Original Article

Microbiological confirmation of tuberculous pleurisy with medical thoracoscopy: targeted pleural washing and pleural biopsy

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Background: Due to the pauci-bacillary nature of tuberculous (TB) pleurisy, clinical diagnosis is common, but microbiological confirmation is necessary to determine drug resistance. This study aimed to investigate the diagnostic yield of medical thoracoscopy (MT) for microbiological confirmation of TB pleurisy.

Methods: Medical records of patients diagnosed as TB pleurisy with microbiological or histologic evidence who underwent MT between May 2015 and July 2023 at Incheon St. Mary's Hospital were retrospectively reviewed. Sensitivities of microbiological results [acid-fast bacilli (AFB) culture or TB-polymerase chain reaction (PCR)] of pre-MT pleural fluid and those of targeted pleural washing fluid and pleural tissues obtained during MT were compared. Difference in sensitivity was verified with McNemar's test.

Results: A total of 72 patients were enrolled. With pre-MT pleural fluid, sensitivities of AFB culture and TB PCR were 5.6% (4/72) and 1.4% (1/72), respectively. With targeted pleural washing fluid, sensitivities of AFB culture and TB-PCR were 23.6% (17/72) and 12.5% (9/72), respectively. With pleural tissues, sensitivities of AFB culture and TB-PCR were 18.1% (13/72) and 40.3% (29/72), respectively. MT showed an additional 27.8% [95% confidence interval (95% CI): 14.2–40.1%, P<0.001] of sensitivity gain in AFB culture and 40.3% (95% CI: 25.7–52.5%, P<0.001) of sensitivity gain in TB-PCR. With pleural washing, additional 19.4% (95% CI: 6.8–31.6%, P=0.001) of sensitivity gain in microbiological confirmation was identified, whereas additional 37.5% (95% CI: 22.6–50.2%, P<0.001) of sensitivity gain was identified with pleural biopsy.

Conclusions: With MT, 44.4% of additional sensitivity gain in microbiological confirmation of TB pleurisy was identified. This underscores the role of MT in the diagnosis of TB pleurisy.

Keywords: Tuberculosis (TB); pleural; thoracoscopy; diagnosis; sensitivity

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Introduction

Extrapulmonary tuberculosis (EPTB) accounts for approximately 17% of total new and relapse tuberculosis (TB) cases globally in 2022 (1). In South Korea, a total of 3,519 patients with EPTB were notified in 2023, accounting for 22.5% of total TB patients (2). EPTB has not been a priority in national TB control as the risk of transmission in EPTB is estimated to be very low. However, some types of EPTB such as central nervous system TB showed higher mortality than pulmonary TB (3,4). In addition, EPTB is associated with more hospitalization and medial expenditure

than pulmonary TB (3), which underscores the necessity of managing EPTB in perspective of public health.

TB pleurisy is the most common type of EPTB in South Korea, which accounts for 45.5% total EPTB patients (2). Diagnosis of TB pleurisy is initiated by obtaining pleural fluid through thoracentesis. Pleural fluid is then sent for basic pleural fluid analysis and microbiological tests such as acid-fast bacilli (AFB) stain, culture, and TB-polymerase chain reaction (PCR). However, due to the pauci-bacillary nature of TB pleurisy, sensitivities of such microbiological tests are low (5-7). Alternatively, clinical diagnosis could be made based on elevated adenosine deaminase (ADA) level among patients showing lymphocyte dominant pleural effusion after excluding other causes of pleural effusion (8). In several previous studies performed in South Korea, one third to two thirds of total enrolled patients were diagnosed clinically (9-12). However, in a previous study, there were many cases of malignant effusion showing elevated ADA level, demonstrating the risk of misdiagnosis in clinical diagnosis of TB pleurisy (13). Furthermore, exclusion of malignant effusion, which is another major cause of pleural effusion especially among elderly population in South Korea, only with the results of pleural fluid analysis is not easy in clinical practice. For example, negative results of pleural fluid cytology could not be interpreted as exclusion of malignant effusion, due to suboptimal sensitivity of pleural fluid cytology for diagnosing malignant pleural effusion (14).

Excellent diagnostic performance of medical thoracoscopy (MT) over other diagnostic tools for diagnosing TB pleurisy has been demonstrated (15). Although some experts have recommended thoracoscopic biopsy only when clinical manifestation is not typical, the role of MT in diagnosis of TB pleurisy has been underscored (13). Moreover, enhanced sensitivity of microbiological test with specimens obtained by MT has been reported (16,17). As World Health Organization recommended the universal drug susceptibility testing (DST) for appropriate treatment (18), which is feasible with isolation of live *Mycobacterium tuberculosis* (MTB) or it's deoxyribonucleic acid (DNA), microbiological confirmation of TB pleurisy has been underscored.

With this background, this study was designed to investigate additional sensitivity gain of MT in perspective of microbiological test such as AFB culture or PCR. Especially, we introduced a novel specimen—targeted pleural washing fluid collected after pleural biopsy and compared its usefulness with pre-MT pleural fluid obtained by thoracentesis and pleural tissue. We present this article in accordance with the STARD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-143/rc).

Highlight box

Key findings

- With targeted pleural washing fluid obtained via medical thoracoscopy (MT), sensitivities of acid-fast bacilli (AFB) culture and tuberculosis (TB)-polymerase chain reaction (PCR) were 23.6% and 12.5%, respectively, resulting in additional 19.4% [95% confidence interval (95% CI): 6.8–31.6%, P=0.001] of sensitivity gain in microbiological confirmation.
- With pleural tissues, sensitivities of AFB culture and TB-PCR were 18.1% and 40.3%, respectively, leading to additional 37.5% (95% CI: 22.6–50.2%, P<0.001) of sensitivity gain.
- Overall sensitivity of MT in aspect of microbiological confirmation of TB pleurisy was 50%, which was 44.4% higher than sensitivity of pleural fluid obtained before medical thoracoscopy.

What is known and what is new?

- Yield of microbiological confirmation for TB pleurisy had been reported to be low, when compared to that of pulmonary TB, due to a pauci-bacillary nature of TB pleurisy.
- Previous studies reporting usefulness of MT in diagnosis of TB pleurisy focused on histological diagnosis with pleural tissue.
- We introduced a novel specimen—targeted pleural washing fluid obtained after pleural biopsy and reported its usefulness in microbiological confirmation of TB pleurisy.

What is the implication, and what should change now?

- MT could be an alternative for enhancing sensitivity of microbiological confirmation for TB pleurisy. The role of MT should be underscored in clinical practice.

Methods

Patient selection and case definition

Medical records of patients who were diagnosed as TB pleurisy by MT between May 2015 and July 2023 at Incheon St. Mary Hospital, the Catholic University of Korea were retrospectively reviewed. Patients who showed scanty amount of pleural effusion (thus thoracocentesis was unfeasible) were excluded as pre-MT pleural fluid was not collected.

Indication for MT was described in our previous article (13). In brief, patients with exudative pleural effusion who showed findings of pulmonary TB on chest computed tomography (CT) scan, waited for results of TB nucleic acid

amplification test [e.g., Xpert MTB/RIF (Cepheid, USA)] with sputum or bronchial washing specimens. If results were positive, patients were diagnosed as TB pleurisy without MT and initiated anti-TB treatment. However, when there were clinical risk factors for malignancy (e.g., past history of malignancy) or when there were chances for concurrent TB and malignancy on chest CT scan, MT was performed to rule out malignancy. If results of sputum or bronchial washing fluid were negative, the patient underwent MT. If there was no clue for diagnosis on chest CT scan, the patient underwent MT.

The diagnosis of TB pleurisy was made histologically, microbiologically, and by exclusion of other pleural diseases in pulmonary TB cases. Histologically, patients who showed chronic granulomatous inflammation in pleura were diagnosed as TB pleurisy unless there were findings suggestive of other granulomatous diseases. To rule out non-tuberculous mycobacterium (NTM), TB/NTM PCR (AdvanSure TB/NTM real-time PCR, LG Lifescience, Seoul, Korea) was performed with formalin-fixed, paraffin-embedded pleura tissue. Cases with both negative TB/NTM results were defined as TB pleurisy considering results of a previous study reporting that most cases of granulomatous pleural inflammation were TB pleurisy in South Korea (19). Microbiologically, patients with at least one positive result among two diagnostic tests (AFB culture and TB-PCR) performed on three specimens (pre-MT pleural fluid, pleural tissue, and pleural washing fluid) were defined as TB pleurisy. Bacteriologically confirmed pulmonary TB patients who showed non-specific findings for diagnosis during MT were diagnosed as TB pleurisy and included in this study.

Procedures of MT

Using flex-rigid scope (LTF-240; Olympus, Tokyo, Japan), the operator obtained pleural tissues under direct visualization. The process of frozen sectioning and the strategy of pleural tissue sampling were described in our previous article (13). At least one pleural tissue was sent for tissue AFB culture without formalin fixation. The operator tried 'deep' pleural biopsy which contained extrapleural fat tissue in addition to pleural layer, indicating a high-quality specimen. After such 'deep' pleural biopsy, more than 200 cc of sterilized normal saline was flushed at and around the biopsy site under direct visualization. This targeted washing fluid was collected and inoculated into BACTEC MGIT960 (Becton Dickinson, USA) and 3% OGAWA media (Eiken Chemical, Tokyo, Japan). In addition, these specimens were sent for TB-PCR [AdvanSure TB/NTM real-time PCR (LG Lifescience, Seoul, Korea)].

Statistical analysis

In this study, additional sensitivity gain in microbiological confirmation of TB pleurisy was investigated, which was defined as at least one positive result in AFB culture or TB PCR. Sensitivities of two diagnostic methods (AFB culture and TB-PCR) performed with two types of specimens obtained during MT (pleural washing fluid and pleural tissue) were compared with those using pre-MT pleural fluid. Difference in sensitivity was verified with McNemar's test, which is a commonly used statistical method to compare the sensitivity of two diagnostic tests conducted on the same patient group. Additional gain in sensitivity was calculated separately with 95% confidence interval (95% CI), considering diagnostic methods and type of specimens.

Continuous variables are presented as median [interquartile range (IQR)]. Categorical variables are presented with numbers (percentage). All statistical analyses were performed using RStudio version 1.2.5033. Two-sided $P<0.05$ was considered statistically significant.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethics approval was obtained from the Institutional Review Board (IRB) of Incheon St. Mary's Hospital, Incheon, Korea (approval No. OC22RISI0111). Considering the retrospective design of this study, the requirement for informed consent was waived by the IRB.

Results

Baseline characteristics of enrolled patients

A total of 72 patients with TB pleurisy were included, finally (*Figure 1*). Clinical characteristics of enrolled patients are described in *Table 1*. Median age was 70 years (IQR, 55.75–77 years). Forty-five (62.5%) patients aged 65 years old or over. Forty-nine (68.1%) patients were males, and 31 (43.1%) patients were smokers. Results of pleural fluid analysis (pre-MT pleural fluid) were presented in *Table 2*. Most of them showed lymphocyte-dominant exudate [median percentage of lymphocyte: 81% (IQR, 66.5–90%)]

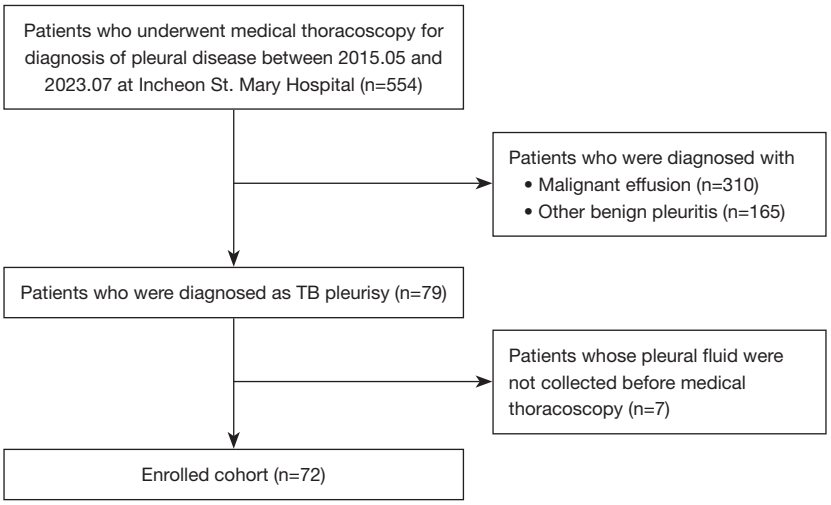

Figure 1 Flow diagram. TB, tuberculosis.

Table 1 Clinical characteristics of enrolled patients (n=72)

Characteristics	Value
Sex	
Male	49 (68.1)
Female	23 (31.9)
Age (years)	70 (55.75–77)
<35	2 (2.8)
35–49	8 (11.1)
50–64	17 (23.6)
≥65	45 (62.5)
BMI (kg/m^2)	22.52 (20.84–23.89)
Smoking	
Non-smoker	41 (56.9)
Ex-smoker	19 (26.4)
Current smoker	12 (16.7)
Comorbidities	
Diabetes mellitus	17 (23.6)
Hypertension	29 (40.3)
Old TB	7 (9.7)
Coronary artery disease	4 (5.6)
Heart failure	2 (2.8)
Chronic kidney disease	8 (11.1)
Liver cirrhosis	6 (8.3)
Cerebrovascular accident	4 (5.6)
Cancer	4 (5.6)

Data are presented as n (%) and median (IQR). BMI, body mass index; TB, tuberculosis; IQR, interquartile range.

Table 2 Pleural fluid analysis results of the enrolled patients (n=72)

Laboratory findings	Value
Protein (pleural fluid) (g/dL)	5.2 [4.6–5.5]
Protein (serum) (g/dL)	7.0 [6.6–7.5]
Pleural fluid/serum protein ratio	0.72 [0.69–0.78]
Albumin (pleural fluid) (g/dL)	2.8 [2.55–3.1]
Albumin (serum) (g/dL)	3.6 [3.2–4.0]
Serum-pleural fluid albumin gradient (g/dL)	0.8 [0.6–1.0]
LDH (pleural fluid) (U/L)	591 [389.5–954]
LDH (serum) (U/L)	399 [343–465.5]
Pleural fluid/serum LDH ratio	1.35 [0.87–2.41]
Glucose (mg/dL)	100.5 [85.25–117.75]
WBC count (/μL)	1,705 [817.5–3,140.5]
Neutrophil (%)	4 [1–13.5]
Lymphocyte (%)	81 [66.5–90]
Macrophage (%)	10 [5–14]
ADA (IU/L)	122 [100–156]

Data are presented as median [IQR]. LDH, lactate dehydrogenase; WBC, white blood cell; ADA, adenosine deaminase; IQR, interquartile range.

with elevated ADA level [median: 122 IU/L (IQR, 100–156 IU/L)]. Diagnostic methods used in the confirmation of TB pleurisy are presented in *Table 3*. Seventy (97.2%) patients showed chronic granulomatous inflammation from pleural tissue pathology. Among them, results of TB PCR and AFB culture were both positive in 17 (23.6%)

Table 3 Diagnosis of TB pleurisy among enrolled patients (n=72)

Tissue pathology (pleura)	TB-PCR[†]	AFB culture[†]	N (%)
Methods of confirm diagnosis			
Chronic granulomatous inflammation	Positive	Growth of MTB	17 (23.6)
		No growth	12 (16.7)
	Negative	Growth of MTB	7 (9.7)
		No growth	34 (47.2)
Other benign	Negative	Growth of MTB	1 (1.4)
		No growth	1[‡] (1.4)
Combined pulmonary TB			
Bacteriologically confirmed pulmonary TB[§]			20 (27.8)
Histologically confirmed pulmonary TB			1 (1.4)
Radiologically diagnosed pulmonary TB			14 (19.4)
No pulmonary involvement			37 (51.4)

[†], combined results from specimens of tissue (pleura), pleural fluid obtained before medical thoracoscopy, and targeted pleural washing fluid obtained during medical thoracoscopy; [‡], bacteriologically confirmed pulmonary TB patients who showed non-specific findings for diagnosis during medical thoracoscopy; [§], patients who showed positive results for smear, culture, and/or rapid diagnostic test recommended by World Health Organization. TB, tuberculosis; PCR, polymerase chain reaction; AFB, acid-fast bacillus; MTB, *Mycobacterium tuberculosis*.

patients. Twelve (16.7%) and 7 (9.7%) patients had positive results of TB PCR and AFB culture, respectively. Results of both tests were negative in 34 (47.2%) patients who were diagnosed not microbiologically but histologically. Among two patients who had benign pathology other than chronic granulomatous inflammation, 1 (1.4%) patient had positive result for AFB culture and the other 1 (1.4%) patient showed negative results for both TB PCR and AFB culture. This patient was included as TB pleurisy by criteria of bacteriologically confirmed pulmonary TB patient who showed non-specific MT findings. Twenty (27.8%), 1 (1.4%), and 14 (19.4%) patients had bacteriologically, histologically confirmed, and radiologically diagnosed pulmonary TB, respectively. The rest 37 (51.4%) patients had no pulmonary involvement.

Additional sensitivity gains of MT by test methods

Table 4 shows sensitivity gains of MT on AFB culture. Sensitivity of AFB culture of pre-MT pleural fluid was 5.6% (4/72), whereas sensitivities of pleural washing fluid and pleural tissue were 23.6% (17/72) and 18.1% (13/72), respectively. Sensitivity for overall specimens obtained during MT was 33.3% (24/72), with an additional 27.8% (95% CI: 14.2–40.1%, P<0.001) of sensitivity gain in AFB culture. Targeted pleural washing showed additional sensitivity gains on AFB culture, when compared to pleural biopsy alone. Eleven patients showed negative results for tissue AFB culture but positive results for pleural washing fluid, leading to an additional 15.3% gain of sensitivity on AFB culture. Sensitivity gains of MT on TB-PCR are presented in *Table 5*. Sensitivity of TB-PCR of pre-MT pleural fluid was 1.4% (1/72), whereas sensitivities of pleural washing fluid and pleural tissue were 12.5% (9/72) and 40.3% (29/72), respectively. Sensitivity of overall specimens obtained during MT was 41.7% (30/72), with an additional 40.3% (95% CI: 25.7–52.5%, P<0.001) of sensitivity gain in TB-PCR. In contrast to AFB culture, additional sensitivity gains of targeted pleural washing on TB-PCR, when compared to pleural biopsy alone were little—only one patient showed negative result with pleural tissue but positive results with pleural washing fluid, leading to 1.4% of sensitivity gain on TB-PCR.

Additional sensitivity gains of MT by type of specimens

Sensitivity gains of pleural washing and pleural biopsy on microbiological confirmation of TB pleurisy are presented in *Table 6*. Sensitivity of pre-MT pleural fluid was 5.6% (4/72), whereas those of pleural washing fluid and pleural

Table 4 Additional diagnostic yield of medical thoracoscopy on AFB culture

Specimens obtained during MT	Pre-MT pleural fluid			Sensitivity (%)			
	Culture positive	Culture negative	Total	Pre-MT pleural fluid	Specimens obtained during MT	Difference (95% CI)	P value
Pleural washing fluid				5.6	23.6	18.1 (5.7–30.0)	0.002
Culture positive	2	15	17				
Culture negative	2	53	55				
Pleural tissue					18.1	12.5 (2.3–23.1)	0.01
Culture positive	3	10	13				
Culture negative	1	58	59				
Overall specimens					33.3	27.8 (14.2–40.1)	<0.001
Culture positive	3	21	24				
Culture negative	1	47	48				
Total	4	68	72				

AFB, acid-fast bacillus; MT, medical thoracoscopy; CI, confidence interval.

Table 5 Additional diagnostic yield of medical thoracoscopy on TB-PCR

Specimens obtained during MT	Pre-MT pleural fluid			Sensitivity (%)			
	PCR positive	PCR negative	Total	Pre-MT pleural fluid	Specimens obtained during MT	Difference (95% CI)	P value
Pleural washing fluid				1.4	12.5	11.1 (2.3–20.7)	0.008
PCR positive	1	8	9				
PCR negative	0	63	63				
Pleural tissue					40.3	38.9 (24.5–51.1)	<0.001
PCR positive	1	28	29				
PCR negative	0	43	43				
Overall specimens					41.7	40.3 (25.7–52.5)	<0.001
PCR positive	1	29	30				
PCR negative	0	42	42				
Total	1	71	72				

TB, tuberculosis; PCR, polymerase chain reaction; MT, medical thoracoscopy; CI, confidence interval.

tissue were 25.0% (18/72) and 43.1% (31/72), respectively. That of overall specimens obtained during MT was 50.0% (36/72), with an additional 44.4% (95% CI: 28.9–57.1%, P<0.001) of sensitivity gain in microbiological confirmation. Targeted pleural washing showed 6.9% of additional sensitivity gains on microbiological confirmation, when compared to pleural biopsy alone. Five patients showed negative results with pleural tissue but positive results with pleural washing fluid. Among them, one patient with non-specific pathologic findings in pleural tissue showed positive AFB culture with targeted pleural washing fluid. The other four patients showed chronic granulomatous inflammation with negative TB PCR in pleural tissue.

Discussion

It is well-known that TB pleurisy often shows a pauci-bacillary nature when compared to pulmonary TB (6,20). In our study, microbiological confirmation was feasible in only 5.6% of total patients with pleural fluid obtained

Table 6 Additional diagnostic yields of targeted pleural washing and pleural biopsy on microbiological confirmation of TB pleurisy

Specimens obtained during MT	Pre-MT pleural fluid			Sensitivity (%)			
	Microbiologically confirmed[†]	Not confirmed	Total	Pre-MT pleural fluid	Specimens obtained during MT	Difference (95% CI)	P value
Pleural washing fluid				5.6	25.0	19.4 (6.8–31.6)	0.001
Microbiologically confirmed	2	16	18				
Not confirmed	2	52	54				
Pleural tissue					43.1	37.5 (22.6–50.2)	<0.001
Microbiologically confirmed	3	28	31				
Not confirmed	1	40	41				
Overall specimens					50.0	44.4 (28.9–57.1)	<0.001
Microbiologically confirmed	3	33	36				
Not confirmed	1	35	36				
Total	4	68	72				

[†], cases were confirmed as TB pleurisy with positive result of TB-PCR or culture. TB, tuberculosis; MT, medical thoracoscopy; CI, confidence interval; PCR, polymerase chain reaction.

by thoracentesis performed before MT. However, MT enhanced the sensitivity of microbiological confirmation up to 50.0%. We demonstrated the additional gain of sensitivity of both AFB culture and TB-PCR using specimens of pleural tissue and pleural washing fluid.

Conventionally, pleural tissue was the only specimen obtained during MT. It was sent for histological examination and microbiological tests such as tissue AFB culture or TB-PCR (16,17,21,22). Several previous studies have presented the sensitivity of microbiological confirmation with pleural tissue obtained during MT. In those studies, the reference standard was defined as microbiologically or histologically diagnosed TB pleurisy, the same as in our study. Casalini *et al.* have reported that sensitivities of AFB culture and TB PCR with pleural tissue were 68.7% and 76.0%, respectively, among patients without pulmonary involvement, and 30.8% and 50.0%, respectively, among those with pulmonary involvement (16). Christopher *et al.* have reported that sensitivities of AFB culture and TB PCR with pleural tissue are 39.1% and 45.0%, respectively (17). Most recently, Li *et al.* have demonstrated that sensitivities of AFB culture and TB PCR with pleural tissue are 56.6% and 69.0%, respectively (22). However, in contrast to those studies, the positive AFB culture rate with pleural tissue was relatively low (18.1%) in our study. This might be because all patients with probable TB pleurisy underwent bronchoscopy if the result of sputum Xpert MTB/RIF was negative. A considerable number of patients were diagnosed with TB pleurisy based on positive Xpert MTB/RIF results in bronchial washing fluid. In other words, we speculate that if bronchoscopy had not been performed, patients with pleural effusion who might have undergone MT and showed positive for AFB culture with pleural tissue, were diagnosed with TB pleurisy based on positive Xpert MTB/RIF results in bronchial washing fluid. As they did not undergo MT, they were excluded from this study. There might be a possibility that patients with low mycobacterial load were selectively indicated for MT, which could have contributed to the lower positive AFB culture rate. Similar to our results, in Casalini's work (16), patients with pulmonary involvement showed lower positive AFB culture rate than those without pulmonary involvement (30.8% *vs.* 68.7%).

In this study, we introduced a novel specimen, the targeted pleural washing fluid. It increased the sensitivity in diagnosis of TB pleurisy with MT. In five patients without microbiological evidence even in pleural tissue examination, pleural washing fluid provided microbiological evidence. Especially, pleural washing fluid showed an advantage of isolating live MTB—additional 15.3% gain of sensitivity on AFB culture when compared with examination of pleural tissue alone. Considering that phenotype DST is feasible only after the isolation of live MTB, targeted pleural washing after pleural biopsy has clear advantage over performing only pleural biopsy during MT.

The pathogenesis of TB pleurisy was explained based on the concept of 'a rupture of subpleural caseous foci' and

'delayed hypersensitivity reaction to MTB antigen'. It was established through several experimental studies (23-25). However, the exact location of the MTB within the thoracic cavity is not known. During MT, the operator removes fibrotic tissue located in pleural cavity as much as possible, which make the loculated effusion becomes mixed together. We postulate that access to MTB confined to loculated effusion and inaccessible via thoracentesis becomes feasible with MT. Another hypothesis is that during the tearing of pleural tissue by forceps, necrotic debris and MTB located at the core of well-formed granulomas may have been released. Further studies clarifying the location of MTB within the thoracic cavity are crucial for microbiological confirmation of TB pleurisy with MT. In addition, as the concept of continuous spectrum of TB pleurisy was suggested (26,27), various spectrum of TB pleurisy should be considered in further studies.

Culture is the gold standard microbiological test for diagnosis of TB (28). In addition to obtaining viable MTB for phenotype DST, we demonstrated an enhanced chance of detecting DNA of MTB with MT, especially in pleural tissues. It was noteworthy that DNA extracted from formalin-fixed paraffin-embedded specimens could be used for DST (29). As various rapid diagnostic tools for detecting nucleic acid of MTB have been introduced (18), the sensitivity of MT in microbiological confirmation would be further improved with these novel diagnostic tools. In this study, we used AdvanSure TB/NTM real-time PCR kit for detection of DNA of MTB, due to the advantage of being able to differentiate NTM. However, in a previous study published in South Korea, Xpert RIF/MTB showed higher sensitivity than AdvanSure TB/NTM real-time PCR among smear negative bronchial washing samples (30). Although there are no direct comparative studies of the sensitivity between AdvanSure TB/NTM real-time PCR and Xpert MTB/RIF in pleural tissue or pleural fluid, we expect further improved sensitivity using Xpert MTB/RIF, considering the pauci-bacillary nature of TB pleurisy.

The usefulness of MT in accurate diagnosis of TB pleurisy among patients with lymphocyte dominant pleural effusion has been reported in our previous article (13). In that study, ADA showed an excellent diagnostic performance. However, clinical diagnosis of TB pleurisy with current ADA cutoff value of 40 IU/L has shown many false positive cases in gray zone showing ADA level between 40–70 IU/L. This could lead to delayed diagnosis of pleural malignancy or unnecessary anti-TB treatment in patients with other benign effusion. Therefore, we suggested MT should be widely performed especially in these patients. In addition, we present another benefit of MT in perspective of microbiological confirmation. Microbiological confirmation is crucial in treatment of TB disease as phenotype or genotype DST could be feasible after obtaining viable MTB or DNA of MTB (31). Considering that prevalence of multi-drug resistance was not different between pulmonary and extrapulmonary TB patients in previous studies carried out in South Korea (32,33), the effort for microbiological confirmation of TB pleurisy should be underscored in clinical practice, as in pulmonary TB. Thus, the role of MT should be more underlined in clinical practice.

Our study has several limitations. First, the number of enrolled patients was small as we did not perform MT among most cases accompanying microbiologically confirmed TB. Despite the small sample size, we demonstrated the statistically significant sensitivity gain of MT. Another limitation of our study was that results of our study were derived from single center experience, which limited the possibility of generalization. Further multi-center studies are needed to verify our results.

Conclusions

In conclusion, despite the pauci-bacillary nature of TB pleurisy, MT could be an alternative for enhancing sensitivity of microbiological confirmation. The role of MT in diagnosis of TB pleurisy should be underscored in clinical practice.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-143/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-143/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-143/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethics approval was obtained from the Institutional Review Board (IRB) of Incheon St. Mary's Hospital, Incheon, Korea (approval No. OC22RISI0111). Considering the retrospective design of this study, the requirement for informed consent was waived by the IRB.

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