Clinical differentiation between pediatric pulmonary tuberculosis and *Mycoplasma pneumoniae* pneumonia (Review)

ZONG WAN, RENJIE QI, QIUSHI YANG, HUAN LI and SHUSONG RUAN

Department of Tuberculosis, Guiyang Public Health Clinical Center, Guiyang, Guizhou 550001, P.R. China

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Abstract. Differentiating between pediatric pulmonary tuberculosis (TB) and *Mycoplasma pneumoniae* pneumonia (MPP) is essential due to their overlapping clinical manifestations yet distinct therapeutic approaches. TB is characterized by a chronic progression, accompanied by constitutional symptoms and specific radiological features such as lymphadenopathy and 'tree-in-bud' patterns. By contrast, MPP typically presents with an acute onset, marked by a severe paroxysmal dry cough, and is associated with patchy consolidation and ground-glass opacities on imaging studies. Accurate diagnosis relies on molecular assays, such as Xpert MTB/RIF and PCR, alongside serological testing. The treatment regimen for TB involves prolonged administration of multiple drugs, whereas MPP is generally managed with macrolide antibiotics, although rising resistance is a concern. Therefore, the integration of clinical, radiological, and laboratory data is imperative for precise diagnosis and effective management.

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Correspondence to: Dr Shusong Ruan, Department of Tuberculosis, Guiyang Public Health Clinical Center, 6 Daying Road, Guiyang, Guizhou 550001, P.R. China
E-mail: 13985417291@163.com

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1. Introduction

Tuberculosis (TB) continues to be a predominant infectious cause of mortality among children globally, exerting a particularly severe burden on those under the age of five (1). The clinical diagnosis of pediatric TB has historically encountered significant challenges, largely attributable to its non-specific symptomatology and generally low bacterial load (2,3). In regions with a high prevalence of TB, the identification of pediatric cases predominantly depends on the screening of individuals who have been in close contact with patients exhibiting active pulmonary TB (4). Nevertheless, it is estimated that a substantial number of cases remain undiagnosed, contributing to a 'hidden' reservoir of the disease (5).

Simultaneously, *Mycoplasma pneumoniae* represents another significant pathogen responsible for community-acquired pneumonia (CAP) in pediatric populations (6). Epidemiological studies suggest that it may account for up to 56.9% of acute lower respiratory tract infections necessitating hospitalization in children (7), thereby presenting a considerable public health challenge. Despite the clinical prevalence of *Mycoplasma pneumoniae* pneumonia (MMP), the intricate molecular mechanisms underlying its pathogenesis and the host immune responses remain inadequately understood. In conclusion, both tuberculosis and MPP contribute substantially to the disease burden of respiratory infections among children in developing countries and resource-constrained settings.

The clinical presentation of pediatric tuberculosis is often characterized by non-specific symptoms, commonly including persistent cough, prolonged low-grade fever, night sweats, and weight loss, which are indicative of chronic consumptive processes (Table I). Nevertheless, the clinical phenotype of pediatric TB demonstrates considerable heterogeneity. In cases of children hospitalized with severe pneumonia, the diagnosis of TB is frequently delayed or overlooked, as it is generally considered by clinicians only after the failure of standard antibiotic treatment or the persistence of symptoms (8).

Children with tuberculosis exhibit a higher susceptibility to developing extrapulmonary TB (EPTB) compared to adults, with clinical manifestations that vary markedly based on the organs involved, such as lymph nodes, the central nervous system and bones (9). In some cases, children may initially present with extrapulmonary symptoms, such as tuberculous meningitis, which is characterized by a gradual onset but carries a severe prognosis (10). Among immunocompromised

children, the clinical presentation of TB tends to be more subtle and atypical, often accompanied by rapid disease progression and a markedly increased mortality rate (11). Consequently, it is imperative for clinicians to maintain a heightened level of suspicion and to perform thorough evaluations to prevent missed or incorrect diagnoses.

The clinical presentation of MMP is diverse, encompassing a variety of acute inflammatory conditions ranging from upper respiratory tract infections and bronchitis to pneumonia (12). Characteristic symptoms typically include a paroxysmal, irritating dry cough, fever, and wheezing (Table I). Research indicates that ~27.75% of pneumonia cases in children are attributable to isolated *M. pneumoniae* infection, with a higher prevalence observed in cases involving co-infection with other pathogens, such as viruses or bacteria (7).

The pathogenicity of MMP is intricately associated with the pronounced pulmonary inflammatory response and immune dysregulation it induces, notably characterized by the impairment of alveolar macrophage function (13). In immunocompromised pediatric patients, such as those receiving chemotherapy for leukemia, MPP may manifest as refractory pneumonia, compounded by issues including antibiotic resistance and drug interactions (14). Additionally, the occurrence of mixed infections can substantially aggravate the clinical condition and extend hospitalization duration, indicating a potential synergistic effect that exacerbates disease severity (15).

The considerable overlap in clinical manifestations between pediatric tuberculosis and MMP presents significant challenges for differential diagnosis, as demonstrated in Table I. The two conditions can exhibit common respiratory symptoms such as cough and fever, rendering differentiation based solely on clinical presentation particularly difficult. For example, typical symptoms of TB intoxication, including low-grade fever, night sweats, and fatigue, may also be observed in some children with severe MPP (16,17). Furthermore, the increasing prevalence of macrolide resistance in *M. pneumonia* (18), coupled with the rising incidence of mixed infections in immunocompromised children (14), exacerbates the complexity of differentiation and management.

Accurate differentiation between these two diseases is of considerable clinical and research importance. First, the fundamental etiological differences necessitate entirely distinct treatment regimens; misdiagnosis may result in ineffective treatment, delayed care, and potentially severe adverse drug reactions. Secondly, a thorough understanding of the key differentiating factors enhances clinical decision-making, facilitates the rational allocation of medical resources, and prevents unnecessary investigations and treatments. Moreover, a comprehensive exploration of differential diagnostic strategies is essential for advancing the diagnostic and treatment framework for pediatric respiratory infectious diseases and for improving the overall quality of healthcare.

2. Clinical diagnostic techniques for pediatric pulmonary tuberculosis and MMP

Current diagnostic techniques for pediatric pulmonary tuberculosis. Diagnosing pediatric tuberculosis presents numerous challenges (Table II). The tuberculin skin test (TST), a conventional immunological method, is extensively utilized; however, its results can be confounded by Bacillus Calmette-Guérin (BCG) vaccination and non-tuberculous mycobacterial infections, resulting in diminished specificity. A study involving 53 children with tuberculosis and 92 healthy children reported a TST sensitivity of 83.0% and a specificity of 100.0%. Nevertheless, specificity is reduced in BCG-vaccinated children (19). Microbiological tests, such as sputum smear microscopy for acid-fast bacilli and culture, are considered the gold standard for diagnosis. However, children often face challenges in producing sputum, and infections are frequently paucibacillary, which leads to low smear positivity rates. Additionally, culture methods are time-consuming and exhibit limited sensitivity, reported to be as low as ~12% in some pediatric studies (20).

The advent of molecular diagnostics has markedly transformed the rapid diagnosis of pediatric tuberculosis. The Xpert MTB/RIF assay facilitates the swift detection of *Mycobacterium tuberculosis* complex and rifampicin resistance, demonstrating greater sensitivity compared to traditional smear microscopy. According to a systematic review and meta-analysis, the Xpert MTB/RIF assay exhibited a pooled sensitivity of 62% and a specificity of 98% when applied to sputum samples for pediatric pulmonary TB. For gastric aspirate samples, the sensitivity was 66% and the specificity remained 98% (20). However, the sensitivity for paucibacillary samples continues to be suboptimal, and the associated costs and equipment requirements pose challenges to its widespread implementation in resource-limited settings.

Current diagnostic techniques for MMP. The diagnosis of MMP is contingent upon an integration of laboratory and radiological assessments (Table II). Serological assays, particularly those detecting *M. pneumoniae*-specific IgM antibodies, are frequently employed in clinical settings to suggest recent infection. Nevertheless, the sensitivity of these tests is constrained by the temporal window of antibody production and the variability in individual immune responses, which may result in false-negative outcomes. In a study involving 183 pediatric patients diagnosed with MPP, it was observed that 31% exhibited seroconversion, while the remaining seropositive individuals demonstrated a four-fold or greater increase in diagnostic IgM antibody titers during their hospitalization (21).

Nucleic acid detection methodologies, such as PCR, facilitate the direct identification of pathogen nucleic acids, thereby providing high sensitivity and specificity, which are particularly advantageous for early diagnostic purposes. Nonetheless, these methodologies necessitate advanced laboratory environments and are susceptible to false-positive results due to contamination, thereby requiring interpretation in conjunction with clinical findings (22).

Imaging modalities, including chest X-ray and computed tomography (CT), can identify pulmonary inflammatory alterations, such as ground-glass opacities and consolidation. However, these imaging findings lack specificity for particular pathogens and necessitate differentiation from pneumonias induced by other infectious agents. A retrospective analysis involving 126 pediatric patients with CAP substantiated that radiological characteristics alone are insufficient for

Table I. Symptom comparison between pediatric pulmonary tuberculosis and *Mycoplasma pneumoniae* pneumonia.

Feature	Pediatric pulmonary tuberculosis	*Mycoplasma pneumoniae* pneumonia
Fever pattern	Chronic low-grade (mainly afternoon, may resolve spontaneously)	Acute high fever (persists 1-3 weeks, requires intervention)
Cough pattern	Mild dry cough, persists for months, no significant worsening	Intense paroxysmal dry cough (worse at night), mild initially, worsens later
Systemic symptoms	Night sweats, weight loss, poor appetite (prominent)	Sore throat, headache (transient, no long-term impact)
Disease duration	Weeks to months (chronic)	1-3 weeks (acute, can resolve with appropriate treatment)

Table II. Comparison of diagnostic methods for pediatric pulmonary tuberculosis and *Mycoplasma pneumoniae* pneumonia.

	Pediatric pulmonary tuberculosis		*Mycoplasma pneumoniae* pneumonia	
Category	Method	Characteristics	Method	Characteristics
Etiological tests	Sputum smear	Rapid screening	Mycoplasma culture	Time-consuming, gold standard
	Sputum Culture	Time-consuming, high accuracy		
Molecular tests	Nucleic acid test (such as Xpert)	Rapid, high sensitivity	Nucleic acid test (PCR)	Rapid, high sensitivity
	Targeted next-generation sequencing	Highest sensitivity, expensive		
Serological tests			*M. pneumoniae* Antibody	Potential false negative early
Immunological tests	Tuberculin skin test (PPD)	Affected by BCG vaccination		
	Interferon-gamma release assays	High specificity, unaffected by BCG		
Imaging	Chest X-ray	Low cost, lower accuracy	Chest X-ray	Non-specific
	Chest CT	High accuracy	Chest CT	Non-specific

CT, computed tomography; BCG, Bacillus Calmette-Guérin vaccine.

distinguishing MMP from viral pneumonia, underscoring the need for integration with clinical and laboratory data (23).

Diagnostic challenges in the context of tuberculosis endemicity. In regions with a high burden of tuberculosis, the diagnosis of both pediatric TB and MMP is fraught with significant challenges. For TB, there exists a dichotomy between the extensive number of suspected cases and the limited availability of diagnostic resources. Additionally, the proliferation of drug-resistant TB strains necessitates the use of diagnostic methods that can swiftly identify resistant strains to inform effective treatment strategies (24).

In the case of MPP, its clinical and radiological symptomatology overlaps with that of TB, as both conditions can manifest with cough, fever, and pulmonary infiltrates, thereby increasing the risk of misdiagnosis. Furthermore, the relatively long incubation period and the early presentation of atypical symptoms associated with *M. pneumoniae* infections often result in delayed medical consultation, thereby missing the optimal window for testing (25). In high TB burden settings, public health resources are frequently allocated primarily towards TB control efforts, which may inadvertently limit the advancement and implementation of diagnostic technologies for other respiratory pathogens, such as *M. pneumoniae*.

Imaging features and differential diagnosis. In pediatric patients, tuberculosis frequently presents on chest imaging as a primary complex, characterized by hilar or mediastinal lymphadenopathy and indications of bronchial compression, with cavitation potentially developing at a later stage (26) (Fig. 1, Table III). High-resolution computed tomography (HRCT) provides enhanced visualization of diffuse miliary nodules, which are predominantly located in the lower lobes (27). In children with compromised immune systems,

Table III. Comparison of imaging features between pediatric pulmonary tuberculosis and *Mycoplasma pneumoniae* pneumonia.

Feature	Pediatric pulmonary tuberculosis	*Mycoplasma pneumoniae* pneumonia
Typical lesion location	Upper lobe apical/posterior segments, lower lobe superior segments	Lower lobes (superior segments, lateral basal segments)
Key associated findings	Hilar/mediastinal lymphadenopathy (common)	No lymphadenopathy
Characteristic lesion morphology	Primary complex, late calcification	No specific morphology, mainly patchy/fluffy opacities
Resolution speed	Slow (months to half a year)	Relatively fast (significant improvement in 1-2 weeks)

Table IV. Comparison of treatment regimens for pediatric pulmonary tuberculosis and *Mycoplasma pneumoniae* pneumonia.

Feature	Pediatric pulmonary tuberculosis	*Mycoplasma pneumoniae* pneumonia
Treatment core	Eradicate *M. tuberculosis*, prevent resistance	Inhibit *M. pneumoniae*, alleviate symptoms
Drug types	Anti-tuberculosis chemotherapy (combination therapy)	Macrolides, etc. (often monotherapy)
Treatment duration	6-24 months (long-term)	3-14 days (short-term)
Stopping criteria	Complete full course plus lesion calcification/ resolution	Symptom resolution plus radiological resolution
Key risks	Self-discontinuation risks resistance, drug-induced hepatotoxicity	Macrolide resistance (some cases), drug-induced gastrointestinal upset

TB may manifest atypically, presenting as segmental consolidation or mass-like pneumonia (26). Positron emission tomography-computed tomography (PET-CT), a functional imaging technique, is capable of detecting heterogeneity in the preclinical stages of TB infection (28).

Characteristic CT manifestations of MMP typically include patchy ground-glass opacities and consolidation predominantly located in the peripheral lung zones (29) (Fig. 2, Table III). In certain instances, multiple pulmonary nodules may be observed, which can persist beyond the resolution of the acute infection, thus becoming a distinctive imaging feature (30). The application of dual-energy CT has enhanced the diagnostic capability for MPP-associated pulmonary embolism by providing more detailed information on pulmonary vascular perfusion (31). In severe cases of MPP, diffuse alveolar damage may occur, which is depicted on imaging as bilateral diffuse exudative lesions, indicative of significant pulmonary inflammation and immunopathological injury (13).

HRCT plays a crucial role in differentiating between pediatric tuberculosis and MMP. In cases of TB, HRCT is adept at accurately depicting characteristic lesions, including subtle miliary nodules, the 'tree-in-bud' sign, and cavitation (27,32). Conversely, in MPP, HRCT is more effective in illustrating changes that predominantly affect the interstitium and exhibit a centrilobular distribution, such as ground-glass opacities, centrilobular nodules, and thickening of the bronchovascular bundles. The variations in distribution patterns and lesion characteristics observed on HRCT provide essential evidence for differential diagnosis.

Serial imaging follow-up is essential for evaluating treatment response and prognosis in both tuberculosis and MMP. In the context of effective anti-TB therapy, radiological improvements are generally gradual, characterized by the slow resolution of pulmonary infiltrates and the reduction in lymph node size. Research indicates that miliary nodules may completely resolve after ~8 months of standard treatment (33).

Conversely, radiological improvements in MPP tend to occur more rapidly, with significant absorption of ground-glass opacities and consolidation typically observable within one to two weeks of effective treatment. Nonetheless, in certain refractory MPP cases, improvement may be delayed, and there may be occurrences of pleural effusion or worsening consolidation, suggesting disease progression. Importantly, even after clinical symptoms have resolved, pulmonary nodules may persist on CT scans in some pediatric patients (30). In specific populations, such as individuals post-chemotherapy for leukemia, immune status plays a critical role in influencing the radiological progression of pulmonary inflammation (13). Consequently, dynamic radiological assessment in complex cases should be consistently integrated with clinical manifestations and laboratory findings (34).

3. Treatment strategies for pediatric pulmonary tuberculosis and MMP

Treatment strategies and drug selection for pediatric pulmonary tuberculosis. The management of pediatric tuberculosis is guided by the principles of 'early, combined, appropriate, regular, and full course' therapy (Table IV). First-line anti-TB medications include isoniazid, rifampicin, pyrazinamide, and ethambutol. The standard initial treatment regimen typically comprises a 2-month intensive phase involving a four-drug combination (HRZE), followed by a 4-month continuation phase with a two-drug combination (HR) (32).

Isoniazid exhibits strong bactericidal activity; however, careful monitoring is required due to its potential hepatotoxicity. A study indicated that ~0.9% of children undergoing a 9-month isoniazid preventive therapy experienced hepatotoxicity (35). Rifampicin is effective against both intracellular and extracellular bacilli, with common adverse effects including gastrointestinal disturbances and liver function abnormalities. Pyrazinamide is particularly effective against persisters in acidic environments, whereas ethambutol primarily acts in a bacteriostatic manner to prevent the development of resistance.

The management of drug-resistant tuberculosis is notably more intricate, necessitating the use of second-line pharmacological agents, which are chosen based on drug susceptibility testing (DST). These agents include fluoroquinolones and injectable aminoglycosides. Nonetheless, there is a paucity of safety and efficacy data regarding the use of second-line drugs in pediatric populations. Additionally, the increased incidence of adverse effects presents significant clinical challenges (36).

Treatment strategies and drug selection for MMP. Macrolide antibiotics, such as azithromycin and clarithromycin, are the preferred treatment for pediatric MMP (Table IV). Azithromycin is frequently administered in short courses of 3-5 days due to its high tissue concentration and prolonged half-life. Research indicates that sequential therapy with azithromycin offers advantages over intravenous erythromycin by reducing the duration of fever and persistence of cough (37).

Nevertheless, the global prevalence of macrolide-resistant *M. pneumoniae*, particularly in Asia where resistance rates can reach 80-90%, poses a significant challenge to treatment efficacy (38). In cases of macrolide resistance or treatment refractory conditions, alternative antibiotics such as tetracyclines (such as doxycycline or minocycline) or fluoroquinolones may be considered. However, the use of tetracyclines in children is associated with potential adverse effects on tooth and bone development, while fluoroquinolones carry risks of cartilage toxicity. Consequently, their use in pediatric patients necessitates a careful assessment of the risks and benefits.

In cases of severe or refractory MMP, immunomodulatory agents such as corticosteroids are employed to mitigate excessive immune-inflammatory responses. For instance, a study demonstrated that the administration of methylprednisolone in pediatric patients with refractory MPP resulted in the resolution of fever within three days in certain instances, accompanied by a marked improvement in cough symptoms (39).

Adjustment of treatment strategies in tuberculosis endemic settings. In regions with a high prevalence of tuberculosis, it is imperative to adapt treatment strategies. Enhancing drug resistance surveillance and DST, as well as implementing individualized treatment regimens, are critical for effective TB management. Simultaneously, it is essential to address drug interactions and the management of pediatric patients with co-infections, such as HIV (40).

Regarding MMP, in areas with limited medical resources, outpatient management of mild cases should be encouraged, provided that rigorous follow-up is ensured. In response to the escalating issue of antimicrobial resistance, it is crucial to enforce stringent antibiotic stewardship while actively exploring new antimicrobials and treatment strategies (25).

4. Technological advances in pediatric pulmonary TB and MMP

Recent advances in diagnosis and treatment of pediatric pulmonary TB. In the field of diagnostics, interferon-gamma release assays (IGRAs) represent advanced immunological techniques that offer greater specificity than the traditional TST and are not influenced by prior BCG vaccination. Research indicates that the sensitivity of IGRAs for diagnosing pediatric tuberculosis varies between 62.3 and 100.0%, with specificity reaching up to 97.8% (19).

Concurrently, molecular diagnostic methods are undergoing continuous optimization, with the development of novel nucleic acid amplification techniques that enhance both sensitivity and specificity. Additionally, the investigation of innovative biomarkers, such as nucleic acid detection from tongue swabs and the identification of specific serum cytokines or proteins, presents promising new diagnostic pathways. Although a number of these approaches remain in the research stage, they hold significant potential for early diagnosis and monitoring of treatment efficacy (41).

In terms of treatment, the introduction of new anti-tuberculosis medications, such as bedaquiline and delamanid, offers alternative options for managing drug-resistant or refractory TB cases. Concurrently, advancements in drug formulations, including fixed-dose combinations tailored for pediatric use, are designed to improve treatment adherence (42).

Recent advances in diagnosis and treatment of MMP. In the field of diagnostics, rapid antigen test kits serve as efficient and expedient early screening tools within primary care environments, despite their sensitivity being ~60%, which is lower than that of PCR (43). Furthermore, the Crispr-based Rapid Assay Device for Field Testing platform has effectively combined CRISPR/Cas12a with RPA technology to develop a portable, integrated point-of-care testing system capable of sample processing, nucleic acid extraction, amplification and detection. This system offers significant advantages, including a rapid detection time of 35 min, a sensitivity of 100 copies/μl, 100% clinical concordance and cost-effectiveness, thereby addressing the existing gap in *Mycoplasma pneumoniae* detection for field applications.

In the field of biomarker research, serum lactate dehydrogenase (LDH) and its isoenzymes, along with C-reactive protein, have been validated as correlates of MMP severity, thereby assisting in the prediction of refractory cases. A particular study demonstrated that the serum levels of LDH isoenzymes (LDH4 + LDH5) were more effective than total LDH levels in diagnosing refractory MPP, achieving an area under the curve of 0.829 and identifying an optimal cutoff value of 109.4 IU/l (44).

In terms of treatment, minocycline has exhibited significant efficacy against macrolide-resistant strains. In addition to antibiotic therapy, bronchoscopic techniques are increasingly employed in the management of MPP complications, such as

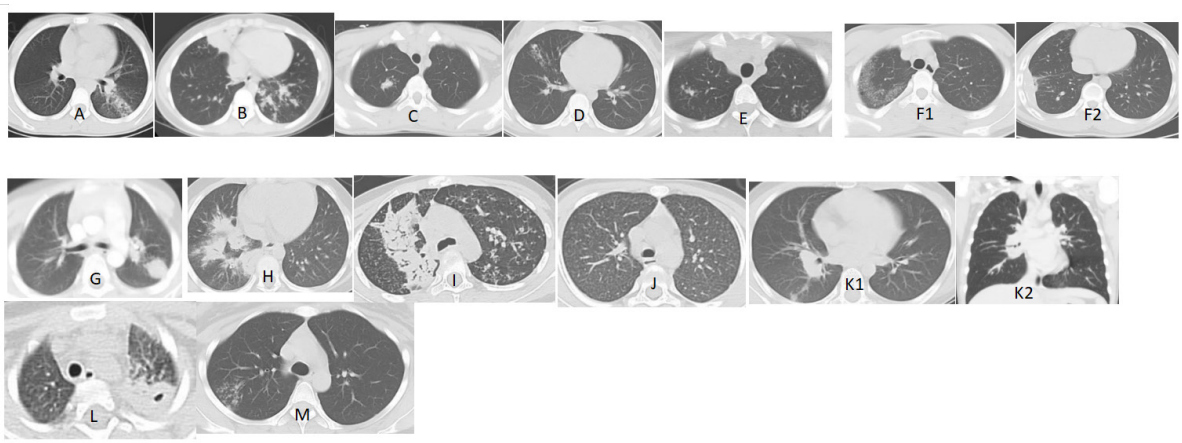

Figure 1. Characteristic imaging images of pediatric pulmonary tuberculosis. (A) Left lower lobe: Patchy, nodular, punctate and linear areas of increased density. (B) Bilateral lower lobes and right middle lobe: Punctate and patchy areas of increased density; lesions with heterogeneous density and ill-defined margins; right middle lobe: Patchy consolidation. (C) Right upper lobe: Patchy and linear areas of increased density, with relatively well-defined margins and punctate calcifications. (D) Right middle lobe: Scattered punctate and nodular areas of increased density. (E) Right middle lobe and left upper lobe: Multiple punctate and nodular areas of increased density. (F1 and F2) Right upper lobe: Multiple patchy areas of increased density, with heterogeneous density; reduced right hemithorax volume; thickened pleura; a spindle-shaped area of high density with partial calcification in the pleural space. (G) Left upper lobe: A nodular opacity measuring ~17 mm, with heterogeneous density, ill-defined margins, and scattered punctate and linear opacities surrounding it. (H) Right upper, middle and lower lobes: Confluent patchy, patchy and nodular areas of increased density. (I) Right upper lobe: Caseous pneumonia. (J) Bilateral lobes: Miliary nodular opacities. (K1 and K2: Primary complex. (L) Left upper lobe: Large, patchy areas of increased density and consolidated lesions with cavities. (M) Right upper lobe: Tree-in-bud pattern.

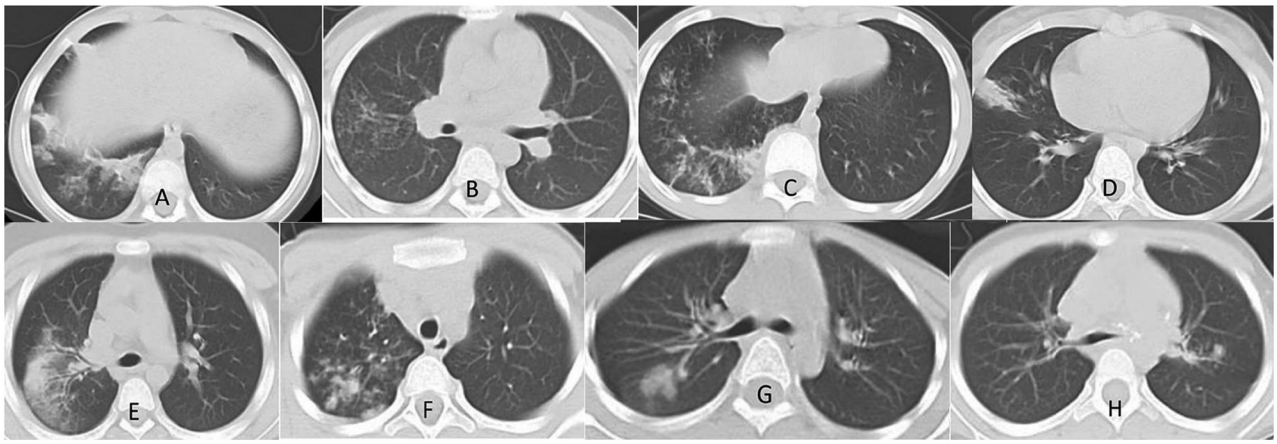

Figure 2. Characteristic imaging images of pediatric *Mycoplasma pneumoniae* pneumonia. (A) Right middle lobe and right lower lobe: Patchy and cloud-like areas of increased density, with heterogeneous density. (B) Posterior and apical segments of the right upper lobe: Multiple punctate and small nodular areas of increased density, with small tree-in-bud pattern. (C) Along the bronchovascular bundles: Patchy, punctate and cloud-like areas of increased density, with ill-defined margins and local connections to the pleura. (D) Right middle lobe: Patchy areas of increased density, with relatively well-defined margins. (E) Right upper lobe: Patchy, ground-glass areas of increased intensity, partially consolidated, with air bronchogram signs. (F) Right upper lobe: Punctate and patchy areas of increased density, with ill-defined margins. (G) Bilateral lobes: Patchy, cloud-like and punctate areas of increased density, with ill-defined margins. (H) Apical-posterior segment of the left upper lobe: Scattered punctate, small nodular and linear areas of increased density, with some ill-defined margins, heterogeneous density, locally punctate nodular densities and partial tree-in-bud pattern.

atelectasis and mucus plugs, facilitating improved ventilation and promoting patient recovery (45).

5. Summary and core conclusions

Summary of key differentiating points. The differential diagnosis between pediatric TB and MMP necessitates the integration of clinical, laboratory, and radiological data. TB typically presents with a chronic progression, often accompanied by symptoms of TB intoxication such as night sweats and weight loss. By contrast, MPP is characterized by an acute onset, frequently manifesting as a pronounced, irritating dry cough (Figs. 3 and 4). From a laboratory perspective, the diagnosis of TB is increasingly moving away from traditional low-sensitivity microbiological techniques towards molecular diagnostics, such as the Xpert MTB/RIF Ultra assay. Conversely, the diagnosis of MPP predominantly relies on serological and molecular biological methods, with targeted next-generation sequencing of bronchoalveolar lavage fluid demonstrating a pathogen detection rate of 99.4% (7).

Radiologically, TB is often associated with features such as hilar lymphadenopathy, the 'tree-in-bud' sign, and cavitation, whereas MPP is primarily indicated by patchy consolidation and ground-glass opacities. In regions with a

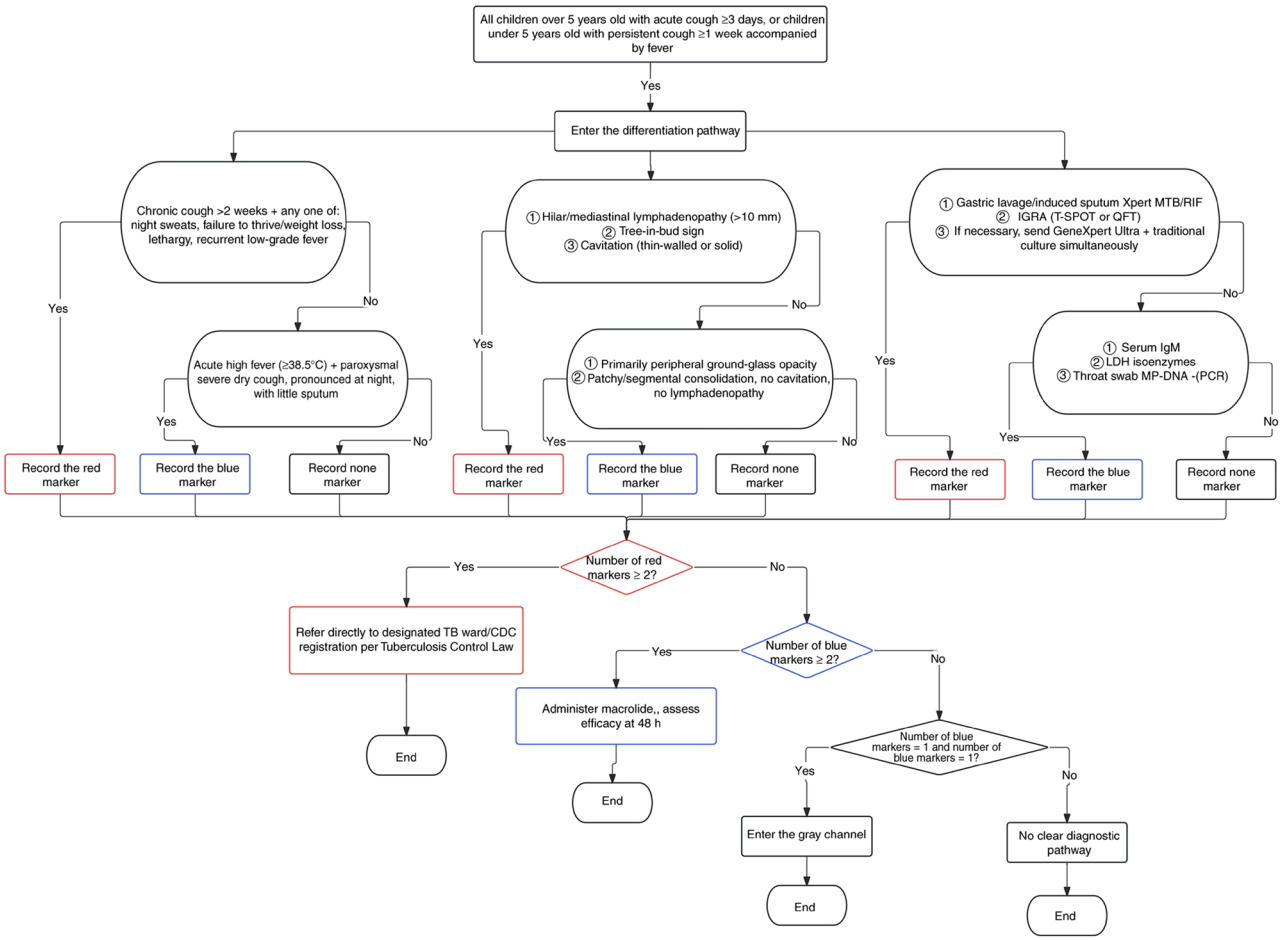

Figure 3. Flowchart for the diagnostic evaluation of pediatric patients with pulmonary tuberculosis and *Mycoplasma pneumoniae* pneumonia infection. IGRA, interferon-gamma release assays; T-SPOT, T-cell spot of tuberculosis test; QFT, QuantiFERON-TB Gold; LDH, lactate dehydrogenase; MP-DNA, M*ycoplasma pneumoniae* DNA.

high burden of TB, the presence of mixed infections and atypical presentations necessitates heightened clinical vigilance. Additionally, serum biomarker analysis has shown promise in the diagnosis of pediatric TB, with sensitivities reaching 87.5 and 83.9% for culture-positive and culture-negative cases, respectively (46).

Clinical practice recommendations. For children with suspected TB, it is advisable to utilize multiple specimen types, such as gastric aspirate, sputum and tongue swab, for molecular testing to enhance detection rates (47). Clinicians must maintain a high level of awareness regarding macrolide resistance in MMP and consider this possibility in cases of treatment failure. In regions with a high burden of TB, systematic TB screening should be integrated into the routine evaluation of children presenting with pneumonia to minimize missed diagnoses and diagnostic delays (8). For complex cases, multidisciplinary team (MDT) consultation to formulate subsequent treatment plans can reduce misdiagnosis.

Radiological assessments should be closely aligned with clinical findings, with HRCT being particularly useful for distinguishing complex cases (23). In immunocompromised children, such as those undergoing post-chemotherapy treatment for leukemia, the possibility of mixed infections should be considered (13). A multidisciplinary, collaborative approach is recommended to develop individualized management plans for complex cases. In resource-limited settings, validated clinical decision support tools should be considered, along with the active implementation of rapid molecular diagnostics.

Treatment strategies should be meticulously tailored according to the etiological diagnosis and DST outcomes. TB management necessitates a comprehensive regimen characterized by the consistent and appropriate use of a combination of drugs throughout the entire course of treatment. By contrast, the management of MMP demands careful consideration of resistance patterns and prompt adjustments to the therapeutic regimen. Simultaneously, it is imperative to enhance health education for patients and their families to bolster treatment adherence, facilitate recovery, and mitigate the risk of transmission.

Research prospects. Future research should prioritize the development of highly sensitive and specific novel biomarkers, such as serum-based assays exemplified by the MAP-TB test, which has demonstrated an 81.7% sensitivity for diagnosing pediatric tuberculosis (46,48). Multi-omics technologies present new opportunities for elucidating the pathogenesis of MMP, although their clinical applicability awaits validation through large-scale studies (10). Artificial intelligence-assisted imaging diagnostic systems hold promise for differential

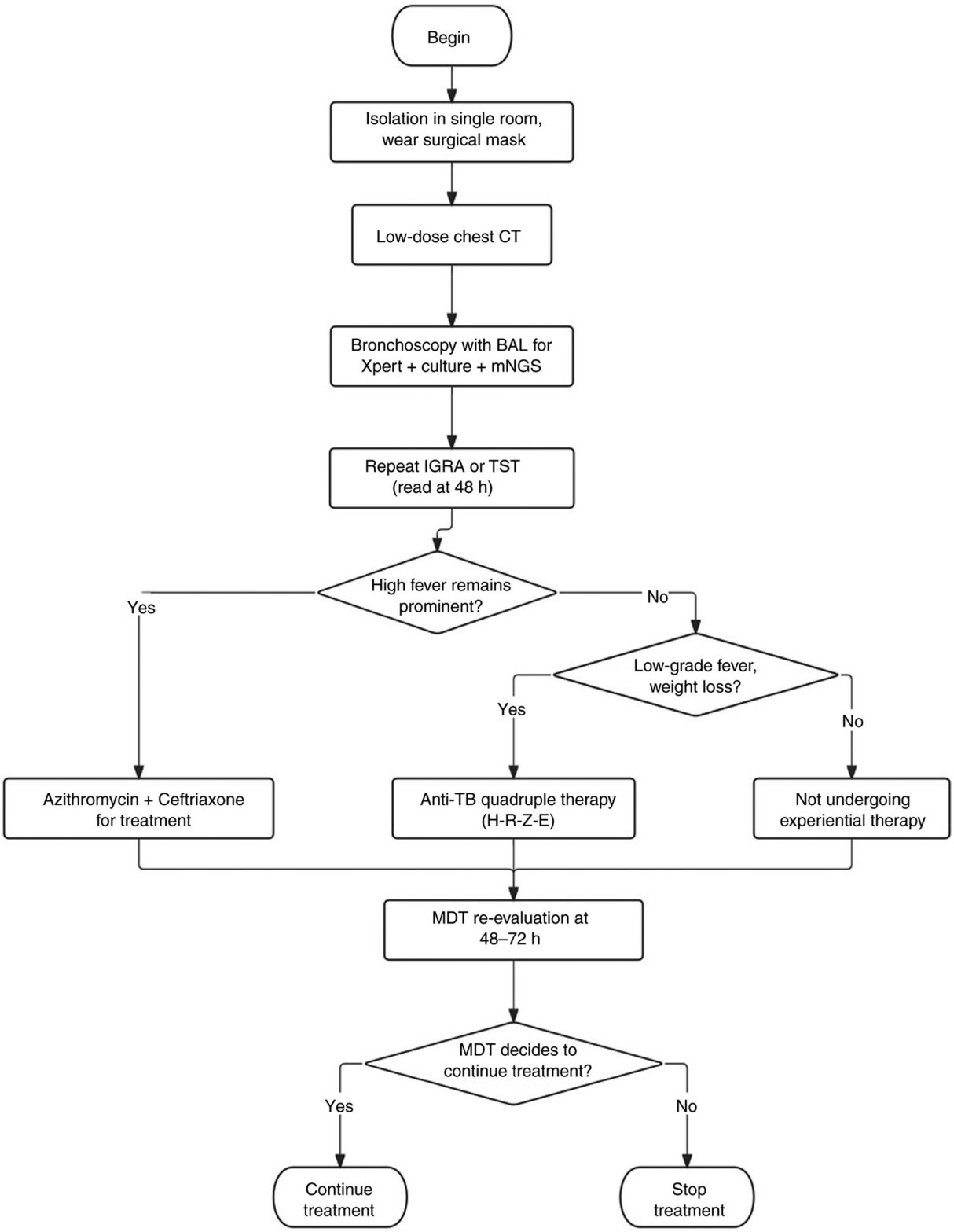

Figure 4. Diagram of the diagnostic process for childhood tuberculosis and *Mycoplasma pneumoniae* pneumonia, depicted in the grey channel. CT, computed tomography; BAL mNGS, bronchoalveolar lavage combined with metagenomic next generation sequencing; IGRA, interferon-gamma release assays; TST, tuberculin skin test; TB, tuberculosis; MDT, multidisciplinary team.

diagnosis, yet require further prospective studies to confirm their efficacy.

In the realm of TB prevention, it is imperative to assess the effect of new vaccines on the pediatric TB spectrum. For MPP, intensified research into resistance mechanisms and the development of new drugs is essential. Additionally, the establishment of international multicenter collaborative networks is crucial for standardizing diagnostic criteria and data collection related to pediatric respiratory infections, thereby facilitating the generation of higher-level evidence-based medical

insights. Finally, optimizing differential diagnostic strategies for special populations, such as HIV-infected and malnourished children, should be prioritized to reduce mortality rates in these high-risk groups (5).

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Availability of data and materials

Not applicable.

Authors' contributions

ZW was responsible for conceptualization, data curation and formal analysis. QY was responsible for data curation and validation. HL was responsible for methodology. RQ was responsible for conceptualization and supervision. SR was responsible for conceptualization, project administration, resources, supervision, writing review, and editing. Data authentication is not applicable. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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