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Long-term outcome of patients with nonspecific pleurisy at medical thoracoscopy

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ABSTRACT

Background: Medical thoracoscopy is an effective and safe procedure for diagnosing pleural effusions of undetermined causes. But there are still a part of patients with pleural effusions were diagnosed as nonspecific pleurisy when no specific biopsy results were found after undergoing thoracoscopic biopsy. The long-term outcome of these patients is unclear, and anxieties about undiagnosed malignancy persist.
Methods: Between July 2005 and June 2014, medical thoracoscopy using the semi-rigid instrument was performed and pleural biopsy was taken in 833 patients with pleural effusions. Fifty-two patients diagnosed with nonspecific pleurisy with available follow-up data were included in the present study and their medical records were reviewed.
Results: Fifty-two patients (31 men and 21 women) were included. Mean follow up was 35.5 ± 40.9 months (range, 1–143 months). No specific diagnosis was established in 21 (40.4%) of the patients. Eight of 52 patients with nonspecific pleurisy (15.4%) were subsequently diagnosed with pleural malignancies. 23 of 52 patients (44.2%) were diagnosed as benign diseases. The recurrence of pleural effusion during followed-up and pleural nodules or plaques found in medical thoracoscopy was associated with malignant disease.
Conclusion: Patients with nonspecific pleurisy after medical thoracoscopy should be closely monitored, especially in those patients with the recurrence of pleural effusion during followed-up, pleural nodules or plaques found in medical thoracoscopy. One year of clinical follow-up for patients found to have nonspecific pleurisy is likely sufficient.

1. Introduction

Pleural effusions are a common clinical problem with more than 60 recognized etiologies including diseases local to the pleura or underlying lung, organ dysfunction, systemic conditions and drugs. It is estimated that approximately 1.5 million people suffer from a pleural effusion in the United States [1]. Medical thoracoscopy (MT) refers to the examination of the pleural space in a nonintubated patient under conscious sedation, and this procedure has been well documented to be highly sensitive for detecting malignant pleural effusion with negative pleural fluid cytology and for diagnosing pleural effusion [2,3]. Unfortunately, for a part of patients, pleural fluid analysis and pleural biopsy fail to yield a definite answer after MT. The cause of the pleural effusion is still uncertain, and the histological finding in pleural biopsies is pleural inflammation (pleuritis/fibrosis), but these are not specific findings such as tuberculous or malignant disease. Published data suggest that 5%–25.5% of these patients will subsequently be diagnosed with pleural malignancy, the most common of which is mesothelioma in 2.5%–15.8% of cases [4–14]. We conducted this study to investigate the incidence of subsequent pleural malignancy among patients diagnosed with nonspecific pleurisy (NSP) after MT and to attempt to determine the appropriate follow-up time for patients diagnosed with NSP after MT.

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Abbreviation list

CT	computed tomography
MT	Medical thoracoscopy
NSP	nonspecific pleurisy

2. Patients and methods

The study protocol was approved by the Institutional Review Boards for human studies of Beijing Chaoyang Hospital, China. Between July 2005 and June 2014, MT using the semi-rigid instrument was performed and pleural biopsy was taken in all suspected areas, systematically in several parts of the parietal pleura for mycobacterial, cytological, and histological examination in 833 patients with pleural effusions [15]. Before this procedure, all patients had completed a detailed medical evaluation, pleural radiological assessments, pleural fluid analyses, and/or closed pleural biopsy examination, but no particular causes of pleural effusions were found. Our pathology database included all cases of parietal pleural biopsy resulting in a nonspecific histological diagnosis of MT, yielding 62 cases. Of these patients, 52 with available follow-up data were included in the study.

The deadline of our follow-up time was Jun first, 2016. During the follow-up, such information was required from the patients or relatives every month by telephone mail or personal interview: 1) the basic status of patients; 2) if there is any new symptoms of patients; 3) if the pleural effusion was recurrence; 4) if there is any subsequent diagnosis of the cause of pleural effusion; 5) when and how the subsequent diagnosis was established. The diagnosis of heart failure was given when impaired cardiac function was identified and the pleural fluid reduced with diuretic treatment. A diagnosis of parapneumonic effusion was given when clinical complaints and biochemical parameters improved after appropriate antibiotic therapy. A diagnosis of tuberculosis-related effusion was given when pleural fluid or hydropericardium tuberculosis was found or pleural fluid regressed following anti-tuberculosis therapy. A diagnosis of pulmonary embolism was given when computed tomography (CT) pulmonary angiography showed the embolism.

MT was performed by chest physicians in our pulmonary procedural suite as described in the previous publications [15]. Pleural fluid samples and pleural biopsies were obtained from all patients and analyzed. Biochemical parameters included total protein, and lactate dehydrogenase, etc. in fluid samples were tested. Cytological examination of pleural fluids and histopathological examination of pleural biopsies from all patients was performed.

3. Statistics

All analyses were performed with SPSS software (version 19.0, SPSS Inc., Chicago, IL, USA). Data of parametric distributions were expressed as mean (±SD. Chi-square or Fisher's exact test was used to compare categorical variables (as appropriate). The Student's *t*-test was performed to compare the mean of two groups. All reported *p* values were two-sided and effects were considered significant if $P < 0.05$.

4. Result

4.1. Summary of patients with NSP

Between July 2005 and June 2014, 833 patients with undiagnosed pleural effusions successfully underwent MT, and pleural biopsy samples were obtained for diagnostic evaluation [15]. Eventually, NSP was the final diagnosis in 62 patients, and 52 of them with available follow-up data were included in our current analysis. Patient characteristics are listed in Table 1. Thirty-one (59.6%) patients were men and 21 (40.4%) were women. Average age was 61.5 ± 16.4 years. Mean follow-up was 35.5 ± 40.9 months (range, 1–143 months).

During the follow-up period, no specific diagnosis was given in 21 (40.4%) of the patients. Mean follow-up of these patients was 54.0 ± 34.2 months (range, 1–133 months). A specific diagnosis was made in 31 (59.6%) patients. The diagnoses are shown in Figure 1.8 of 52 patients with NSP (15.4%) were subsequently diagnosed as pleural malignancies (Table 2), with 5 of them were mesothelioma, 2 adenocarcinoma, and 1 thymoma. 23 of 52 patients with NSP (44.2%) were diagnosed as benign diseases, with 8 of them were tuberculosis, 6 heart failure, 5 parapneumonic effusion, 2 pulmonary embolism, and 2 pneumosilicosis.

4.2. Detailed description of 8 malignant cases

Patient 1 was a 70-year-old female who underwent tracheotomy and invasive ventilator assisted ventilation with rapid deterioration in her basic status. Space-occupying lesion in the right lung was found in CT. Biopsies taken at a percutaneous needle lung biopsy showed malignant mesothelioma. She died 3 months later.

In patients 2 and 3, clinical suspicions of pleural malignancies were low. No specific findings were found in CT. Both of them experienced effusion recurrence in 3 months. Biopsies taken at a second MT showed malignant mesothelioma.

Patient 4 was a 48-year-old female suffering re-accumulation of her pleural effusion 2 months after the initial MT. No specific findings were found in CT before the initial MT. Biopsies taken at a open-lung biopsy showed malignant mesothelioma 8 months later, and she died 28 months later.

Patient 5 was a 77-year-old male with space-occupying lesions in the right lower lobe of lung. Clinical suspicion of pleural malignancy was high, but pleural biopsy in MT only showed mesothelial

Table 1
Patient details.

Patient details	n = 52
Age (yr)	61.5 ± 16.4
Sex	
Male	31 (59.6)
Female	21 (40.4)
Tobacco use (pack-years)	
0	29 (55.8)
0–25	11 (21.1)
25–50	7 (13.5)
>50	5 (9.6)
Follow up duration (months)	35.5 ± 40.9
Diagnosis of pleural malignancy during follow-up	
Mesothelioma	5 (9.6)
Adenocarcinoma	2 (3.8)
Thymoma	1 (1.9)
Time from NSP biopsy to cancer diagnosis (months)	4.1 ± 3.4
Diagnosis of pleural benign disease during follow-up	
Tuberculosis-induced	8 (15.4)
Heart failure	6 (11.5)
Parapneumonic effusion	5 (9.6)
Pulmonary embolism	2 (3.8)
Pneumosilicosis	2 (3.8)

Results are mean ± standard deviation or number (percentage).