



Clinical features of endobronchial tuberculosis

Kliničke karakteristike endobronhijalne tuberkuloze

Natalija Samardžić*, Dragana Jovanović*[†], Ljiljana Marković-Denić*[†], Marina Roksandić-Milenković*, Spasoje Popević*, Vesna Škodrić-Trifunović*[†]

*Clinic for Lung Disease, Clinical Center of Serbia, Belgrade, Serbia, [†]Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [‡]Institute of Epidemiology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Abstract

Background/Aim. Endobronchial tuberculosis (EBTB) is a specific type of pulmonary tuberculosis which often affect the tracheobronchial tree, and can be microbiologically and/or pathohistologically confirmed. The aim of the study was to determine the clinical features and diagnostic aspects of EBTB. **Methods.** This retrospective study was conducted at the Clinic for Lung Diseases, Clinical Center of Serbia, Belgrade, from January 1997 to December 2007. All patients with EBTB confirmed by bronchoscopy with biopsy during a study period were analysed. Data included the patient's medical history, a physical exam, chest X-ray, mycobacterial analysis of sputum samples, endoscopic types and pathohistological confirmation. **Results.** In the study, 57.6% of the patients were males. The most frequent symptoms were cough (71.2%), malaise (54.2%), fever (49.2%), weight loss (40.7%), and hemoptysis (13.6%). Most of the patients were diagnosed within 30 days of symptoms onset. Sputum examination showed acid-fast bacilli in 31.4% of the patients, while sputum culture for tuberculosis bacilli were positive in 55.9% of the patients. The most common radiographic localization was in the upper lung lobes (63.5%). Cavities were present in 60.4% of the patients. The most common endoscopic subtype determined by bronchoscopy were nonspecific bronchitis (39.9%) and edematous-hyperemic subtype (36.4%). **Conclusion.** EBTB was more frequent among men, and among people in their fifties in our country. Detailed bronchoscopic examination, correlated with clinical and laboratory findings, will improve diagnostic rate and provide timely therapy.

Key words:

tuberculosis; pulmonary; diagnosis; signs and symptoms; radiography; bronchoscopy; histological techniques.

Apstrakt

Uvod/Cilj. Endobronhijalna tuberkuloza (EBTB) je tuberkuloza traheobronhijalnog stabla, mikrobiološki i/ili patohistološki potvrđena. Cilj rada bio je da se odrede kliničke karakteristike i dijagnostički aspekt endobronhijalne tuberkuloze. **Metode.** Ova retrospektivna studija sprovedena je u Klinici za plućne bolesti Kliničkog centra Srbije u Beogradu u periodu od januara 1997. do kraja decembra 2007. god. Analizirani su svi bolesnici sa EBTB koja je potvrđena bronhoskopski i biopsijom u navedenom periodu. Prikupljeni su anamnestički podaci bolesnika, podaci o fizikalnom pregledu i radiografiji pluća, laboratorijske analize sputuma, uz bronhoskopsku i patohistološku potvrdu. **Rezultati.** U studiji je bilo 57,6% osoba muškog pola. Najčešći simptomi bolesti bili su kašalj (71,2%), znojenje (54,2%), povišena telesna temperatura (49,2%), gubitak telesne mase (40,7%) i hemoptizije (13,6%). Kod većine bolesnika dijagnoza je postavljena unutar 30 dana od početka simptoma. U sputumu je kod 31,4% bolesnika potvrđen *Mycobacterium tuberculosis*, a kultura je bila pozitivna kod 55,9% bolesnika. Na radiografskom nalazu najčešće su bili zahvaćeni gornji režnjevi pluća (kod 63,5% bolesnika). Kaverne je imalo 60,4% bolesnika. Bronhoskopski nalaz je kod najvećeg broja pokazivao nespecifični bronhitis (39,9%) i edemohiperemični podtip EBTB (36,4%). **Zaključak.** U našoj zemlji EBTB je značajno češća kod muškaraca i osoba u pedesetim godinama života. Bronhoskopski nalaz koreliše sa kliničkim i laboratorijskim nalazom i omogućava lakše postavljanje dijagnoze i pravovremenu terapiju.

Ključne reči:

tuberkuloza pluća; dijagnoza; znaci i simptomi; radiografija; bronhoskopija; histološke tehnike.

Introduction

Endobronchial tuberculosis (EBTB) is a specific type of pulmonary tuberculosis (TB) which often injures the tracheobronchial tree, and can be microbiologically and/or pathohistologically confirmed¹. The diagnosis of EBTB is frequently delayed until the onset of serious bronchial stenosis with resultant atelectasis and bronchiectasis². EBTB often presents a diagnostic challenge because the clinical presentation varies, and some patients can have normal chest radiography, even though the acid-fast bacilli (AFB) positive sputum sample is present³. EBTB may have a prolonged and insidious course and mimic lung cancer, or an acute course, and imitate bronchial obstruction, aspiration of a foreign body or pneumonia, and sometimes the clinical course can be asymptomatic. Because of the complexity and different prognosis, an endoscopic EBTB classification was adopted based on morphological characteristics of the seven subtypes (actively caseating, edematous hyperemic, fibrostenotic, tumorous, granular, ulcerative, and nonspecific bronchitic) proposed by Chung and Lee⁴. The course of EBTB differs according to the endoscopic type. Actively caseating, edematous hyperemic, and fibrostenotic subtypes most frequently lead to the formation of bronchostenosis that is the most serious complication of EBTB⁵. All subtypes can be transformed one into another. The outcome of the treatment for all subtypes is predictable, except for the tumorous form. Fibrostenosis may develop later, after a nine-month doctrinaire treatment (a combination regimen composed of four kinds of anti-tuberculosis drugs – the commonly used drugs include isoniazid, rifampicin, pyrazinamide and ethambutol), which was observed in one third of cases. Endoscopic type can predict bacillar prominence and anticipate the extent and duration of the disease (the edematous hyperemic form, the granulous form, and non-specific bronchitis occur in the early stages, while other forms indicate a widespread disease). The proportion of EBTB in pulmonary TB is about 10–40%³. Although the TB incidence has decreased during the last few decades in Serbia⁶, this disease remains an important public health problem especially among patients older than 65 years⁷. The incidence rates being for the last few decades 32–36 *per* 100,000 inhabitants, up to the last few years when they decreased to 24–26 *per* 100,000 inhabitants. However, there are a few data about EBTB in our country, and in the region of Balkan and Southern Europe as well, even in the countries with high TB prevalence⁸.

The aim of this study was to determine common clinical features and diagnostic aspects of EBTB in our patients.

Methods

This retrospective study was conducted at the Clinic for Lung Diseases, Clinical Center of Serbia, Belgrade, from January 1997 to December 2007. A total of 118 consecutive patients with EBTB were hospitalized and treated in our hospital, during the study period. All the cases with EBTB confirmed by bronchoscopy with biopsy during study period were analysed. For each patient we had a questionnaire filled

out. Data included the patient's medical history, physical exam, chest X-ray, bronchial examination with bronchial biopsies and mycobacterial analysis of sputum samples. Statistical Package for Social Sciences (SPSS) program-version 15.0 was used for data entry and analysis. Statistical differences were evaluated using the chi-square test and *t*-test.

The Institutional Ethics Committee approved the study.

Results

There were 68 (57.6%) men and 50 (42.4%) women, the ratio being 1.4 : 1. The mean age was 44.3 ± 4.32 years (ranged from 16 to 73 years). Twenty four (20.3%) of the patients were older than 60 years. At the time of diagnosis, there was a significant tendency for the women that had EBTB to be younger than 40 years, compared to the men ($p = 0.05$) (Figure 1).

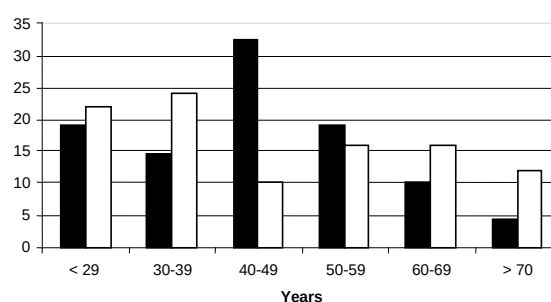


Fig. 1 – Percentage of patients with endobronchial tuberculosis according to age and sex.

Closed bars – men; open bars – women.

Nearly half (47.8%) of the patients were diagnosed within 30 days of symptom onset. The clinical presentation of EBTB varied. Five (4.2%) patients were asymptomatic, all the other patients have at least one symptom of TB. Symptoms and their duration before diagnosis are presented in Table 1, the dominant being cough 84 (71.2%) and general weakness 64 (54.2%), followed by fever 58 (49.2%), weight loss 48 (40.7%), and hemoptysis 16 (13.6%), respectively. Hemoptysis were significantly more frequent in males than in females ($p = 0.04$), but without differences according to age. Beside that, other complaints included chest pain (31.4%), sweating (17.8%), and dyspnea (12.4%), and 3.4% patients were hoarse. A predisposing disease or condition was recorded in 43 (36.4%) patients. Fourteen (11.9%) patients had diabetes mellitus. A small number of patients, 5 (4.2%) had been previously treated for TB, on average 28.5 years earlier, ranging between 10 and 40 years.

In patients with EBTB, a unilateral process was more frequent (59.5%) than bilateral (41.5%). Upper lung fields were the most frequently involved in 63.5% of the patients (Table 2). Cavernous lesions were notified in 60.4% patients.

TB was confirmed by direct microscopy and/or culture. Sputum examination for acid-fast bacilli (AFB) was positive in 31.4%, and culture in 55.9% of the patients.

The most common bronchoscopic findings were nonspecific bronchitis and edematous-hyperemic subtype (Table 3).

Table 1

Symptoms of endobronchial tuberculosis

Symptoms	Patients n (%)	Duration of symptoms (days)		
		$\bar{x} \pm SD$	median	min-max
Cough	84 (71.2)	98.6 $\pm$ (96.9)	60.0	1–450
Hemoptysis	16 (13.6)	55.7 $\pm$ (110.7)	10.0	1–365
Fever	58 (49.2)	47.3 $\pm$ (37.8)	30.0	2–150
General weakness	64 (54.2)	87.4 $\pm$ (84.9)	60.0	10–450
History of weight loss	48 (40.7)	90.1 $\pm$ (91.8)	60.0	20–450

*The total number of patients is higher than 118 because some of the patients had more than one symptom.

Roentgenographic site in 118 patients with endobronchial tuberculosis

Localisation	Patients, n (%)
Right upper lobe	27 (22.9)
Left upper lobe	22 (18.6)
Both side – upper lobes	26 (22.0)
Middle lobe	6 (5.1)
Right lower lobe	8 (6.8)
Left lower lobe	6 (5.1)
Both side – diffusely	23 (19.5)
Total	118 (100.0)

Table 2

The bronchoscopic findings in 118 patients with endobronchial tuberculosis

Bronchoscopic findings	Patients, n (%)
Actively caseating	10 (8.5)
Edematous-hyperemic	43 (36.4)
Fibrostenotic	10 (8.5)
Tumorous	5 (4.2)
Granular	3 (2.5)
Nonspecific bronchitis	47 (39.9)
Total	118 (100.0)

Table 3

Of the 118 patients, 111 (94.0%) cases presented with chronic tuberculous bronchitis on the pathological findings of biopsy obtained by bronchoscopic procedures while only 6% cases presented tuberculous granuloma.

Discussion

This research encompassed one of the largest numbers of a series of EBTB cases in the region of Balkan. We found that there were more male than female EBTB patients in the fifth decade of life (sex ratio 1.4 : 1), which is confirmed by papers from different regions (Hong Kong, Korea, China, Japan, Brazil)^{9–13}. In contrast, the preponderance of females among patients with EBTB is stated in the works of other authors¹⁴.

Respiratory symptoms in EBTB, according to our results, were nonspecific. Cough and fatigue dominate, followed by fever, weight loss and hemoptysis. Cough was the most common symptom according to the results of other studies^{1,15}. Thoracic pain was present in almost a third of our patients (31.4%), whereas this symptom was less frequently observed (15%) by other authors^{3,9}. In our study group, 13.6% of the patients had hemoptysis, while accord-

ing to other papers, 25% to 40.2% of the patients had hemoptysis⁹. General symptoms, such as weakness, fever, and weight loss, were present in a significant number of patients, according to the results of this study and other studies, as well^{3,9}. As for the duration of symptoms prior to diagnosis of TB, according to our results, the interval varies from 1 week to 1 year, but the severity of symptoms (most commonly cough and fatigue) most likely contributed to the fact that almost half of patients came for a checkup during the first 30 days of the onset of symptoms. Short average period from disease onset to diagnosis of EBTB, when compared to overall pulmonary TB in the same settings, could be explained by clear clinical symptoms that lead to suspicion to EBTB and faster implementation of diagnostic procedure. Other authors describe precisely this diversity of symptoms and their intensity: with symptoms that mimic asthma^{9,13,14}, aspiration of a foreign body, and lung cancer^{16–18}. An asymptomatic form of the disease is also possible and it was observed in five patients in our study.

In terms of the bacillarity of sputum in EBTB, several different results have been published. Thus, some studies^{1,4,13} confirm the assumption of high infectivity of patients with EBTB by the presence of simple sputum positive for AFB in 51.8–91% patients. On the other hand, some studies^{1,9,14} report on a significantly lower (9.1–17%) positive sputum for AFB. The results of the present study confirm AFB in one third of the patients, while the Löwenstein-Jensen culture of sputum samples were positive in over half the cases, which is consistent with the results reported by other authors⁴. Certainly, different histological types EBTB correspond to these contradictory findings. It was noted that the endoscopic ulcerative form and actively caseating type of EBTB have higher sputum positivity, which is not the case with edematous-hyperemic and fibrostenotic type⁵, so that in these cases the histological confirmation of disease fibro-bronchoscopy is required, while negative sputum for AFB does not exclude the diagnosis of EBTB.

Radiographic analysis of the lungs of the patients in our study showed that cavernous changes in the lungs were present in about two-thirds of the patients with EBTB and this finding did not differ significantly from the results in the literature¹³. None of the patients had chest radiography without pathological changes, in our study. In contrast to our work, many studies have ascertained the presence of normal chest radiographs in 10–20% of cases^{9,10,14,19}. Normal chest radiography is a diagnostic trap for EBTB that is why the diagnosis of the disease is often delayed²⁰. The authors agree

that the most common radiographic localization of pulmonary TB is in the upper lobes which was confirmed by our results, as well (63.5%). The middle and lower lobes, as atypical radiographic presentations, in our work were affected in 17% of the patients, while the same results, were found in up to 42–90% of patients, according to the literature^{21,22}.

The most common endoscopic forms of EBTB determined by bronchoscopy in our study were nonspecific bronchitis in 39.8% of the patients, followed by the edematous hyperemic form in 36.4%, while the granular form was recorded in only 2.5% of the cases, and no patient had ulcerative EBTB form. These results differ from those in the study by authors who made a proposal of classification, Chung and Lee⁴ and Lee et al.²³, which showed the most frequent occurrence to be the actively caseating form (43%), while nonspecific bronchitis (7.9%) and ulcerative type (2.7%) were the rarest represented. The differences could most likely be explained by the duration of the disease until bronchoscopy, that is, endoscopic exploration. In our study, in approximately half of the patients the disease was diagnosed by bronchoscopy during the first month, which resulted in the highest frequency of nonspecific bronchitis and edematous-hyperemic type, which confirmed the observation that these forms occur in the early stages of EBTB⁸. Bronchoscopy was performed in order to obtain good aspirate sample for bacteriologic analysis, and later to use the same sample to test the susceptibility to antituberculosis (AT) drugs. Concerning difficulties of *Mycobacterium tuberculosis* isolation, it was the case in the past from time to time up to 3–4 years ago, due to the periods when sputum induction could not be performed at all because of a lack of essential equipment (the nineties of 20th century and first few years of new millennium). This diagnostic procedure was conducted in the patients with radiological findings which were not enough persuasive of TB process, and in a certain proportion in the patients without bacteriologic confirmation of TB. They were

treated with AT drugs for 3–4 weeks, and when at the first check-up, chest x-ray did not show any initial improvement (initial regression of lesions) and who did not provide good or not at all sputum sample for bacteriologic diagnosis, even after sputum induction, so there was a problem how to confirm the suspicion of TB process. Bronchoscopy was also used to exclude any other underlying or concomitant disease. Due to a serious problem of increasing incidence of lung cancer in our country, in the last decade more than 27%²⁴, it is very important to use bronchoscopy as diagnostic tool.

A histologic confirmation of EBTB is of great importance in the prevention of further spread of TB and to eliminate the suspicion of malignancy²⁵. It is also useful in differentiation from the other granulomatosis, mostly sarcoidosis. We found TB granuloma in 6% of the patients. When EBTB cannot be diagnosed by histologic confirmation findings after repetitious examinations, diagnosis should be established by a combination of clinical, bacteriological and bronchoscopic findings and aggressive treatments must be performed to eradicate *Mycobacterium tuberculosis* to avoid tracheobronchial stenosis²⁶.

Conclusion

In our patients, EBTB was more frequent among men, and among people in their fifties. Detailed bronchoscopic examination is unavoidable as being a simple and reliable diagnostic procedure, correlated with clinical and laboratory findings. This procedure alone will improve diagnosis accuracy rate and provide timely therapy.

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