

Clinical Manifestations and Diagnosis of Extrapulmonary Tuberculosis

Hee Jung Yoon, Young Goo Song, Woo Il Park, Jae Pil Choi, Kyung Hee Chang, and June Myung Kim

Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea.

Since the diagnosis of extrapulmonary tuberculosis (EPT) is largely depended on the physician's suspicion in respect of the disease, we believed that it would be worthwhile to scrutinize the clinical characteristics of EPT. Thus, here we present retrospectively evaluated clinical manifestations of patients who were diagnosed as EPT cases in a tertiary referral care hospital.

Medical records of 312 patients, diagnosed as having EPT at Yongdong Severance hospital from January 1997 to December 1999, were reviewed retrospectively.

In total 312 patients, 149 (47.8%) males and 163 (52.2%) females aged from 13 years to 87 years, were included into this study. The most common site of the involvement was pleura (35.6%). The patients complained of localized symptoms (72.4%) more frequently than systemic symptoms (52.2%). The most common symptom was pain at the infected site (48.1%). Leukocytosis, anemia, and elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were found in 12.8%, 50.3%, 79.3% and 63.1% of the patients, respectively. Twenty-four percent of the patients had underlying medical illnesses such as, diabetes mellitus or liver cirrhosis, or were over 60 years old. In 67.3% of patients, tuberculosis was suspected at the initial visit. However, tuberculosis was microbiologically proven in only 23.7% of the patients. The time interval from the symptom onset to the diagnosis varied, with the mean duration of the period 96 days. Pulmonary parenchymal abnormal lesions were found in 133 patients (42.6%) on chest radiographs.

EPT has a wide spectrum of clinical manifestations, so it is difficult to diagnose it. Based on our studies, only 11.2% of the patients were confirmed as EPT. So it is important that the physician who first examines the patient should have a high degree of suspicion based on the chest radiography, localized or systemic symptoms and several laboratory parameters reviewed in this study.

Key Words: Tuberculosis, extrapulmonary tuberculosis, diagnosis

INTRODUCTION

According to a survey study on tuberculosis (TB) prevalence in Korea, the incidence of active TB based on the chest X-ray results was 5.1% and the bacteria positive rate 0.94% in 1965. These rates decreased to 1.0% and 0.22%, respectively, in the 7th survey performed in 1995, with the annual decrease in the incidence of 5.0%,¹ which is identical to the annual decrease found in the United States, according to the study by Hans et al.² Although many studies have been performed on the incidence, clinical pattern and the standard treatment for TB, studies on the incidence and bacteria positive rate of extrapulmonary tuberculosis (EPT) are scarce. The reason is that the diagnostic criteria of this type of TB are limited, and the diagnosis is made according to the histologic examination and tissue biopsy results. Moreover, the treatment is started in the patients clinically or radiologically suspected of having EPT in many cases. Thus, we have retrospectively reviewed changes in the number and the affected sites of patients diagnosed as having EPT in the university hospital and observed the relationships between the overall clinical patterns, diagnostic methods, underlying diseases, and chest X-ray findings.

MATERIALS AND METHODS

Changes in the incidence of EPT were reviewed

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Reprint address: requests to Dr. Young Goo Song, Department of Internal Medicine, Yongdong Severance Hospital, 146-92 Dogok-dong, Kangnam-gu, Seoul 135-270, Korea. Tel: 82-2-3497-3319, Fax: 82-2-3463-3882, E-mail: imfell@yumc.yonsei.ac.kr

retrospectively in patients diagnosed as EPT cases from January 1992 to December 1999 at Severance Hospital (affiliated with the College of Medicine), Yonsei University. We have retrospectively reviewed the medical records and chest X-rays results of 312 patients who were diagnosed as EPT cases during the period from January 1997 to December 1999 at Yongdong Severance Hospital. The patients were divided into 9 groups, according to the affected site, i.e., pleura, lymph nodes, bone and joints, gastrointestinal tract, CNS, genitourinary tract, miliary TB, respiratory tract (the trachea, bronchus, larynx and epiglottis) or other locations (skin, soft tissue, pericardium, and the endocrine system). The clinical patterns were divided into the systemic symptoms, such as fever, weight loss, sweating, loss of appetite and malaise, and the local symptoms, such as pain at the infected site, cough, sputum and dyspnea. The underlying diseases were divided into chronic wasting diseases, such as diabetes, liver cirrhosis, renal failure, and congestive heart failure, malignancy, history of malnutrition, status after surgery and history of treatment with steroid drugs as well as no underlying diseases. Blood tests were done to determine whether the levels of white blood cells (WBC), hemoglobin, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated. The patients were also divided into those with history of pulmonary TB and EPT and those without it. The degree of agreement between the suspected initial diagnosis (divided into EPT at the suspected site, tumor, bacterial infection and non-bacterial infection) and the final diagnosis was also determined. Non-bacterial infection was defined as fever of unknown origin, a viral infection or an adverse drug reaction. The patients were divided into 3 groups, according to the methods of the diagnosis, in which "the patients with confirmed TB" had a positive culture, "patients with suspected TB" had a positive smear or chronic granulomatous inflammation, and "patients with possible TB" showed a favorable radiological and clinical response to the TB treatment.³ To establish a relationship between the abnormal findings of the X-ray examination and the development of EPT, the X-ray findings were divided into 3 types, namely: normal findings, the presence of tuberculous scar formations, and the

presence of cavity lesions or parenchyma with active TB.

RESULTS

Number of EPT

The number of EPT was 496, 496, 464, 490, 463, 457, 430, and 440 in 1992, 1993, 1994, 1995, 1996, 1997, 1998 and 1999, respectively.

Incidence

As for the incidence by organs, the most frequently affected site was the pleura in 111 cases (35.6%), followed by lymph nodes in 57 (18.3%), bone and joints in 41 (13.1%), the upper airways in 28 (9.0%), the gastrointestinal tract in 23 (7.4%), miliary TB in 9 (3.2%), and other locations in 9 cases (3.2%). Other affected organs included the pericardium, skin, soft tissue, middle ear, adrenal gland and thyroid gland (Table 1).

Demographic characteristics

The age of the patients ranged from 13 years to 87 years, with the overall average age of 41.3 ± 17.9 years. They included 149 males (47.8%) and 163 females (52.2%). TB lymphadenitis was present in 11 males (19.3%) and 46 females (80.7%), and was 4.2 times more prevalent in females than in males. Miliary TB was present in 7 males (77.8%) and 2 females (22.2%), and was 3.5 times more prevalent in males (Table 1).

Clinical manifestations

In one hundred and sixty-three cases (52.2%) systemic symptoms and in 226 cases (72.4%) local symptoms were noted. The most prevalent local symptom was pain at the affected site, in 150 cases (48.1%), and the most prevalent systemic symptom was fever, in 103 cases (33.0%). Other systemic symptoms included malaise, in 64 cases (20.5%), anorexia, in 46 (14.7%), loss of weight, in 45 (14.4%), and sweating, in 12 (3.8%). The local symptoms included cough and sputum in 117 cases (37.5%) and dyspnea in 79 (25.3%). Charac-

Table 1. Demographic Characteristics of Patients with Extrapulmonary Tuberculosis

	Age*(years)	No.	
		M/F	Total
Pleura	39.6 ± 18.4	66/45	111 (35.6%)
Lymph nodes	38.4 ± 16.1	11/46	57 (18.2%)
Bone and joints	43.0 ± 17.8	16/25	41 (13.1%)
Airways	44.6 ± 20.6	10/18	28 (9.0%)
G-I [†] organ	45.0 ± 17.5	9/14	23 (7.4%)
CNS [‡]	38.3 ± 14.2	12/8	20 (6.4%)
G-U [§] tract	40.1 ± 15.7	8/6	14 (4.5%)
Miliary	56.6 ± 21.8	7/2	9 (2.9%)
Other	45.7 ± 16.1	5/4	9 (2.9%)
Total	41.3 ± 17.9	149/163	312 (100%)

*Values are mean ± SD; [†]Gastrointestinal. [‡]Central nervous system; [§]Genitourinary.

Table 2. The Incidence of Systemic and Localized Symptoms of Extrapulmonary Tuberculosis (n=312)

	No.(%)							
	Fever	Wt.loss	Sweat	Anorexia	Malaise	Pain	C/S*	Dyspnea
Pleura	52 (46.8)	12 (10.8)	5 (4.5)	15 (13.5)	24 (21.6)	65 (58.6)	73 (65.8)	60 (54.1)
Lymph nodes	13 (22.8)	6 (10.5)	3 (5.3)	2 (3.5)	5 (8.8)	12 (21.1)	8 (14.0)	2 (3.5)
Bone and joints	1 (2.4)	2 (4.9)	1 (2.4)	0	2 (4.9)	31 (75.6)	1 (2.4)	2 (4.9)
Airways	8 (8.6)	8 (28.6)	0	7 (25.0)	14 (50.0)	3 (10.7)	22 (78.6)	4 (14.3)
G-I [†] organ	5 (21.7)	11 (47.8)	1 (4.3)	9 (39.1)	8 (34.8)	15 (65.2)	5 (21.7)	2 (8.7)
CNS [‡]	13 (65.0)	0	1 (5.0)	8 (40.0)	2 (10.0)	14 (70.0)	1 (5.0)	1 (5.0)
G-U [§] tract	2 (14.3)	1 (7.1)	0	2 (14.3)	2 (14.3)	7 (50.0)	1 (7.1)	1 (7.1)
Miliary	9 (100.0)	4 (44.4)	1 (11.1)	3 (33.3)	6 (66.7)	2 (22.2)	3 (33.3)	5 (55.6)
Other	0	1 (11.1)	0	0	1 (11.1)	1 (11.1)	3 (33.3)	2 (22.2)
Total	103(33.0)	45 (14.4%)	12 (3.8%)	46 (14.7%)	64 (20.5%)	150 (48.1%)	117 (37.5%)	79 (25.3%)

*Cough/sputum, [†]Gastrointestinal, [‡]Central nervous system, [§]Genitourinary.

Systemic symptoms:163(52.2%): fever, weight loss, sweat, anorexia, malaise.

Localized symptoms: 226(72.4%): pain, cough/sputum, dyspnea.

teristically, fever was present in only one of 41 cases (2.4%) in tuberculous osteoarthritis, and in all 9 patients with miliary TB. Despite the fact that pain at the affected site was the most prevalent clinical symptom, it was present only in 3 of 28 cases (10.7%) and in one of 9 cases (11.1%) in miliary TB and upper airways TB, respectively. Weight loss was prevalent in gastrointestinal TB and miliary TB, with frequencies of 47.8% and 44.4%, respectively. General weakness was prevalent in miliary TB and upper airways TB. Of the local symptoms, cough and sputum were pre-

valent in pleural TB and upper airways TB. However, dyspnea was prevalent only in pleural TB. At least one of the systemic symptoms was present in miliary TB, CNS TB and gastrointestinal TB, with the frequencies of 100%, 80.0% and 78.3%, respectively. The systemic symptoms were less prevalent in tuberculous osteoarthritis, with only 5 of 41 cases (12.2%) showing systemic symptoms. The local symptoms were most prevalent in pleural TB, followed by upper airways TB and tuberculous osteoarthritis (Table 2).

Laboratory characteristics

WBC count increased to more than 10,000/mm³ in 40 out of 312 cases (12.8%), with the least affected in TB lymphadenitis in 2 of 57 cases (3.5%). Anemia, according to the WHO definition, was present in 157 cases (50.3%) and was most prevalent in gastrointestinal TB, with 17 of 23 cases (73.9%) (Table 3). ESR was elevated in 69 of 87 cases (79.3%), and was high in all 9, 5, and 2

Table 3. Laboratory Characteristics of Extrapulmonary Tuberculosis

	No. (%)	
	Leukocytosis*	Anemia
Pleura	9 (8.1)	53 (47.7)
Lymph nodes	2 (3.5)	18 (31.6)
Bone and joints	8 (19.5)	23 (56.1)
Airways	6 (21.4)	18 (64.3)
G-I [†] organ	3 (13.0)	17 (73.9)
CNS [†]	6 (30.0)	7 (35.0)
G-U [‡] tract	4 (28.6)	9 (64.3)
Miliary	1 (11.1)	6 (66.7)
Other	1 (11.1)	6 (66.7)
Total	40 (12.8)	157 (50.3)

*WBC \geq 10,000/mm³, [†]Gastrointestinal, [‡]Central nervous system, [§]Genitourinary.
n=312.

cases of gastrointestinal TB, upper airways TB and miliary TB, respectively. CRP was elevated in 41 of 65 cases (63.1%).

History of TB and underlying disease of EPT

Forty-eight cases (15.4%) were diagnosed as pulmonary TB, and 7 (2.2%) had history of EPT. Seventy-five cases (24%) had chronic wasting diseases or similar entities as the underlying diseases, and the underlying diseases were present in 7 of 9 cases (77.8%) of miliary TB. The underlying diseases and conditions included; age older than 60 years, diabetes, renal failure, liver cirrhosis, malignancies (stomach cancer and hepatoma), history of surgery, severe malnutrition, and long-term steroid treatment (Table 4).

Initial impression

TB was suspected at the first contact with the physician in 210 of 312 cases (67.3%). Other than TB bacterial infection was suspected most frequently in 35 cases (11.2%), followed by non-bacterial infection in 34 cases (10.9%), and neoplasms in 33 (10.6%). A neoplasm at the infected site was suspected most frequently in the gastrointestinal TB subgroup in 8 of 23 cases (34.7%) (Table 5).

Table 4. History of Tuberculosis and Underlying Disease of Extrapulmonary Tuberculosis

	No. (%)		
	History of pulmonary tuberculosis	History of extrapulmonary tuberculosis	Underlying diseases and conditions
Pleura	20 (18.0)	2 (1.8)	24 (21.6)
Lymph nodes	6 (10.5)	1 (1.8)	12 (21.1)
Bone and joints	4 (9.8)	0	8 (19.5)
Airways	7 (25.0)	1 (3.6)	8 (28.6)
G-I* organ	3 (13.0)	2 (8.7)	8 (34.8)
CNS [†]	1 (5.0)	0	3 (15.0)
G-U [‡] tract	1 (7.1)	1 (7.1)	3 (21.4)
Miliary	3 (33.3)	0	7 (77.8)
Other	3 (33.3)	0	2 (22.2)
Total	48 (15.4)	7 (2.2)	75 (24.0)

*Gastrointestinal, [†]Central nervous system, [‡]Genitourinary.
n=312.

Table 5. Initial Impression and Diagnostic Method of Extrapulmonary Tuberculosis

	Impression				Diagnosis		
	Tuberculosis	Neoplasm	Bacterial infection	Non-bacterial inflammation	Definite	Probable	Possible
Pleura	95 (85.6)	4 (3.6)	9 (8.1)	3 (2.7)	10 (9.0)	71 (64.0)	30 (27.0)
Lymph nodes	37 (64.9)	9 (15.8)	8 (14.0)	3 (5.3)	3 (5.3)	48 (84.2)	6 (10.5)
Bone and joints	28 (68.3)	2 (4.9)	4 (9.8)	7 (17.1)	6 (14.6)	23 (56.1)	12 (29.3)
Airways	17 (60.7)	6 (21.4)	4 (14.3)	1 (3.6)	6 (21.4)	18 (64.3)	4 (14.3)
G-I [§] organ	9 (39.1)	8 (34.8)	2 (8.7)	4 (17.4)	1 (4.3)	11 (47.8)	11 (47.8)
CNS [†]	4 (20.0)	0	4 (20.0)	12 (60.0)	2 (10.0)	1 (5.0)	17 (85.0)
G-U [‡] tract	6 (42.9)	3 (21.4)	3 (21.4)	2 (14.3)	3 (21.4)	8 (57.1)	3 (21.4)
Miliary	9 (100.0)	0	0	0	4 (44.4)	4 (44.4)	1 (11.1)
Other	5 (55.6)	1 (11.1)	1 (11.1)	2 (22.2)	0	7 (77.8)	2 (22.2)
Total	210 (67.3)	33 (10.6)	35 (11.2)	34 (10.9)	35 (11.2)	191 (61.2)	86 (27.6)

[§]Gastrointestinal, [†]Central nervous system, [‡]Genitourinary.
n=312.

Diagnostic methods and the period before diagnosis

Thirty-five (11.2%) patients were confirmed to have TB, with the susceptibility tests sensitive to all TB drugs. The number of suspected TB cases was the most prevalent, with 191 cases (61.2%), among whom the smear was positive in 39 cases (12.5%), and chronic granulomatous inflammation by tissue biopsy was found in 152 cases (48.7%). Possible TB was diagnosed in 86 cases (27.6%). Characteristically, CNS TB showed a negative culture or smear in most cases treated for TB in 14 of 17 cases (82.4%). A positive culture or smear was present only in 74 of the 312 cases (23.7%), demonstrating that EPT cannot be neglected even in cases with a negative culture or smear (Table 5).

The period between the manifestations of the initial symptoms to the diagnosis varied from one day to 7 years, with the average of 96 days. The diagnosis was the quickest in CNS TB, taking 1 to 30 days. This period was greater than 30 days in only 2 patients. When these 2 patients were excluded, the average period became 8.6 days. In genitourinary TB, the time necessary to make the final diagnosis was the longest, ranging from 2 days to 4 years, and in 6 out of 14 cases (42.9%) it took more than 200 days.

Chest X-rays

Normal parenchyma was noted in 179 cases (57.4%), and abnormal findings, in 133 (42.6%). Among the cases with abnormal findings, 65 (20.8%) showed signs of TB that could not be evaluated or scars, such as calcification, in 65 cases (20.8%), and, in addition, 68 cases (21.8%) showed cavitary formations or signs of active TB. The possibility of concurrent active TB was high in the airways TB and miliary TB subgroups, with the frequencies of 20 of 28 cases (71.4%) and 5 of 9 cases (55.5%), respectively. Normal parenchyma was observed in 19 of 20 cases (95.0%) of CNS TB (Table 6).

DISCUSSION

Despite our deep understanding of the pathology, natural course and treatment of TB, the disease remains an important health issue throughout the world. In 1993 the WHO declared TB an emergent disease, because approximately 8 million people are infected worldwide. Moreover, significant challenges, such as the pandemic HIV infection, have contributed to the failures of its treatment, and an increased drug resistance have been noted.^{4,5} Although the incidence of TB

Table 6. The Findings of Pulmonary Parenchyme on ChestRadiographs in Extrapulmonary Tuberculosis

	No. (%)		
	Normal	Inflammatory evidence	Active
Pleura	61 (55.0)	27 (24.3)	23 (20.7)
Lymph nodes	37 (64.9)	12 (21.1)	8 (14.0)
Bone and joints	30 (73.2)	6 (14.6)	5 (12.2)
Airways	3 (10.7)	5 (17.9)	20 (71.4)
G-I* organ	15 (65.2)	4 (17.4)	4 (17.4)
CNS [†]	19 (95.0)	1 (5.0)	0
G-U [‡] tract	10 (71.4)	3 (21.4)	1 (7.2)
Miliary	2 (22.2)	1 (11.1)	6 (66.7)
Other	2 (22.2)	5 (55.6)	2 (22.2)
Total	179 (57.4)	64 (20.5)	69 (22.1)

*Gastrointestinal, [†]Central nervous system, [‡]Genitourinary.
n=312.

decreased steadily at 5% per year in the United States from 1963,² its rate since 1990, has continued to increase at 9% per year, probably due to the increase in the number of the patients infected with HIV.^{6,7} Many studies have been performed on the incidence, the rates of development, treatment failures and drug resistance since TB management systems, such as prevention, early detection and treatment, were established. However, few studies have examined the management of EPT. According to the statistical data collected in the United States, 3,492 cases (17.5%) were affected by EPT among the total of 22,506 patients infected with TB in 1986,² whereas 4,887 patients (18.6%) were affected by EPT among 26,283 cases infected with TB in 1991. Suresh et al.⁸ in their retrospective study covering a 5-year period at a university hospital reported that 44% of the culture positive TB patients had EPT. The incidence of EPT is also expected to be high in Korea, since the incidence of TB here is significantly higher than in Western countries.

Although the mainly affected by EPT sites vary, the lymph nodes are affected most of all, followed by the pleura, bones and joints, genitourinary tract, miliary tuberculosis, meninges, and gastrointestinal tract.^{2,9} However, in the present study, the mainly affected site was the pleura (35.6%), not the lymph nodes. Turkey, one of a developing countries, also shows a similar distribution of EPT, with TB pleuritis being at the top.³ Generally,

it is accepted that tuberculous pleuritis is expressed as the primary infection and is deemed present when caseated lesions are present under the pleura rupture.¹⁰ However, Antoniskis et al.¹¹ report that tuberculous pleuritis was not primary but recurrent in 27 (46%) of their 59 patients, due to the possibility of an alternative mechanism of tuberculous pleuritis development. We have found parenchymal abnormalities in 45.0% by chest X-rays examinations in the present study, supporting the postulation that tuberculous pleuritis occurs as a recurrent form of TB. Korea is a nation with a high prevalence of TB - this finding could be provided by the evidence of the cause of dominating tuberculous pleuritis.

According to the gender distribution, TB lymphadenitis is 4.2 times more prevalent in females than in males, and miliary TB is 3.5 times more prevalent in males than in females. Generally, TB lymphadenitis is reported to be more prevalent in females¹² and miliary TB is more prevalent in males.¹³ TB pleuritis was more prevalent in males, and Ozbay B et al.³ report that TB pleuritis is prevalent among the young personnel in military service. Women are prone to progression of the disease, because they are more immunodeficient and are characterized by poorer conditions with respect to socioeconomic and cultural factors.^{14,15} Considering the fact that the mechanism of TB pleuritis involves reactivation, this result is consistent with the fact that women are less prone

to TB pleuritis.

In terms of clinical symptoms, 52.2% of the patients complained of at least one systemic symptom, and 47.8% had no systemic symptoms. Characteristically, fever was present in only one of 41 cases (2.4%) in tuberculous osteoarthritis and no systemic symptoms were noted in 36 cases (87.8%) of tuberculous osteoarthritis. Generally, systemic symptoms such as fever, chill, weight loss and malaise, have been reported to be present in about 20% of patients.¹⁶ That is why TB is often misdiagnosed as some other systemic diseases, and TB becomes chronic and difficult to diagnose. Because miliary TB shows hematogenous or lymphatic spread, fever was found in all 9 cases of miliary TB in the present study. Gastrointestinal TB was accompanied by weight loss more than other types of EPT (47.8%) but showed no occlusion, rupture, hemorrhage or adhesion symptoms that could be noted in neoplasm. A direct connection between the symptoms on admission and the anatomical localization of TB was not established in this study. However, L.EBDRUP et al.¹⁷ report the percentage between these two issues to be 83%, and the clinical manifestation is an important clue in the places such as sub-Saharan Africa including Malawi, with the lack of assessing facilities in the diagnostic practice, so its importance to the diagnosis cannot be ignored.¹⁸

Although blood tests produce diverse results in TB, the possibly presented symptoms include anemia, leukocytosis, thrombocytosis, hyponatremia, and increased ALP due to chronic diseases.¹⁹ Anemia has been relatively frequently noted in the present study, in 54% of cases, and leukocytosis has been noted only in 13.7%. ESR was elevated in 69 of 87 cases (79.8%), which was higher than the 67% reported by Al-Marrie et al.,²⁰ though this rate would have little clinical significance since 20.7% of our patients showed normal ESR levels, and ESR is a non-specific acute phase reactant. CRP was increased in 63.1%, which was slightly lower than the percentage with elevated ESR.

Only 17.6% of our patients were diagnosed as EPT or TB cases; perhaps this rate was low because the history was taken from the medical records or in the course of the interview with the

patients. Because the abnormal parenchymal findings were noted in 42.0% of the patients, the percentage of patients with EPT having a history of TB or EPT is likely to be much higher than 17.6%, considering the patients with latent TB, with no symptoms and those with no knowledge of having been previously infected with TB or EPT.

The underlying diseases and conditions including the old age, chronic renal failure, hemodialysis, long-term use of steroid drugs and liver cirrhosis were found in only 24% of the EPT patients, which is significantly different from the rate reported by Denis-Delpierre et al.²¹ This difference may be related to the fact that the number of younger patients infected with TB in Korea is significantly higher than in Western countries. So EPT would frequently occur with no underlying disease in Korea. In Western countries, patients infected with EPT are usually immunocompromised and have a higher incidence of the underlying diseases. However, in the case with miliary TB, underlying diseases and conditions, such as old age, liver cirrhosis, and chronic renal failure were noted in 77.8%. Although in the past miliary TB was prevalent in children younger than 3 years of age, it affects older people and occurs frequently in patients of high-risk, such as undergoing chemotherapy, taking immunosuppressants, receiving hemodialysis or post surgical patients.²²

Because EPT shows complex clinical patterns, and the histologic diagnosis is not easy, efforts must be applied in various directions to provide the diagnosis.²³ Only 16% cases were diagnosed in the present study through microbiologic approaches, including cultures and smears. Despite Engin et al.²⁴ report that chest X-rays or skin tests could help in the diagnosis, the possibility of EPT cannot be ignored after obtaining negative responses in these tests. Furthermore, skin tests for TB would have little significance in Korea, where BCG is mandatory, so that the usefulness of skin tests as an adjunct method of diagnosis would be very limited.²⁵ Therefore, one of the most important aspects in the diagnosis of EPT would be a strong suspicion of EPT at an early stage. Despite the fact that the patterns of the clinical manifestation varies significantly in the present

study, TB was suspected as a differential disease at the very high rate of 70.3%, probably due to its high incidence in Korea. Rieder et al.²⁶ report that the post-mortem diagnosis of TB was made in 5.1% of patients from 1985 to 1988 and emphasize the importance of consideration of this curable disease at an early stage. Though they report that the rate of this diagnosis is very low, despite the various methods used for the diagnosis of TB, including surgery and histologic examinations, Denis-Delpierre et al.²¹ suggest beginning of an early treatment when EPT is first suspected, rather than delaying the treatment until the laboratory or microbiologic results are available.

The period between the onset and diagnosis could be as short as a few days or as long as several years, with the average of about 2 months. The diagnosis is reported to be made the earliest in pleural TB and the latest in tuberculous osteoarthritis.⁹ The average period from the onset to the diagnosis is 97.5 days in the present study, which is significantly longer than the 8 weeks period as reported by Adamsson et al.²⁷ The period between the hospital visit and the diagnosis could be shorter in Korea, because patients do not visit hospitals for early symptoms mainly due to economic and social reasons. In the case with the asymptomatic CNS TB, the average period for the diagnosis was 3 months, according to Vasakova et al.²⁵ However, this was only 10 days in the present study. CNS TB was diagnosed the earliest, and genitourinary tract TB was diagnosed the latest, taking more than 200 days in 42.9%.

Accompanying abnormal lung parenchymal findings were present in 43.3% of our patients, by chest X-rays examination, which is significantly higher than the 15% reported by the US Department of Health and Welfare in 1982 and the 37% reported by Weir et al.⁹ Findings of active pulmonary tuberculosis were present in 71.4% of the upper airways TB cases, and abnormal parenchymal findings were noted in 89.3% of these patients. Abnormal parenchymal findings were noted in 7 of 9 cases (77.8%) of miliary tuberculosis. Direct adhesion of the tuberculosis bacteria through the bronchial mucosa, spread of TB to the surrounding organs, such as the trachea and bronchi, by pus secreted by the tuberculous cavities, and direct infiltration by the tuberculous

lesions of the lung parenchyma are the mechanisms of tracheal and bronchial tuberculosis.²⁸

Robert et al.²⁹ in their extremely large study done over an extended period reported that the incidence of TB in patients with positive HIV test results had increased from 2% in 1983 to 28% in 1990. It is inevitable that the incidence of EPT increases according to the increased number of patients infected with HIV, since HIV promotes latent infection to infection. HIV infection being scarce in Hong Kong, HIV is unlikely to be an important source of TB infection.³⁰ There was no HIV positivity as an underlying disease or condition in this study. However, when the patient is diagnosed as EPT, HIV test should be done because recently the number of HIV-positive patients has drastically increased.

The present study was undertaken to promote early diagnosis through a clinical review of EPT in Asian patients at a tertiary referral care hospital. By focusing on the pattern and the clinical manifestation of the non-typical EPT detected in the increasing number of patients infected with HIV, thorough TB management is strongly recommended to include an early detection and treatment.

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