Brief Report

The Evaluation and Cluster Analysis of Parapneumonic Effusion in Childhood

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Summary

We studied 80 children with parapneumonic effusion (PPE) with respect to the clinical manifestations and treatment alternatives as well as prospective follow-up for 1 year. Out of the 80 patients, 59 per cent were male. The mean age of the patients was 4.0 ± 3.1 years. Mild effusion was successfully treated by antibiotic alone in 33 per cent of the patients. Tube thoracostomy (TT) was utilized in 63 per cent of the patients. In this group, 11 healed completely, 13 patients required surgical treatment, and 25 required fibrinolytic therapy (FT). FT was successful in 18, and no complication due to FT was observed. Six patients who received FT required surgical therapy later in the course of treatment. Cluster analysis revealed a group of patients with rapid progression and a short history of symptoms (4–6 days) that showed significantly higher rate of complicated prognosis ($p < 0.05$). Successful FT prevented surgical operation in 22 per cent of the patients who were candidates for surgical treatment. The follow-up for one year revealed sequelae on chest X-ray in 28 per cent of the patients most of whom had an operation for necrotizing pneumonia. Pulmonary function tests performed over seven years of age were abnormal in 57 per cent of the patients.

Introduction

The treatment of parapneumonic effusion (PPE) may be conservative or surgical. The optimal choice of therapy depends on the stage of PPE which may be assessed by the clinical and laboratory findings. Delayed or inadequate treatment of PPE is a common cause of progression of its stage. However, other risk factors that may play a role in the prognosis or evolution of the disease are not clear. There are many studies that report fibrinolytic therapy (FT) is successful in the treatment of empyema in adults, but there are not as many studies in children.[1–6]

In this study, the clinical properties, treatment options, and early, and late (for 1 year) consequences of PPE admitted to a tertiary reference hospital over a period of 3 years are evaluated. The clinical parameters were studied by cluster analysis to see whether or not there are distinct groups that would provide predictive factors to guide the management of PPE.

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Materials and Methods

A total of 80 children over two months of age admitted to the Uludag University Hospital with pneumonia and PPE were included and prospectively evaluated. The patients were staged as acute exudative, fibropurulent, and chronic organized stage according to the pleural fluid findings and sonography.[2,7]

If drainage of tube thoracostomy (TT) was inadequate (<30–50 ml/day according to age) in spite of large effusion, after 48–96 h, or viscous or septated fluid persisted on X-ray or US, FT was given through the thoracostomy tube. Hemorhagic diathesis was excluded before the procedure. The FT consisted of 30 000–100 000 units of urokinase repeated 1–7 times at 24-h intervals according to drainage and US findings. Surgical operation was performed when indicated either at the time of initial presentation, or during follow-up. All patients were followed for at least one year after discharge.

Cluster analysis[8] of our cases was utilized to identify the clinical and laboratory properties of the patients. Kruskall-Wallis test, χ^2, and Fisher's exact χ^2 tests were used for statistical analyses.

Results

Clinical parameters and evaluation of the patients are presented in Tables 1–3.

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TABLE 1
The clinical parameters of the patients at presentation

Parameter	X ± SD (distribution)
Age (years):	4.0 ± 3.1 (3 months–14 years)
<2 years *n* (%)	33/80 (41%)
3–6 years *n* (%)	30/80 (38%)
>7 years *n* (%)	17/80 (21%)
Male/Female	47/33
Duration of symptoms (days)	11 ± 9.4 (1–60 days)
AB prior to admission (%)	75/80 (94%)
Prior hospitalization elsewhere (%)	42/80 (53%)
Duration of prior hospitalization (days)	7.6 ± 6.6 (1–35)
Findings of pneumosepsis (%)	57/80 (71%)
Pleural effusion (%):	
Right	39/80 (49%)
Left	34/80 (42%)
Bilateral	7/80 (9%)
Stage of effusion (%):	
Exudative	22/80 (28%)
Fibropurulent	43/80 (54%)
Chronic-organized	15/80 (18%)
Duration of symptoms (days):	
Exudative	7.1 + 4.3 (2–15)
Fibropurulent	7.1 + 4.9 (1–20)
Chronic-organized	15.0 + 3.5 (10–20)

TABLE 2
Analysis of pleural fluid

Parameter	X ± SD (distribution)
Fluid thickness (mm) on US	25 + 16 mm (1–75 mm)
Cell count	12,673 ± 22,508
Granulocytes (%)	(75 ± 25)
Granulocyte predominance (>50%) (%)	46/46 (100%)
Glucose (mg/dl)	29.6 ± 27.8 (2–100)
<40	8/46 (17%)
40–60	6/46 (13%)
>60	32/46 (70%)
Protein (g/dl)	4.0 ± 1.3 (1–7)
<2	5/46 (11%)
2–2.9	2/46 (4%)
>3	39/46 (85%)
LDH (IU/l)	973.8 ± 851.1 (0–2967)
<200	8/46 (17%)
201–600	8/46 (17%)
601–1000	11/46 (24%)
>1001	19/46 (42%)
pH	7.35 ± 0.5 (5.0–8.0)
<7.2	16/46 (35%)
7.2–7.35	9/46 (20%)
>7.35	21/46 (45%)
Gram positive microorganism (%)	10/56 (18%)
Positive culture (%)*	6/56 (11%)
Serology (Mycoplasma IgM positive)	2/56 (4%)
Total no of patients with identified etiology (%)	15/56 (27%)

*Three of the patients with positive culture also had positive gram stain.

Cluster analysis revealed two distinct groups (N1 = 6, N2 = 7 patients). There were significant differences ($p < 0.05$) between these two groups. The first group with a shorter duration of symptoms (mean 4.3 vs. 14.7 days), prior hospital care (0 per cent vs. 100 per cent), higher rate of AST elevation (86 ± 87 U/L vs. 38 ± 12 U/L), longer duration of hospitalization (33 ± 9 vs. 22 ± 9 days), and longer normalization time of CRP (15 ± 3 vs. 11 ± 2 days) had a higher frequency of necrotizing pneumonia and all of the patients in this group required surgical operation ($p < 0.05$). Surgical operation was performed in 28 per cent of the patients because of large necrotizing pneumonia, bronchopleural fistula, restriction in the lungs, due to severe pleural thickening, and/or loculated organized empyema. Surgical operation involved decortication, repair of bronchopleural fistula (BPF), and lobectomy.

One year follow-up could be completed in 43 of the surviving 77 patients (56 per cent). Twenty-four of 34 patients who did not come for re-evaluation, were contacted by telephone and no complaints were reported other than nonspecific infections. Chest X-ray revealed sequela in 12 patients (28 per cent), 8 of whom were operated on because of necrotizing pneumonia. Pulmonary function tests were performed in seven patients who were over seven years of age at follow-up visit and found abnormal in 4 (57 per cent).

Discussion

More than half of our patients were hospitalized for a mean duration of 7 days elsewhere with complaints of a mean duration of 4 days prior to referral to our hospital. It took about 11 days from the beginning of the symptoms to the initiation of a multidisciplinary treatment protocol in our hospital. Various studies have reported a mean of 8–18 days between the beginning of the symptoms and the time of admission.[9–12] Heffner, *et al*. have demonstrated the significant increase in hospital stay and cost of treatment when therapy or drainage is delayed.[13] As these studies have emphasized, loss of time with inadequate and inappropriate treatment in PPE leads to complicated progression and decreased or lost possibility of medical therapy. However, the cluster analysis in our patients has revealed a more complicated clinical course characterized with

TABLE 3
Clinical evaluation of the patients

Number of febrile days (X ± SD)	7.0 ± 4.1 (1–19)
Hospital stay for antibiotic only group ($n = 26$) (days) (X ± SD)	15.3 ± 6.8 (4–34)
AB + TT ($n = 50$)	
Performed (%)	50/80 (63%)
Duration of TT (days) (X ± SD)	9.2 ± 3.7 (3–20)
Success (%)	11/50 (22%)
Failure (%)	39/50 (78%)
FT	25/50 (50%)
Surgery	13/50 (26%)
Exitus	1/50 (2%)
Hospital stay (days) (X ± SD)	
Successful TT	25.3 ± 11.8 (12–36)
Direct surgery	26.4 ± 6.5 (18–39)
AB + TT + FT (N = 25)*	
Performed (%)	25/80 (43%)
Total drainage before FT (ml) (X ± SD)	148 ± 94
Total drainage after FT (ml) (X ± SD)	276 ± 104
Success (%)	18/25 (72%)
Hospital stay (days) (X ± SD)	22 ± 7.21
Failure (%)	7/25 (28%) (1exitus, 6 surgery)
Total surgical operation (%)	22/80 (28%)
At presentation (%)	3/80
During TT (%)	13/80
During TT + FT (%)	6/80
Mortality	3/80 (3.75%)
Nosocomial infection	4/80 (5%)

*Twenty-five patients are considered as potential candidates of surgery before the trial of FT.

a high risk of necrotizing pneumonia, surgical operation, need for therapy change, prolonged hospitalization, and delayed normalization of CRP in a group of patients who had rapid onset of symptoms (4–6 days) and who were hospitalized in our institution without prior hospitalization. Although the reason for this observation is not clear, it may be due to the invasive pathogen and/or impaired or exaggerated immune response of the host. Only 28 per cent of our patients after a mean delay of 11 days were still at exudative stage (mean 7 days delay) with 54 per cent at fibropurulent (mean 7 days delay), and 18 per cent at chronic organized stage (mean 15 days delay) (Table 1). Fibropurulent or empyema stage at admission was reported in 36–83 per cent, and chronic organized stage in 0–19 per cent in pediatric literature.[14–16] Regarding the data mentioned above, we can speculate there are two groups of patients with complicated course requiring operation. The first group not mentioned previously as a risk group in the literature, is characterized by rapid onset and short duration of symptoms (<6 days), and no prior hospital admission and antibiotic therapy with high incidence of necrotizing pneumonia. The second group is characterized by prolonged symptoms (mean 15 days) with delayed or inappropriate therapy, and prior hospital admission with high incidence of chronic organized stage.

The characteristics of the pleural fluid of the patients treated with antibiotics alone (33 per cent) was generally supportive of acute exudative stage. The patients with higher quantity of fluid and characteristics of empyema or complicated empyema (63 per cent) had TT. Twenty-two percent of them recovered completely, 26 per cent was given to surgery, and 50 per cent had FT. There are a few studies in the literature that report the success rate of therapy in children as 20–38 per cent with antibiotic alone and 45–96 per cent with TT.[10,17] The lower rate of success in our patients could be due to delayed treatment, complicated course, and difficulty in draining the fluid because most of the patients were at chronic organized stage.

Urokinase was given in 50 per cent of our patients who had TT and was successful in 72 per cent. This ratio was comparable with the literature where the highest success rate was reported as 86 per cent.[1,2,5,6,18] We thought that the need for surgical operation could be eliminated by successful FT in most of these patients in chronic organized stage.

Many authors recommend surgical decortication in the beginning for patients with PPE at chronic organized stage (complicated empyema).[16,19] The rate of surgical operation in PPE in childhood ranges between 6 and 90 per cent in various studies,[10–12,17,19] however, this rate is very dependent on the clinical findings of the patients at presentation and delay in treatment. Despite an average delay of 11 days in our patients, the rate of decortication at presentation was 4 per cent. However, failure of TT in some patients were compensated by FT, and the need for surgical intervention was minimized.

The duration of hospital stay of our patients were comparable with literature which ranged between 13 and 40 days.[12,14,15,19]

The mortality rate of empyema in our children (3.75 per cent) is considered acceptable when compared to the incidence of <10 per cent in the literature.[10,17,19,20] The optimal therapy and the low mortality rate could be achieved by close follow-up and early introduction of the appropriate therapy by a multidisciplinary approach.

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