Diagnostic value of closed percutaneous pleural biopsy vs pleuroscopy in suspected malignant pleural effusion or tuberculous pleurisy in a region with a high incidence of tuberculosis: a comparative, age-dependent study

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Objective. To compare the value of closed percutaneous pleural biopsy versus pleuroscopy for diagnosis of undiagnosed exudative pleural effusion in an age-dependent manner.

Design. Prospective clinical study.

Setting. University hospitals.

Patients. Forty-nine consecutive patients with undiagnosed exudative pleural effusion following the initial clinical and paraclinical investigations, including bronchoscopy. Cases were divided into younger and older groups according to their ages.

Intervention. Closed pleural biopsy immediately followed by pleuroscopy with a flexible fiberoptic bronchoscope from the same incision site.

Results. In the older age group, pleuroscopy was superior to closed pleural biopsy for the diagnosis of the underlying pleural disease (P=0.0007), while they were almost equally diagnostic in the younger cases (P=0.58).

Conclusion. For those patients with undiagnosed exudative pleural effusion who are older than 50 years of age, pleuroscopy could be chosen as the first procedure of choice as compared to closed pleural biopsy if malignant pleural effusion is suspected.

Introduction

Pleural effusion is a frequently encountered clinical condition. Tuberculosis, malignancy, congestive heart failure, parapneumonia, and pulmonary embolism are the main causes of pleural effusions (1,2). Exudative pleural effusions are usually of infectious origin in youth, while malignancies are common in the aged (1,3). They are the second most common cause of pleural effusions in patients over the age of 50 (1,4,5). If cytological and microbiological analysis of an exudative pleural effusion obtained by thoracentesis cannot elucidate the cause of pleural effusion, closed pleural biopsy and, less often, fiberoptic bronchoscopy, is suggested as the next procedure (6–9). Closed pleural biopsy may reveal granuloma or mycobacteria in 50–80% of such cases with tuberculous pleurisy, which is relatively common in the young age groups (10–11). It may also detect the pleural involvement by malignancies in about 46 57% of these cases (12,13).

Diagnostic pleuroscopy is indicated when all the above-mentioned investigations are not able to make a final diagnosis (14). It can elucidate the cause of exudative pleural effusion in the majority of patients (14). Pleuroscopy with a flexible bronchoscope has a high diagnostic accuracy too (13,15), especially for the diagnosis of malignancies (16).

Whether or not these invasive procedures – closed pleural biopsy versus pleuroscopy with a flexible bronchoscope – have a similar diagnostic yield in young and elderly patients with undiagnosed exudative pleural effusions has not yet been systematically studied. To clarify this issue, therefore, we have carried out a preliminary study for the first time and then completed this prospective study on 49 cases with an exudative pleural effusion in whom the usual investigations, such as biochemistry, cytology and bacteriology of fluid obtained by thoracentesis, were not diagnostic. Since we live in an area where pulmonary tuberculosis is quite frequent in the young, and malignant pleural effusions are
seen mainly in our elderly, the value of these procedures for identification of the underlying causes of undiagnosed exudative pleural effusions were compared with each other in an age-dependent manner.

**Patient and Materials**

Since our university hospitals are the main referral centres for patients with pulmonary and pleural disorders, only patients with the following criteria for undiagnosed exudative pleural effusion were selected for this study: (a) those having the generally accepted criteria of an exudative pleural effusion (17); (b) those for whom a thorough history, physical examination, and the usual biochemical and laboratory (including acid-fast stains), cultural, and cytological studies of the pleural fluid and sputum (three times) were not diagnostic; (c) those having a negative fiberoptic bronchoscopic study which included both washings and brushings. Forty-nine consecutive cases with an undiagnosed pleural effusion were divided into two groups.

Group I (n=27) consisted of 15 males and 12 females with an age range of 17-76 years (28.55 ± 7.96). Group II (n=22) included 13 males and 9 females with an age range of 52-70 years (60.00 ± 4.95). All cases signed a written consent.

The chest roentgenograms were carefully reviewed to make sure that there were no grossly detectable atelectatic lesions, masses or parenchymal infiltrates. All patients underwent a percutaneous pleural biopsy with Abrams needle as described by Morrone et al. (18). At least four pleural biopsies were done, and the pleural specimens were sent for histological studies as well as culture for Mycobacterium tuberculosis. Immediately after this, all cases underwent pleuroscopy through the same biopsy site with a gas-sterilized flexible fiberoptic bronchoscope (Olympus BF-B2 instrument).

**PROCEDURE OF PLEUROSCOPY**

Atropine 0.6 mg intravenously and 50 mg pethidine were used before performing percutaneous closed pleural biopsy by Abrams needle. Local anaesthesia using 2% lidocaine was performed for all patients. One minute later, after taking blind pleural biopsies by Abrams needle, while the patient was placed in the lateral decubitus, a metal trocar with cannula was inserted through a 3-cm skin incision of the chest wall of the 6th intercostal space which was made during percutaneous closed pleural biopsy by Abrams needle into the pleural space. The patients were on 4-51 nasal oxygen. In order to provide an air-tight seal, a purse-string suture of black silk was tied around the trocar. The tip of an Olympus BF-B2 gas-sterilized flexible bronchoscope was inserted into the pleural space through the metal cannula after removing the trocar (15). A 20-30% pneumothorax was made to allow visualization of the pleural space. The degree and extent of the pneumothorax could be controlled by using the bronchoscopic suction channel. The pleura was carefully studied. At the end of the procedure, the pneumothorax was suctioned. The bronchoscope was gradually removed while applying suction through the suction channel. The purse-string ligature was tightened.

After termination of the procedures, a chest X-ray film was taken, and cases were hospitalized and observed for the next 24 h for detection of possible complications.

**FOLLOW-UP**

Those patients with a diagnosis of non-specific pleuritis by either closed percutaneous pleural biopsy (CPB) or pleuroscopy were followed regularly for a period of a mean of 21.3 ± 4.2 months.

**Statistical Analysis**

Only the histopathological diagnostic yield of each of these procedures was compared with that of the other—first among the patients of the same group, and then among those of the two groups. A test was assumed to have a positive diagnostic yield when there was definite histopathological evidence of a disease process such as tuberculosis or malignancy. Signs of non-specific pleuritis, or those which were subjectively assessed by the pathologist to be inadequate, were considered a negative test result. In some cases a definite diagnosis was established by subsequent thoracotomy and/or clinical follow-up.

Chi-square (Pearson) and Fisher’s exact test were used to analyse the data. A P value of less than 0.05 was considered statistically significant. Statistics were determined using SAS program language (SAS Institute Inc., Cary, NC).

**Results**

Of 27 patients of group I (young group), 11 and 13 cases were diagnosed using closed percutaneous pleural biopsy (CPB) and pleuroscopy, respectively (Table 1). There was no statistically significant difference between the overall positive diagnostic capabilities of the two procedures in this group (P=0.58). Five cases with initial histopathological evidence of non-specific pleuritis turned out to have either tuberculosis (n=3) or malignancy (n=1) during the period of follow-up. Resolution of effusion occurred in three cases with antibiotics, so that a presumptive diagnosis of pneumonia was made. Spontaneous resolution of effusion was seen in seven cases (Table 2).

As a whole, there were 15 patients with a final diagnosis of tuberculous pleurisy in group I patients (Table 2). Thus, the diagnostic sensitivity of CPB for diagnosis of tuberculous pleurisy was 66-66% (10/15), and it was 80% (12/15) for the pleuroscopy in group I patients (P=0.40).

Of 22 group II patients (n=22), the diagnosis was made in eight and 19 using CPB and pleuroscopy, respectively (Table 1). The overall positive diagnostic yield of pleuroscopy turned to be significantly superior to that of closed pleural biopsy in patients over the age of 50 (P=0.0007). There were three cases with an initial tissue diagnosis of non-specific pleuritis in this group, two of whom turned out
TABLE 1. The overall diagnostic yield of CPB* and pleuroscopy among the patients of both groups

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number of patients</th>
<th>Number diagnosed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I</td>
<td>Group II</td>
</tr>
<tr>
<td>CPB*</td>
<td>27</td>
<td>22</td>
</tr>
<tr>
<td>Pleuroscopy</td>
<td>27</td>
<td>22</td>
</tr>
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</table>

*Closed pleural biopsy.

TABLE 2. Results obtained by CPB* and pleuroscopy in group I patients, compared with the final diagnoses in the same group during their follow-up

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Final diagnoses</th>
<th>Diagnosed by CPB</th>
<th>Diagnosed by pleuroscopy</th>
<th>Diagnosed by either CPB or pleuroscopy</th>
<th>Diagnosed by neither CPB nor pleuroscopy</th>
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<tbody>
<tr>
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<td>12</td>
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<td>0</td>
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<td>0</td>
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<tr>
<td>Metastatic squamous-cell carcinoma</td>
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<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other and undifferentiated carcinoma</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
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<td>0</td>
<td>0</td>
<td>3</td>
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<tr>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<tr>
<td>Non-specific pleuritis</td>
<td>7</td>
<td>16</td>
<td>14</td>
<td>14</td>
<td>-</td>
</tr>
</tbody>
</table>

*Closed pleural biopsy.

TABLE 3. Results of CPB* and pleuroscopic examinations in group II patients, compared with the final diagnoses in the same group during their follow-up

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Final diagnoses</th>
<th>Diagnosed by CPB</th>
<th>Diagnosed by pleuroscopy</th>
<th>Diagnosed by either CPB or pleuroscopy</th>
<th>Diagnosed by neither CPB nor pleuroscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
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<td>1</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Mesothelioma</td>
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<td>Other and undifferentiated carcinoma</td>
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<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Non-specific pleuritis</td>
<td>1</td>
<td>14</td>
<td>3</td>
<td>3</td>
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</table>

*Closed pleural biopsy.

to have mesothelioma after thoracotomy during their follow-up (Table 3). The effusion of the third one was spontaneously resolved during the follow-up.

There were 18 patients with mesothelioma or metastatic pleural carcinomatosis in the older group (group II) during their clinical follow-up (Table 3). Therefore, the diagnostic sensitivity of CPB for malignant pleural effusions was 38.88% (7/18) and 88.88% (16/18) for the method of pleuroscopy (P=0.001).

When the overall diagnostic yields of both percutaneous pleural biopsy and pleuroscopy were compared between the patients of the two groups, it was only the latter procedure which was more diagnostic in the older than younger patients (P=0.005). There was no statistically significant difference between the overall diagnostic yield of closed pleural biopsy in the two groups (P=0.75).

There were no life-threatening complications secondary to either procedure. Four patients developed a small pneumothorax which did not require treatment. Nine patients complained of having pain during the pleuroscopy which was not significant. Mild, transient hypotension occurred in four cases; this was managed by merely putting them into the supine position.

Discussion

In this study we performed concomitant closed pleural biopsy and pleuroscopy (one after the other) for the
diagnosis of pleural disease in 49 consecutive cases with exudative pleural effusion where the routine biochemical, cultural, and cytological study of fluid were not diagnostic.

The arbitrary division of group I and group II on the basis of age under or over 50 was made because of two facts. First, although the average age of patients with tuberculous pleural effusion is increasing in some areas (5), the majority of patients with tuberculous pleurisy are relatively young in our region. Second, the most malignant pleural effusions are seen in patients over the age of 50 (1,4,5). The histopathological results obtained at these procedures were compared with each other according to the patients' age groups.

Tuberculous pleurisy, which is a frequent cause of exudative pleural effusion among young adults in our area, may present with an acute illness or with an indolent illness with non-specific constitutional symptoms (11). Cultures of all potentially diagnostic specimens such as pleural, sputum, gastric washing, and pleural biopsy tissue combined with histological examination of needle pleural biopsies may confirm the diagnosis of tuberculosis in most cases (5,6). In our patients of group I (young age), pleuroscopy had a 48.15% overall diagnostic yield, which was higher than that of closed pleural biopsy (40-74%) and could make the diagnosis of tuberculosis more frequent than the latter procedure; however, these differences were not statistically significant, implying that both procedures were equally diagnostic for these patients. Casardoy and his coworkers (19) have found pleuroscopy to be a very good technique for the diagnosis of tuberculous pleuritis, although others (20) have claimed it to be superior to the closed pleural biopsy for diagnosis of tuberculosis. However, these findings are contrary to those reported by Menzies and Charbonneau (16) who found that pleuroscopy increases the yield for malignancy but not for tuberculosis.

Pleural fluid cytology is one of the best procedures for confirming the diagnosis in malignant pleural effusion (21). Approximately, up to 71% of patients with malignant pleural effusions have a positive cytology for cancer cells in the pleural fluid specimens (2,22). The remaining cases need a pleural biopsy and/or, sometimes, pleuroscopy. Up to 57% of malignant pleural effusion can be confirmed by closed needle biopsy (13). Sahn (12) has found a lower diagnostic yield for diagnosis of malignancy by means of closed pleural biopsy when cytological study of fluid was negative.

In this study, in the older age group – those over the age of 50 years (group II) – the overall diagnostic value of pleuroscopy was 88.88%, and it could make the diagnosis of malignancy much more frequent than closed pleural biopsy, both of which were statistically impressive. The reasons for these differences are clear. Thoracoscopy allows visualization of large areas of both parietal and visceral pleural surfaces (23), and specimens for biopsy can be taken directly from grossly abnormal looking parts of the pleura. This is especially true for cases in whom the visceral and diaphragmatic pleura are involved since these areas are not accessible to routine percutaneous pleural biopsy (9,16).

Thoracoscopy with a rigid scope is a safe and highly accurate procedure, especially in those centres which are interested in performing diagnostic thoracoscopy (24,25). Menzies and Charbonneau (16) have reported a sensitivity of 91%, a specificity of 100% and a negative prediction value of 93% for the diagnosis of malignant pleural effusions. Oldenburg and Newhouse (25) have found the diagnostic accuracy of rigid thoracoscopy to be superior to that of a flexible one. However, others (15) have used fiberoptic bronchoscopy successfully, and we had close to 89% diagnostic yield with it as well.

According to this study, we can conclude that the combination of culture and histological examination obtained by closed pleural biopsy, and less often fiberoptic bronchoscopy, in young or adolescent patients with undiagnosed exudative pleural effusion may be ample for diagnosis of tuberculous pleurisy. In the setting of the failure of a pleural biopsy to demonstrate granulomatous pleuritis, the patients should be individualized. In those patients who are strongly suspected of suffering from tuberculosis, an antituberculous chemotherapy trial is justified in spite of negative histological results obtained by closed pleural biopsy, especially in an area with a high incidence of tuberculosis. Usually, no pleuroscopy is required in these patients. It may be reasonable to observe these patients for a period of time before performing any further invasive procedure.

Given the above-mentioned advantages, as well as cost effectiveness (24), low rate of complications (16,25), and the high overall diagnostic yield as shown in this study, it seems reasonable to suggest pleuroscopy as the procedure of first choice in older patients with suspected malignant pleural effusions if and when initial results of clinical and paraclinical investigations, including bronchoscopy and pleural fluid cytology studies, are negative.

References


