Original Article

DOCTOR'S DELAY IN ENDOBRONCHIAL TUBERCULOSIS

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Abstract [Objective] The aim of this study was to investigate the current status of doctor's delay in diagnosing endobronchial tuberculosis (EBTB) and to elucidate the risk factors contributing to the delay. [Methods] Retrospective clinicopathological analysis. [Patients] Sixty-two patients with EBTB were admitted at our hospital between 1999 and 2010. Their backgrounds, symptoms, diagnoses at initial consultation, delay in diagnosis, and clinical examination results were analyzed. [Results] Of the 62 patients, 59 had acid-fast, bacilli-positive sputum smear test results at admission. Among the 40 patients with total diagnostic delay of more than 2 months, only 11 experienced long patient's delay exceeding 2 months. However, 22 patients experienced long doctor's delay of more than 2 months (28% vs. 55%, respectively, $p<0.05$), suggesting that doctor's delay contributes more to total delay than patient's delay. Fever was less frequent in patients with long doctor's delays than in those without (0% vs. 18%, respectively), at the initial consultation. In addition, radiographs showed that patients with long doctor's delays more frequently presented with shadows in the lower lung field (50% vs. 23%, $p<0.05$), and most of these patients had noncavitary shadows on admission. All 7 patients diagnosed with bronchial asthma at the initial consultation had long doctor's delays. [Conclusion] These findings demonstrate that long doctor's delays in diagnosing EBTB remain an issue. The clinical features of EBTB with long doctor's delays were confirmed to be quite different from those of pulmonary tuberculosis.

Key words: Endobronchial tuberculosis, Doctor's delay, Radiographic findings, Bronchial asthma

Introduction

Tuberculosis is one of the most prevalent infectious diseases in Japan. In 2010, there were 23,261 newly diagnosed tuberculosis patients and the incidence of tuberculosis was 18.2 per 100,000 population, which makes Japan a middle-incidence country for tuberculosis[1]. However, amid the trend towards a long term, slow decline in the incidence rate of tuberculosis, the total diagnostic delay of tuberculosis remains an ongoing problem in clinical practice[2]. The total delay in diagnosis is called total delay, which is a combination of the patient's and doctor's delays. Patient's delay is defined as the interval between the onset of symptoms and the initial consultation, whereas doctor's delay is defined as the interval between the initial consultation and diagnosis of tuberculosis[3]. The length of doctor's delay in pulmonary tuberculosis (PTB) diagnosis has been decreasing because of recent advances in examination methods[2] such as polymerase chain reactions[4] and Quanti FERON-TB[5].

Unfortunately, total delay, especially doctor's delay, is known to be high in the diagnosis of endobronchial tuberculosis (EBTB) associated with PTB[6)~10)]. This is because EBTB is difficult to distinguish from common diseases such as cold, bronchitis, or bronchial asthma on the basis of symptoms, considering the following features[6)~12)]: (i) EBTB is common in women and young individuals; (ii) it is frequently associated with severe cough as the chief complaint and is often accompanied by wheezing; and (iii) on radiography, the X-ray shadows often appear as minimal shadows without cavities as a result of comorbid PTB. EBTB patients have a high rate of sputum smear positivity for acid-fast bacilli (AFB)[6)~12)], and the risk of contact infection is high. Therefore, decreasing the length of doctor's delay is essential, not only for the doctors themselves, but also for maintaining public health, in general.

The objective of this study was to investigate the current status of doctor's delay in EBTB. We also aimed to elucidate the risk factors that can prolong doctor's delay in EBTB patients.

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Subjects and methods

From 4272 patients with culture-positive active tuberculosis who were admitted to the tuberculosis ward of National Hospital Organization Tokyo National Hospital, Tokyo, Japan, between 1999 and 2010, 62 patients (1.5%) who fulfilled all the following criteria were selected: (i) underwent fiberoptic bronchoscopy while receiving tuberculosis treatment during initial hospitalization; (ii) tuberculous lesion confirmed bronchoscopically in the region between the laryngopharynx and segmental bronchi; and (iii) data regarding clinical course, bacteriological findings, radiographic findings, and bronchoscopic findings were available.

The total delay, patient's delay, and doctor's delay were calculated for these 62 patients from information obtained before their admission to our ward. In addition, their further clinical course, radiographic findings, bronchoscopic findings, bacteriological findings, and other data from the period of admission were analyzed. Finally, retrospective analyses were performed. In this study, doctor's delay was defined as the time interval between the initial consultation at a medical institution and referral examination of patients at the hospital, with a diagnosis of tuberculosis or suspected tuberculosis. All 62 patients were admitted to the ward within days of their consultation at the hospital. Chest radiography findings on admission were classified according to the classification of PTB recommended by the Japanese Society for Tuberculosis (Gakkai classification)[13]: Extent 1, morbid foci that do not cross the area from the lung apex to the horizontal line on front upper edge of second rib; Extent 3, morbid foci that cross the hemi-thorax area; Extent 2, morbid foci between Extent 1 and Extent 3; Type I, widespread cavities that cross the area of Extent 1 and morbid foci that cross the hemi-thorax area in total; Type II, morbid foci with cavities other than Type I; Type III, active infiltrative morbid foci with no cavities[14]. Various methods for classifying EBTB from bronchoscopic findings, such as Chung's classification[15] or Arai's detailed classification[16], have been proposed in Japan. For this study, patients were evaluated according to our own proposed classification[17]: phase I (intramucosal nodules), phase II (ulcer), phase III (polyp), and phase IV (fibrous scar). This classification system is simple and corresponds accurately with the pathological findings, which is advantageous because disease status can be easily classified even from a review of images archived in medical records.

The chi-square test, Fisher's exact test, and McNemar's test were used for the statistical analysis of frequency of various factors, as appropriate. Differences with p value of <0.05 were considered significant. SPSS, version 20.0 (SPSS Inc., Chicago, IL, USA) statistical software was used. This study was approved by the institutional review board of the hospital, and the need for informed consent was waived.

Table 1 Patient characteristics

Factors	Number of patients (n=62)
Sex	
Male/female	21/41
Age (years)	
≦39/40−69/70≦	22/26/14
Underlying disorders and past history	
None	53
Major symptoms*	
Cough/wheeze/fever/hoarseness	50/9/7/5
Sputum smear for AFB†	
Positive/negative	59/3
Chest radiography findings†	
Type II/III	12/50
Extent 1/2	22/40
Lower lung field−predominant shadow	20
Bronchoscopic findings‡	
Phase I/II/III/IV	1/45/7/9
Location of main tuberculosis lesion	
L/Tr-MB/IB-SB	3/33/26

*at the first consultation, †on admission to our hospital, ‡during hospitalization,
AFB: acid-fast bacilli, L: larynx, Tr: trachea, MB: main bronchus, IB: intermediate bronchus, SB: segmental bronchus

Results

Table 1 shows the clinical characteristics of the 62 patients. The majority of patients were women (41 patients). Comparing the patient demographics for classical PTB, the proportion of older patients was small. With regard to underlying diseases, 2 patients had a history of cancer-related surgery, 2 had diabetes mellitus, 2 were positive for human immunodeficiency virus, 2 had a history of PTB treatment, and 1 had pulmonary nontuberculous mycobacteriosis. The remaining 53 patients did not have any underlying diseases or past history relevant to the onset of tuberculosis. The prevalence of symptoms was analyzed according to the referral letter or the documented history at the time of admission, and each patient was allowed to register up to 2 chief complaints at the initial consultation. The chief complaint was cough in 50 patients (81%), followed by wheezing (9 patients) and hoarseness (5 patients). Some patients had systemic symptoms such as fever (7 patients) or weight loss (3 patients). No patient had expectoration as a chief complaint. However, on admission, spontaneous or induced sputum revealed AFB-positive sputum smear test results in 59 of the 62 patients. On radiographic findings, many patients had Type III tuberculosis (noncavitary, 50 patients) with Extent 2 (not extensive, 40 patients), and 20 showed localized tuberculosis in the lower lung fields. Lobar atelectasis was observed in 6 patients. Fiberoptic bronchoscopy was performed immediately after hospitalization in 3 patients whose sputum smears were negative on admission. In the remaining 59 patients, bronchoscopy was performed during tuberculosis treatment when deemed appropriate by the attending physician. Phase II features (ulcers), which were the most characteristic and active findings, were observed in 45

patients. Many ulcers were found in large airways, including the trachea and main bronchus (33 patients), and these ulcers are known to often cause the sequela of tuberculosis[18].

The total delays for all 62 patients are shown in Fig. 1. Of the 62 patients, 22 (35%) were diagnosed with tuberculosis within 2 months from the onset of symptoms, whereas diagnosis was delayed for more than 2 months in the remaining 40 patients. Diagnosis was delayed for more than 6 months in 16 % patients (10 patients). A delay greater than 2 months was considered a long delay, considering the following facts: most of the 62 patients had AFB-positive sputum smear tests on admission, and the risk of contact infection was relatively high. The ratio between patient's delay and doctor's delay in the 40 patients with a total delay more than 2 months was calculated (Fig. 2). Although 11 patients experienced patient's delays of more than 2 months (over 6 months in 2 patients), 22 patients experienced doctor's delays greater than 2 months (over 6 months in 5 patients) (28% vs. 55%, respectively, $p<0.05$).

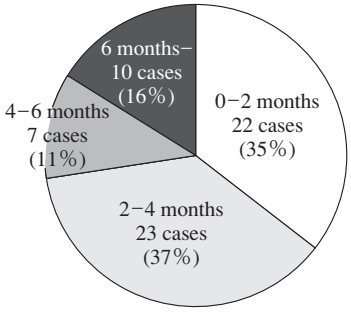

Fig. 1 Total delay* in all 62 patients
*time interval between onset of symptoms and diagnosis of tuberculosis

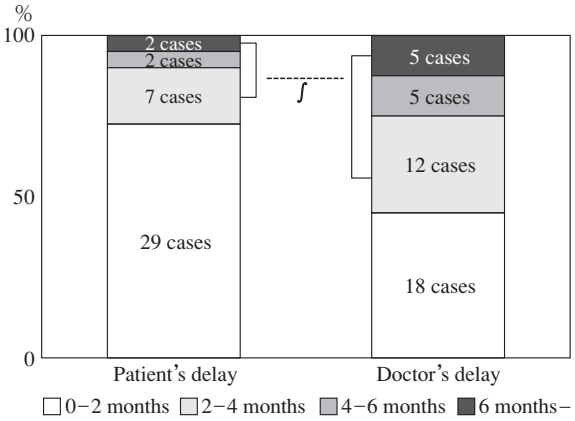

Fig. 2 Patient's delay* and doctor's delay† in 40 patients with total delay‡ of over 2 months
*time interval between onset of symptoms and the first consultation
†time interval between the first consultation and diagnosis of tuberculosis
‡time interval between onset of symptoms and diagnosis of tuberculosis
∫ $p<0.05$

This finding suggests that prolonged doctor's delay, which is an iatrogenic factor, has a larger role in long total delay than in patient's delay, which is a patient-related factor or a social factor. The 62 patients were then divided into 2 groups on the basis of doctor's delay > 2 months (22 patients) or within 2 months (40 patients). Subsequently, clinical presentations of patients in the groups were compared (Table 2). There were no differences between the 2 groups in terms of the background factors such as gender and age, but patients in the group with long doctor's delays presented with fever less often than those with short delays (0% vs. 18%, respectively), and the incidence of wheezing in these patients was higher (27% vs. 8%, respectively).

The relationship between doctor's delay as well as radiographic and bronchoscopic findings is shown in Table 3. The data regarding the number of patients who underwent chest radiography at the initial consultation was unavailable. However, on admission, patients in the group with long doctor's delays more often showed a lower lung field shadow than those with short delays (50% vs. 23%, respectively, $p<$

Table 2 Relationship between doctor's delay* and patient background

Factors	Doctor's delay	
	≦2 months (n=40)	>2 months (n=22)
Demographics		
Female	28 (70%)	13 (59%)
Young age (<40 years)	14 (35)	8 (36)
Major symptoms†		
Cough	31 (78)	19 (86)
Wheeze	3 (8)	6 (27)
Fever	7 (18)	0 (0)
Hoarseness	3 (8)	2 (9)

*time interval between the first consultation and diagnosis of tuberculosis
†at the first consultation

Table 3 Relationship between doctor's delay* and radiographic/bronchoscopic findings

Factors	Doctor's delay		
	≦2 months (n=40)		>2 months (n=22)
Chest radiography findings†			
Type III	31 (78%)		19 (86%)
Extent 2	26 (65)	∫	14 (64)
Lower lung field localization	9 (23)		11 (50)
Bronchoscopic findings‡			
Phase II (ulcer)	29 (73)		16 (73)
Tr-MB localization	21 (53)		12 (55)

*time interval between the first consultation and diagnosis of tuberculosis
†according to the classification of pulmonary tuberculosis designated by the Japanese Society of Tuberculosis, on admission to our hospital
‡during hospitalization,
Tr: trachea, MB: main bronchus, ∫ $p<0.05$

Table 4 Relationship between doctor's delay* and diagnosis in 32 patients who had not been diagnosed with tuberculosis at the first consultation

Diagnosis	Doctor's delay	
	≦2 months (n=10†)	>2 months (n=22)
Pneumonia/bronchitis (n=11)	6 (60%)	5 (23%)
Laryngeal diseases (n=3)	1 (10)	2 (9)
Common cold (n=4)	1 (10)	3 (14)
Bronchial asthma (n=7)	0 (0)	7 (32)
Unknown (n=4)	2 (20)	2 (9)
Others (n=3)	0 (0)	3 (14)

*time interval between the first consultation and diagnosis of tuberculosis
†30 patients who had diagnosis of tuberculosis at the first consultation were excluded in this group

0.05); moreover, 19 of the 22 patients in the groups with long doctor's delays showed noncavitary shadows. It has been noted that bronchoscopic findings of EBTB consist mostly of ulcers at the beginning of treatment, irrespective of the duration of presenting symptoms (i.e., the length of the delay)[8)10)]. Our study results also showed no differences in the bronchoscopic findings between the groups with different delay lengths.

After excluding 30 patients diagnosed with tuberculosis or suspected of having tuberculosis at the initial consultation, the clinical diagnoses at the initial consultation were compared between the groups with long doctor's delays and short doctor's delays (within 2 months) (Table 4). Six of 11 patients who had been diagnosed with pneumonia and/or bronchitis at the initial consultation experienced short doctor's delays, whereas all 7 patients who had been diagnosed with bronchial asthma experienced long doctor's delays.

Discussion

EBTB has been once considered as a type of PTB while calculating the statistics for tuberculosis in Japan, and the statistical details regarding the disease were unclear until 2006. However, previous studies have shown that EBTB has clinical characteristics different from those of classical PTB. In addition, Kurasawa[19)] stated the need to consider EBTB as a different type of tuberculosis. The present study also showed the following characteristics of EBTB that were different from those of typical PTB: (i) a predominance of female patients; (ii) a relative predominance of younger patients; (iii) chief symptoms of cough, hoarseness, and wheezing; (iv) AFB-positive sputum smear test results in almost all cases; (v) noncavitary shadow and predominantly lower lung field shadow on radiographs; and (vi) a high frequency of ulcers in the region from the trachea to the main bronchus on fiberoptic bronchoscopy.

Regarding doctor's delay for diagnosing EBTB, a study by Komatsu et al.[6)], involving 40 EBTB patients in the 1970s, showed that several patients were misdiagnosed with bronchial asthma and lung cancer. A study by Kurasawa et al.[7)], involving 61 EBTB patients in the 1980s, showed no significant difference between the number of patients (n=9, 15%) who experienced doctor's delays of 3 months or more compared with those who experienced patient's delays of 3 months or more (n=7, 11%). In contrast, a study by Sasaki et al.[8)] involving 50 EBTB patients in the 1980s and 1990s found the mean length of doctor's delay to be 16.4 weeks, which was much longer than that of patient's delay (5.7 weeks). The reason attributed to this difference was that many EBTB patients lacked characteristic tuberculous cavities on radiographs and had a low Spread level. Toyota et al.[9)] also reported that in 48 patients with EBTB in the 1990s, the mean doctor's delay was longer than the mean patient's delay (3.3 months vs. 2.4 months). Furthermore, in our previous study involving 103 EBTB patients, conducted from the 1990s to the 2000s, 26 of the 59 patients who visited medical institutions where tuberculosis was not diagnosed, experienced total delays of more than 3 months, suggesting that a medical consultation that did not give an accurate diagnosis of tuberculosis may have contributed to a longer total delay of EBTB[10)]. The present study involving 62 EBTB patients, who were predominantly diagnosed in the 2000s, showed that about one-third of the patients experienced doctor's delays of more than 2 months. Moreover, in a few of the patients, tuberculosis diagnosis was delayed for more than 6 months. These results suggest that doctor's delay in EBTB remains a problem in clinical practice.

Analysis of the clinical data in the present study aimed at determining which factors prolonged doctor's delay showed that neither gender nor young age was a contributory factor, but indicated that shadows localized in the lower lung fields on radiographs and absence of fever may be important risk factors. In addition, the presence of wheezing mimicking bronchial asthma and noncavitary shadows on radiographs may be influential factors.

Comparison of diagnoses at the initial consultation showed that doctor's delays were prolonged in all patients diagnosed with bronchial asthma. In contrast, the results suggested that a comparatively large number of the patients diagnosed with pneumonia and/or bronchitis were diagnosed with EBTB earlier. It is possible that radiographic and sputum examinations (even if expectoration was not a major complaint) were commonly performed after the diagnosis of infectious diseases such as bronchitis and/or pneumonia. However, those examinations would not likely be performed with a diagnosis of noninfectious diseases such as bronchial asthma in which fever is absent. On the basis of the present study findings, we speculate that early EBTB patients lacking fever and expectoration, but having cough and wheezing, might receive only steroid inhalation therapy, depending on whether they are diagnosed with bronchial asthma. This delay may further prolong doctor's delay and disease progression in EBTB.

The present study demonstrated that long total delays in EBTB diagnosis, especially the part contributed by doctor's

delay, may not be resolved in the 21st century; in fact, it suggests that the problem may worsen. Solving this problem requires greater attention from pulmonologists treating typical EBTB cases presenting with wheezing, without fever, and with shadows in the lower lung field or noncavitary lesions on radiographs, as well as increased awareness about such cases among general physicians, allergy specialists, and otolaryngologists in various clinical settings.

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