital, the number of malignancies may have been unusually high. Open thoracotomy has also been recommended for the diagnosis of unexplained pleural effusions. However, Black43 reported diagnostic findings in only 57 percent of these patients even after exploratory thoracotomy. Accordingly, the indications for pleuroscopy or thoracotomy are not well established. These procedures may be indicated in selected patients.

Despite all efforts, a substantial number of patients who are evaluated for a pleural effusion will have no diagnosis. This was the case in 46 percent of our patients with a mean follow-up of 21 months and 41 percent of patients followed by Gunnels4 for a mean of 24 months. The long-term outcome of these patients was addressed by Ryan and associates4 in a group that remained undiagnosed after thoracotomy. Sixty-one percent of their patients had no apparent cause and no recurrence of the pleural effusion in a follow-up that ranged from 1.5 to 15 years after surgery. In 25 percent, the cause of pleural effusion was discovered from two weeks to five years after thoracotomy. The majority of these patients proved to have malignancy, with lymphoma or malignant mesothelioma accounting for most cases. The remaining diagnoses were made months to years after thoracotomy and included systemic lupus erythematosi s, rheumatoid arthritis, and the yellow nail syndrome.

In our study, we have also examined the role of FOB in 17 patients with a malignant pleural effusion and no obvious primary tumor. Since up to 33 percent of malignant pleural disease is due to bronchogenic carcinoma,6,14 the examination of the tracheobronchial tree would seem justified. Fiberoptic bronchoscopy in our patients with malignant effusion but an otherwise normal chest roentgenogram was diagnostic in only two patients (12 percent). In both instances, adenocarcinoma was discovered. The low yield in our cases of adenocarcinoma metastatic to the pleura (two of 12 patients) is consistent with the literature relating to adenocarcinoma of unknown primary. Stewart et al45 found only one of 17 FOBs helpful in a group of patients with unknown primary metastatic carcinoma. This study and others46,47 suggest that an exhaustive diagnostic work-up in this setting is not indicated. In our group, the second most common diagnosis was malignant mesothelioma, a tumor that would not be found by examining the tracheobronchial tree.

In conclusion, we have examined the yield of FOB in a retrospective analysis of patients presenting with pleural effusion and no other indication for this procedure. The yield of FOB in the patient with an undiagnosed pleural effusion is low, and we suggest these patients simply be followed. Although the yield in patients with malignant pleural effusions is slightly higher, the recent literature does not support a search for the primary tumor in these patients. We suggest that FOB not be routinely performed in these settings.

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