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Diagnostic Utility of Bronchoalveolar Lavage Fluid in Cases of Tuberculosis

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ABSTRACT

This article explores the clinical features and diagnostic utility of bronchoalveolar lavage associated with tuberculosis.Early diagnosis of pulmonary tuberculosis (PTB) is essential to reduce the spread, morbidity, mortality, and escalating costs associated with advanced disease.In this article 45 cases of tuberculosis are presented, highlighting the role of bronchoalveolar lavage . Mycobacterial culture is considered gold standard but time taken for results is 2-6 weeks. Bronchoalveolar lavage (BAL) is a safe, minimally invasive and inexpensive diagnostic technique commonly used to obtain cells, infectious agents and noncellular elements from the lower respiratory tract in patients with bilateral diffuse lung diseases.Bal fluid sample is also being used for applying Gene Xpert for MTB in our hospital sectors. Evaluation FOB/BAL is a useful diagnostic tool, and seems to have changed the course of therapy in more than half of patients, by initiation or cessation of treatment.

Key Words: *Bronchoalveolar lavage, minimally invasive ,pulmonary tuberculosis (PTB),Gene Xpert.*

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INTRODUCTION

Tuberculosis (TB) is one of significant infectious disease which can be avoided and treated, yet it is causing death. It is a critical health problem around the world. World Health Organization (WHO) has identified tuberculosis as 1 of the top 10 leading causes of death worldwide [1]. Thus early diagnosis of pulmonary tuberculosis (PTB) is essential to reduce the spread, morbidity, mortality, and escalating costs associated with advanced disease.

"Direct sputum smear microscopy" continues to be crucial tool of diagnosis, but might turn out negative in up to 50% case of active pulmonary TB. In patients who are strong suspects of PTB and yet are sputum smear negative, are a diagnostic challenge. Fiberoptic bronchoscopy is considered a good option for such cases. Mycobacterial culture is considered gold standard but time taken for results is 2-6 weeks. Bronchoalveolar lavage (BAL) is a safe, minimally invasive and inexpensive diagnostic technique commonly used to obtain cells, infectious agents and noncellular elements from the lower respiratory tract in patients with bilateral diffuse lung diseases [2]. It help to sample the terminal airways and the lung parenchyma. Although frequently used, there is lack of contemporary literature regarding the diagnostic utility of BAL for various pulmonary diseases. Bronchoalveolar lavage fluid (BALF) analysis is both qualitative (recognition of BALF constituents) and quantitative (measurement of total cell count and differential count of inflammatory cells). The guidelines for BAL methodology were published and it is recommended to follow them in the laboratories in clinical practice [3, 4]. The lavage of the part of the lung allows harvesting cellular and non-cellular compounds of this space. Normal BALF pattern is defined by the presence of about 10 million cells with differential cell proportion, as follows: >80% of macrophages and <20% of lymphocytes. Any changes in normal pattern can be used to rule out the pathology. Thus it is a frequently used diagnostic modality in pulmonary practice for a variety of indications including infections, especially tuberculosis, interstitial lung diseases and malignancies.

MATERIAL AND METHODS

This study was conducted in 45 cases at tertiary Hospital, between 2019 and 2022 in northern india. We retrospectively identified all patients aged >= 15 years with clinical suspicion of pulmonary tuberculosis, who were

sputum scarce or sputum AFB smear-negative and underwent bronchoscopy. This was a retrospective study performed over a period of 4 years. All BAL samples reported on cytology were studied, their clinical details were retrieved, and the corresponding smears were reviewed. Cyto-histopathologic correlation was done, wherever possible. All procedures were performed in the hospital endoscopy suite under intravenous sedation. BAL of the target segment was performed with sterile saline. This was followed by transbronchial lung biopsy (TBLB) of the affected segments under X-ray fluoroscopy in three of the patient. BAL were sent for cytology, AFB smear microscopy as well as Xpert assay. Three TBLB samples were sent for histological examination.

A mean fluid volume of 40 mL was retrieved. Cells were collected by centrifugation, and slides were stained with H&E and May-Grunwald-Giemsa stains. When requested, additional stains, ziehl neelsen, was applied. Smears were eventually examined. Differential cell count is evaluated in the slides stained with May– Grunwald–Giemsa (MGG), which makes possible identification of non-epithelial and lymphoid cells. All smears were further reviewed.

RESULTS

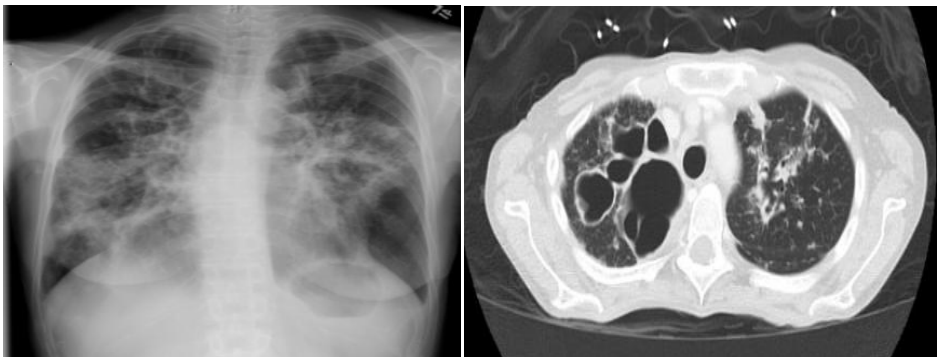
Bronchoalveolar lavage was done in 45cases at tertiary cancer centre in northern India (Table1). Age of patients ranged from 15 years to 72 years (average age 47.2); 27(60%) were males and 18(40%) were females. In majority of the cases, clinical presentation of the patients was cough with minimal expectoration, fever, loss of appetite and hemoptysis. Four patient presented with dyspnea on exertion for few months. Additionally one patient was known case of cardiac sarcoidosis and four patient were defaulter with prior history of antitubercular treatment. Chest X-Ray was done in our patient. CT scan shows right,left or bilateral lung cavitary consolidation or cavitory lesions. Some cases shows centrilobular nodules and tree in bud appearance in lung lobe.

Table 1: Distribution of cases based on cytological diagnosis

DIAGNOSIS ON BALF CYTOLOGY	NUMBER OF CASES	FUNGAL CULTURE	GENE EXPERT	HISTOPATHOLOGICAL CONFIRMATION
TUBERCULOSIS	45	POSITIVE 3 NEGATIVE 42	POSITIVE 38 NEGATIVE 7	3

Grossly bronchoalveolar lavagewere about 6-30 ml. 35 samples were mucoid to straw colour and mildly turbid fluid grossly when received in the laboratory.10 sample were hemorrhagic fluid. Gene expert done on BALF was positive in 38 cases and negative in 7 cases. Fungal culture was negative in 42 cases and positive in 3 cases. Culture of these positive cases showed scanty growth of Candida albicans after 48 hrs of incubation. Majority of tuberculosis cases cytology showed neutrophilic infiltrate on a necrotic background. Granulomas were less frequantly reported in case of Bal fluid. Further for these cases, zeihl neelsen stain was applied which eventually came out to be positive. Even if there was mild inflammation, it was noted the bacilli were frequantly noted in zeihl neelsen stain thus helping to come to a definite diagnosis. A diagnosis of tuberculosis was perhaps made on following clinical presentation and investigations.

Histopathological confirmation was done in only three cases. First case was CT guided trucut biopsy from left upper and lower lobe lung mass. Histomorphology showed only necrosis. Zeihl Neelsen stain highlighted the acid fast bacilli. Second case was taken as CT guided biopsy from left lung mass and it was reported as necrotizing granulomatous inflammation. Third case was endobronchial biopsy from mucosal infiltrate over carina which was suggestive of granulomatous pathology. These 45 cases were followed up. 40 patients showed good response to ATT both clinically and radiologically, and 4 patients lost to follow up and 1 patient died during course of disease.



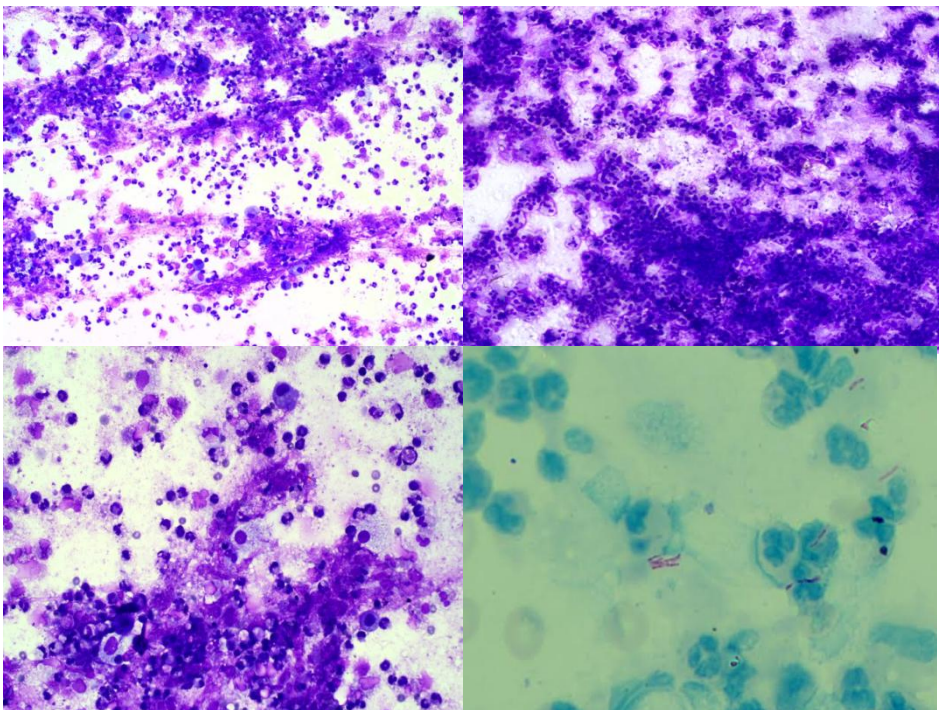


Figure 1: Chest X-RAY showing multiple cavitarypredominately in upper lobe of lung. **Figure 2:** CT scan shows multiple cavitary lesion in upper lobe of right lung. **Figure 3, 4:** Photomicrograph showing cellular smear displaying predominately inflammatory infiltrates including polymorphs along with occasional alveolar macrophages and respiratory epithelial cells, [H&E stain, x100] and [H&E stain, x400]. **Figure 5:** Photomicrograph showing another cellular smear displaying predominately inflammatory infiltrates including polymorphs along with occasional alveolar macrophages and respiratory epithelial cells on a necrotic background [H&E stain, x400]. **Figure 6:** Photomicrograph showing acid fast bacilli highlighted by Ziehl neelsen stain [H&E stain, x1000].

DISCUSSION

Baughman et al. studied 2524 BAL fluid samples and diagnosed tuberculosis in 50 patients. Additionally, they observed that BAL facilitates early detection of tuberculosis, especially in sputum negative cases [5]. Tuberculosis was diagnosed in 45 subjects in our study. Altaf Bachh et al. [6] 66.7% were males and 33.3% were females. Sweta Madas et al. [7] reported 74% males and 26% females and Surendra k Sharma et al. [8] 65 % males and 35% females. In this study majority of case were male (60 %) and rest were female (40 %).The most common symptom observed in this study was cough with or without expectoration (74 %) followed by fever (52 %). Four patient presented with dyspnea on exertion for few months. One patient had medical history of cardiac sarcoidosis and four patient had prior history of antitubercular treatment. Since the BAL samples are from the alveolar spaces, the rate of detection of tuberculosis is high. In all 45 cases, Ziehl-Neelsen stain was positive for acid-fast bacilli.

Traditional diagnostic tools, including sputum acid-fast bacillus (AFB) smear and Mycobacterium culture, are fraught with challenges. Mycobacterium tuberculosis culture based on solid media takes up to 4 to 8 weeks, and the sensitivity of the traditional AFB smear can be as low as 20% [9]. Additionally, although Mycobacterium tuberculosis liquid culture method is faster, it still takes 2 to 4 weeks. Moreover, tuberculosis culture methods to support the diagnosis of PTB are not widely available in high-burden settings. In 2011, the WHO recommended the Xpert MTB/RIF assay (Cepheid, Sunnyvale, CA) for the diagnosis of PTB and the detection of rifampicin resistance [10]. The Xpert MTB/RIF. assay is an automated, single-cartridge-based nucleic acid amplification test that is able to simultaneously detect M. tuberculosis and rifampicin resistance within 2 to 3 hour. Currently, Xpert MTB/RIF often uses sputum samples as well as BAL fluid to diagnose PTB.

Even in ICU patients, diagnosis of TB may be an incidental co-morbid finding as previously undiagnosed sub clinical disease which only manifests during hospitalization [11, 12]. Mortality is high for patients with active TB and respiratory failure, mainly associated with delay in the TB diagnosis. Patients with TB required ICU care in worldwide, may have high rates of co-morbidities related complications.

Bal fluid sample is being used for applying Gene Xpert for MTB in hospital sectors. In our setup Bal fluid was frequent specimen used for Gene Xpert for MTB. 38 cases (84.4 %) were positive for Gene Xpert. The results of our study also indicate how to minimize risk of starting of antitubercular treatment in patient, in turn decreasing the financial burden and the pill load who present similar to PTB clinically and radiologically. Fiberoptic bronchoscopy (FOB) with

bronchoalveolar lavage (BAL) can identify infectious causes in this population. Accurate diagnosis is required for the rational use of medications. Evaluation FOB/BAL is a useful diagnostic tool, and seems to have changed the course of therapy in more than half of patients, by initiation or cessation of treatment.

CONCLUSION

BAL has been an integrated method of respiratory tract examination for about 40 years. It is dedicated to the diagnosis of interstitial lung diseases, infections and malignancy. BAL is a safe and useful procedure for primary diagnosis of infections such as tuberculosis and fungal infections, which has special significance in developing nations where prevalence of such infections is high. BAL cytology should also be employed as a diagnostic modality for early diagnosis of suspected lung infections and malignancies, especially in cases where biopsies cannot be performed.

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