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Analysis of High-Risk Warning Factors for Severe Mycoplasma Pneumoniae Pneumonia in Children

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Abstract: Severe Mycoplasma pneumoniae is a serious respiratory disease caused by Mycoplasma pneumoniae and is characterized by persistent high fever, frequent coughing and shortness of breath. The disease is relatively common in children, and if left untreated, it may rapidly lead to serious complications and even death. In this paper, we systematically summarize the high-risk early warning factors of severe Mycoplasma pneumoniae pneumonia in order to be helpful for the early identification of high-risk factors and the adoption of effective interventions in the clinic.

1. Introduction

Mycoplasma pneumoniae (MP) is an important pathogen of respiratory infections in children, accounting for 20-40% of pediatric community acquired pneumonia (CAP), with an even higher incidence in epidemic seasons, and most MP infections are self-limiting and have a good prognosis[1–4] . MP has long been recognized as an important pathogen of pneumonia[5] . Most children with mycoplasma pneumoniae pneumonia (MPP) are curable, but some present with worsening clinical symptoms and imaging manifestations called severe mycoplasma pneumoniae pneumonia (SMPP)[6,7] . Severe pneumonia is the leading cause of death in children under 5 years of age, with an estimated 740,180 deaths per year globally due to severe pneumonia, 22% of which are in children under 5 years of age[6,8–10] . MP has been detected in the majority of children with pneumonia, with a significant increase in hospitalization and severe conversion cases since 2022[11] .The incidence of MPP is has increased significantly, and some children with SMPP may be combined with serious intrapulmonary and intrapulmonary complications, such as respiratory failure, cardiac insufficiency, dizziness, coma, and impaired consciousness, which leads to increased difficulty in clinical treatment, and seriously affects children's health and quality of survival. Early clinical recognition of severe Mycoplasma pneumoniae pneumonia is crucial in order to improve treatment outcomes and reduce morbidity and mortality[12] . By systematically reviewing the high-risk early warning factors of SMPP, this paper aims to provide a scientific basis for clinical practice and public health interventions.

2. Main features of severe Mycoplasma pneumoniae pneumonia

The clinical manifestations of SMPP patients often include persistent high fever, paroxysmal dry cough, which may be accompanied by shortness of breath, cyanosis, wheezing, etc. Some patients are accompanied by intrapulmonary and extrapulmonary complications, which are often difficult to be detected and diagnosed at an early stage, and in severe cases, may lead to death[13,14] SMPP Most of the SMPP occurs around 1 week of the disease duration, and the common intrapulmonary complications include plasmablastic bronchiolitis, embolism, pleural effusion, necrotizing pneumonia, bronchial asthma, and mixed infections. In case of plastic bronchitis, medium-to-large pleural effusion, extensive pulmonary consolidation and necrosis, and pulmonary embolism, children may suffer from shortness of breath or respiratory distress; children with pulmonary embolism may also suffer from chest pain and hemoptysis[15]; extrapulmonary complications may occur in the neurological system, the blood system, the circulatory system, and the skin and mucous membranes, etc [16,17], and may present with damage to the corresponding systems.

3. Diagnostic criteria for severe Mycoplasma pneumoniae pneumonia

SMPP means MPP is severe and meets any of the following manifestations[1,18] :

(1) Persistent high fever (above 39° C)≥ 5d or fever≥ 7d, with no downward trend in peak temperature;

(2) One of wheezing, shortness of breath, dyspnea, chest pain and hemoptysis. These manifestations are associated with severe lesions, combined plastic bronchitis, asthma attacks, pleural effusion and pulmonary embolism;

(3) Extrapulmonary complications occurring, but not meeting the criteria for critical care;

(4) Finger pulse oximetry at rest with air inhalation≤ 0.93;

(5) Imaging manifestations of one of the following conditions: 1) a single lung lobe≥ 2/3 involved, the presence of uniform high-density solid lesions or two or more lobes of high-density solid lesions (regardless of the size of the area of involvement), may be accompanied by moderate to large amounts of pleural effusion, can also be accompanied by limited fine bronchiolitis manifestations; 2) single-lung diffuse or bilateral≥ 4/5 lobes of the lungs have fine bronchiolitis manifestations, can be combined with the formation of bronchiolitis, and mucus embolus The formation of mucus plugs may lead to atelectasis;

(6) Progressive exacerbation of clinical symptoms, with imaging showing more than 50% progression of lesion extent in 24-48h;

(7) Those with markedly elevated CRP, LDH, or one of the D-dimers.

4. SMPP high-risk warning factors

4.1 Persistent hyperthermia

The association between duration of fever and SMPP was reported in a study by[19–22] , which showed that the duration of fever was an influential factor in the development of SMPP. The results of a study by Gao Hua et al[19] showed that fever duration of more than 5 d was a risk factor for the development of SMPP in children.

4.2 Lower lobe lesions and large lamellar lesions of the lungs

Imaging examination is one of the main bases for clinically determining the severity of MPP and assessing the prognosis. The degree and distribution of lung lesions can be clarified through visual

imaging. In terms of imaging performance, there are differences in the chest imaging performance of children with MPP of different severity. Chest imaging changes are valuable in predicting the occurrence of SMPP, and related studies[19,23] showed that imaging manifestations of lower lobe lung lesions were influential factors in the occurrence of SMPP in children. A study by Liu Liping and other scholars[20,19,24] showed that large lamellar solid lesions in the lungs were strongly correlated with SMPP, suggesting that large lamellar lesions in the lungs are an influential factor in the development of SMPP in children. Therefore, when children with MPP present with lobar lesions, large lamellar shadows or pleural effusion, the possibility of SMPP should be highly alerted[25] .

4.3 Peripheral blood routine related indexes

Neutrophils are key cellular components of the body's host defense system against infections; Neutrophil-to-lymphocyte ratio (NLR) reflects the body's systemic inflammatory state and immune response[26] . Some studies have shown that peripheral blood neutrophil percentage, lymphocyte percentage, and NLR levels can reflect the inflammatory state and severity of the disease in children with MPP; compared with children with normal MPP, SMPP patients had higher peripheral blood neutrophil percentage and NLR and lower lymphocyte percentage, which suggests that the neutrophil percentage and NLR can be used for early prediction of the occurrence of SMPP[26,27] .

4.4. Inflammation and blood biochemistry-related indicators

Significantly elevated white blood cell (WBC) are associated with a strong inflammatory response in the body, which is consistent with the mechanism of immune damage in SMPP. The immune system mounts a strong immune response to infection or inflammation, leading to an increase in WBC in response to potential threats. However, if the immune response is too strong or inappropriate, it may contribute to the development of SMPP by making the disease difficult to control and increasing the risk of complications. Therefore, WBC is also a risk factor for SMPP[28] . interleukin (IL-6) promotes the secretion of protective antibodies and enhances the production of other inflammatory factors to exacerbate inflammatory injury, and it has been demonstrated that the level of IL-6 in the bronchoalveolar lavage fluid of children with SMPP is significantly higher than that of children with normal MPP[29] . Chen Mengxue et al. showed that C-reactive protein (CRP) was significantly elevated in patients with SMPP and correlated with the degree of lung tissue injury[30–32] . erythrocyte sedimentation Rate (ESR) is an important and effective marker of inflammatory infections and disease activity, it increases with disease activity to a more significant degree than CRP and can monitor the degree of inflammatory response in children with MPP[33–35] . Serum levels of lactate dehydrogenase (LDH) reflect the extent of cell membrane damage and can be used to monitor cell and tissue damage. A related study reported the association between LDH and SMPP, and the results showed that LDH was an influential factor in the development of SMPP in children[19,20,36,37] . D-dimer is a fibrin degradation product, which is usually elevated in the context of increased coagulation and fibrinolysis, which is common in systemic inflammatory responses. A related study reported the association between D-dimer and SMPP, and the results showed that D-dimer was an influential factor in the development of SMPP in children[38,24,39,40] . Procalcitonin, (PCT) is a precursor substance of calcitonin produced by thyroid C-cells, but when the body is infected with bacteria and undergoes an inflammatory response, tissues and organs such as the liver, lungs, and kidneys may produce large amounts of PCT However, when the body is infected with bacteria and reacts to inflammation, the liver, lungs, kidneys and other tissues and organs may produce large amounts of PCT and release it into the bloodstream, resulting in a significant increase in its serum level[41]. Studies have shown that PCT is an influential factor in the

development of SMPP in children[42,38] . Therefore, in clinical practice, a significant increase in WBC, IL-6, CRP, ESR, LDH, D-dimer, PCT and other indicators can be used as an early warning for the development of SMPP.

4.5 Other early warning factors

MPP is a common respiratory infectious disease in children, while the airways of asthmatic children are in a hypersensitive state, and respiratory infections can trigger acute attacks, the two diseases interact with each other, leading to complication of the condition, and related studies have shown that the risk of severe disease is increased in children with MPP who have combined with asthma[43] Delayed treatment with macrolide antimicrobial drugs, and MP infections in combination with other pathogenic infections need to be guarded against the SMPP occurs. Also allergic children (with a clear history of allergy, allergens, and significantly elevated serum IgE levels) are at high risk for developing SMPP[44] .

5. Conclusions

This article analyzes the high-risk warning factors for severe Mycoplasma pneumoniae pneumonia in children, aiming to provide a scientific basis for early clinical recognition and intervention. SMPP is a serious respiratory disease, and its early recognition is crucial for improving prognosis. Studies have shown that persistent high fever, imaging manifestations (e.g., lower lobe lesions, large patchy shadows, and pleural effusion), and abnormalities in related indicators (e.g., neutrophil percentage, NLR, WBC, IL-6, CRP, ESR, LDH, D-dimer, PCT) are important early warning factors for the development of SMPP. In addition, comorbid asthma, allergies, and delayed macrolide therapy are also high risk factors for SMPP.

Although current studies have identified a variety of high-risk warning factors, early diagnosis of SMPP remains challenging, especially if symptoms are atypical or combined with other infections. Future studies should further explore new biomarkers to improve the sensitivity and specificity of early diagnosis. In addition, the development and clinical application of novel antibiotics against drug-resistant strains should also be a focus of research. Through multidisciplinary cooperation and precision medicine, it is expected to further reduce the morbidity and mortality of SMPP and improve the prognosis of children.

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