European Review for Medical and Pharmacological Sciences 2014; 18: 1487-1495

The visual diagnosis of tuberculous pleuritis under medical thoracoscopy: a retrospective series of 91 cases

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Abstract. – BACKGROUND: Despite progress of medical, the fast and accurate diagnosis of tuberculous pleuritis (TP) continues to be a challenge, mainly because of the lack of specific clinical features and the difficulty in isolating the *Mycobacterium tuberculosis*.

OBJECTIVES: To investigate the role of medical thoracoscopy in definite diagnosis of tuberculous pleuritis, especially the feature of visual diagnosis in tuberculous pleuritis via medical thoracoscopy. We performed a retrospective review of the utility of medical thoracoscopy in tuberculous pleuritis.

PATIENTS AND METHODS: A retrospective chart review was performed of 91 patients who had medical thoracoscopy for suspected TP at the Second Xiangya Hospital from October 1, 2006 to July 30, 2012.

RESULTS: In ninety one cases, 76 patients were diagnosed with TP by pathologic diagnosis. The visual findings via thoracoscopy of 76 TP patients included the following: (1) necrosis (76.32%, n=58), (2) diffuse miliary nodules (64.67%, n=49), (3) single or multiple pleural nodules (14.47%, n=11), (4) hyperemic, edematous and thickened pleura (56.58%, n=43), and (5) pleural adhesions or fibrotic septa (78.95%, n=60), and all of these samples had hydrothorax or loculated effusion. The diagnostic efficiency of visual diagnosis via medical thoracoscopy about tuberculous pleuritis was 93.41%. In the non-invasive test, ADA > 40 u/l with LDH > 200 u/l for TP showed relatively high sensitivity and specificity (73.68%, 80.00%, respectively).

CONCLUSIONS: TP presents a variety of scopic phenotypes under medical thoracoscopy. The experienced pulmonologists visually diagnose TP efficiently and directly via medical thoracoscopy. Medical thoracoscopy with combined biopsy is an accurate and safe method for diagnosing TP.

Key words:

Tuberculous pleuritis, Pleural effusion, Medical thoracoscopy, Visual diagnosis, Pathology.

Introduction

Despite the efficacious treatments of decades, tuberculosis (TB) remains a major global health problem. One-third of the world's population carry the TB bacteria, more than 9 million of whom become sick each year with "active" TB which can be spread to others in 2010[1]. Tuberculous pleuritis (TP), the most occurrence of extrapulmonary TB, accounts for 30-80% of all pleural effusions[2].

Some TP patients present typical clinical symptoms, which include current cough, chest pain (pleuritic-sharp, stabbing, associated with respiration), fever, chill, dyspnea, night-sweat, weight loss[3]. The presence of these symptoms often provides an important clue in early diagnosis of TP. In addition, some nonivasion tests, such as c-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR) level, lactate dehydrogenase (LDH) level, adenosine deaminase (ADA) level, radiologic test, purified protein derivative (PPD) of tuberculin skin test level, microscopic examination of acid-fast bacilli (AFB) stained smears, and cultures for *Mycobacterium tuberculosis*, may confirm this diagnosis. Especially, the positive results of AFB smears (preferably three) and cultures for mycobacteria provide strong inferential evidence for TP diagnosis[4]. Although there are these developed diagnositic tools, it is still difficult to diagnosis TP quickly and accurately, due to the absence of spe-

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cific clinical features and the difficulty with isolating the *Mycobacterium tuberculosis*[5].

Currently, biopsy is considered as the final and decisive tool to diagnose tuberculous pleuritis[6]. Biopsy methods include percutaneous thoracentesis, closed pleural biopsy (CPB), video-assisted thoracic surgery (VATS), thoracotomy, and medical thoracoscopy[7-9]. Since 1990, medical thoracoscopy has been used widely in developed countries as an efficient and safe means of evaluating pleuritis[10], but it remains a novel technology in developing countries. The visual features are the first and most direct findings of medical thoracoscopy, which could afford physicians the early impression and management of patients. Furthermore, the experienced doctor could diagnose tuberculosis by visual finding of endoscopy[11,12]. However, there are limited date about visual findings of TP. The aim of this study is to describe the view appearance of tuberculous lesions in pleura and investigate the role of visual diagnosis in TP under medical thoracoscopy.

Patients and Methods

Patient selection

Ninety-one patients who had diagnostic medical thoracoscopy for suspected TP in the Department of Respiratory Medicine at the Second Xiangya Hospital between October 1, 2006, and June 30, 2011 were recruited. Patients with incomplete clinical or histologic data were subsequently excluded. Clinical data was obtained from the hospital records and Follow-up visits. The medical records of these patients were reviewed for demographic, clinical data, laboratory data, histologic diagnosis, and medical thoracsocopy features. This study was approved by the Ethical Committee of the Second Xiangya Hospital, and written informed consent was obtained before participation.

The classic diagnosis of TP was established on the basis of caseous granuloma, caseous necrosis, or positive bacteriologic results for *Mycobacterium tuberculosis*[4,13]. However, some presumed or probable cases of TP without positive bacteriologic results present suggestive clinical and medical thoracoscopy findings. A favorable clinical response of chemotherapy would provide further evidence of TP in these cases.

Prethoracoscopy Evaluation

The noninvasive test valued patients initially with blood routine, c-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR) level, lactate dehydrogenase (LDH) level, adenosine deaminase (ADA) level and radiographic characteristics. AFB smears and culture for *Mycobacterium tuberculosis* were used in sputum or pleural effusions before the procedure of medical thoracoscopy. Most patients had carried out thoracocentesises at least once before thoracoscopy. The pleural fluid was analysed for biochemical markers, Gram stain, bacterial and TB culture, as well as for cytology and differential white blood cell (WBC) count, ADA level, LDH level, and protein level, Rivalta test and character of effusion.

Medical Thoracosocopy

Medical thoracosocopy (LFT 240, Olympus, Tokyo, Japan) was carried out in 91 patients, with spontaneous breathing and under local anesthesia by the experienced pulmonologists in the medical thoracoscopy room. During the procedure, patients were placed in the lateral decubitus position with the affected side upward (for 23 patients who had bilateral effusions, the side with a higher effusion was selected for entrance). The portal of entry was usually along the mid-axillary line between the fourth and ninth intercostal spaces[14]. After skin sterilization, 5-10 ml of 2% lidocaine was administered as local anesthesia. A 1 to 2cm skin incision was made with a scalpel, and then all layers of the intercostal muscles were dissected bluntly to visualize the pleura. A disposable flexible trocar was inserted through the chest wall, followed by the flexible thoracoscopy to aspirate the pleural fluid. Then the pleural effusion was submitted for laboratory tests. Adhesions or fibrotic septa between the two pleural leaves were removed when necessary. The parietal, visceral, and diaphragmatic pleura were successively inspected, together with the mediastinal vessels and lymph nodes. A 24-Fr chest tube was introduced via the entry portal before wound closure to evacuate fluid[15]. ECG leads, a BP cuff, and an oxygen monitor were placed on patient during the process of medical thoracoscopy, as well as supplemental oxygen was provided by nasal cannula.

At least 6 biopsies were obtained from the involved pleura using biopsy forceps under direct visual control[16,17]. The histological and microbiologic diagnoses were defined within these biopsy samples. The visual diagnosis of TP was made according to the 5 types, as follows: necrosis, diffuse miliary nodules, single or multiple pleural nodules, hyperemic, edematous and thickened pleura, pleural adhesions[11,12].

Therapy and Follow-up Visit

Seventy six TP patients were given anti-tuberculous drugs after the definite diagnosis of TP. Therapy consisted of a at least 2 month initial phase of isoniazid (300 mg/day), rifampicin (600 mg/day), ethambutol (15 mg/kg/day), and pyrazinamide (1500 mg/day); and a continuation phase in which isoniazid and rifampicin were given on a daily basis for another 4-8 months[2,4]. These patients were checked hepatic function, renal function and radiology every month, then valued the anti-tuberculous treatment outcomes. They were invited for Follow-up visits at one year after the end of standard chemotherapy (October 2006 to July 2012). Finally, all of 91 patients were followed up in order to establish the correctness of the diagnosis in 2012.

Data Analysis

This study discussed the accuracy of noninvasive diagnostic method and the medical thoracoscopy. Population, demographic features, clinical symptoms and conventional laboratory results, and the thoracoscopy findings were also evaluated.

Data analysis was performed with the SPSS software package, version 16.0 (SPSS Inc., Chicago, IL, USA). Data was showed as percentage or median/mean ± standard deviation. The variables were compared by the Student's *t* test and chi-square statistics. The level of statistical significance was set at 0.05. The accuracy of various diagnostic tests was expressed as sensitivity and specificity, positive and negative predictive values, and diagnostic efficiency.

Results

Patient population

Ninety one patients, who had undiagnosised pleural effusion with suspect TP (n=22) or presumed TP that needed to be differentiated from malignant effusion (n=69), were enrolled in this study. To primarily define the character of pleural effusion, the thoracocentesis was done in all patients. In the latter 69 cases, in order to rule out the malignant pleural disease, 35 of them received the CT-guided biopsy without special findings. All of the latter 69 cases undertook empirical anti-tuberculous treatment over a period of 17 ± 7.2 days (range: 3-28 days) before medical thoracoscopy procedure, though none of them responded to this therapy. Ultimately, 76 patients were diagnosed with TP by histology or bacteriology, and confirmed by the Follow-up vists. The other 15 patients were defined with the following diagnoses: 7 pulmonary carcinoma cases, 4 pleural mesothelioma cases, 2 lymphoma cases and 2 connective tissue disease cases. Though these 15 patients were not described in detail in our study, their available data was used to observe the accuracy and complication of medical thoracscopy in TP diagnosis.

Clinical data of the TP

The seventy-six TP cases consisted of 55 male and 21 female, ages ranging from 16 to 84 years old (average age: 50.60 ± 18.41 years old). Only Fifteen patients (15/76, 19.74%) have had a previous TB history. Symptom duration before visiting hospital was 45.49 ± 53.23 days (range: 3-367 days). Twenty patients (20/76, 26.32%) underlied diabetes mellitus, and one patient (1/76, 1.32%) had existing renal failure.

The most common manifestations for 76 TP patients were pleural effusion (76/76, 100%), fever (57/76, 75.00%), night-sweat (55/76, 72.37%), cough (54/76, 71.05%), fatigue (54/76, 71.05%), the positive PPD test (≥ 5 mm with or without hypersensitivity reaction) (50/76, 65.79%). The other clinical data was summarized in Table I.

Noninvasive diagnostic results

The thorax ultrasonography was used in all of 91 patients. All cases were confirmed and characterized by ultrasonic detection. These 76 TP effusion cases were divided into three groups: small pleural effusion (15/76, 18.42%), moderate pleural effusion (33/76, 43.42%), and large pleural effusion (28/76, 36.84%). Small pleural effusion was defined as under 30mm, moderate pleural effusion was defined as between 30mm and 50mm, and large pleural effusion was defined greater than 50mm during ultrasonography.

Chest radiological test also was used in all of 91 patients. The abnormalities of chest X-ray were summarized as follows: 91 cases of pleural effusion (100%), 17 cases of fibroplasias (17/91, 18.68%), 15 cases of nodular infiltration (15/91, 16.48%), and 13 cases of cavity (13/91, 14.29%). The abnormalities of computerized CT scan also seen in 91 patients: 91 cases of pleural effusion (100%), 22 cases of thickened and nodular pleura (22/91, 24.18%), 19 cases of fibroplasias (19/91, 20.88%), 15 cases of nodular infiltration (15/91, 16.48%), and 13 cases of cavity (13/91, 14.29%). From these radiological abnormalities, more than a half of patients needed to be differentiated between TP and malignant pleural disease. The interpretation of radiological findings could be ei-

Table I. The demographic and clinical features of 76 TP patients.

Patient information	Range (mean ± SD) or n (%)
Age (years)	16-84 (50.60 ± 18.41)
Gender (male/female)	55/21
Location (unilateral /bilateral)	53/23
Body mass index (kg/m^2)	19.1-32.5 (22.3 ± 4.8)
Previous TB history*	15 (19.74%)
TB contacts history	31 (40.79%)
Active concomitant pulmonary TB	13 (17.11%)
Empirical TB treatment	69 (90.79%)
Symptom duration (days)	3-67 (15.5 ± 17.3)
Cough	54 (71.05%)
Chest pain	34 (44.74%)
Fever (> 37.5°C)	57 (75.00%)
Night-sweat	55 (72.37%)
Fatigue	54 (71.05%)
Loss of appetite	38 (50.00%)
Weight loss	28 (36.84%)
Dyspnea	27 (35.53%)
Expectoration	24 (31.58%)
Lymphadenopathy	39 (51.32%)
Small pleural effusion	15 (19.74%)
Moderate pleural effusion	33 (43.42%)
Large pleural effusion	28 (36.84%)
Hemoptysis	18 (23.68%)
PPD skin test§	50 (65.79%)
Operation time of medical thoracoscopy (min)	30-130 (52.23 ± 15.87)
Day of drainage¶ (day)	3-19 (5.67 ±3.12)

*TB tuberculosis;
§ Positive PPD test (≥ 5 mm with or without hypersensitivity reaction);
¶After process of medical thoracoscopy.

Table II. The laboratory findings in 76 TP patients.

Patient information	Range (mean ± SD)
Blood	
Hemoglobin (g/l)	58.00-159.00 (102.34 ± 16.85)
White blood cell count (×10^9/l)	3.60-19.80 (10.35 ± 3.53)
% Neutrophils (×100%)	65.00-92.00 (82.86 ± 14.01)
ESR (mm/h)	13.00-120.00 (45.45 ± 21.23)
CRP (mg/l)	8.00-109.00 (32.12 ± 20.24)
LDH (u/l)	120.20-412.30 (191.11 ± 58.73)
Protein (g/l)	20.00-60.00 (35.67 ± 9.83)
Albumin	25.00-40.50 (30.12 ± 4.23)
CEA (ng/ml)	0.05-11.31 (3.84 ± 1.73)
Pleural effusion	
Number of cells (×10^6/l)	250.00-800.00 (517.52 ± 150.41)
% Neutrophils (×100%)	25-85 (45.86 ± 15.01)
% Lymphocytes (×100%)	15.00-85.00 (52.29 ± 16.17)
% Mesothelial cells (×100%)	0.00-10.00 (1.86 ± 1.46)
ADA (u/l)	10-70 (39.34 ± 8.90)
LDH (u/l)	122.10-529.40 (140.21 ± 60.21)
Protein (g/l)	10.00-40.00 (20.11 ± 8.63)
CEA (ng/ml)	0.05-21.14 (2.10 ± 1.09)
Acid-fast stain positive	0
Mycobacterium tuberculosis culture positive	0

SD, Standard Deviation, ESR, erythrocyte sedimentation rate, LDH, lactate dehydrogenase, ADA, adenosine deaminase, CEA, carcinoembryonic antigen

ther TP or malignant disease, according to the radiologist's experience and decision. Therefore, the TP diagnosis varied in a range from radiology (17-36/76 for X-ray, 29-38/76 for CT scan).

In such TP cases, hemoglobin level was 102.34 ± 16.85 g/L, and 64 patients (64/76, 84.21%) were anemic (as defined by a hemoglobin <140 g/L in men and <120 g/L in women). The peripheral white blood cell (WBC) was (10.35 ± 3.53) ×10^9/L, and percentage of neutrophils was 82.86 ± 14.01%. Sixty-seven patients (67/76, 88.16%) were acute infection (as defined by WBC >10.00×10^9/L or neutrophils percentage >75%). The active TB parameters, ESR and CRP were high in most patients.

All of 91 patients have had thoracocenteses at least once before thoracoscopy. Effusion from 22 patients was suspected as tuberculous pleural effusion with all the six abnormal index from laboratory tests as follows: lymphocytic effusion (lymphocytic rate > 50% in effusion), raised ADA level in effusion (ADA > 40 u/L), increased LDH (LDH > 200 u/L), increased ratio of pleural effusion/serum about ADA which was

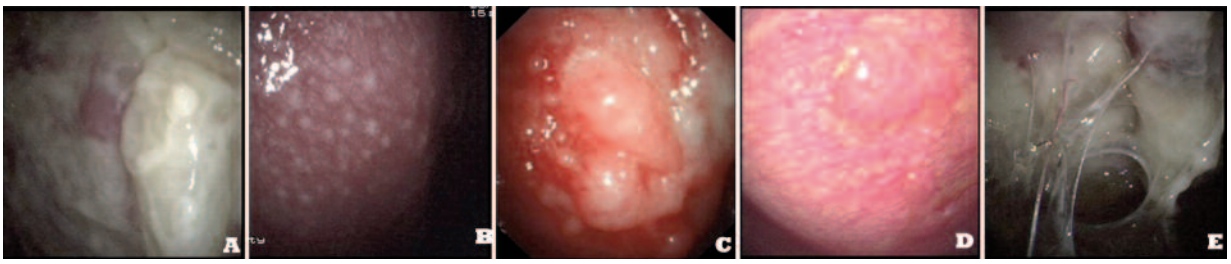

Figure I. Thoracoscopic pleural findings in 76 patients with tuberculous pleuritis. **A**, Necrosis; **B**, Diffuse miliary nodules; **C**, Single or multiple pleural nodules; **D**, Hyperemic, edematous and thickened pleura; **E**, Pleural adhesions and fibrotic septa.

greater than 1, increased ratio of pleural effusion/serum about LDH which was greater than 0.6, and increased ratio of pleural effusion/serum about protein which was greater than 0.5[2,3,16,18]. Because of high CEA level, thirteen effusion cases were thought to be malignant. The acid-fast staining and culture of pleural effusion for Mycobacterial detection were negative in all patients. The other laboratory findings are summarized in Table II.

Visual findings of the TP patients under medical thoracoscopy

The visual findings during the thoracoscopies of 76 TP patients including the following: hydrothorax in 76 patients (76/76, 100.00%), pleural adhesions or fibrotic septa in 60 cases (60/76, 78.95%), necrosis in 58 cases (58/76, 76.32%), diffuse miliary nodules in 49 cases (49/76, 64.47%), hyperemic, edematous and thickened pleura in 43 cases (43/76, 56.58%), and single or multiple pleural nodules in 11 cases (11/76, 14.47%) (Figure 1, Table III).

Based on the visual inspection at thoracoscopy, 74 patients of 91 patients were suspected to have tuberculous pleurisy, 11 patients of 91 patients were suspected to have mesothelioma, and 6 patients of 91 patients were suspected to have a metastatic malignancy. However, it was demonstrated that 2 malignant patients present thoracoscopic feature of TP with visual observation. On the contrary, 4 TP cases were misdiagnosed with malignant diseases from visual diagnosis.

Table III. Medical thoracoscopy findings in patients with TP.

	Number (%)
Medical thoracsocopy appearance	
Necrosis	58/76 (76.32%)
Diffuse miliary nodules	49/76 (64.47%)
Single or multiple pleural nodules	11/76 (14.47%)
Hyperemic, edematous and thickened pleura	43/76 (56.58%)
Pleural adhesions or fibrotic septa	60/76 (78.95%)
Pleura histopathology	
Caseous necrosis	58/76 (76.32%)
Caseous granuloma	53/76 (69.74%)
Nonspecific findings	5/76 (6.6%)
Pleura microbiology	
AFB stain positive	3/76 (3.95%)
Mycobacterium tuberculosis culture positive	5/76 (6.58%)

Pathological findings of the TP patients via medical thoracoscopy

Under pathological microscopy, 58 (58/76, 76.32%) necrosis cases and 53 (53/76, 69.74%) caseous granuloma cases were found in the whole 76 TP cases. After the targeted biopsy, the AFB test of tissue was positive in 3 cases (3/76, 3.95%). And the culture of tissue was positive in 5 cases (5/76, 6.58%) (Table III).

Accuracy and predictive value of the diagnostic tools

Based on the radiological findings, the TP diagnosis varied in a range (17-36 /76 for X-ray, 29-38/76 for CT scan). Therefore, the accuracy and predictive value of radiology were variation during a range.

In the laboratory test, pleural ADA level over 40 U/L, pleural LDH level over 200 U/L and predominant pleural lymphocytosis (> 50% cells are lymphocytes) present relatively high sensitity (81.58%, 76.32%, 82.89% respectively) and positive predictive value (91.18%, 89.23%, 90.00% respectively) with low specificity (60.00%,

53.33%, 53.33% respectively). When pleural ADA level combined with pleural LDH level or lymphocyte rate test, they perform raised specificity (80.00%, 66.67%,respectively) than any single test as previous research[19]. Pleural ADA level combined with pleural LDH level also presents a high diagnostic efficiency (74.73%).

The visual diagnosis of TP was established at medical thoracoscopy in 72 of 76 TP patients (72/76, 94.74%). In terms of diagnostic efficiency, the visual diagnosis showed more accurate than these noninvasive tools (93.41%, $p < 0.005$). The other diagnostic accuracy and predict value of these different methods was shown in Table IV.

Medical thoracoscopy outcomes

The mean interval between admission and medical thoracoscopy was 15.5 ± 17.3 days (range: 3-67 days). The mean operative time was 52.23 ± 15.87 min (range: 30-130 min). After the operation of medical thoracoscopy, 35 of the 91 patients complained of chest pain for an average of 3 days, which was relieved by oral nonsteroidal anti-inflammatory drugs (celecoxib capsules) or opiates (such as tramadol and bucinnazine). No other complications, such as aeroembolism, re-expansion pulmonary edema, wound infection or hemorrhage occurred. Average days of drainage were 5.67 ± 3.12 days, ranged from 3 to 19 days.

Table IV. The accuracy and predictive value of the diagnostic tests for tuberculous pleuritis.

	TP (n=76)	Non-TP (n=15)	Sensitiity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic efficiency (%)
Abnormal CR	17-36/76	6-10	22.37-47.37	33.33-60.00	62.95-85.71	7.81-18.37	24.18-49.45
Abnormal CT	29-38/76	5-8	38.16-50.00	46.67-66.67	78.38-88.37	12.96-20.83	39.06-52.75
Acid-fast stain positive in sputum	0/56	0/13	0	100	∝	18.84	18.84
Culture positive in sputum	0/56	0/13	0	100	∝	18.84	18.84
Pleural effusion							
PPD skin test	48/68	2/13	70.59	81.82	96.00	31.03	72.15
ADA >40	62/76	6/15	81.58	60.00	91.18	39.13	78.02
LDH >200	58/76	7/15	76.32	53.33	89.23	30.77	72.53
Lymphocytes % >50%	63/76	7/15	82.89	53.33	90.00	38.10	78.02
ADA >40 and LDH >200	56/76	3/15	73.68	80.00	94.92	37.50	74.73
ADA >40 and Lymphocytes % >50%	58/76	5/15	76.32	66.67	92.06	35.71	74.73
Acid-fast stain positive	0/56	0/13	0	100	∝	18.84	18.84
Culture positive	0/56	0/13	0	100	∝	18.84	18.84
Medical thoracoscopy							
Visual diagnosis	72/76	2/15	94.74	86.67	97.30	76.47	93.41
Necrosis	58/76	1/15	76.32	93.33	98.31	43.75	79.12
Diffuse miliary nodules	49/76	2/15	64.47	86.67	96.08	32.50	68.13
Pleural adhesions or fibrotic septa	60/76	1/15	78.95	93.33	98.36	46.67	81.32
Acid-fast stain positive	3/76	0/2	3.95	100	100	2.67	6.41
Culture positive	5/76	0/2	6.58	100	100	2.74	8.97

CR Chest radiology, CT Computed tomography, PPV Positive predictive value, NPV negative predictive value, PPD Purified protein derivative, ADA Adenosine deaminase, LDH Lactate dehydrogenase, CEA Carcinoma embryonic antigen.

Follow-up result

Four patients died during the period of the chart review (from October 2006 to July 2012) of unrelated causes: 1 died from encephalorrhagia, 2 died from coronary heart disease, and 1 died from lung cancer.

Seventy six TP patients were treated with standard anti-tuberculous chemotherapy (isoniazid 300 mg, rifampicin 450 mg, pyrazinamide 1500 mg and ethambutol 15mg/kg/day taken at a draught per day) for 6-10 months, and all of them completed the anti-tuberculous chemotherapy under the direct observation. The follow-up visits comfirmed that all of TP patient had clinical improvements after chemotherapy.

Discussion

Pleural effusion is a common clinical condition in daily practice, which is mostly caused by TP in developing countries[19]. It was previously believed that delayed hypersensitivity plays an important role in the pathognenesis of tuberculous pleural effusion[3]. Because of that, the positive dectection of *Mycobacterium tuberculosis* in pleural fluid was rare[20]. Recently, it is reported that tuberculous effusion also can occur as a result of direct spread of bacilli from cavitary lung lesions[16]. However, the rate of positive Mycobacterial result might be decreased to a rarer level through the untargeted thoracocentesis[18,21,22]. Similar to these studies, the AFB smear and the culture positivity were 0% in pleural fluid samples after our "blind" thoracocentesis. However, might due to the difficulty of isolating and culturing the *Mycobacterium tuberculosis*, the AFB and culture positivity were still poor after targeted biopsy.

Thirty-five patients were underwent CT-guided biopsy in this study. None of them showed positive result of *Mycobacterium tuberculosis*. This unsatisfying result of CT-guided biopsy might be explained by these followed reasons: 1) aspiration sample might be too little to define the character of cytology. 2) abnormal pleural appearance are not always seen on thoracic CT scan, and only 20 percent of tuberculous effusion associated pulmonary lesions at most[13]. Agreed with the BTS guideline of local anesthetic thoracoscopy[30], this research data showed medical thoracoscopy was one of the techniques with the highest diagnostic yield in aspiration cytology negative TP. And the abnomal chest CT scan of TP showed enhanced pleural fulid, thickened and nodular pleura, fibroplasias and cavity. However, these abnormalities could be found in other diseases, especially pleural malignant disease, indicating the CT scan in the diagnosis of TP might be of limited value.

Testing for pleural ADA levels is an easy and inexpensive method for establishing the diagnosis of TP[19]. In China, pleural fluid ADA is routinely employed in the diagnostic flow chart. The pleural ADA level over 40 U/L had relatively high sensitity and positive predictive value (PPV) with low specificity in this study, suggesting it might be appropriate to screen TP with pleural ADA level. ADA is a common enzyme present in lymphocytes, so high pleural ADA level has also been reported in malignancies (5%, particularly lymphomas), infectious disease, and connective tissue disease[22,33,34]. This can explain why 6 non-TP patients showed high ADA level in this study. And our study replicated previous studies[19], presenting that the accuracy of pleural ADA level appeares to be higher after combination with pleural LDH or lymphocyte level. However, those accuracy were still lower than medical thoracoscopy's ($p < 0.005$).

Previous studies valued the medical thoracoscopy in diagnosing of pleural effusion, which might include some other non-suspect TP cases. In this study, medical thoracscopy was performed in all of 91 pleural effusion patients who were suspected with TP. According to some other tuberculous series studies[11,23-25], this study classified the characteristic TP appearance under medical thoracoscopy into five types:

1. Necrosis scattered over the pleura;
2. Diffuse milliary nodules (< 5 mm) on the pleura;
3. Single or multiple pleural nodules (> 5 mm) on the pleura;
4. Hyperemic, edematous and thickened pleura;
5. Pleural adhesions or fibrotic septa; and all of these samples had hydrothorax or loculated effusion.

The most common appearances of TP were diffuse milliary nodules (64.47%), necrosis (76.32%), and adhesions (78.95%). The authors have reported their preliminary diagnosis of TP with these visual findings, before the combined bacteriologic and histologic results coming out. This visual diagnosis showed high efficiency (93.41%) for TP. However, this high efficiency depends on the interpretation of the medical thoracoscopist. In this study, all of these medical

thoracoscopists are senior and experienced specialists of TB in the high burden country-China. The more experience might bring the higher efficiency. And in the lower burden country-Korea, the visual diagnosis efficiency for tuberculosis (88%) was less than our study[11], which might be attributed to the less experience.

Another advantage of medical thoracoscopy is the speed of diagnosing[26]. Though the conventional microbiological studies show high prevalence of negative result, they could take up to 4-6 weeks. The visual diagnosis could be defined just during medical thoracoscopy, even combined with the histological verification usually takes 5-7 days in our hospital and allows quick diagnosis. Although mortality has been decreasing, it has been estimated that tuberculosis causes 1.7 million deaths each year[27]. Meanwhile, there are increasing multidrug-resistant TB (MDR-TB)[5,21]. Both the high mortality and increasing MDR-TB could be partially induced by delay treatment. With quick diagnosis under thoracoscopy, the anti-tuberculosis treatment can be initialed instantly. On the other hand, medical thoracoscopy could provide larger quantities of tissue required for culture in suspected MDR-TB. Of note is that 2 malignant patients in this series present thoracoscopy feature of TP. Conversely, 4 TP cases were misdiagnosed with malignant disease. These findings demonstrated the importance of biopsies under medical thoracoscopy.

In this retrospective study, medical thoracoscopy, combined with bacteriologic and histologic observation, presented excellent availability of TP diagnosis. It confirmed TP in 76 cases, even though all of bacteriologic and histologic results were negative before thoracoscopy procedure. This extraordinary diagnostic yield of TP might be due to the targeted biopsy under direct observation of pleural space.

Medical thoracoscopy is also useful when lysis of adhesions and fibrotic septa is indicated for more effective drainage[19]. In this study, all of the pleural effusion smples were exudate as Light's study3]. We also found that the most common appearance of pleural lesion in TP was adhesions and fibrotic septa under medical thoracoscopy. Exudate is full of fibrin, which can deposit and concentrate. Then, fibrin might construct the pleural adhesions, fibrotic septa and even loculation chronically[28,29]. Especially, some of TP patients, who might be underwent thoracocentesis times for drainage, have more potential of coagulation. Though physicians could clear the adhesion or fibrotic septa with direct observation, an obvious and thick fibrous adhesion might prevent medical thoracoscopy. Therefore, the authors suggested that medical thoracoscopy might be performed in the early stage of TP. Since the adhesion or fibrotic septa might block vision, authors also suggested avoided and cleared the obvious fibro-adhesion with caution.

Most of previous research showed that the mortality and chance of systemic complication after medical thoracoscopy were lower, compared with surgical thoracoscopy or thoracotomy biopsy[30-32]. Because of local anesthesia and minimized cut, the medical thoracoscopy objects ranged from 16 to 84 years-old, including poor health who might not endure the general anesthesia and surgical trauma. In this study, chest pain was the only encountered complication for an average of 3 days, relieved by oral non-steroidal anti-inflammatory drugs or opiates. All of these findings might imply the less side effect of medical thoracoscopy.

Conclusions

TP presents a variety of scopic phenotypes under medical thoracoscopy. The experienced pulmonologists visually diagnose TP efficiently and directly via medical thoracoscopy. Medical thoracoscopy with combined biopsy is the most accurate and safe method for diagnosing TP.

Acknowledgement

This study was supported by National Nature Science Foundation of China 30770931, 30800503, 81070039 and the National Natural Science Foundation of Hunan Province 09JJ3036 and 2008FJ3151.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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