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Diagnostic implications of bronchial lavage in patients with pleural tuberculosis

Abstract

Introduction: The presence of *Mycobacterium tuberculosis* in a respiratory specimen is diagnostic in patients with pleural effusion. It is difficult to obtain sputum even after induction in these patients. An alternative method of acquiring respiratory specimens is via bronchial lavage. This study was undertaken to evaluate the diagnostic yield of acid-fast bacilli (AFB) smear, AFB culture, and Xpert assay of bronchial lavage fluid in the workup of pleural tuberculosis patients.

Material and methods: All patients who met the inclusion criteria of the study underwent thoracentesis, pleural biopsy, and bronchial lavage. Specimens of pleural fluid, pleural biopsy, and bronchial lavage fluid were sent for acid fast bacilli smear, culture, and Xpert assay.

Result: Bronchial lavage AFB smear, culture, and Xpert assay was positive in 9.5%, 17.9%, and 26.2% of patients, respectively. It gave an immediate diagnosis in 22 (26.2%) patients.

Conclusion: Bronchial lavage, though not a surrogate to pleural biopsy, offers an additional approach to the early diagnosis of pleural tuberculosis in patients not producing sputum. Besides being diagnostic, this method also has epidemiologic significance in containing the tuberculosis epidemic because detecting *Mycobacterium* in bronchial lavage confirms that the patient is infectious.

Key words: bronchial lavage, bronchoscopy, pleural tissue, pleural tuberculosis, Xpert assay

Adv Respir Med. 2020; 88: 389–393

Introduction

Globally, tuberculosis (TB) remains one of the most important public health problems. Tuberculous pleural effusion affects approximately 5% of people infected with *Mycobacterium tuberculosis* (MTB) and is one of the most common forms of extrapulmonary tuberculosis [1]. According to the World Health Organization, Pakistan is ranked fifth among high-burden TB countries worldwide with an estimated 510,000 new TB cases emerging each year.

Diagnosing pleural tuberculosis is difficult due to paucibacillary infection and often requires invasive procedures like pleural biopsy [2]. For a confirmatory diagnosis of tuberculosis, isolation of the bacterium from pleural fluid or pleural tissue is required which is mostly not possible due to the pathogenesis of the disease [3]. It is known that

pleural space infections are acquired from initial parenchymal lesions which are usually not obvious on chest radiography [4, 5]. With the use of computed tomography, parenchymal lesions and focal areas of subpleural cavitation can be visualized [6].

The presence of *Mycobacterium tuberculosis* in a respiratory specimen is diagnostic in patients with pleural effusion. Sputum specimens are often not tested because these patients usually do not produce sputum even after efforts of sputum induction. An alternative to getting respiratory samples in such patients is by testing fluid acquired via bronchial lavage. It is a safe and minimally invasive procedure done under local anesthesia. In addition to having diagnostic value, it can also be used to monitor the progress of patients who test positive and are given anti-tuberculous treatment (ATT). Apart from these diagnostic implications, it may have epidemio-

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DOI: 10.5603/ARM.a2020.0149

Received: 16.04.2020

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ISSN 2451–4934

logic significance as patients in whom MTB is isolated in bronchial lavage are likely contagious and demand thorough contact tracing, especially in endemic countries like Pakistan.

This study was carried out to evaluate the diagnostic yield of acid-fast bacilli (AFB) smear, AFB culture, and Xpert assay in bronchial lavage in the workup of pleural tuberculosis patients.

Material and methods

This was a prospective study completed from September 2016 to December 2018 in Fatima Jinnah General and Chest Hospital and Taj Medical Complex. All patients aged 18 years or older with lymphocytic exudative pleural effusion who were not expectorating and who had failure of sputum induction were included in the study. Patients with known HIV infection, parenchymal abnormalities on chest imaging (radiograph or computed tomography scan), or those who were already on antituberculous drugs for more than 1 week were not included in the study.

The diagnosis of pleural tuberculosis was made if any of the microbiologic tests came out positive or clinically if the patient responded to antituberculous drugs (resolution of fever, weight gain on 2 months of treatment). Patients not meeting the diagnostic standards for tuberculosis were treated as controls.

All patients underwent thoracentesis, pleural biopsy, and bronchial lavage. Pleural fluid was sent for AFB smear, AFB culture, and Xpert assay (Gene Xpert). An ultrasound of the chest was done in all study participants. Abram’s pleural biopsy was done in patients with no intrapleural septations on ultrasound. Medical thoracoscopy under local anesthesia was done for those with multiseptated or multi-loculated pleural effusions. Pleural tissue specimens were sent for AFB smear, AFB culture, and histopathology in formalin. Tissue for the Xpert assay was sent in normal saline. Bronchial lavage was done under local anesthesia using flexible bronchoscope. Normal saline was instilled into large airways of both lungs and aspirated back. Bronchial lavage fluid was sent for AFB smear, AFB culture, and Xpert assay. The investigation which confirmed the diagnosis of tuberculosis earliest was also documented as the test giving an ‘immediate microbiologic diagnosis’.

Out of a total of 188 patients, 148 patients were included in the final analysis. A study flow diagram is shown in Figure 1.

Written informed consent was obtained for the procedures from study participants. Ethical

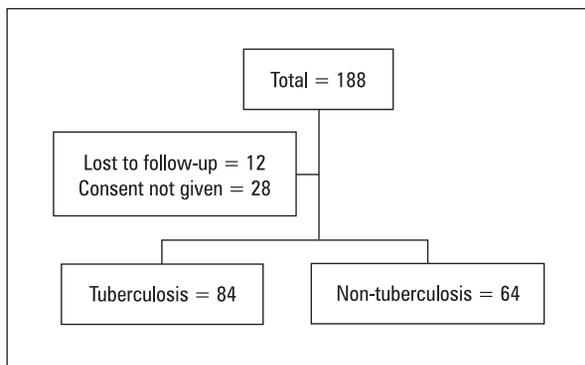


Figure 1. Study flow diagram

approval was obtained from the study hospitals ethical review committee. The study was done according to the principles laid down in the Declaration of Helsinki.

SPSS (version 23) was used for statistical analysis. Mean and standard deviation were calculated for age. The independent samples t-test was used to compare the mean between groups where the data was normally distributed. Frequencies and percentages were calculated for categorical variables and compared using the Chi square test and Fisher’s exact test (if cells had an expected count of less than 5). A P-value of < 0.05 was identified as being statistically significant. Sensitivity and specificity was calculated for various diagnostic tests.

Result

A comparison of the demographic variables between tuberculosis and non-tuberculosis patient groups is shown in Table 1. The sensitivity of bronchial lavage fluid AFB smear, AFB culture, and Xpert assay was 9.5%, 17.9%, and 26.2%, respectively. The yield of different diagnostic methods is shown in Table 2. The immediate microbiologic diagnosis of tuberculosis based exclusively on bronchial lavage was obtained in (22) 26.2% patients. The yield of different microbiologic tests for immediate diagnosis of pleural tuberculosis is shown in Table 3. The overlap of positive results among various diagnostic methods is shown in Figure 2. No significant complications of bronchoscopy were noted in any of the patients.

Discussion

In Pakistan, as a result of TB being a common infection, a mostly exudative lymphocytic pleural

Table 1. Demographic characteristics of patients

Characteristic	Tuberculosis (n=84)	Non tuberculosis (n=64)	p-value
Age in years \pm SD	37.39 \pm 16.74	39.48 \pm 15.60	0.43
Gender			
Male	54	44	0.56
Female	30	20	
Co morbidities			
Nil	68	49	0.24
Hypertension	4	0	
Diabetes mellitus	9	9	
Chronic liver disease	2	4	
Malignancy	1	2	
Smoking status			
Non-smoker	64	51	0.44
Ex-smoker	2	0	
Current smoker	18	13	

Table 2. Yield of different diagnostic methods in pleural tuberculosis

Investigation	Tuberculosis (n=84)	Non-tuberculosis (n=64)	Sensitivity (%)	Specificity (%)	p-value
Pleural fluid					
AFB smear	1	0	1.2	100	1.00
Xpert assay	9	0	10.7	100	0.005
AFB culture	1	0	1.2	100	1.00
Pleural tissue					
AFB smear	14	0	16.7	100	0.001
Xpert assay	46	0	54.8	100	<0.001
AFB culture	32	0	38.1	100	<0.001
Caseous necrosis on histopathology	56	0	66.7	100	<0.001
Bronchial lavage fluid					
AFB smear	8	0	9.5	100	0.10
Xpert assay	22	0	26.2	100	<0.001
AFB culture	15	0	17.9	100	<0.001

AFB: acid fast bacilli

Table 3. Yield of different diagnostic methods for immediate microbiologic diagnosis of pleural tuberculosis

Diagnostic methods	Immediate diagnosis	Only investigation giving immediate diagnosis
Pleural tissue	45 (53.6%)	38 (45.2%)
Pleural fluid	9 (10.7%)	0
Bronchial lavage fluid	22 (26.2%)	12 (14.3%)

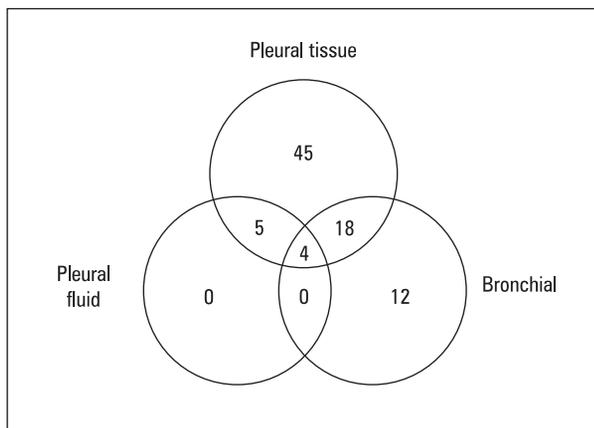


Figure 2. Diagram showing diagnostic overlap among various microbiologic investigations (numbers show the frequency of positive results for tuberculosis)

effusion is treated as TB until proven otherwise. However, without microbiologic confirmation, there remains a problem of delayed diagnosis or misdiagnosis. Due to the low amount of MTB in pleural fluid, tests are often negative for MTB. The current study demonstrates that microbiologic tests done on bronchial lavage fluid in patients with no parenchymal lesions can help in diagnosing tuberculosis.

In our study, the sensitivity of bronchial lavage fluid AFB smear, AFB culture, and Xpert assay was 9.5%, 17.9%, and 26.2%, respectively. Levine and colleagues described that 33% (7/21) of patients with a tuberculous effusion had positive sputum, gastric, or bronchial lavage specimens [7]. There has not been a significant amount of research done on the role of bronchial lavage, but studies have demonstrated that induced sputum has a good diagnostic yield in pleural tuberculosis in patients with and without parenchymal lesions. Conde *et al.* [8] demonstrated that the yield of sputum culture was 6% to 13% higher than that described previously (4–9%) in patients with no parenchymal lesions and similar to those with lesions on chest radiograph [3, 9, 10]. Other similar studies from Los Angeles [11] and India [5, 12] also reported a high yield of sputum induction in pleural tuberculosis.

In our study, AFB was detected in pleural fluid in 1 (1.2%) case on smear, 1 (1.2%) in culture, and 9 (10.7%) on Xpert assay. Antoniskis *et al.* [11] found that 7% of patients had a positive AFB smear on pleural fluid testing. Other studies have shown that AFB culture is positive in < 30% of pleural fluid specimens [9, 13–15].

In the current study, it is shown that pleural tissue AFB smear, culture, and Xpert assay was

positive in 16.7%, 38.1% and 54.8% of cases, respectively. The yield of the microbiological tests on pleural fluid and tissue reported by Christopher *et al.* agrees with our results; pleural tissue Xpert was 45%, pleural tissue culture was 39%, pleural fluid culture was 17%, and pleural fluid Xpert was 14% [16].

Bronchial lavage gave an immediate diagnosis in 22 (26.2%) patients and was the only investigation giving an immediate diagnosis in 12 (14.3%) patients. Hence, it gives another approach in the early diagnosis of pleural tuberculosis and it can also help in monitoring patients who test positive during their treatment course.

In contrast to other forms of extrapulmonary tuberculosis, pleural TB can be infectious as demonstrated by the finding of AFB in bronchial lavage. Questions arise whether pleural tuberculosis patients should be isolated until they cease being infectious and whether contact tracing should be done like in pulmonary TB cases. Further studies are needed to evaluate the infectivity of this form of disease as it has significant implications on public health.

Conclusion

Bronchial lavage, though not a surrogate to pleural biopsy, offers an additional approach in the early diagnosis of pleural tuberculosis in patients not producing sputum. Besides being diagnostic, this method also has epidemiologic significance in containing the tuberculosis epidemic as detecting Mycobacterium in bronchial lavage fluid shows the infectivity of pleural tuberculosis.

Conflict of interest

The authors have no conflict of interest to disclose.

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