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Case Report

Severe Fulminant Hypoxemic Respiratory Failure Secondary to *Mycoplasma Pneumoniae* in a Previously Healthy Adult Patient: A Case Report

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Abstract

Background: *Mycoplasma pneumonia (M. pneumoniae)* is a common cause of community-acquired pneumonia, usually presenting as a mild respiratory illness. However, severe complications, including Acute Respiratory Distress Syndrome (ARDS), can occur, even in previously healthy individuals. The Centers for Disease Control and Prevention has reported an increase in *M. pneumoniae* infections, particularly among young children, coinciding with rising cases of macrolide-resistant strains. Early diagnosis remains challenging due to the organism's atypical presentation, and the need for targeted therapy is critical to managing severe cases effectively.

Case Presentations: A 40-year-old previously healthy male presented with one week of progressively worsening respiratory symptoms, including fatigue, myalgias, and a productive cough. Initial investigations revealed leukocytosis, and chest imaging showed bilateral pneumonia with areas of consolidation. Despite empiric therapy with ceftriaxone and azithromycin, his condition worsened, and he required mechanical ventilation for ARDS on Day 3. Bronchoalveolar Lavage (BAL) confirmed *M. pneumoniae* as the causative pathogen. After de-escalating antimicrobial therapy and following the ARDS mechanical ventilation protocol with prone positioning, the patient was extubated on Day 8 and, by Day 14, required only minimal oxygen support.

Conclusions: Severe *M. pneumoniae* infections, such as ARDS, can occur in previously healthy individuals, requiring rapid diagnosis and intensive care. This case underscores the importance of Polymerase Chain Reaction (PCR) testing and Bronchoalveolar Lavage (BAL) for accurate diagnosis. With the increasing virulence of *M. pneumoniae*, potentially due to macrolide resistance, early diagnosis and timely treatment with azithromycin remain essential, although alternative therapies may be needed for resistant strains. Ongoing surveillance and updated treatment strategies are critical to managing this evolving clinical challenge.

Keywords: *Mycoplasma pneumoniae*; Acute Respiratory Distress Syndrome; Fulminant pneumonia; Macrolide resistance; Bronchoalveolar lavage

Introduction

Mycoplasma pneumoniae (*M. pneumoniae)* is a common cause of community-acquired pneumonia, typically presenting as a mild respiratory illness. However, in rare cases, it can result in severe complications, including fulminant respiratory failure, even in previously healthy individuals. Recent case reports have documented severe manifestations of *M. pneumoniae* infections, such as Acute Respiratory Distress Syndrome (ARDS), cavitating pulmonary lesions, cardiogenic shock, and electrical storm [1-4]. In response to a surge in *M. pneumoniae* infections, the Centers for Disease Control and Prevention (CDC) has reported a notable increase across the United States, particularly among young children. This resurgence, observed since late spring 2024, coincides with a rise in pneumonia-associated emergency department visits and growing concerns over macrolide-resistant strains. These findings emphasize the importance of heightened clinical vigilance, prompt diagnostic testing, and the judicious use of targeted antibiotic therapies [5]. Despite advancements in diagnostic tools, *M. pneumoniae* remains challenging to detect early due to its atypical presentation, subclinical onset, and delayed confirmation through microbiological methods. The organism's unique pathophysiology, including its ability to evade

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immune defenses by adhering to respiratory epithelium and inducing a robust inflammatory response, plays a critical role in the progression to severe disease [6]. This case report aims to contribute to the existing literature by presenting a fulminant case of *M. pneumoniae* pneumonia in a young, previously healthy adult, highlighting the diagnostic complexities, therapeutic approaches, and clinical outcomes involved in managing such severe presentations.

Case Presentation

A 40-year-old previously healthy male presented to the emergency department with a one-week history of progressively worsening symptoms. His illness began one week prior to his admission with upper respiratory tract symptoms, including fatigue, myalgias, and mild fever. The 48 hours prior to his admission, he developed a productive cough with yellow sputum, dyspnea, and persistent fatigue, which he managed with over-the-counter acetaminophen. On the day of admission, his condition further deteriorated, prompting him to seek medical attention.

At presentation, the patient reported fever (Tmax 38.5°C), myalgias, fatigue, and significant shortness of breath. Initial oxygen saturation was 77% on room air, improving to 92% with high-flow oxygen therapy (Airvo) at FiO_2 60%. He denied any recent travel, smoking, or substance use but identified a sick contact in his child, who had a recent cough. Laboratory investigations revealed leukocytosis (WBC 12.7 × 10^9/L) with neutrophilia (9.9 × 10^9/L) and normal lactate levels. Chest CT performed on admission demonstrated bilateral pneumonia with areas of consolidation and ground-glass opacities, without pleural effusion.

Despite empiric treatment with ceftriaxone and azithromycin, the patient's respiratory status worsened, requiring escalating oxygen support. On Day 3 of admission, he was transferred to the intensive care unit and eventually was intubated for ARDS secondary to severe bilateral pneumonia. His antimicrobial agents were escalated to include piperacillin-tazobactam and he was empirically treated for blastomyces with amphotericin B. A bronchoscopy with Bronchoalveolar Lavage (BAL) was performed on November 22, confirming *M. pneumoniae* as the causative agent. His antimicrobial therapies were de-escalated thereafter and he continued mechanical ventilation with ARDS protocol, including prone positioning for three days.

The patient's condition gradually improved, and he was extubated to non-invasive ventilation on admission day 11. By his 14th day of admission, he required minimal oxygen with significant clinical and radiologic improvement.

Investigations

The initial diagnostic workup for this 40-year-old male patient, presenting with severe community-acquired pneumonia and Acute Respiratory Distress Syndrome (ARDS), included various tests to rule out common causes. A nasal swab collected on hospital day 3 tested positive for *M. pneumoniae* via Nucleic Acid Amplification Testing (NAAT) by PCR. Additionally, Bronchoalveolar Lavage (BAL) samples revealed a positive result for *M. pneumoniae*, while fungal cultures and tests for Legionella, Blastomyces serology, Histoplasma serology, and Pneumocystis jirovecii returned negative. His HIV and IgG, IgA, IgM, Rheumatoid factor and ANA screening were also all negative (see Appendix: Table 1 & 2 for more details).

Chest imaging revealed significant changes over time. A CT pulmonary angiogram on November 18, 2024, initially ruled out pulmonary embolism but showed bilateral pneumonia with right lower lobe consolidation and lingula opacity, consistent with underlying pneumonia. A follow-up CT on November 23 showed worsening left lower lobe consolidation, while improvements were noted in the right lower lobe.

Follow-up CT scan of the chest on admission day 11 revealed resolution of some acinar opacities with improvements overall in the consolidation. Additionally, the patient's central pulmonary arteries were enlarged, suggesting pulmonary arterial hypertension, and a small hypodense nodule in the right adrenal gland, likely an adenoma, was identified.

Given that follow-up imaging showed no evidence of ARDS, the patient's clinical improvement, supported by radiologic resolution and diagnostic findings, allowed for successful extubation to non-invasive ventilation on the same day. He was subsequently required only minimal oxygen with continued progress.

Treatment

Upon admission on Day 1, the patient presented with a one-week history of upper respiratory symptoms and diagnosed with suspected community-acquired pneumonia. Given his presentation and imaging findings, ceftriaxone (2g IV) and azithromycin (500mg IV) were initiated to cover both typical and atypical pathogens, including *M. pneumoniae*. A chest CT revealed bilateral pneumonia with consolidation in the right lower lobe with ground-glass opacities in the upper lobes. Initial laboratory results indicated leukocytosis with a WBC of 12.7 × 10^9/L, supporting the need for antibiotic therapy.

Despite initial treatment, the patient's condition deteriorated, with increased hypoxia and work of breathing. On Day 3, the patient was transferred to the Level 2 ICU for closer monitoring and non-invasive ventilation. Given the progression to acute hypoxemic respiratory failure and concern for ARDS, the patient was intubated and initiated on the ARDS mechanical ventilation protocol, which included prone positioning.

Piperacillin-tazobactam (4.5g IV) was started on Day 3 for broader coverage, while azithromycin was continued for a 10-day course (Day 1–10). Amphotericin B (IV) was initiated on Day 4, given concern for possible fungal infection, and hydrocortisone (50mg IV Q6H) was started on Day 4 for suspected sepsis and the inflammatory response associated with ARDS.

Throughout the patient's ICU course, Infectious Disease and Respiratory specialists were consulted to guide therapy. ID confirmed the diagnosis of *M. pneumoniae* pneumonia and supported the continuation of azithromycin, while initially advising the use of amphotericin B given the severity of the illness and the potential for co-infection. Respiratory consultations focused on managing the ARDS, advising prone positioning, and guiding mechanical ventilation strategies, including the use of ARDS protocol ventilation. On Day 7, after no evidence of fungal infection, amphotericin B was discontinued. By Day 8, the patient's respiratory status showed

significant improvement, allowing for extubation to non-invasive ventilation. At this time, hydrocortisone was tapered and stopped. The patient continued azithromycin through Day 10 while piperacillin-tazobactam was also discontinued on Day 8, as the patient no longer required broad-spectrum coverage.

By Day 10, the patient transitioned to room air with continued improvement in respiratory function. He remained in the ICU for additional monitoring, and his antibiotics were completed as per the treatment plan. On Day 12, the patient was transferred from Level 1 ICU to Level 2 ICU for continued observation and recovery. Respiratory and ID consultations remained involved to ensure ongoing recovery and to address any potential complications. The patient demonstrated ongoing recovery with steady improvement, requiring only minimal supplemental oxygen during this phase (refer to Appendix: Table 3 for additional details).

Discussion

The increasing severity of *M. pneumoniae* infections has become a growing concern in recent years, with more severe cases of pneumonia, ARDS, and respiratory failure requiring intensive care [7-9]. Many health organizations have reported a rise in *M. pneumoniae* infections, particularly among young children, and an increasing number of these cases have been associated with severe complications [10].

The pathophysiology of *M. pneumoniae* pneumonia involves the bacterium's ability to adhere to the respiratory epithelium, particularly in the small airways. *M. pneumoniae* uses specific adherence proteins to attach to the epithelial cells of the respiratory tract. Once attached, it produces hydrogen peroxide and superoxide, which cause damage to the epithelial cells and cilia, leading to inflammation and impaired mucociliary clearance. The bacterium also exhibits a gliding movement, facilitated by specialized tip organelles, allowing it to burrow between cilia, causing further epithelial sloughing. This damage triggers an inflammatory response, activating cytokines that contribute to airway obstruction and impaired gas exchange. In severe cases, this can progress to ARDS, as seen in this patient [11]. Additionally, antibodies against *M. pneumoniae* may cross-react with human tissues, acting as autoantibodies and leading to extrapulmonary manifestations such as immune thrombocytopenic purpura, autoimmune hemolytic anemia, and neurological complications like transverse myelitis [12]. The absence of a cell wall in *M. pneumoniae* makes it resistant to beta-lactam antibiotics, complicating treatment. This, along with its ability to cause both respiratory and systemic inflammatory responses, presents challenges in managing severe cases of *M. pneumoniae* infection.

The increasing virulence of *M. pneumoniae* infections can be attributed to several factors. A key contributor is the emergence of macrolide-resistant strains, which have become more prevalent and make treatment more challenging. These resistant strains, primarily due to mutations in the 23S ribosomal RNA gene, reduce the effectiveness of macrolides, such as azithromycin, leading to prolonged illness and severe complications, including pneumonia progressing to ARDS [13]. Host factors also play a significant role; individuals with weakened immune systems, such as those with chronic diseases, immunosuppressive therapies, or previous respiratory infections, are more vulnerable to severe outcomes. Their immune response may be less effective, leading to prolonged inflammation, tissue damage, and greater risk of complications like ARDS [14]. Additionally, genetic adaptations within *M. pneumoniae* may enhance its virulence, enabling the bacterium to better adhere to and invade respiratory epithelial cells, evade the immune system, and persist within the host [15]. These genetic changes may make the infection more difficult to control and contribute to more severe disease. Lastly, crowded environments such as schools, healthcare facilities, and dormitories facilitate the rapid spread of *M. pneumoniae*, particularly more virulent strains, which increases the risk of severe infections in otherwise healthy individuals [16]. The close proximity in these settings accelerates transmission, making it easier for resistant and virulent strains to propagate. Together, these factors—macrolide resistance, host immune factors, genetic adaptations, and crowded settings—contribute to the growing severity of *M. pneumoniae* infections, emphasizing the need for enhanced diagnostics, treatment strategies, and surveillance to address this rising concern.

Accurate diagnosis of *M. pneumoniae* pneumonia is crucial for appropriate treatment. Traditionally, diagnosis has relied on antigen detection tests, such as enzyme immunoassays or lateral flow tests, but these can lead to false positives due to cross-reactivity with other pathogens [17]. Polymerase Chain Reaction (PCR) testing, however, offers greater sensitivity and specificity, allowing for more accurate detection even in the absence of viable bacteria. Nasopharyngeal swabs or Bronchoalveolar Lavage (BAL) specimens are commonly used to collect samples for PCR, with BAL being particularly useful in more severe cases. The improved accuracy of PCR in detecting *M. pneumoniae* makes it the preferred method for diagnosis, particularly in hospitalized patients with suspected severe disease [18].

In terms of treatment, azithromycin remains the first-line therapy for *M. pneumoniae* pneumonia, as recommended by current guidelines from the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) [18]. Azithromycin is effective against *M. pneumoniae* due to its ability to inhibit bacterial protein synthesis and its favorable pharmacokinetic properties. The 10-day course of azithromycin administered to this patient aligns with current recommendations and has been shown to reduce the duration of symptoms and prevent progression to more severe forms of pneumonia. While alternatives such as doxycycline and fluoroquinolones are recommended for macrolide-resistant strains, azithromycin remains a cornerstone of treatment in uncomplicated cases [18]. The patient's successful response to azithromycin and other supportive treatments, such as mechanical ventilation and ARDS protocol management, underscores the importance of early diagnosis and timely intervention.

There are limitations to this case report, most notably, the retrospective nature of the study may have impacted the thorough identification, reporting, and documentation in the patient's medical chart. Absence of genomic analysis to identify strain-specific virulence factors and reliance on BAL for diagnosis, which may not be feasible in all clinical settings. Additionally, the lack of serial imaging comparisons limits the visualization of radiologic progression. The increasing severity of *M. pneumoniae* infections highlights the need for heightened clinical awareness, particularly in previously healthy individuals. The pathophysiology of *M. pneumoniae* involves

complex interactions between the bacterium and the host immune system, leading to severe complications such as ARDS. With the rise of macrolide-resistant strains, accurate diagnosis through PCR and appropriate antimicrobial therapy, including azithromycin, remain critical in managing these infections. The patient in this case responded well to a 10-day course of azithromycin, highlighting its continued efficacy in treating severe *M. pneumoniae* pneumonia. As the clinical landscape evolves, ongoing surveillance and timely treatment adjustments will be essential in managing the growing threat of severe *M. pneumoniae* infections.

Conclusion

In summary, severe infections caused by *M. pneumoniae* can manifest as ARDS, even in healthy individuals, necessitating prompt recognition and ICU-level care. This case underscores the importance of considering atypical pathogens as a cause in fulminant respiratory failure and the utility of PCR and BAL in establishing a definitive diagnosis. Further research into the evolving virulence of *M. pneumoniae* and its clinical implications is essential for optimizing management strategies.

Highlights

- This case highlights a rare progression of *Mycoplasma pneumoniae* leading to severe hypoxemic respiratory failure in a previously healthy adult.
- PCR testing and bronchoalveolar lavage (BAL) were essential in confirming *M. pneumoniae* as the cause, demonstrating the value of advanced diagnostic tools in severe cases.
- The emergence of macrolide-resistant strains is a growing concern, stressing the need for accurate diagnosis and timely intervention.
- Azithromycin remains the mainstay of therapy for *M. pneumoniae* pneumonia, despite rising concerns over resistance, due to its efficacy and favorable pharmacokinetics.
- Early recognition and targeted therapy were crucial for the patient's recovery, underscoring the importance of prompt treatment in severe *M. pneumoniae* cases.

Author Statements

Ethical Approval

Ethical approval for the publication of this case report was obtained in accordance with the hospital's guidelines for ethical conduct in case reporting.

Consent for Publication

Written informed consent was obtained from the patient for the publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of Supporting Data

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

Competing Interests: The authors declare that they have no competing interests.

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Author's Contributions

All authors were involved in the conception and design of the article. The primary author drafted the initial manuscript, while the co-authors provided critical revisions for significant intellectual content. All authors reviewed and approved the final version to be published and accepted responsibility for all aspects of the work.

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