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ORIGINAL ARTICLE

CLINICAL PROFILE OF TUBERCULOUS PLEURAL EFFUSION IN CHILDREN

Ankita Shah[1], Sunayna Gurnani[2].

[1]H B T Medical College and DR R N Cooper Municipal General Hospital, Mumbai, India;
[2]Seth G S Medical College, KEM Hospital, Mumbai, India.

ABSTRACT

Aim: To determine the age distribution, clinical and laboratory findings, and outcomes of patients with tuberculous pleural effusion (TPE).

Methods: This retrospective study was done over a period of 5 years in children between 1 month-15 years of age who were referred to our tertiary referral center with TPE.

Results: Seventy-six (5.3%) children were diagnosed with pleural effusion of which 43 (56.6%) patients had right-sided affection, 31 (40.8%) had left sided affection and 2 (2.6%) bilateral involvement. Mean age of presentation was 6.8±3.2 years. Mean ADA values in pleural fluid were 107.6±115.7 IU/L. High ESR was found in 58 (77.8%) with mean values of 79.1±28.5 mm at end of 1 hour. Left sided effusion was seen at a mean age of 7.9±3.5 whereas right sided effusion was seen at a mean age of 6.1±2.8 (p=0.016).

Conclusion: Most of the pleural effusions are seen in children <10 years of age and does not have a predilection for adolescents as mentioned in literature. Elevated ADA and ESR may suggest TPE. Though right sided effusion is more common, left sided effusion is seen in older children.

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Introduction

Tuberculosis (TB) is most common cause of infections related death globally. It is estimated that childhood TB constitutes 10-20% of all TB in high-burden countries.[1] Tuberculous pleurisy is the second most common form of extrapulmonary tuberculosis (TB)[2] and a common cause of pleural effusion in endemic TB areas. There is limited data regarding the prevalence of tuberculous pleural effusion (TPE) in children but estimated literature has shown that frequency of pleural involvement in pediatric tuberculosis ranges from 2-38%.[3,4,5,6] 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.[7] The aim of this study was to describe the age distribution of pediatric patients with TPE, with the clinical and laboratory findings and outcome of these patients.

Methods & Materials

This was a retrospective study done over 5 years in children between 1 month-15 years of age who were referred to our tertiary referral center. Patients identified as TPE were included in the analysis. TPE was diagnosed if the chest radiograph depicted a pleural effusion and at least one of the following criteria: (1) positive culture or positive cartridge based nuclear acid amplification test (CBNAAT) or presence of acid-fast bacilli (AFB) for *Mycobacterium tuberculosis* (MTB) from pleural fluid, (2) Compatible clinical picture with pleural fluid showing lymphocytic predominance or levels of adenosine deaminase activity (ADA) more than 35 IU/l with/without a positive tuberculin skin test or contact with an adult having TB. Records of all patients were evaluated and clinical history; examination findings and laboratory investigations were noted. Malnutrition was defined as weight or height less than 3 centile as per Agarwal charts.[8] Associated serositis in form of pericardial effusion or ascites was noted. Drug resistance TB was diagnosed as per World Health Organization (WHO) criteria.[9] Pulmonary TB was defined by WHO as a patient with tuberculosis disease involving the lung parenchyma.[10] TB contact was defined as defined as person who shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with the index case during the 3 months before commencement of the current treatment episode.[11] High ESR was defined as >20 mm at end of 1 hour. The patients were followed up regularly and the outcome of their treatment was charted, along with a specific mention of those requiring an intercostal drainage (ICD) tube and those needing steroid therapy. Those developing any form of resistance to treatment or development of hepatitis were also monitored.

Prevalence of TPE in all patients with TB was determined and clinical profile of patients with TPE was analyzed. Difference between left and right sided pleural effusion and various clinical and laboratory parameters was analyzed. Proportions were analyzed using the Chi square tests and Fisher Exact test. P value <0.05 was

Address for Correspondance: Dr Ankita Shah, 501, Rose villa, next to filmalaya studio, ceaser road, amboli, andheri west, Mumbai 400058, India.
Email: drankitashah@hotmail.com

taken as significant. All data was statistically analyzed using SPSS software version 18 and Primer.

Results

Total 1425 children suffering from TB were studied of which 76 (5.3%) children were diagnosed with pleural effusion. Of these, 43 (56.6%) patients had right-sided affection, 31 (40.8%) with left sided affection and 2 (2.6%) bilateral involvement. Factors associated with left or right-sided pleural effusion are depicted in Table 1. Male:female ratio was 1.96. Mean age of presentation was 6.8±3.2 years with range of 1-14 years. Of the total, 23 (30.3%) children were <5 years, 41 (53.9%) children were 5-10 years and 12 (15.8%) children were >10 years. Malnutrition was seen in 32 (42.1%) patients. Only 5 (6.6%) patients had associated serositis (4 had pericardial effusion and 1 had ascites with pericardial effusion). ADA values were done in 28 patients of whom 24 (85%) children had high values with a mean value of 107.6±115.7 IU/L. Only 24 (32.4%) patients had contact with a patient having TB. Cultures of pleural fluid were positive for MTB in 7 (15.6%) patients out of 45 tested of which 4 (57.1%) cases were DR-TB of which 2 were multi-drug resistant (MDR), 1 was monoresistant and 1 polyresistant. Thirty (39.5%) patients had TB in other organs, of which associated pulmonary TB was present in 22 (73.3%) cases (21 of which had primary complex and 1 had miliary TB), 8 (26.7%) had extrapulmonary TB (6 had mediastinal adenopathy and 2 had intracranial tuberculomas). High ESR was found in 58 (77.8%) with mean values of 79.1±28.5 mm at end of 1 hour. Twenty six (43.3%) children had a positive mantoux test. BCG vaccination was given in 71 (93.4%) patients. Sixty (78.9%) patients completed treatment and 16 (21.1%) did not follow up. The mean duration of treatment was 7.1±2.5 months. Forty-eight (63.2%) patients were treated with steroids and 12 (15.8%) children required ICD. Drug induced hepatitis occurred in 2 (2.6%) patients and paradoxical reaction in 1 (1.3%) patient.

Discussion

Though frequency of pleural involvement in pediatric TB ranges from 2-38%[3,4,5,6], in our study TPE prevalence was 5.3%. This wide difference in the prevalence rates can be attributed to the different diagnostic modalities used around the world. The gold standard to diagnose TPE is demonstration of MTB in the pleural fluid either by culture, microscopy or PCR testing.

PCR testing itself has a variable sensitivity of 37-77%.[12] However, due to cost restraints, in high TB burden areas, the diagnosis of TPE is made on the basis of pleural fluid ADA levels in adults, which may be the contributor to the wide variation of prevalence globally.[13] The difference can also be attributed to environmental conditions, since pleural TB accounts for fewer than 1% of all exudative effusions in western countries, however, in developing countries like India, it is responsible for 30-80% of all pleural effusions encountered.[14]

Published literature so far has shown that TPE is very uncommon in young children and is more likely to be observed in adolescents and adults. Merino et al in his study found that mean age of patients with TPE was higher (13.5 years) than children without pleural effusion (7 years)[7], but in our study we found that majority of patients were between 5 to 10 years of age. Similar findings have been noted in other studies.[15,16]

Pleural effusions secondary to TB are largely unilateral with a slight right-sided predominance. Valde et al reported right-sided predominance to occur in 55% of cases[17] In our study also; we had similar right-sided predominance (56%). The reason for predominance of right-sided involvement is not understood. In our study, right-sided involvement was found more commonly in younger children as compared to left sided involvement, whereas left-sided predilection was seen in older children. This variation remains unexplained and further studies will be required to determine why a particular side is affected at a particular age. Other factors such as gender, contact with TB, malnutrition did not influence the site of pleural effusion in our study.

Boloursaz et al found in his study that history of TB contact was present in 55% cases[18] however in our study we had only 32.5% cases with history of TB contact. There is a wide variation of tuberculin test sensitivity among children with pleural TB. Up to 30% of patients with tuberculous pleurisy have a negative

Table 1. Factors associated with Left or Right sided Pleural Effusion.

	RIGHT	LEFT	P VALUE
1) AGE (YRS)	6.1±2.8	7.9±3.5	0.016
2) Age group:			
<5 years	13 (30.2%)	9 (29.0%)	
5-10 years	23 (53.5%)	17 (54.8%)	0.884
>10 years	7 (16.2%)	5 (16.1%)	
3) GENDER			
Male	30 (69.8%)	19 (61.3%)	0.609
Female	13 (30.2%)	12 (38.7%)	
4) Associated other organ TB	16 (37.2%)	12 (38.7%)	0.911
5) Contact with TB	14 (32.5%)	10 (32.3%)	0.822
6) Malnutrition	18 (41.8%)	13 (42%)	0.816
7) Past TB	1 (2.3%)	2 (6.4%)	

tuberculin test[19] In our study, 43.3% had a positive MT test. This low mantoux sensitivity can be attributed to the increased number of malnourished children (42.1%) in our study.

Estimation of ADA level in pleural fluid is extremely helpful in establishing the etiology of tubercular pleural effusion in adults. At present, ADA is the most cost-effective pleural fluid biomarker and is routinely employed as a screening tool, particularly in countries where TB is endemic.[20] It has a high accuracy with sensitivity and specificity of up to 100% and % respectively for diagnosis of TPE in adults.[21] According to Marnet et el, this specificity can be further increased by measuring the ADA-1 fraction which is elevated in TB. The most widely accepted cut-off level of ADA for the diagnosis of TPE is 40 U/l[22] In children, though estimation of ADA in pleural fluid is still not routinely practiced, it appears to be a good diagnostic tool as in our study, we could do ADA only in 28 patients and most of them had a high ADA levels. Thus, ADA may be an inexpensive, rapid and useful test to aid in diagnosis of TB pleural effusion in children. However, ADA is not specific for TB and is elevated in many other conditions as well, thus should not be used as the sole diagnostic parameter.[23]

Though pleural fluid grew MTB only in 15% of our patients, the diagnostic yield in various studies has been similar.[22] TPE was earlier thought to be a hypersensitivity reaction, but now due to the discovery of superior culture media, higher culture rates of MTB from pleural fluid are seen. Thus the disease is now considered a paucibacillary infection of the pleural space, which maybe part of the primary infection or due to secondary reactivation in immunocompromised children.[12] So all patients with suspected TB pleural effusions should undergo testing of the pleural fluid for PCR and TB cultures. All patients with suspected TPE should undergo testing screening for drug resistance as in our study, 4 out of the 7 samples tested for MTB showed DR strains.

Screening for associated TB or serositis elsewhere in the body will be a helpful practice as in our study, associated TB was found in 30% patients. Serum ESR values were elevated in 77% patients in our study, and has been shown to be elevated in other studies on TPE as well. Thus ESR should be used as a corroborative evidence of TPE in the pediatric population.[24]

Intercostal drainage was done in 15.3% patients in our study suggesting that some patients may have persistence of effusion inspite of aspiration and drugs and they may require drainage. The exact reason for ICD was not clear in the records of these patients. Similar use of therapeutic thoracocentesis has been done successfully in other studies in the past.[12] Though the use of steroids in TPE has not yet been justified, 63.2% of our patients had been given steroids as per the records. Main indication for steroids was for relief of symptoms as well as to prevent loculations and adhesions within the pleural fluid.

Conclusion

The prevalence of TPE in children was lower than the general TPE prevalence of the region. Amongst children, the maximum prevalence was found in the 5-10 year age group though it was previously reported to be a disease of adolescence. Further, the distribution was such that younger children developed right-sided effusion and older children more commonly developed left-sided effusion. Elevated pleural ADA may be useful in diagnosis of TPE but more studies in children are required to determine its accuracy. All patients of TPE should undergo pleural culture for MTB, smear for AFB and testing for drug resistance as we found resistance in 4 out of 7 tested patients.

Compliance with Ethical Standards

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Conflict of Interest: None

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