
DIAGNOSTIC ROLE OF FIBEROPTIC BRONCHOSCOPY IN INDETERMINATE LUNG INFILTRATES

Javid Ahmad Malik, Shabir Ahmad Lone, Ramees Mohi Ud Din Mir

Author's affiliations **Javid Ahmad Malik, Shabir Ahmad Lone, Ramees Mohi Ud Din Mir :**
Department of Pulmonary Medicine,
Medical College Srinagar, India

Abstract

Background: Bronchoscopy has been used to diagnose various infectious, inflammatory and neoplastic pulmonary diseases by retrieving samples from bronchial, alveolar and interstitial compartments of patients with lung infiltrates. We prospectively assessed the diagnostic role of bronchoscopy in patients who had respiratory symptoms, radiographic infiltrates and sputum smear test negative for acid-fast bacilli (AFB).

Methods:

We prospectively performed bronchoscopy in 40 consecutive patients between December 2013 and November 2014, who had respiratory symptoms, radiographic findings not consistent with any specific diagnostic entity and had sputum smear negative for AFB.

Results: Cohort of 40 patients had a mean age of 44 years (SD 14.5) with 55% male participants. Comorbidities were present in 35% patients and 52% participants were current smokers. Most common presenting symptoms were cough (55%) and hemoptysis (20%) followed by fever (15%) and weight loss (10%). Tuberculosis was confirmed in 16 (40%) patients. Nontubercular diseases were diagnosed in 24 (60%). Interstitial lung disease (ILD) was diagnosed in 7.5%, lung cancer in 2.5%, hydatid cyst in 5.0%, bronchiectasis in 12.5%, pneumocystis jirovici (previously known as PCP) in 2.5%, pneumonia in 7.5%, lung abscess in 2.5% and non-specific infection in 20.0%. There was no difference in the comparative age of the study subjects in relation to final diagnosis.

CONCLUSION: Given its high diagnostic yield and safety, bronchoscopy should be considered in the evaluation of patients with respiratory symptoms, indeterminate radiographic infiltrates and negative sputum AFB test.

Keywords: Fiberoptic bronchoscopy (FOB), Tuberculosis, Acid-fast bacilli (AFB)

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Correspondence: Dr Javid Ahmad Malik , M.D.(Internal Medicine), PGI Chandigarh , D.M. (Pulmonary & Critical Care Medicine) PGI Chandigarh , Associate Professor and Head Department of Pulmonary Medicine , SKIMS Medical College, Srinagar, India . Phone: 09419479600 ,e-mail: javidmalik2009@yahoo.co.in

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Introduction:

In the era of interventional pulmonology one big problem that today's pulmonologists face is patients whose chest roentgenograms (CXR) reveal infiltrates and sputum smears are negative for acid-fast bacilli (AFB) regardless of immune status. In developing countries one must exclude pulmonary tuberculosis (PTB) in such patients though differential diagnosis includes various non-mycobacterial infections, inflammatory and neoplastic etiologies as well. By giving an access to lung tissue and other specimens from lower respiratory tract, bronchoscopy and its related procedures have made a tremendous contribution in diagnosis of various lung diseases. Detection of AFB in respiratory specimens is recommended by world health organization as the initial approach to the diagnosis of PTB but in those patients who cannot produce sputum spontaneously this method has a low sensitivity¹. Though relatively easy to perform sputum microscopy and culture can be negative in a significant proportion of PTB patients with sensitivities ranging from 25 to 45%². In the diagnosis of PTB both in terms of higher microscopy and higher culture positivity, results from various studies have confirmed the higher diagnostic yield of bronchoscopy over sputum examination^{3,5}. In contrast some studies have shown no additional yield of bronchoscopy over sputum examination^{6,7}. Nearly 50% of PTB cases are sputum smear negative for AFB⁸ and thus samples other than sputum have an important role in patients not only having occult tuberculosis but also in other conditions that mimic tuberculosis. Unanswered question is whether an invasive investigation like bronchoscopy is must or should we treat tuberculosis empirically on clinico-radiological grounds particularly in tuberculosis endemic countries. But we need to keep in mind that empiric treatment may not only result in unnecessary cost and toxicity of ATT but we may also miss other mimicking diseases particularly malignancy and interstitial lung disease (ILD). To address this issue we designed the present study to answer whether fiberoptic bronchoscopy (FOB) provides any additional diagnostic yield in patients who have respiratory symptoms, sputum AFB negative and indeterminate radiographic infiltrates.

METHODS:

We prospectively evaluated 40 consecutive patients in the current study between December 2013 and November 2014, aged 20 years and above who had respiratory symptoms and radiographic findings not consistent with any specific diagnostic entity. All participants had at least two induced sputum (IS) reports negative for AFB. Written informed consent was obtained from all eligible participants. Exclusion criteria included previous history of PTB, severe COPD, pregnancy and respiratory or cardiac failure. Detailed history, physical examination, complete blood count, coagulation profile, HIV serology and CT scan chest were obtained in all the patients included in the study.

Standard bronchoscopic premedication protocol was used⁹ however we minimized the use of lidocaine as much as possible because of its known antimicrobial properties¹⁰. We obtained BAL specimens in all patients by wedging the bronchoscope into the radiologically most involved pulmonary segment and instilling four to six aliquots of 20 ml normal saline and aspirated until a total of 30 to 40 ml of fluid return was obtained. Bronchial biopsy (BB) or transbronchial lung biopsy (TBLB) was performed if deemed necessary depending upon bronchoscopic and radiological findings. Using standard techniques all specimens were stained with Ziehl-Neelsen (ZN) stain for AFB and cultured in Löwenstein-Jensen (LJ) medium for the detection of mycobacterium tuberculosis (MTB). Definite PTB was defined as a positive culture for MTB in bronchoalveolar lavage fluid (BALF). Qualified pathologist reported biopsy results. All the participants were followed for at least 6 months after enrollment in the study.

RESULTS:

Present study included 40 patients who had a mean age of 44 years (SD 14.5) with 55% male participants (Table 1). Diabetes, chronic kidney and liver diseases the main comorbidities were present in 35% of our cohort whereas 52% participants were current smokers. Most common presenting symptoms were cough (55%) and hemoptysis (20%) followed by fever (15%) and weight loss (10%). Tuberculosis was confirmed in 16 (40%) patients. Other nontubercular etiologies were diagnosed in 24(60%) and included

interstitial lung disease (ILD), lung cancer, infected hydatid cyst, bronchiectasis, pneumocystis jirovici (previously known as PCP), pneumonia, non-specific pulmonary infection (NSPI) and lung abscess (Table 2). There was no difference in the comparative age of the study subjects in relation to final diagnosis (Fig 1). In tuberculosis group 5 patients (31%) had bronchoscopic abnormalities like endobronchial nodularity, mucosal irregularity and increased secretions in the radiographically involved lung. These patients had tuberculosis confirmed by BAL-MTB culture in 14 (88%) cases and by bronchial biopsy or TBLB in 2 (12%) patients demonstrating caseating granulomas consistent with tuberculosis. The two patients who had only biopsy evidence of PTB

Table 1: Demographic characteristics of the study population:

Age (years) Mean \pm SD	44 \pm 14.5	Percentage
Sex (male / female)	22/18	55.0 / 45.0
Smoker	21	52.5
Co-morbidities	14	35.0
Presentation:		
Cough	22	55.0
Hemoptysis	8	20.0
Fever	6	15.0
Weight loss	4	10.0

Table 2: Final diagnostic categories of the study subjects:

	Tuberculosis	ILD	Bronchiectasis	Lung cancer	PCP	NSPI	Pneumonia	Hydatid cyst	Lung Abscess
Number (%)	16 (40.0)	3 (7.5)	5 (12.5)	1 (2.5)	1 (2.5)	8 (20.0)	3 (7.5)	2 (5.0)	1 (2.5)
Mean age (years)	45.00	55.33	26.60	43.0	55.0	52.42	51.21	28.00	23
SD	15.57	4.04	7.27			14.32	14.76	4.24	

ILD: interstitial lung disease

PCP : pneumocystis jirovici pneumonia (previously known as pneumocystis carinii)

NSPI: nonspecific pulmonary infection

responded to six months ATT with complete clinical and radiological improvement. In three patients (7.5%) a diagnosis of ILD was made on the basis of transbronchial lung biopsy (TBLB) and radiological findings. A 43 year chronic smoker was diagnosed to have small cell lung cancer from bronchial biopsy. This gentleman had fleeting infiltrates in serial radiographs and endobronchial growth in left upper lobe bronchus. A 55 year old male smoker who had poorly controlled diabetes with diffuse ground glass opacity (GGO) on high resolution CT (HRCT) scan of chest had pneumocystis jirovici previously known as PCP in BAL fluid. Pseudomonas was isolated from BAL fluid of two of the 5 (12.5%) bronchiectasis patients. Two young males who had cavitation

in upper lobes, hydatid membranes intrabronchially and positive hydatid serology were diagnosed to have infected hydatid cysts. Community acquired pneumonia (CAP) and lung abscess were found in 3 (7.5%) and 1 (2.5%) subjects respectively. Finally we labeled 8 (20%) patients who did not fit in to any known clinical entity as cases of nonspecific pulmonary infection (NSPI) because bronchoscopy and BAL fluid analysis could not reveal any specific etiology and with broad spectrum antibiotic therapy there was complete clinical improvement and resolution of radiographic infiltrates. Bronchoscopic procedures were well tolerated by most patients, there were no major complications and no deaths in the present study.

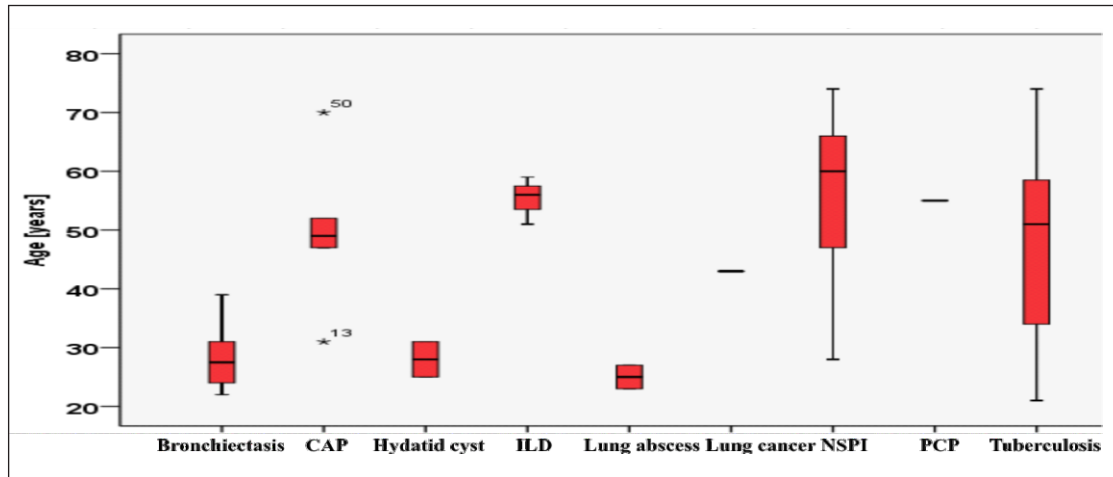


Fig. 1: Comparative age of the study subjects in relation to final diagnosis.

DISCUSSION:

Interventional pulmonology particularly bronchoscopy has revolutionized the concept of approach to the diagnosis of various lung diseases. Bronchoscopy related procedures like bronchoalveolar lavage (BAL), bronchial biopsy (BB), transbronchial lung biopsy (TBLB) and endobronchial ultrasonography guided needle aspiration (EBUS-TBNA) have immensely enhanced the understanding of evidence based respiratory medicine by providing tissue diagnosis. BAL based studies have been found to be useful for assessing the lower respiratory tract inflammation and studying the pathogenesis of various lung diseases. BAL in miliary tuberculosis shows lymphocytic alveolitis, elevated levels of fibronectin and immunoglobulins (IgG, IgA, IgM).

Pulmonary tuberculosis (PTB) is a communicable disease with adverse public health consequences throughout the world. Nearly 50% of PTB cases are sputum smear negative for AFB and the transmission rate of smear negative TB may be as high as 22%⁸. In countries with a high prevalence of TB and a high clinical suspicion, anti-tuberculosis therapy is often initiated without further investigations. Ideally any patient with suspected PTB on clinical and radiological grounds requires further investigations to confirm the diagnosis. A study that compared the yield between spontaneous sputum, induced sputum and bronchoscopy in patients with suspected PTB concluded that bronchoscopy had a significantly higher diagnostic yield¹¹. Contrary to this two small

studies in patients with negative sputum AFB did not find any additional yield by performing bronchoscopy^{6,12}.

Both in terms of higher microscopy and higher culture positivity, results from various studies have confirmed the higher diagnostic yield of bronchoscopy over sputum examination³⁻⁵. In the present study we report the diagnostic yield of bronchoscopy in 40 patients who had respiratory symptoms, indeterminate radiographic infiltrates and AFB negative sputum specimens. Our results suggest that bronchoscopy is a useful and largely safe tool in the workup of such patients. Bronchoscopic procedures in the present study confirmed the diagnosis of PTB in 40% patients by BAL and biopsy. Across the studies considerably different yields have been reported regarding the yield of bronchoscopy in the diagnosis of PTB^{3,4,6,7,13-15} reflecting differences in study design and the patient population being studied. In the present study like an earlier report by Mohan¹⁶ we have proven clearly the diagnostic utility of bronchoscopy in culture confirmation of TB after negative results on induced-sputum samples.

From our results it is very clear that bronchoscopy and its related procedures including BAL, bronchial biopsy and TBLB have a definite diagnostic role in patients who have similar clinical and radiological presentation. It not only helps us in precise culture based diagnosis of mycobacterial pulmonary infection but also in other diseases like lung cancer, interstitial lung diseases, hydatid lung disease and PCP. In India where the prevalence of tuberculosis is high, patients

having clinical and radiological picture compatible with TB but a negative sputum smear for AFB usually receive ATT at peripheral hospitals. One may argue in favor of this strategy as it is useful in most cases with the advantage of avoiding an invasive bronchoscopic procedure because smear-negative TB is a common problem in clinical practice. However, our study has exposed a serious limitation of this strategy by diagnosing non-tubercular conditions particularly ILD, lung cancer, PCP and hydatid lung disease for which ATT will not only mean toxicity of unnecessary treatment but at the same time patient may be losing the crucial

time by delayed diagnosis of the actual disease. Therefore bronchoscopy and its related procedures should be offered to the patient and the procedure is largely safe.

CONCLUSIONS:

Based on our results we conclude that, given its high diagnostic yield and safety, bronchoscopy should be considered in the evaluation of patients with respiratory symptoms, indeterminate radiographic infiltrates and negative sputum AFB. All that looks alike on clinico-radiological grounds is not actually so and bronchoscopy can pick up alternative diagnoses.

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