ORIGINAL ARTICLE

The diagnostic role of fiberoptic bronchoscopy in cases of suspected pulmonary tuberculosis*

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Background: Pulmonary tuberculosis is an infectious disease of high prevalence and incidence. The use of sputum bacilloscopy is a sure and speedy way of reaching a diagnosis. However, in light of the fact that 30% to 50% of pulmonary tuberculosis patients have negative sputum cultures or present no sputum, fiber bronchoscopy acquires a special importance.

Objectives: To evaluate the sensitivity of the specimens collected by means of fiber bronchoscopy (bronchoalveolar lavage and transbronchial biopsy) for the diagnosis of patients suspected of having pulmonary tuberculosis, without confirmation through sputum bacilloscopy.

Methods: By review of the records of fiber bronchoscopies carried out from March 1997 to March 2001, we identified and included in the study adult patients who were referred to two different respiratory endoscopy clinics with suspicion of tuberculosis and who had had at least three negative sputum cultures. Data regarding age, gender, changes detected at thorax imaging and endoscopy were collected.

Results: Fifty-two patients ranging from 19 to 77 years of age (median, 39), were included, 58% were of male and 37% were patients from the Public Health System (i.e. without private health insurance). The prevalent finding in chest X-rays was alveolar infiltrate (80%). In 35 patients, tuberculosis was the final diagnosis (1 with concomitant neoplasia). In 28 (80%) of the patients, diagnosis was achieved through bronchoscopy. Other bronchoscopy confirmed diagnoses included neoplasias, histoplasmosis, chronic alveolitis, *Pneumocystis carinii* pneumonia and pulmonary fibrosis.

Conclusion: The results of this study point out the value of fiber bronchoscopy in cases of suspected tuberculosis, specifically those not diagnosed thorough sputum bacilloscopy. Fiber bronchoscopy is useful for diagnosis of not only pulmonary tuberculosis but other, differential diagnoses as well.

Key Words: Tuberculosis, pulmonary/diagnosis. Bronchoscopy/methods.

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Abbreviations used in this paper:

AFB – Acid-fast bacilli

BAL – Bronchoalveolar lavage

TBB – Transbronchial biopsy

INTRODUCTION

In the late 1800s and early 1900s, after the discovery of radiology and effective chemotherapy, it was expected that a cure for *Mycobacterium tuberculosis* would be found. This would have been a significant advance in public health.[1,2-25] In the beginning of the 1980s, there was an increase in the incidence of pulmonary tuberculosis. This occurred as a result of various factors, including the advent of AIDS, increased migration from areas of high tuberculosis prevalence to areas in which the disease was under control, increased poverty, greater life expectancy and disorganization within tuberculosis

control centers. It is believed that, during the 1990s, 1.7 billion people (one-third of the global population) were infected by *M. tuberculosis* and that 30 million died from this disease.[1, 4,3,-22]

Direct examination of sputum is a fast, simple, and inexpensive way to diagnose pulmonary tuberculosis. However, from 30% to 50% of patients infected with pulmonary tuberculosis are not diagnosed through sputum culture.[1,25,23,5-24] In the literature, there is much controversy over what is the best method for investigating suspected cases of tuberculosis.[1,25,23,6,7,8,9,26,27,10,12,28-29] Fiber bronchoscopy has been evaluated for this purpose. This study was carried out in order to evaluate the sensitivity of methods used in the detection of bacillus in specimens collected by means of fiberoptic bronchoscopy for the diagnosis of tuberculosis and of other diseases with similar clinical manifestations.

METHODS

Patients suspected of having pulmonary tuberculosis and presenting negative sputum cultures (in at least 3 samples) were evaluated using fiberoptic bronchoscopy. Only patients above the age of 18 were included. The study was carried out at the Hospital Universitário Prof Edgard Santos (HUPES) and at the Hospital São Rafael (HSR). The records of all (940) fiberoptic bronchoscopies performed at the HUPES and at the HSR from March 1997 to March 2002 were reviewed, and 52 were found to have been performed based on suspicion of tuberculosis. Clinical demographic data were collected from the files of the HUPES and HSR respiratory endoscopy clinics or from patient medical charts. Data on the clinical evolution of tuberculosis patients in whom fiberoptic bronchoscopy failed to identify the disease were also collected (at least 6 months after the exam). Fiberoptic bronchoscopies were always performed by the same (2) clinicians, using Fujinon or Pentax 4.8-mm flexible bronchoscopes. Prior to the procedure, patients were sedated with 20 mL of intravenous 2% xylocaine, and no vasoconstrictors were administered during the exam. Thorough inspection of the tracheobronchial tree was always performed, followed by the collection of bronchoalveolar lavage (BAL) fluid, bronchial biopsy (when endobronchial lesions were found) and transbronchial biopsy (TBB) when necessary. The BAL and TBB were performed at sites where radiological changes, according to standard criteria, were previously found. The BAL consisted of 5 samples of 20 mL of saline solution each, manually aspirated and stored in sterile containers. Samples were sent to the microbiology laboratory and submitted to direct examination and culture for BK viruses and fungi, Gram stain and quantitative culture for pyogenic microorganisms. The same samples were then sent to the pathology laboratory. The TBB procedure was performed through a channel of the bronchoscope using forceps to reach the lung parenchyma with no visual access, and approximately 6 tissue samples were collected. Samples were stored in a formaldehyde solution and sent to the pathology laboratory for anatomopathological examination and specific staining for acid-fast bacilli (AFB) and fungi.

Continuous variables are expressed as mean ± standard deviation (SD), median and limits. Categorical variables are expressed as percentages. The calculation of the sensitivity of fiberoptic bronchoscopy – using Ziehl-Nielsen staining, BAL culture, and TBB anatomopathological examination – was performed taking into consideration all criteria for the diagnosis of tuberculosis. The 95% confidence interval (95% CI) was used for the estimation of sample variability. Statistical analyses were performed using SPSS 7.5 and Epi Info 6.04 software. Criteria for diagnosis of pulmonary tuberculosis included positive bacilloscopy (in the BAL culture, or in the TBB or open-lung biopsy), *M. tuberculosis*-positive culture, granuloma with caseous necrosis (with negative findings for fungi in TBB or open-lung biopsy) and positive response to the use of regimen I, according to standards of the national tuberculosis control plan.

RESULTS

Of a total of 940 patients submitted to fiberoptic bronchoscopy, 52 presented suspected tuberculosis and negative sputum smears (from at least 3 samples). Ages ranged from 19 to 77 (median, 39). The most common radiographic finding was alveolar infiltrate (in 78.8%). A final diagnosis of tuberculosis was made in 35 patients. Table 1 shows the results.

Diagnostic and therapeutic methods used to define diagnosis are shown in Table 2. The methods found to have the best diagnostic potential were BAL bacilloscopy, BAL culture and TBB.

Bronchoscopy helped determine a final diagnosis of tuberculosis in 28 patients. Table 3 shows the diagnostic methods used.

The sensitivity of bronchoscopy for the diagnosis of tuberculosis was 80% when compared with all other sampling methods, although the percentage was lower when compared to only some of the other methods, as can be seen in Table 4. The specificity of bronchoscopy was 100%, there were no false-positive results, 20% of the exams yielded false-negative results, the positive predictive value was 100% and the negative predictive value was 70%.

Of the 17 patients whose diagnosis was not tuberculosis, 11 were diagnosed through bronchoscopy, 3 through open-lung biopsy and 3 on the basis of clinical evidence (Table 5). For these patients, the sensitivity of bronchoscopy was 77%, there were no false-positive results and 25% false-negative results.

Bronchoscopic sampling, as a diagnostic tool for use in suspected cases of tuberculosis or other diseases, demonstrated a sensitivity of 78% (95% CI = 63.7 to 88) and a specificity of 100%. There were no false-positive results and the negative predictive value was 15.4% (95% CI = 2.7 to 46.3).

DISCUSSION

When there is suspicion of active tuberculosis, patients in whom direct examination of sputum is inconclusive represent a diagnostic and therapeutic challenge. When there are no other diagnostic resources, analysis of clinical data in together with chest radiograph findings has proven to be inappropriate in determining treatment regimens, especially when diseases for which there is no specific treatment progress.[15-17, 24-25] Our study confirms this observation since other infectious, neoplastic and immunologic diseases were diagnosed in these patients who were originally though to be suffering from pulmonary tuberculosis.

The most common radiological finding in pulmonary tuberculosis in adults is alveolar infiltrate in the upper lobes (right or left).[25] In this study, radiographs of all the patients diagnosed with neoplasia revealed alveolar infiltrate in the upper lobe of a lung, whereas alveolar infiltrate was observed in other areas of the lungs of some patients diagnosed with tuberculosis. Although we did not study some factors, such as diabetes, AIDS, and other causes of immunosuppression, any of which could masquerade as tuberculosis with atypical radiological findings, we reassert the lack of specificity of chest radiographs in the diagnosis of pulmonary tuberculosis.[20, 24-25]

The *Mycobacterium tuberculosis* culture process, despite its 80% sensitivity, is time consuming, and thereby delays diagnosis. The use of DNA amplification techniques is mainly restricted to laboratory research and does not determine the viability of the bacillus.[2] Tuberculosis is a pathology with one of the highest diagnostic sensitivities for transbronchial biopsy,[26,27] a method of sample collection that uses a fiberoptic bronchoscope and has a low incidence of complications (pneumothorax in less than 5% of cases and less than 1% requiring drainage). Anatomopathological study of biopsy fragments may immediately indicate a diagnosis of tuberculosis, as well as helping define the diagnosis of other diseases with varying etiologies.[27] In this group of patients, the sensitivity of bronchoscopy for diagnosis of tuberculosis was 80% when we studied the results of the direct examination of BAL fluid, BAL culture and the anatomopathological examination of the transbronchial biopsy together. When we analyzed only the results of the direct examination of BAL fluid and BAL culture, sensitivity was 60%. The sensitivity of the direct examination of BAL fluid alone was 48.6%.

The study of the sensitivity of different sample collection methods using bronchoscopy in this group of patients reinforces the idea that, whenever there are no contraindications (for example, in patients who suffer from coagulopathy), transbronchial biopsy should be used in concert with other collection methods (direct examination and BAL culture).

A study comparing HIV-positive (HIV+) and HIV-negative (HIV–) patients was performed in the city of São Paulo between January 1994 and June 1998.[20] The objective of the study was to evaluate the contribution of bronchoscopy to the diagnosis of tuberculosis in patients with no expectoration or with negative bacilloscopy. The conclusion was that the overall sensitivity of BAL culture and direct examination of BAL fluid were similar: 30% and 50%, respectively. The sensitivity of transbronchial biopsy was found to be 89% in the HIV– group and 67% in the HIV+ group, quite similar (regarding the HIV– group) to our results, and the authors suggested that this could be attributed to the lower

tendency for granuloma formation in the HIV+ group. Lung neoplasia was diagnosed in 10 HIV+ patients and in 4 HIV– patients. Inconclusive results were found in only 17/214 HIV+ patients and 4/105 HIV– patients. Similar to our results, the authors found the contribution of bronchoscopy to diagnosis confirmation to be significant and emphasized the use of transbronchial biopsy for the immediate diagnosis of tuberculosis and other diseases of varying etiologies, such as infectious diseases and neoplasias.

In the present study, bronchoscopy was useful not only for the diagnosis of tuberculosis but also for the identification of other pathologies, especially neoplasias, whose delayed diagnosis may exclude the possibility of a surgical cure. Some authors even suggest that the higher the possibility of neoplasia, the sooner bronchoscopy should be performed.[26-27] Other infectious diseases (*Pneumocystis carinii* pneumonia and histoplasmosis) were also diagnosed through bronchoscopy during this study. The initial method of diagnostic investigation for these pathologies is also sputum culture[3] and the consequent delay in diagnosis may cause progressive pulmonary deterioration, which can lead to respiratory insufficiency. Another type of lesion that may occur in patients with histoplasmosis is fibrosing mediastinitis, creating a risk of chronic deterioration of respiratory mechanics.

Endobronchial changes detected by bronchoscopy are not always predicted prior to the examination, and must be investigated through bronchial biopsy. Anatomopathological findings from this type of biopsy show a higher sensitivity when neoplasia is diagnosed, ranging from 90% to 95%. In a study that evaluated 280 patients diagnosed with neoplasia, Castella detected changes ranging from 65% to 95% during the endoscopic examination, with varied histological types, the most common of which was the small-cell subtype and the least common was the alveolar bronchiole subtype.[26] Some authors believe that false-negative results in bronchial biopsies from patients diagnosed with neoplasia are caused by areas of necrosis within the tumor tissue.[27] Of the 52 patients evaluated in the present study, endobronchial lesions were found in 4 patients, 3 of them diagnosed with neoplasia (28% of the patients with neoplasia) and 1 with tuberculosis (3% of the total number of patients with tuberculosis). Endobronchial lesions were present in about 20% of patients diagnosed with tuberculosis, and it was quite common that no evidence of those lesions appeared in chest radiographs. This is consistent with the smaller percentage of endobronchial lesions expected in patients with pulmonary tuberculosis and negative sputum bacilloscopy.[26-27]

Cytopathological analysis was not performed on sputum cultures from patients with a final diagnosis of neoplasia. This method has low sensitivity for the diagnosis of neoplasia and, even in sputum culture confirmed cases, endoscopic evaluation must be performed in patients diagnosed with neoplasia in order to determine the exact location (which could include the oropharynx or the larynx) and endobronchial extension of the neoplasm, as well as the staging and whether surgical treatment will be necessary.[25-27]

In this study, no investigative method other than bronchoscopy was used for detection of tuberculosis. Therefore, no comparative study was possible. However, Since more than 15% of the patients studied were diagnosed with neoplasia, no other method could replace bronchoscopy in the endoscopic evaluation of these patients.

The sensitivity of bronchoscopy for tuberculosis (80%) and the determination of the diagnosis of other pathologies (neoplasia, infectious diseases or diseases mediated by the hypersensitivity mechanism) reinforce data in the literature indicating this type of examination when there is suspicion of tuberculosis but no confirmation in the sputum bacilloscopy. This is especially true if we consider the fact that immediate results are obtained through anatomopathological examination of the transbronchial biopsy.

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TABLE 1
Final Diagnosis

Diagnosis	N (%)
Tuberculosis	35 (67.3%)
Spinocellular carcinoma	4 (7.7%)
Cicatricial lesion	3 (5.8%)
Bronchioloalveolar carcinoma	2 (3.8%)
Adenocarcinoma	2 (3.8%)
Tuberculosis and spinocellular carcinoma	1 (1.9%)
Pulmonary fibrosis	1 (1.9%)
Infection by *P. Carinii*	1 (1.9%)
Histoplasmosis#	1 (1.9%)
Chronic eosinophilic alveolitis + BOOP	1 (1.9%)
Pyogenic abscess	1 (1.9 %)
Bacterial pneumonia	1 (1.9%)

Diagnosis confirmed without clinical intervention; # transbronchial biopsy demonstrating fungal inclusion in macrophage, positive stain with silver; BOOP: bronchiolitis obliterans organizing pneumonia

TABLE 2
Diagnostic method/therapeutic procedures used to define diagnosis

Method/Procedure	N (%)
BAL bacilloscopy	52 (100%)
Culture	49 (94.2%)
Transbronchial biopsy	35 (67.3%)
Therapeutic test for tuberculosis	6 (11.5%)
Empirical antibiotic therapy	1 (1.9%)
Follow-up without intervention	2 (3.8%)

Total number of patients = 52

BAL: bronchoalveolar lavage

TABLE 3
Diagnostic method and proportion of positive results for tuberculosis

Method	N (%)
Bronchoscopy (all kinds of collection methods)	28/35 (80%)
Transbronchial biopsy	18/35 (51.4%)
Culture	18/35 (51.4%)
Ziehl	17/35 (50%)
Open lung biopsy	1/4 (25%)
Therapeutic test	6/6 (100%)

Endobronchial changes were detected in 4 patients: 3 diagnosed with neoplasia (28% of patients with neoplasia) and 1 with tuberculosis (3% of patients with tuberculosis)

Table 4
Sensitivity of bronchoscopy in the diagnosis of tuberculosis

Diagnostic method	Sensitivity(%) / (95% CI)
Ziehl + culture +TBB	80 / (62.5 to 90.9)
Ziehl +culture	62.9 / (44.9 to 78)
Culture	56.6 / (37.9 to 73.2)
Ziehl	48.6 / (31.7 to 65.7)

TBB: transbronchial biopsy; 95% CI: 95% confidence interval

TABLE 5
Diagnostic method and final diagnosis in patients not diagnosed with tuberculosis

Method	Diagnosis	N (%)
Bronchoscopy (all collection methods)		11 (64.7%)
	Squamous cell carcinoma	4 (23.5%)
	Adenocarcinoma (1 bronchioloalveolar)	3 (17.6%)
	Pulmonary fibrosis	1 (5.8%)
	CEA + BOOP	1 (5.8%)
	Histoplasmosis	1 (5.8%)
	Infection by *P. carinii*	1 (5.8%)
Open lung biopsy		1 (5.8%)
	Bronchioloalveolar carcinoma	1 (5.8%)
	Pyogenic abscess	1 (5.8%)
	Scarring	1 (5.8%)
Clinical evidence	Bacterial pneumonia	3 (17.6%)
	Cicatricial lesion	2 (11.8%)

Total number of patients = 17; CEA: Chronic eosinophilic alveolitis; BOOP: bronchiolitis obliterans organizing pneumonia