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Review Article

Update in the Diagnosis and Treatment of Mycoplasma Pneumoniae Pneumonia in Children

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Abstract

This paper analyzes and studies the diagnosis and treatment of Mycoplasma pneumoniae pneumonia (MPP) by referring to relevant domestic and international literature, aiming to provide new methods and references for the clinical diagnosis of MPP in children.

Mycoplasma pneumoniae pneumonia (MPP) is a common community-acquired pneumonia in pediatrics, a lower respiratory tract infection caused by Mycoplasma pneumoniae. Mycoplasma pneumoniae is a unique microorganism capable of growing and reproducing in cell-free culture media. It primarily attacks the human respiratory tract and lungs, and in severe cases, can affect multiple organs throughout the body. Its clinical manifestations are diverse, ranging from mild self-limiting cases to severe pneumonia or extrapulmonary complications. Timely and accurate diagnosis is crucial for treatment. Traditional methods such as serological antibody detection, while widely used, still have limitations including a diagnostic "window period" and delayed results. Molecular diagnostic methods centered on nucleic acid detection technology, such as real-time fluorescent PCR, have become a core tool for early clinical diagnosis due to their rapidity and high sensitivity. Additionally, direct antigen detection, biomarkers for assessing disease severity and prognosis, and imaging examinations like high-resolution CT collectively form a more comprehensive and multi-dimensional diagnostic system. Referring to domestic and international literature on MPP, this paper analyzes and studies its diagnosis and treatment. It is anticipated that future developments in diagnostic technology will focus more on the popularization of rapid point-of-care testing and the deepening of artificial intelligence-assisted analysis. The aim is to provide new methods and references for the clinical diagnosis of MPP in children, thereby comprehensively improving the diagnostic and therapeutic standards for pediatric MPP.

Keywords: Children, Mycoplasma pneumoniae pneumonia, Diagnosis, Molecular detection, Biomarker, High-resolution CT

Introduction

Mycoplasma pneumoniae is a unique pathogen lacking a cell wall, primarily transmitted through respiratory droplets among populations, especially children and adolescents. It is one of the important pathogens causing community-acquired pneumonia (CAP) in children, accounting for 20%–40% of CAP cases, and up to 50% during epidemics [6]. Post-infection clinical manifestations vary, ranging from mild cold-like symptoms to severe pneumonia. Some children may also

experience extrapulmonary involvement affecting the skin, nervous system, etc. [10], [11]. In recent years, the incidence of MPP in children in China has shown an upward trend, with a relatively high rate of severe cases. During the 2023 epidemic, severe cases accounted for approximately 20% of all cases. Coupled with the increasingly prominent issue of macrolide antibiotic resistance (azithromycin resistance rate approached 100% during the 2023 epidemic) [7] and the common occurrence of co-infections, higher demands are placed on the early recognition and accurate diagnosis of pediatric MPP. Traditional diagnostic methods have shortcomings in timeliness and sensitivity. However, the rapid development of new technologies such as molecular biology provides powerful tools for achieving early and precise diagnosis. The following sections will review the traditional diagnostic methods, novel detection technologies, relevant biomarkers, and the application and advances of imaging assessment for pediatric MPP, aiming to provide a clear diagnostic framework for clinical practice.

Traditional Diagnostic Methods: Value and Limitations

Traditional diagnostic approaches mainly include pathogen isolation culture and serological testing, which remain important components of the diagnostic system.

Pathogen Isolation and Culture

This involves inoculating patient samples such as throat swabs, sputum, or bronchoalveolar lavage fluid onto special culture media. It is considered the "gold standard" for confirming M. pneumoniae infection. This method allows direct acquisition of the pathogen for subsequent drug resistance studies. However, its main drawbacks are the high requirements for culture conditions and the very slow growth of M. pneumoniae. Primary culture typically takes 7–14 days or even longer, failing to meet the need for early rapid clinical diagnosis. Therefore, it is primarily used in pathogen research, drug resistance testing, or epidemiological investigations.

Serological Testing

This is currently a very widely used method in clinical practice. It primarily relies on detecting specific antibodies against M. pneumoniae in the blood to determine infection.

- **IgM Antibody Detection:** IgM antibodies typically appear about one week after infection, peak at 3–4 weeks, and persist for several months. A rising IgM level suggests recent infection. Commonly used methods like enzyme-linked immunosorbent assay (ELISA) are relatively simple to perform. However, it is important to note that "false negatives" may occur during the early infection stage due to antibodies not yet being produced (i.e., window period). Additionally, antibody detection in some children, especially infants and young children, may be affected by their weaker immune response.
- **IgG Antibody Avidity Testing:** Helps distinguish between recent and past infections. IgG antibodies produced during recent infection have lower avidity, whereas those from past infections have higher avidity. This is valuable for differentiating cases with negative IgM but high clinical suspicion.
- **Dynamic Monitoring of Antibody Titers:** Comparing paired serum samples from the acute phase and convalescent phase (2–4 weeks apart). A fourfold or greater increase in antibody titer (e.g., IgG) during convalescence is considered diagnostically significant. This method is more reliable but is retrospective and cannot be used for early decision-making.

Application Advances in Novel Detection Technologies

With continuous technological progress, a series of rapid and sensitive novel detection methods have become the mainstay of clinical diagnosis.

Molecular Diagnostic Techniques

These techniques directly detect the pathogen's nucleic acid (DNA or RNA), offering advantages of high sensitivity, high specificity, and rapid turnaround time.

- **Real-time Fluorescent Quantitative PCR (qPCR):** This is currently the most widely used molecular diagnostic method in clinical practice. It can detect extremely small amounts of M. pneumoniae DNA from samples like throat swabs or sputum very early in the disease course, providing results within hours, greatly shortening diagnostic time. Quantitative results can also, to some extent, reflect the pathogen load.
- **Multiplex PCR and Targeted Sequencing:** Can simultaneously detect M. pneumoniae and dozens of other common respiratory pathogens, making it highly suitable for identifying co-infections. Targeted sequencing can also detect gene mutations associated with drug resistance (e.g., mutations at positions 2063, 2064, 2617 on the 23S rRNA gene) [7], providing direct reference for clinical drug selection.
- **Isothermal Amplification and CRISPR Technology:** For example, Loop-mediated Isothermal Amplification (LAMP) does not require complex thermal cycling equipment, making it more suitable for use in primary healthcare institutions. Detection technologies based on CRISPR-Cas systems (e.g., CRISPR-Cas12a) can even achieve rapid detection without pre-amplification, simplifying operation. This represents an important future direction for point-of-care testing (POCT) [3].

Antigen Detection Technology

Directly detects specific antigen components of M. pneumo-

niae in samples, bypassing the window period issue associated with antibody detection and directly indicating current pathogen presence.

- **Ultra-sensitive ELISA Detection:** For example, detection methods targeting the M. pneumoniae P30 adhesion protein offer high sensitivity, can yield positive results early in infection, and their levels may correlate with disease severity.
- **Rapid Antigen Testing:** Aims to develop simple-to-operate, rapid-result POCT tools, similar to influenza antigen test strips. For instance, research has explored using bio-nanozyme technology for non-invasive detection via saliva samples, a method particularly suitable for children [4].
- **Chemiluminescent Probe Detection:** Utilizes hydrogen peroxide produced by M. pneumoniae metabolism as a target to develop specific chemiluminescent probes (e.g., MPCL). This enables direct quantitative detection of M. pneumoniae, with reported clinical sample sensitivity of 100% and specificity of 96.5%, providing a new pathway for rapid diagnosis [8].

The Role of Biomarkers in Disease Assessment

While biomarkers cannot directly confirm M. pneumoniae infection, they hold significant value in assessing disease severity, predicting the risk of severe disease, and identifying complications.

1. **Inflammatory Markers:** C-reactive protein (CRP) is elevated in most affected children, and significant elevation often indicates intense inflammatory response. Combined detection of markers such as lactate dehydrogenase (LDH), interleukin-6 (IL-6), and D-dimer has been confirmed by multiple studies to be closely associated with refractory or severe MPP and can serve as early warning signals [2]. Additionally, procalcitonin (PCT), erythrocyte sedimentation rate (ESR), interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α), etc., have also been confirmed to correlate with MPP severity and can be used in combination for severe disease risk assessment [6].
2. **Coagulation-related Markers:** Severe cases often present with coagulation dysfunction. A significant elevation in D-dimer not only suggests severe inflammation but may also indicate a risk of secondary thrombosis. Thromboelastography provides a more comprehensive assessment of coagulation status.
3. **Novel Prognostic Assessment Markers:** Peripheral blood levels of Ficolin-3 and P2X7 receptor are significantly elevated in children with MPP. Levels are higher in severe cases compared to mild cases, and in cases with poor prognosis compared to those with good prognosis. Combined detection of these two markers shows superior predictive efficacy for poor prognosis compared to single indicators [9].

Auxiliary Diagnostic Value of Imaging Examinations

Imaging examinations can more directly visualize the nature, extent, and severity of pulmonary lesions.

1. **Chest X-ray (CXR):** The most basic imaging examination. Typical findings include increased and blurred lung markings, as well as scattered patchy or cloudy opacities. However, it may not clearly show very early or mild lesions.
2. **Chest High-Resolution Computed Tomography (HRCT):** More sensitive and precise than CXR in assessing the condition. It can clearly display characteristic changes such as ground-glass opacities, centrilobular nodules, and bronchial wall thickening. For severe cases, CT can accurately show the extent of lung consolidation, the presence of necrosis, pleural effusion, etc. The incidence of pleural effusion and lung consolidation in children with severe MPP is significantly higher than in those with mild MPP [6]. Furthermore, the appearance of signs like "tree-in-bud" or atelectasis on CT images should raise awareness of potential long-term sequelae such as bronchiolitis obliterans [12].

Conclusion and Perspectives

Current diagnostic practice for pediatric MPP has evolved from primarily relying on a single traditional technique to a comprehensive diagnostic strategy combining multiple approaches and different technologies. In clinical practice, physicians typically select appropriate tests flexibly based on the child's duration of illness, disease severity, and the testing capabilities of the healthcare facility. Nucleic acid detection can be prioritized when early rapid diagnosis is needed. For children presenting later, serological antibody testing plays an important auxiliary role. Biomarkers and chest CT are mainly used to assess disease severity and monitor complications [1], [5]. Clinical diagnosis should also pay attention to differential diagnosis from adenovirus pneumonia, influenza virus pneumonia, bacterial pneumonia, etc., to avoid over-diagnosis or misdiagnosis [13].

Future evolution of diagnostic technology may focus on three directions: First, developing faster and easier-to-operate point-of-care testing tools to enhance the diagnostic capabilities of primary healthcare units. Second, researching optimal combinations of biomarkers to achieve more precise prediction of a child's risk of developing severe disease or drug resistance, and even constructing prognostic prediction nomograms based on multiple factors [10]. Third, promot-

ing the deep integration of artificial intelligence technology with medical image recognition to improve the objectivity and overall efficiency of imaging assessment. Through continuous improvement of the existing diagnostic system, we anticipate laying a more solid foundation for the earlier detection, more timely treatment, and ultimately better recovery outcomes for children with Mycoplasma pneumoniae pneumonia.

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