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**Original Article**

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## **Tuberculous Pleural Effusion in Children**

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### **ABSTRACT**

**Background and Aim:** Pleural effusion is the second most common type of extra pulmonary tuberculosis with an incidence of 4.9%. This study aims to describe the age distribution, main clinical, laboratory and radiographic findings and outcome of patients with Tuberculous Pleural Effusion (TPE).

**Materials and Methods:** This is a retrospective study of TPE patients admitted in pediatric ward of Masih Daneshvari Hospital from 2002 to 2008. Eighteen patients under 18 years of age were included in our study.

**Results:** The patients in our study were 12 boys (66.7%) and 6 girls (33.3%) who were all in the 10-18 age bracket. The most common presenting symptoms and signs were cough (17 patients, 94.4%), anorexia (14 patients, 77.8%), fever (13 patients, 72.2%), chest pain (10 patients, 55.6%), tachypnea and respiratory distress (2 patients, 11%), cyanosis (1 patient, 5.5%). All subjects showed exudative pleural fluid with lymphocytosis >50%. Acid fast bacilli (AFB) were not detected in the sputum, gastric and/or pleural fluid of any of the patients. Sputum culture was positive in 4 (23.5%). Positive pleural culture was not seen in any of the patients. Pleural biopsies were available in 88% of which showed necrotizing granulomatous inflammation. The most common radiographic findings were unilateral PE (100%), mediastinal lymphadenopathy (22%) and consolidation (11.1%). Eighteen patients received medical treatment.

**Conclusion:** The clinical manifestation of childhood TPE is not specific and especially in countries with high prevalence of TB it should always be considered in the differential diagnosis for older children suffering from parapneumonic effusion.

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**Keywords:** Children, Sputum culture, Tuberculous pleural effusion

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## INTRODUCTION

Tuberculosis (TB) is a significant health problem in developing and under developed countries (1-3). Children account for 5-15% of all tuberculous cases. Although pulmonary tuberculosis is the main manifestation of the disease in childhood, the proportion of extra pulmonary tuberculosis has risen (1). Tuberculous pleural effusion is classified as extra pulmonary disease (4-6). Pleural effusion (PE) is the second most common type of extra pulmonary tuberculosis with an incidence of 4.9% (1,5). Pleural effusion is also more commonly found in patients with TB (7).

The frequency of pleural involvement in TB has been variably reported (from 4% in the US to 23% in Spain) (8). Pleural effusion complicated by tuberculosis may be mixed up with other pathogen related pleural effusions (9,10). Effusion is not a common characteristic of primary pulmonary TB in young children and it is more probable to be detected in adolescents and adults (4,11,12).

Confirming the diagnosis of tuberculous pleural effusion (TPE) can be difficult because of the classic findings of lymphocytic exudative PE, pleural granuloma, and cutaneous sensitivity to purified protein derivative (PPD) have low specificity and sputum, pleural fluid, and pleural biopsy cultures have a low achievement rate (3,4,7,13). More than 50% of the patients with pleural tuberculosis who are not cured develop pulmonary tuberculosis in the next 5 years (9). Hence, early diagnosis and treatment are clinically significant both for the betterment of patient outcome and in preventing further spread of the disease. Thus, understanding the clinical factors suggestive of tuberculous pleurisy is vital (14). The aim of this study was to describe 1) the age distribution of pediatric patients with tuberculous pleural effusion; 2) main clinical and laboratory findings; and 3) outcome of patient with tuberculous

pleural effusion. The decision to conduct such a study was made due to shortage of studies carried out on TPE and considering the fact that Masih Daneshvari hospital is a referral center for pulmonary tuberculosis.

## MATERIALS AND METHODS

This is a retrospective study of patients admitted in the Pediatric ward of Masih Daneshvari hospital with TPE from 2002 to 2008. Our study was conducted on 18 patients with less than 18 years of age. The data extracted included epidemiologic, clinical, laboratory (CBC, ESR, CRP, PPD), radiological and pathological findings and pleural fluid analysis.

The patients were included in the study if: they showed chest radiograph interpreted by a radiologist as portraying a pleural effusion and at least one of the following criteria 1) positive culture for *Mycobacterium tuberculosis* from sputum, gastric aspirate, pleural fluid, or pleural biopsy specimen, 2) detection of acid fast bacillus by stain in sputum, gastric aspirate, pleural fluid or pleural tissue (obtained by closed biopsy), 3) the presence of caseating granulomas in histological sections, 4) positive tuberculin test if the palpable induration was  $\geq 10$  mm along with one of the following items: lymphocytic pleural fluid  $>50\%$ , exudative fluid (protein  $>4\text{gr/dl}$  or lactate dehydrogenase  $\geq 200$  U/L) or pleural fluid levels of adenosine deaminase greater than 40 Units per liter. Data analysis was carried out with a statistical software package (SPSS, version 16.0; SPSS Inc, Chicago, IL).

## RESULTS

Thirty three patients suffering from pleural effusion were examined from 2002 to 2008; 18 of whom had TPE and were included in our study. Among these patients there were 12 boys and 6 girls who were all between 10 to 18 years of age. Twelve

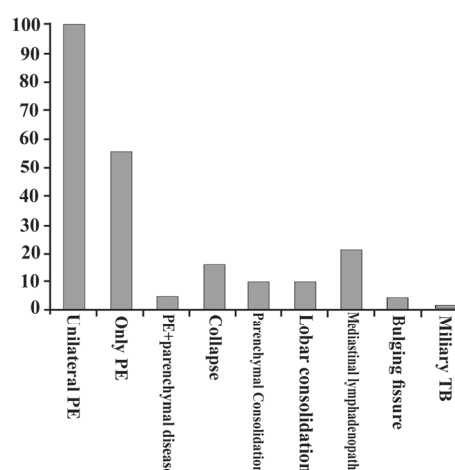
**Table 1.** Tuberculin test data

Tuberculin test, induration (mm)	No.	%
5≥	5	27/8
5-9	1	5/6
10-14	6	33/3
15≤	6	33/3

patients (66.67%) had a tuberculin skin test (positive) by induration  $\geq 10$  mm. Tuberculin skin test results are summarized in table 1. Common symptoms among patients were cough (94.4%), anorexia (77.8%) and fever (72.2%). Clinical findings are shown in table 2. History of contact with a TB patient was present in 10 (55.5%); 6 of whom showed PPD  $\geq 10$ mm and 4 showed a positive sputum culture. Eleven patients (73.3%) had a positive CRP test assessed semi quantitatively. Fourteen (87.5%) showed high ESR; all of the patients showed exudative pleural fluid. Leukocytosis was not seen in any of the cases. Acid fast bacillus was not observed in sputum, gastric washing or pleural fluid lavage of any of the patients. Sputum culture in 4 of the 18 (23.5%) patients was positive. Table 3 shows the cytological and biochemical analyses of pleural fluid. Radiological records were available in all patients. Chest radiographic findings in all patients with tuberculous pleural effusion are shown in figure 1.

**Table 2.** Clinical findings

Finding	No.	%
Malaise	4	22
Fatigue	5	27
Anorexia	14	77.8
Respiratory distress	2	11
Dyspnea	10	55.6
Tachypnea	2	11
Cough	17	94.4
Chest pain	10	55.6
Orthopnea	2	11.1
Cyanosis	1	5.5
Fever	13	72.2
Chills	6	33.3
Weight loss	6	33.3
Decreased breath sounds	12	66.7

**Figure 1.** Radiological features

The most common radiographic findings were unilateral pleural effusion (100%), mediastinal lymphadenopathy (22.2%) and parenchymal consolidation (11.1%). Histological finding from pleural biopsy specimens were available in 9 patients; eight (88%) of which showed necrotizing granulomatous inflammation and one had non-diagnostic features, but no one showed positive culture. Hospitalization period was 1 week in 4 patients (22.2%) and 2 weeks in 14 patients (77.8%). Eighteen patients received medical treatment. Average duration of symptoms prior to admission to the hospital in patients with TPE was 30.2 days. Fourteen (77.8%) patients having TPE

**Table 3.** The cytological and biochemical analyses of pleural fluid in the studied patients

Laboratory data	No.	%
Cell/L <2000	10	55.6
2001-4000	5	27.8
4001-6000	3	16.7
Lymphocytosis, % >50%	18	100
Protein <4 (g/dL)	2	11.1
4-5	6	33.3
>6	4	22.2
Glucose, g/dL	16	Mean: 75.06
LDH <500 (U/L)	4	23.5
500-1000	12	70.6
1001-1500	1	5.9
ADA <40 (U/L)	2	11.1
40-60	6	35.3
61-80	3	17.6
>80	6	35.3

had received antibiotic treatment before final diagnosis.

## **DISCUSSION**

Our study group included 12 boys (66.7%) and 6 girls (33.3%), ranging in age from 10-18 years old. In a similar report from Taiwan, boys outnumbered girls; the reported age ranged from 10 to 17 years old (9). Tuberculosis pleural effusion is common in older children, but it is not common in young children (4,9). In contrast TPE was found in young children in a Philippine investigation (3).

Tuberculous PE usually appears as an acute illness with fever (72%), cough (94%), and respiratory distress (33.3%). Our findings are similar to those reported from Taiwan and Malaysia (9,15). Results of a report from Pakistan showed fever (97%), cough (91%) and chest pain (80%) as the main clinical manifestations (16). A number of clinical findings (such as fever) reported from a research conducted in Athens was similar to our study (11). The clinical features of childhood TB is not definite. In the present work, patients with TPE frequently had chest pain (56%). A survey from Pakistan revealed chest pain in 80% of their patients (16). Clinical findings, chest radiography, tuberculin skin testing and a history of contact with a case of active pulmonary TB provide a basis for the diagnosis of childhood TB (17-20). A positive tuberculin skin test result is helpful evidence in the diagnosis of TB pleural effusions in areas of low prevalence (or no vaccination). However, a negative tuberculin skin test result may occur in roughly one third of patients (8). In our series, 12 patients (33.3%) showed an induration of  $\geq 10$  mm in the skin test. A history of contact with tuberculous case was present in 10 patients (55.5%). In Taiwan's study positive history was identified in 6 patients (46%) (9). In the present investigation all our patients had normal leukocyte count, while C-

reactive protein was normal in seven (27%). In the Taiwanese study, 92% of patients had normal leukocyte count and C-reactive protein was normal in 31% of the patients (9). TPE is usually unilateral (4,8). In our series, unilateral PE was seen in all of the subjects. A research was carried out in Taiwan (2007) and Spain in which unilateral PE was seen in 92% and 100% of patients, respectively (9,4). Mediastinal lymphadenopathy (22.2%) was the most common radiographic feature followed by parenchymal consolidation (11.1%). Parenchymal consolidation was the most common finding reported from a survey conducted in Spain in 2008 (4). Results from Athens study demonstrated mediastinal lymphadenopathy in 33% of the patients (11). Analysis of effusion showed lymphocytic exudative effusion in all our patients. A research from Spain showed lymphocytic fluid in 71% of the patients (4). A neutrophil predominance was not found in our series. In our series, smears and cultures of pleural fluid and pleural biopsy were negative. Tuberculosis is associated with lack of positive cultures of pleural fluid (4). Some reports have shown higher specificity and sensitivity rates for the measurement of ADA activity in the diagnosis of pleural TB (1,4,13). In our series 2 of the 18 patients (11.1%) showed ADA activity  $< 40$  U/L (Table 3) which was similar to the results reported by Merino et al (4). Histological examination of pleural biopsy disclosed granulomatous inflammation which is frequently used as a diagnostic test for pleural TB (5,8,12). In our series 8 patients (88%) showed necrotizing granulomatous inflammation. In Merino et al study, 78% of the pleural biopsy specimens showed granulomatous inflammation (4).

## **CONCLUSION**

Given the prevalence of TPE in developing countries, this disease has to be considered among

differential diagnoses for older children and adolescents suffering from parapneumonic effusion. Therefore, prompt diagnosis can prevent adverse effects and progression of the disease. In children with TPE, mediastinal lymphadenopathy and pulmonary parenchymal consolidation are the most frequent radiological findings and correct diagnosis of TPE can be achieved by detecting a normal leukocyte count with an exudative effusion.

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