Analysis of the concise etiology of pleural effusion in 3707 pediatric patients in a single clinical center

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Purpose: To summarize the concise etiology of pleural effusion in 3707 patients over a period of 13 years at the Children’s Hospital of Chongqing Medical University.

Methods: A total of 3707 patients with pleural effusion were included from January 2007 to December 2019 at our hospital. According to etiology, pleural effusion was divided into infectious pleural effusion and noninfectious pleural effusion. The infection factors were further subdivided as being caused by tuberculous, paragonimiasis, parapneumonic factors (including multiple bacteria, multiple viruses, mycoplasma, chlamydia, chlamydia, fungus and fever, blood routine examination shows increased white blood cells and neutrophils). The noninfectious factors were further subdivided into neoplastic, trauma, other causes. They were also divided into the infants and young children group (3 y and below), the preschool group (3–6 y) and the school-age group (above 6 y) depending on age.

Results: Among the 3707 children, there were 2925 (78.9%) patients with infectious pleural effusions, and 782 (21.1%) patients with noninfectious pleural effusions. The incidence of infectious pleural effusions caused by parapneumonic factors decreased significantly with increasing age; however, parapneumonic factors remained the primary etiology of infectious pleural effusion in each group. The incidence of infectious pleural effusions caused by tuberculosis and paragonimiasis increased significantly with increasing age. Tumor was the primary cause of noninfectious pleural effusion. The incidence of noninfectious pleural effusion caused by tumor and other causes increased significantly with increasing age. The incidence of noninfectious pleural effusion caused by trauma in the preschool group was significantly greater than that of the infants and young children group and school-age group. The number of noninfectious pleural effusion caused by other causes in the school-age group were significantly greater than those in the infants and young children group and preschool group.

Conclusion: In our center, pediatric pleural effusion was primarily caused by infections, parapneumonic factors were the primary causes of infectious pleural effusions. The proportion of noninfective pleural effusions in the etiology of pleural effusion in children was small; however, some were difficult to treat, requiring long-term treatment and possibly poor prognosis. Therefore, multidisciplinary treatment should be combined.

Keywords: Pleural effusion, Pediatric, Etiology, Concise analysis

Pleural effusion is the most common manifestation of pleural diseases. The most common causes of pleural effusion in adults are cancer and tuberculosis. However, children have their own characteristics associated with pleural effusion, and the etiologies of pleural effusion are diverse, involving not only several systems, organ diseases and dysfunctions but also lung, pleura, mediastinum, diaphragm and subphrenic or other adjacent tissue lesions[1], and they have a variety of clinical manifestations. Timely determination of the causes of pleural effusion is important for treatment and better prognosis. Despite the fact that there have been many studies regarding pleural effusion in children, reports of the etiology of large cases of pediatric pleural effusion are rare. The data from 3707 patients with pleural effusion were retrospectively analyzed in our hospital over the past 13 years, and the etiologies were approximately summarized to provide references for clinical treatment.

Data and methods

Clinical data
A total of 3707 hospitalized patients with pleural effusion were collected in the Children’s Hospital of Chongqing Medical
University in southwest China from January 2007 to December 2019, including 2438 males and 1269 females, with a sex ratio of 1.92:1. The ages ranged from 1 day to 17 years old.

**Laboratory testing**

Sputum testing: bacterial culture, detection of 7 common respiratory viruses, mycoplasma and chlamydia DNA testing, and acid-fast staining smears, etc.

Blood test: blood analysis and CRP, lung fluke antibody, tuberculosis antibody, T-spot TB test, etc.

Pleural fluid culture and pathologic examination of pleura.

Diagnostic criteria: all cases were confirmed as pleural effusion by chest radiology and/or B-ultrasound.

**Methods**

Read the cases, the following information was extracted: a: according to the age, the subjects were divided into infants and young children group (3 y and below), preschool group (3–6 y), and school-age group (above 6 y); b: according to etiology, pleural effusion was divided into infectious pleural effusion and noninfectious pleural effusion. The infection factors were further subdivided as being caused by tuberculous (sputum and pleural fluid culture, pleural biopsy and imaging diagnosis), paragonimiasis (with a history of eating freshwater crabs and prawns, pulmonary paragonimiasis antibody in the blood were positive, blood routine examination and pleural biopsy show increased eosinophils), parapneumonic factors (including multiple bacteria, multiple viruses, mycoplasma, chlamydia, fungus and fever, blood routine examination shows increased white blood cells and neutrophils). The noninfectious factors were further subdivided into neoplastic (including mediastinal, thoracic, or other tumors), trauma, other causes (including heart failure, immune system diseases such as nephropathy, purpura, Kawasaki disease, etc.).

**Statistical methods**

Several groups of disordered and multiple classification data were analyzed by the Kruskal-Wallis H test, and comparison between groups was performed using the Bonferroni correction. Statistical significance was accepted at $P < 0.05$.

**Results**

**Etiology comparison**

Among the 3707 cases of pleural effusion, 2925 cases were infectious cases, accounting for 78.9%, and 782 patients had noninfectious cause, accounting for 21.1% (Table 1), indicating that the primary cause of pediatric pleural effusion was infection in our hospital over 13 years.

**Comparison of infectious pleural effusion among different ages**

The causes of infectious pleural effusion in different age groups were significantly different. The infectious pleural effusion caused by parapneumonic factors decreased significantly with the increase of age. Nevertheless, parapneumonic factors remained the principal cause of infectious pleural effusions. The incidence of infectious pleural effusions caused by paragonimiasis and tuberculosis increased significantly with increasing age. The patients with pleural effusion associated with paragonimiasis were more frequently seen in the preschool and school-age groups, while the patients with tuberculous pleural effusion were more common in the school-age group (Table 2).

**Comparison of noninfectious pleural effusion among different ages**

The causes of noninfectious pleural effusion in different age groups were significantly different. The incidence of noninfectious pleural effusions caused by tumor factors increased significantly with increasing age, and tumor factors were also the primary cause of noninfectious pleural effusions in different age groups. The number of noninfectious pleural effusions caused by traumatic factors in the preschool group were significantly higher than those of infants and young children group and school-age group. The number of noninfectious pleural effusion caused by other causes (such as nephritis, kidney disease, purpura, Kawasaki disease, etc) in the school-age group were significantly greater than those of in infants and young children group and preschool group (Table 3).

**Discussion**

Pleural effusion is the most common clinical manifestation of pleural diseases. It can be caused by lung, pleural and extrapulmonary diseases. The pathogenesis of pleural effusion includes increased hydrostatic pressure in the pleural capillary (as for example in heart failure), increased pleural permeability (as in pleurisy), decreased colloid osmotic pressure in pleural capillaries (hypoproteinemia) or the obstruction of parietal pleural lymphatic drainage. The fluid in the thoracic cavity is secreted by the parietal pleura at high hydrostatic pressure and is absorbed by the venous side of the visceral pleura capillary in a dynamic

<table>
<thead>
<tr>
<th>Table 1</th>
<th>The number of pleural effusion.</th>
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<tbody>
<tr>
<td>Etiology</td>
<td>Infectious</td>
</tr>
<tr>
<td>Data</td>
<td>Number</td>
</tr>
<tr>
<td>Number</td>
<td>2925</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Comparison of different types of infectious factor.</th>
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<tbody>
<tr>
<td>Group, N (%)</td>
<td>Infants and Young Children Group</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
</tr>
<tr>
<td>Tuberculous</td>
<td>12* (1.1)</td>
</tr>
<tr>
<td>Paragonimiasis</td>
<td>18† (1.6)</td>
</tr>
<tr>
<td>Parapneumonic factor</td>
<td>1076* (97.3)</td>
</tr>
</tbody>
</table>

Notes: comparison of multiple groups of disordered and multiple classification data, $H=203.490$, $P=0.0001$.

* $H=16.683$, $P=0.001$.

† $H=173.013$, $P=0.0002$.

‡ $H=139.160$, $P=0.0002$. 

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equilibrium under normal conditions. If the pleural secretion increases or the absorption of the venous side of the visceral pleura decreases, the balance is destroyed and pleural effusion results.

There are many classification methods for pleural effusion\[^{2}\]. In this study, pleural effusion was divided into infectious and noninfectious factors. The infectious factors were further subdivided as being caused by tuberculous, paragonimiasis, parapneumonic factors. Bacteria were not detected for some patients because antibiotics had been used outside the hospital for some cases of parapneumonic pleural effusions\[^{3}\], for the convenience of statistical analysis, parapneumonic pleural effusions had not been specifically classified into which kind of bacteria, virus, mycoplasma, chlamydia, fungi, etc. Noninfectious factors were further subdivided into neoplastic, traumatic and other causes. For the sake of the convenience of statistical analysis, other causes for noninfectious pleural effusion were heart failure, autoimmune diseases (such as kidney disease, purpura and Kawasaki disease, etc.) and reactive pleural effusion caused by appendicitis, except for tumor and trauma.

The causes of pleural effusion in children are different from those of adults. Tumor and tuberculosis are the main causes of pleural effusion in adults\[^{4}\]. Our study confirmed that infectious factors accounted for 78.9% in children. We also found that there were significant differences in terms of the cause of infectious pleural effusion in different age groups. Pleural effusion caused by parapneumonic pleural effusion decreased significantly with increasing age, the reasons were that children with a young age have lower immunity and poorer ability to limit bacterial infection. With the increase of age and enhancement of immunity, the ratio of parapneumonic pleural effusion was significantly decreased in the preschool and school-age groups. However, the proportion of parapneumonic effusion remained highest among infected pleural effusions in different groups. In the present study, its percentages were above 50% in the 3 groups of patients, similar to values reported in previous studies\[^{5,6}\]. It has been reported that the most common pathogens causing pneumonia in children are bacteria, followed by viruses, mycoplasmas, chlamydia and fungi\[^{7,8}\], therefore, the infectious factors should be firstly considered in the treatment of pleural effusion. The pleural effusion caused by paragonimiasis increases significantly with the increase of age. The number of paragonimiasis pleural effusion were more commonly seen in the preschool and school-age groups, which was related to the diversity of food intake and the fewer supervision by parents. The children during this period are susceptible to eating raw crabs and raw shrimps. In some remote mountainous areas of southwestern China, there is even a misconception that raw fresh water crabs can increase the physical strength of children. Pleural effusion due to paragonimiasis has the following characteristics\[^{9-11}\]: (1) history of eating fresh water crabs; (2) increased eosinophils in the peripheral blood; (3) increased eosinophil in pleural effusion. Paragonimiasis is more common in rural areas at the past\[^{12-14}\], due to traffic and economic development, more children with paragonimiasis are also coming to cities for treatment now. Therefore, there have been more cases of paragonimiasis pleural effusion in our hospital. The incidence of tuberculous pleurisy in school-age group was significantly higher than other groups, the cause is that children of school-age are more likely to be infected with tuberculosis due to the long-term clustering together. This result differed from other studies which reported that tuberculosis was more common in infants and young children\[^{15}\]. The positive of acid-fast staining or culture of tuberculous bacteria is the gold standard for diagnosis of tuberculous pleural effusion, but it has low positivity in pleural effusion and sputum. Tuberculosis can also be diagnosed by pleural biopsy, imaging, INF-γ and specific nucleic acid amplification techniques.

The proportion of noninfectious factors among childhood pleural effusions was low, and the noninfectious factors were primarily tumor, blood system disease, immune disease, trauma, kidney disease, and others. For the sake of convenience of statistical analysis, noninfectious factors were further subdivided into tumor, trauma and other causes (including heart failure, autoimmune diseases and reactive pleural effusion caused by appendicitis). We found tumor was the primary cause of noninfectious pleural effusion in all age groups, and noninfectious pleural effusions caused by tumor factors increased significantly with increasing age, the most common causes of neoplastic pleural effusion in children were mediastinal tumor, thoracic tumor, lymphoma, and leukemia. The number of noninfectious pleural effusions caused by traumatic factors in the preschool group were significantly higher than that of infancy and toddler and school-age groups, the reasons are that preschool children’s activity begins to increase significantly, and reduced adult supervision, and increased various forms of trauma. As nephritis, kidney disease, purpura and Kawasaki disease etc increased with increasing age, noninfectious pleural effusions from other causes were significantly higher in the school-age group than in infants and young children group and the preschool group. The primary pathogeneses of noninfectious pleural effusions were tumor, blood system disease, immune disease, kidney disease and others, all being difficult to treat and requiring long-term treatment. Therefore, multidisciplinary treatment should be combined.

In summary, the primarily etiology of pleural effusion in children was parapneumonic factor in our center. Although the proportion of noninfective pleural effusion in children was small, some of them were difficult to treat, requiring long-term treatment and possibly with poor prognosis, therefore, clinicians should pay more attention to this type of effusion. Early identification of the etiology is conducive to favorable prognosis. In addition to treat the etiology, for children with moderate to severe pleural effusion, our experience suggesting placement of closed thoracic drainage rather than thoracocentesis, avoiding multiple thoracic punctures to form multiseptum effusion requiring surgery and alleviating the fear of multiple thoracic punctures for children.

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**Table 3**

Comparison of different types of noninfectious factors.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Infants and Young Children Group</th>
<th>Preschool Group</th>
<th>School-age Group</th>
</tr>
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<tbody>
<tr>
<td>Tumor</td>
<td>74(^{1}) (45.0)</td>
<td>121(^{1}) (40.6)</td>
<td>226(^{1}) (60.5)</td>
</tr>
<tr>
<td>Trauma</td>
<td>29(^{1}) (17.7)</td>
<td>65(^{1}) (26.6)</td>
<td>36(^{1}) (9.5)</td>
</tr>
<tr>
<td>Others</td>
<td>61(^{1}) (37.3)</td>
<td>58(^{1}) (23.8)</td>
<td>112(^{1}) (30.0)</td>
</tr>
</tbody>
</table>

Comparison of multiple groups of disordered and multiple classification data, \(H=8.246, P=0.016\).

\(^{1}\)\(H=12.897, P=0.002\).

\(^{2}\)\(H=8.567, P=0.001\).

\(^{3}\)\(H=8.567, P=0.013\).
Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards for retrospective studies. Ethical approval is not required. This article does not contain any studies with human participants performed by any of the authors, there is no need for informed consent.

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Author contribution


Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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None.

Guarantor

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