Original Article

Morphological manifestation of tuberculous pleurisy in children under medical thoracoscope and diagnostic value

Qian Li, Xiaodi Tang, Xiuli Yan

Abstract:

OBJECTIVE: Our study analyzed the main manifestations of tuberculous pleurisy (TBP) in children under medical thoracoscopy (MT). This article aimed to explore the clinical application value of MT in the diagnosis and treatment of TBP in children.

METHODS: In our study, we selected 23 TBP patients diagnosed in our hospital. We analyzed the clinical data and thoracoscopic morphology of these patients. At the same time, we also observed the pathological manifestations, acid-fast staining, and treatment effects of the patient's diseased tissue under MT.

RESULTS: The MT clinical findings of TBP patients include pleural hyperemia and edema, miliary nodules, scattered or more white nodules, simple pleural adhesion, wrapped pleural effusion, massive cellulose exudation, yellow-white caseous necrosis, pleural hyperplasia and hyperplasia, and mixed pleural necrosis. The positive rate of pleural biopsy was 73.91% and that of acid-fast staining was 34.78%. The main pathologic types of these patients were tuberculous granulomatous lesions (16 cases), caseous necrosis (5 cases), and fibrinous exudative, multinucleated giant cell and other inflammatory cell infiltration lesions (13 cases). The average time of diagnosis of the 23 patients was 8.32 days (5.0–16.0 days), and they were transferred to specialized hospitals for treatment after diagnosis. The mean time of chest drainage was 3.0–5.0 days after treatment. The average time for their body temperature to return to normal was 3.31 days (2.0–5.0 days).

CONCLUSION: Thoracoscopic lesions of TBP in children are varied. The use of MT is not only helpful for the early diagnosis and treatment of TBP. It also protects and improves lung function. Therefore, the use of MT has high clinical value.

Keywords:

Child, diagnostic value, medical thoracoscopy, performance under thoracoscopy, tuberculous pleurisy

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Tuberculous pleurisy (TBP) is one of the types of extrapulmonary tuberculosis in developing countries.[1] TBP is inflammation caused by a high allergic reaction to direct or indirect infection with *Mycobacterium tuberculosis*.[2] It is also one of the main causes of pleural effusion in children. There are no typical clinical symptoms in the early stage of TBP. At the same time, most of the patients had no active tuberculosis focus in their lungs.[3] Therefore, early patients with TBP are easy to be misdiagnosed, thus delaying their treatment time. Middle-stage or late-stage TBP patients develop a series of clinical manifestations, such as pleural adhesions, hypertrophy, thoracic collapse, and scoliosis.[4] TBP in children tends to occur in children or adolescents over 5 years old, ranking second in the etiology of pleural effusion in children, accounting for 12.6%.[5] The existing clinical basic treatment methods include chemotherapy, hormone therapy, and surgery.[6] However, the

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complexity of TBP often leads to the limitations of the clinical application of these treatment options.

The diagnosis of TBP in children is mainly based on tuberculosis contact history, clinical manifestations, chest imaging features, tuberculin examination, interferon-γ release examination, laboratory examination of pleural effusion, pathology, and diagnostic antituberculosis efficacy.[7] In TBP, depending on the radioimaging test, computed tomography (CT) scan chest can show lung parenchymal involvement in more than 50% of cases. However, sometimes, TBP is difficult to diagnose, which is easy to cause misdiagnosis and mistreatment, so it is necessary to rely on pleural biopsy under medical thoracoscopy for diagnosis.[8] MT is a minimally invasive procedure. It is usually performed by an interventional pulmonologist in the endoscopy room or operating room under local or general anesthesia or moderate sedation.[9] Pleural biopsy is currently considered to be an effective means of diagnosing TBP. MT provides endoscopic access to the chest cavity. The doctor observed the lesions in the pleural cavity directly and biopsied the lesions.[10] This is helpful for histopathological examination and analysis of pathogen-related etiology. Therefore, MT is also considered a safe means of examination and treatment.[11] For the treatment of infectious diseases, MT is used in early-stage patients to release adhesive bands, remove abscesses, and encapsulated effusion. This helps patients to promote pulmonary recruitment. Compared with other treatment schemes, MT is more beneficial to the recovery of patients' conditions.[12] For clinical examination of extrapulmonary tuberculosis, MT is used to examine and obtain the biopsies of pleural tissue and perform therapeutic interventions. Studies have shown that 20%–40% of exudative pleural effusion and suspected TBP patients are still misdiagnosed.[13,14] Whether the clinical application of MT reduces this rate of misdiagnosis is unknown.

Our work explored the clinical application value of MT in the diagnosis and treatment of TBP in children by analyzing the characteristics of 23 children diagnosed with TBP in the Department of Respiratory Intervention of Shandong University Qilu Children's Hospital after MT diagnosis and treatment. We hypothesize that the clinical application of MT is more accurate in the diagnosis of early TBP in children. At the same time, MT contributes to the treatment process of TBP in children by promoting pulmonary recruitment or other ways.

Methods

General information

This study was a retrospective study. From October 2013 to February 2020, 23 children with TBP were admitted to the Department of Respiratory Intervention of Shandong University Affiliated Children's Hospital. All of them were healthy before and had no other underlying diseases. To identify the etiology of pleural effusion, they performed pleural adhesion release. After obtaining approval from the Medical Ethics Committee of our hospital and the informed consent of their guardians, we conducted an MT examination. The selection of cases was consistent with MT examination indications, without absolute contraindications. There were 18 males and 5 females, with a sex ratio of 3.60:1.00. The mean age was 8.1 years old, and the course of the disease was 1–36 weeks, with an average of 5.02 weeks. The clinical symptoms included fever, cough, sputum, chest pain, and chest tightness. All cases were secondary, and 10 cases had a history of tuberculosis contact. After admission, unilateral or bilateral pleural effusion was confirmed by chest CT or B-ultrasound, and closed drainage by pleural puncture was required in all cases. Chest CT or chest radiograph combined with or without pulmonary parenchyma lesions. The basic information is shown in Table 1.

Medical thoracoscopy inspection

Checking equipment and instruments

(1) EVIS LIFT240 Flexible front-end MT (Olympus, Tokyo, Japan). (2) EVIS LUCERA BF-P260F series electronic bronchoscope produced (outer diameter 4.0 mm) (Olympus). (3) EVIS 260 image processing system (Olympus). (4) Biopsy forceps, trocar, thoracic drainage system.

Table 1: Basic information

Classification	Cases	Ratio (%)
Course of disease <2 weeks	7	30.43
Course of disease ≥2 weeks	16	69.57
Fever	23	100
Cough	15	65.21
Chest pain	4	17.39
Chest tightness	2	8.70
Distribution of pleural effusion		
Right pleural effusion	12	52.17
Left pleural effusion	9	39.13
Bilateral pleural effusion	2	8.70
Hydrothorax examination		
Mainly composed of mononuclear cells	18	78.26
Mainly composed of lobulated nuclear cells	5	21.4
Hydrothorax TB-DNA/RNA		
Negative	22	95.65
Positive	1	4.35
PPD test		
Negative	8	34.78
Positive	15	65.22
T-SPOT test		
Negative	13	56.52
Positive	10	43.48
PPD and T-SPOT tests were negative	8	34.78

PPD=Purified protein derivative, TB=Tuberculosis

Preoperative preparation

All patients underwent routine examinations before surgery. Examinations included blood routine, activated partial thromboplastin time, clinical biochemistry, electrocardiogram, HIV1/2-Ab, HCV-Ab, TP-Ab, HBcAb, and blood pressure measurement. Preoperative chest CT and B-ultrasound were performed to select the puncture site. The 6th to 8th intercostal incision of the posterior axillary line of the lateral chest wall was selected for puncture.

Examination procedure

All patients underwent MT examination under general anesthesia. General anesthesia was performed by intravenous and inhalation anesthesia. During the operation, the laryngeal mask was connected to the anesthesia machine for ventilation, and heart rate, respiration, blood pressure, and oxygen saturation were monitored during the operation. Patients laid on the side. They were raised laterally. The upper limb was raised at the right angle to the body. Moreover, the lower chest wall was padded with a circular pad, making the upper spine arched. This helped to fully expose the intercostal space. At the incision, 5% lidocaine was anesthetized layer by layer to the parietal pleura. The surgeon made an incision of about 1 cm with a scalpel, bluntly separated each subcutaneous layer to the pleura, and placed a human puncture cannula perpendicular to the intercostal space. Next, MT was placed through the cannula into the pleural cavity. We observed the visceral layer, parietal layer, diaphragmatic pleura, and peri-incision pleura in the order of internal, anterior, superior, posterior, lateral, and inferior. The pleural tissue was taken by forceps at the lesion site for pathology examination. Biopsy forceps were used at the adhesive zone for local release. After the examination, the drainage tube was placed, and the negative pressure drainage box or water seal bottle was connected. Patients were then observed for any adverse reactions. After MT surgery, all patients underwent bronchoscopy to rule out pulmonary hemorrhage and active tuberculosis. The anesthesiologist performed resuscitation, and the patient returned to the ward. Postoperative temperature changes, dyspnea, chest pain, and chest tightness were observed. At the same time, we also recorded the drainage volume and liquid properties in the drainage bottle.

Diagnostic criteria

Pathological diagnostic criteria of MT biopsy:

1. Chronic granulomatous inflammation with caseous necrosis
2. Chronic granulomatous inflammation, acid-fast staining positive
3. Chronic granulomatous inflammation, acid staining negative, the diagnostic antituberculosis treatment effective
4. Cellulose exudation, multinucleated giant cells and other inflammatory cell infiltration, acid-fast staining negative, the diagnostic antituberculosis treatment is effective.

Among them, (1) and (2) were considered the gold criteria for TBP diagnosis, and the diagnosis was made by referring to the TBP diagnostic criteria formulated by the Tuberculosis Branch of the Chinese Medical Association.[15,16]

Results

Morphological manifestations of tuberculous pleurisy under medical thoracoscopy

As shown in Figure 1, we observed pleural hyperemia and edema in 4 cases (17.39%), miliary nodules in 1 case (4.35%), scattered or more white nodules in 5 cases (26.08%), simple pleural adhesion in 6 cases (26.09%), encapsulated pleural effusion in 5 cases (21.73%), massive cellulose exudation in 5 cases (21.73%), yellow-white caseous necrosis in 7 cases (41.18%), pleural hyperplasia and hypertrophy in 1 case (4.35%), and mixed type under MT in 17 cases (73.91%).

The main manifestations of tuberculous pleurisy histopathology

As shown in Figure 2, we have observed tuberculous granulomatous lesions in 16 cases (69.57%), caseous necrosis in 5 cases (21.74%), and fibrinous exudative and inflammatory cell infiltrating lesions in 13 cases (56.52%). Meanwhile, the pathologic positive rate of pleural biopsy under MT was 73.91% and that of acid-fast staining was 34.78%. Overall, there were 8 children diagnosed using gold standard, 9 children diagnosed using serial 3rd criteria, and 6 children diagnosed using serial 4th criteria [Table 2].

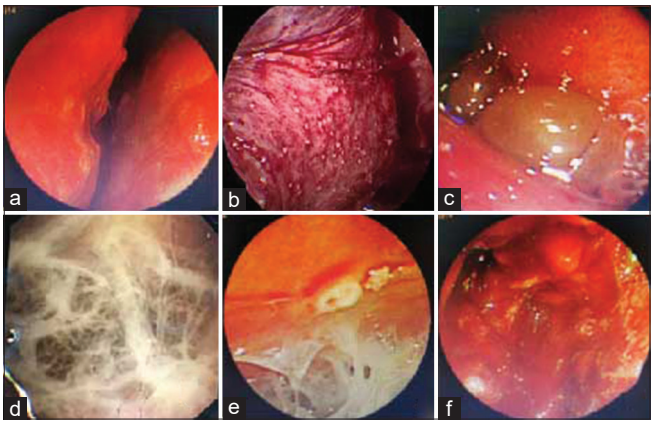

Figure 1: Various pathological changes of tuberculous pleurisy under medical thoracoscopy. (a) Pleural congestion and edema. (b) Miliary nodules. (c) Encapsulated pleural effusion. (d) Cellulose exudates. (e) Cheese like spoilage. (f) Pleural hypertrophy and hyperplasia

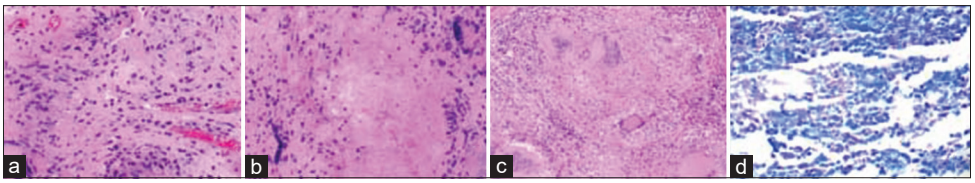

Figure 2: Histopathological manifestations and acid-fast staining of tuberculous pleurisy. (a) Tuberculous granuloma. (b) Caseous necrosis. (c) Cellulose exudation and multinucleated giant cell infiltration. (d) Positive acid-fast staining

Analysis of disease course and medical thoracoscopy morphologic results

As shown in Table 3, seven patients had a course of disease <2 weeks (30.43%). In addition, five patients showed pleural adhesion, multiple nodules, miliary nodules, and caseous necrosis (21.74%). In addition, two patients presented with pleural adhesion hypertrophy, cellulose exudation, and multiple encapsulated effusion (8.70%). The course of disease was >2 weeks in 16 patients (69.57%). Four patients presented with pleural adhesion, multiple nodules, miliary nodules, and caseous necrosis (17.39%). Twelve patients showed pleural adhesion hypertrophy, cellulose exudation, and multiple encapsulated effusion (52.17%).

Pleural biopsy for primary tuberculosis

There were five patients who were negative for X-ray Pert in pleural fluid. Among five negative patients, two cases were tested for half a month, one case was tested for 20 days, one case was tested for 1 month, and one case was tested for 2 months. In addition, pleural biopsy X-ray Pert found that four of these cases were positive. Next, we conduct a pleural biopsy for high throughput detection of pathogens. Among five negative patients, we found that three of these cases were positive for the *M. tuberculosis* complex group. This suggested that the pleural biopsy results are more accurate.

Therapeutic effect

During MT, samples were taken from different parts of the patient for biopsy. During the operation, the adhesive band was fully released, the encapsulated pleural effusion was removed, and the patient was fully attracted. The mean time to diagnosis was 8.32 days (5.0–16.0 days). The mean time of chest drainage was 3.0–5.0 days. The average time for their body temperature to return to normal was 3.31 days (2.0–5.0 days). As shown in Figure 3, the patient's chest imaging improved after review. After diagnosis, patients were referred to specialized hospitals for regular antituberculosis treatment. Eventually, we found that the patient's clinical symptoms gradually disappeared.

Complications

All patients had postoperative incision site pain, which was tolerated by most patients. 3–5 days after the operation, the pain gradually relieved, and the local pleural bleeding appeared slight. The patient's bleeding stopped after a topical spray of 1:10, 000 epinephrine. In this process, we also found two patients with mild subcutaneous emphysema without dyspnea or shortness of breath. However, the symptoms disappeared after 2–3 days.

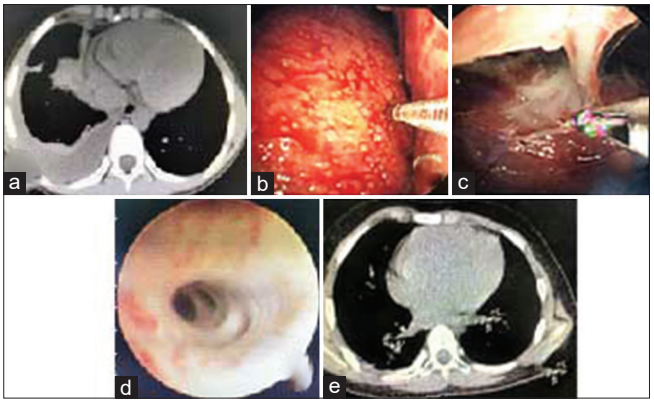

Figure 3: Thoracoscopic treatment of tuberculous pleurisy. (a) Chest computed tomography (CT) before treatment. (b) Pleural biopsy. (c) Loosen the adhesive joint. (d) Smooth and unobstructed lumen mucosa under bronchoscopy. (e) Chest CT after treatment

Discussions

TBP is one of the main causes of pleural effusion in children.[17] If it is not treated promptly, TBP in children leads to pleural adhesion, hypertrophy, thoracic collapse, and scoliosis. The early clinical symptoms of this disease are not typical, mostly without active tuberculosis, which is easy to be misdiagnosed.[18] With the exudation of a large amount of protein and cellulose in the chest, the patient will have pleural adhesion hypertrophy, thoracic collapse, and scoliosis.[19] This brings great harm and loss to TBP in children and their parents. Our study aimed to explore the application value of MT in clinical diagnosis and treatment by analyzing the main morphological manifestations under MT of TBP in children.

MT examination is the main diagnosis and treatment technique for interventional respiratory diseases at present. It observes the full picture of the pleural cavity in detail and performs multipoint biopsy under direct vision. It has the characteristics of high diagnosis rate, few complications, safety, and simple operation. Foreign studies have shown that the diagnostic rate

Table 2: Proportion of pathological results of pleural biopsy under medical thoracoscopy

	Pathological characteristics	Cases	Ratio (%)
Pathologically positive (17 cases; 73.91%)	Chronic granulomatous inflammation, caseous necrosis, and positive acid-fast staining	8	34.78
	Chronic granulomatous inflammation, considering TB and negative acid-fast staining	9	39.13
Pathologically negative (6 cases; 26.09%)	Cellulose exudation, inflammatory cell infiltration, and negative acid-fast staining	6	26.09

TB=Tuberculosis

Table 3: Relationship between the course of disease and the morphology of lesions under medical thoracoscopy

Course of disease (days)	Pleural congestion, edema, and white nodules	Diffuse miliary nodules	Pleural adhesions, cellulose, and encapsulated effusion	Caseous necrosis	Pleural hypertrophy and hyperplasia
14–21	2 (8.70)	0	2 (8.70)	3 (13.04)	0
21–28	2 (8.70)	0	7 (30.43)	2 (8.70)	0
>28	0	1 (4.35)	3 (13.04)	0	1 (4.35)

of MT for unknown causes of pleural effusion is more than 80%.[20,21] Compared with traditional closed pleural biopsy, MT pleural biopsy has the characteristics of direct vision, thus reducing the number of pleural biopsies and improving the accuracy of pleural biopsy.[22] Studies have shown that in the diagnosis of TBP, the diagnostic rate of the pleural biopsy under MT is 94.46%.[20,23,24] Here, we found that the positive rate of MT pleural biopsy was 73.91%, and the positive rate of fast staining was 34.78%. The average time of diagnosis was 8.32 days (5.0–16.0 days). Therefore, pleural biopsy under MT is of great significance in the diagnosis of TBP. Attention is paid to biopsies at multiple sites of pleura to improve the positive rate, shorten the time of diagnosis, provide a reliable pathological basis for clinical diagnosis, and avoid misdiagnosis and mistreatment.

The morphology of pleural lesions in different stages of the course of TBP is also different. MT is visually observed and provides a basis for diagnosis. Sugiyama[24] divided the morphological manifestations of TBP lesions under MT into four stages. Stage I is mucosal hyperemia and edema, which could be accompanied by scattered white nodules. Stage II is the diffuse nodule stage. The patient has extensive parietal pleural edema and diffuse white nodules of varying sizes. Stage III is the cellulose hypoplasia stage. The patients have reticular or lamellar adhesions between the visceral parietal pleura. Stage IV is pleural atresia or hypertrophy. The patient's pleura thickened, whitened, and hardened, making forceps difficult to extract. The clinical characteristic changes in Stages II and III lasted for 3–4 weeks. At this time, the positive rate of biopsy in patients is the highest, and typical tuberculous granuloma and caseous necrosis can be seen in the pathology. In our study, we found that there were 7 cases in Stage I, 15 cases (65.22%) in Stage II and III, and 1 case (1.4%) in Stage IV. It has been found that the lesion forms under TBPMT include pleural congestion and edema, scattered or multiple grayish or white nodules, miliary nodules, parietal pleural adhesion, wrapped effusion, fibrinous exudation and caseous material, and pleural hyperplasia, which was consistent with a previous report.[25] In addition, it was found that when the course of TBP was short, the main morphological changes of pleural lesions were multiple pleural nodules and caseous necrosis. In the longer course of the disease, the main symptoms were pleural adhesion hypertrophy, cellulose exudation, and multiple encapsulated effusion.

Therefore, MT technology not only has the advantages of less trauma and biopsy of diseased tissues under direct vision but also has the therapeutic significance of attracting pleural fluid and releasing intrathoracic adhesions.[26] All the children in this study had mild chest pain after MT examination and treatment. Among them, 2 cases had mild subcutaneous emphysema without dyspnea or shortness of breath. However, symptoms disappeared after 2–3 days. Therefore, we believe that MT treatment of TBP in children can shorten the length of hospital stay and reduce the occurrence of sequelae. MT therapy is an effective, safe, and reliable method to treat TBP.

Conclusion

To sum up, the morphological manifestations of TBP in children under MT are varied. As a minimally invasive examination and treatment method, MT has the advantages of safety and fewer complications. Under MT, pleural biopsy, pleural adhesion band release, exfoliation of encapsulated pleural effusion, pleural fluid aspiration, and local administration of antituberculous drugs can be performed. At the same time, we also found that MT has an extremely important clinical value of TBP in early diagnosis and disease control. It improves clinical symptoms and reduces the occurrence

of sequelae. However, there were still some limitations in this study, and the included clinical sample size is relatively small. In the future, we will include more cases, as well as cases of children with immunosuppression or late reporting, for more comprehensive research.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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