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CASE REPORT

An Atypical Pneumonia Case of Quinolone-Refractory *Chlamydia Pneumoniae* Successfully Treated With Omadacycline

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Abstract: Atypical pneumonia caused by *Chlamydia pneumoniae* often presents diagnostic challenges due to its nonspecific symptoms and slow progression. While most cases are mild and self-limiting, severe infections in immunocompetent adults are rare. This report describes a 32-year-old Chinese female with progressive pneumonia unresponsive to empirical quinolone therapy. Bronchoalveolar lavage (BAL) and next-generation sequencing (NGS) identified *C. pneumoniae* as the causative pathogen. The patient showed significant clinical improvement following treatment with omadacycline, a novel tetracycline-class antibiotic. This case highlights the importance of bronchoscopic evaluation, BAL cytology, and NGS in diagnosing atypical pneumonia. It also underscores omadacycline's potential in treating quinolone-refractory *C. pneumoniae* pneumonia.

Keywords: *chlamydia pneumoniae*, atypical pneumonia, bronchoalveolar lavage, next-generation sequencing, omadacycline

Introduction

Pneumonia remains a leading global cause of morbidity and mortality, with atypical pathogens posing significant diagnostic and therapeutic challenges.[1,2] *Chlamydia pneumoniae* (*C. pneumoniae*) is an obligate intracellular bacterium that causes community-acquired pneumonia (CAP).[3,4] Its clinical presentation often mimics viral or mycoplasma infections, leading to frequent misdiagnoses.[1] While most *C. pneumoniae* pneumonia cases are mild, severe and rapidly progressive infections in immunocompetent adults are rare.[5]

Recent meta-analysis data indicate that atypical pathogens—such as *C. pneumoniae, Mycoplasma pneumoniae*, and *Legionella pneumophila*—contribute significantly to severe pneumonia, with an overall pooled prevalence of 8.1% among critically ill patients.[6] Notably, *C. pneumoniae* showed a prevalence of 1.8%, with regional and diagnostic variability influencing detection rates. These pathogens remain endemic in regions such as East Asia and Northern Europe, where delayed diagnosis in immunocompetent individuals may still lead to severe disease progression. Such findings highlight the need for improved early microbiological screening and targeted antibiotic strategies in community-acquired and severe pneumonia cases.

Due to the intracellular nature of *C. pneumoniae*, conventional antimicrobial susceptibility testing is unreliable.[7] Quinolones, macrolides, and tetracyclines are commonly used for treatment.[8] Quinolone-resistant *Chlamydia pneumoniae* has poor viability, and the development of quinolone resistance in this bacterium is not straightforward.[9] Consequently, cases of quinolone-resistant *C. pneumoniae* pneumonia are rarely reported.

Quinolone resistance in *Chlamydia pneumoniae* has been increasingly linked to specific gene mutations, particularly in the *gyrA* gene, which alters DNA gyrase and reduces drug-binding affinity. In addition, mutations in *rpoB* have been associated with resistance to rifamycins, and broader resistance mechanisms—such as alterations in 23S rRNA—may compromise

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macrolide efficacy. These findings, supported by molecular surveillance studies, underscore the growing concern regarding antibiotic resistance in intracellular pathogens.[10] Given the limited number of effective treatments, especially for respiratory *Chlamydia* infections, novel agents such as omadacycline have shown promise. Omadacycline, a next-generation aminomethylcycline, retains activity against tetracycline-resistant strains due to its evasion of efflux-based resistance mechanisms and superior intracellular penetration, offering a viable therapeutic option amidst rising resistance trends.[11]

This report details the case of a previously healthy 32-year-old female whose pneumonia progressed despite empirical ceftazidime and moxifloxacin therapy. Bronchoscopy and BAL supported the diagnosis of atypical pneumonia, while NGS confirmed *C. pneumoniae* as the causative pathogen. Following treatment adjustment to omadacycline, the patient's condition improved. This case underscores the diagnostic value of bronchoscopy, BAL cytology, NGS, and computed tomography severity scoring (CTSS) in pneumonia of unknown origin. Additionally, it explores the role of novel antibiotics in managing resistant atypical pneumonia, contributing to advancements in precision medicine for respiratory infections.

Case Present

Initial Symptoms and First Treatment

On November 17, 2024, a 32-year-old Chinese female developed myalgia without an apparent cause. The patient had been previously healthy with no underlying medical conditions. The next day, she experienced a dry cough without fever, nasal congestion, or rhinorrhea. She visited the emergency department on November 19, where a chest CT scan revealed a left upper lobe lesion covering 50–75% of the area (2, CT Severity Score: 4 Figure 1). The other lung lobes were unaffected (score: 0), bringing the total CTSS to 4. She was administered intravenous moxifloxacin (0.4 g once daily) and ceftazidime (2 g twice daily) for infection control, along with ambroxol for mucus clearance and aspirin for cough relief. Her symptoms showed slight improvement.

CT Image Scoring

To better quantify the extent of lung lesions and their changes over time, the CT Severity Score (CTSS) system is applied.[12] The lungs are divided into five lobes, and each lobe is scored based on the degree of involvement:

- 0. points: No involvement
- 1. point: < 5% involvement
- 2. points: 5% - 25% involvement
- 3. points: 26% - 50% involvement
- 4. points: 51% - 75% involvement
- 5. points: > 75% involvement

Total Score Calculation:

The total score is obtained by summing the scores of all five lobes, ranging from 0 to 25. A higher score indicates more severe pneumonia.

Disease Progression and Second Treatment Phase

On November 20, the patient traveled to Hunan Province for work. During this period, her cough worsened, and she developed a fever. She returned to the emergency department on November 24 with a peak temperature of 38.8°C. Moxifloxacin (Bayer Pharmaceuticals, Germany) and ambroxol were continued, but by November 28, her cough had worsened, with thick sputum, nausea, and vomiting. A follow-up CT scan showed lesion progression, with the left upper lobe involvement increasing to >75% (score: 5), and new involvement in the left lower lobe (25–50%, score: 3), bringing the total CTSS to 8 (Figure 1).

Hospital Admission and Diagnostic Workup

Upon admission, laboratory tests revealed a white blood cell count of 6.7×10^9/L, neutrophil percentage of 75.7% (↑), lymphocyte percentage of 18.0% (↓), hemoglobin of 138 g/L, and platelet count of 222×10^9/L. High-sensitivity

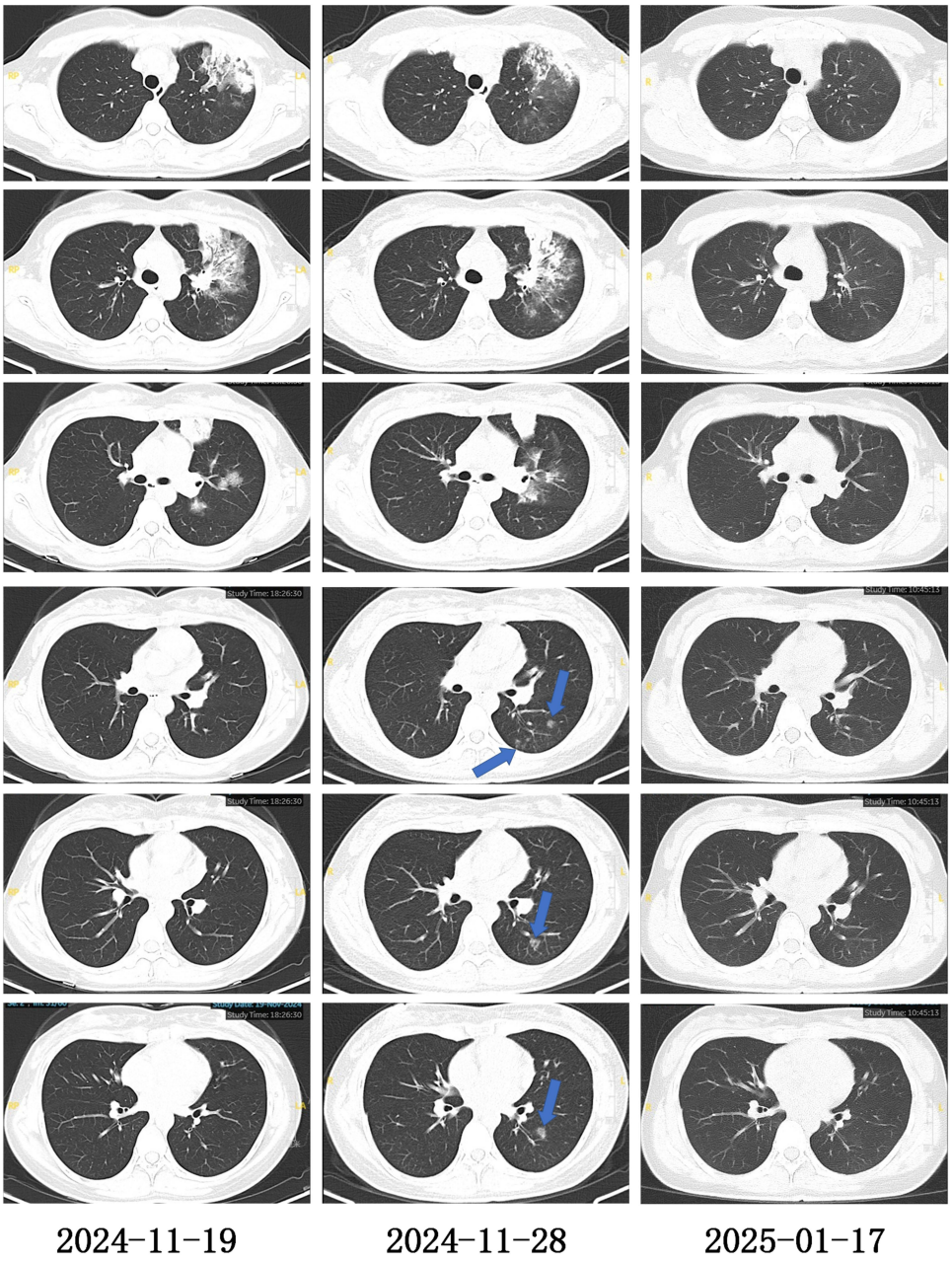

Figure 1 Sequential CT scans with CTSS scores. November 19, 2024: Lesion in the left upper lobe involving 50–75% of the area (score: 4). No significant abnormalities in other lobes (score: 0). Total: 4. November 28, 2024: Lesion in the left upper lobe expanded to >75% (score: 5). New lesion in the left lower lobe affecting 25–50% (score: 3). No abnormalities in other lobes (score: 0). Total: 8. January 17, 2025: Residual lesion in the left upper lobe (≤25%, score: 2). No abnormalities in other lobes (score: 0). Total: 2. Arrows (→) in each panel indicate newly developed pneumonia lesions relative to the prior scan, which were scored in the CTSS assessment.

C-reactive protein was 3.12 mg/L, and erythrocyte sedimentation rate (ESR) was 19 mm/h. Biochemical, coagulation, infectious disease panels, tumor markers, sputum cultures, cryptococcal antigen, and GM tests were normal.

Bronchoscopy on November 29 showed mucus obstruction in the left upper lobe bronchus, with resolution after suctioning (Figure 2). The bronchial mucosa appeared swollen. BAL revealed a reduced macrophage percentage (10.00%↓), increased eosinophils (2.0%↑), and segmented neutrophils (88.0%↑). Microscopy showed enlarged and irregularly shaped macrophages with multinucleation, indicative of *C. pneumoniae*-induced cytoskeletal disruption (Figure 3). Pathological examination confirmed significant lymphocyte and plasma cell infiltration with scattered eosinophils (Figure 4).

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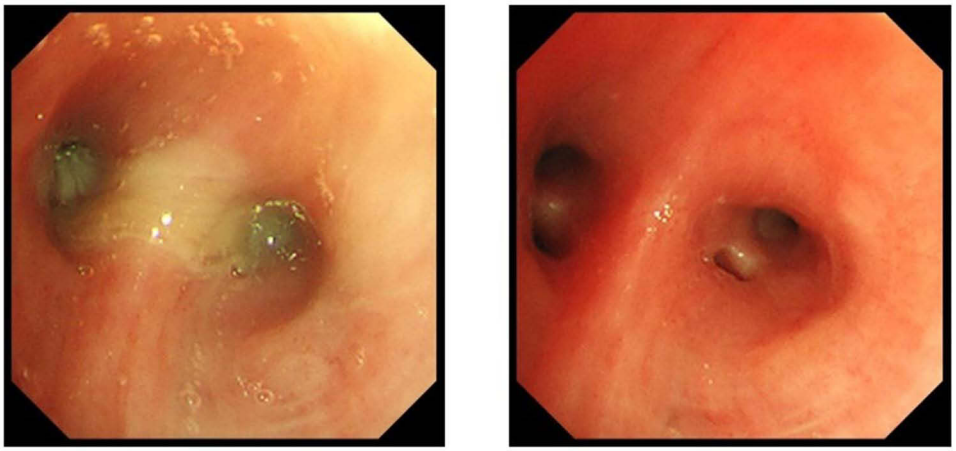

Figure 2 Bronchoscopy revealed mucus obstruction in the lumen of the left upper lobe bronchus. After suctioning, the airway became patent, but bronchial mucosal swelling was observed.

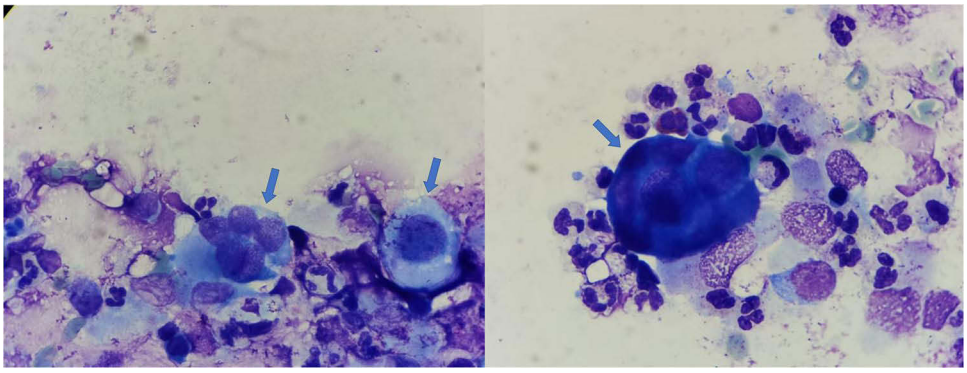

Figure 3 Bronchoalveolar lavage (BAL) fluid cytology. Micrographs demonstrating enlarged, irregularly shaped macrophages with multinucleation. Arrows (→) point to representative multinucleated macrophages, confirming cellular atypia consistent with *Chlamydia pneumoniae* infection.

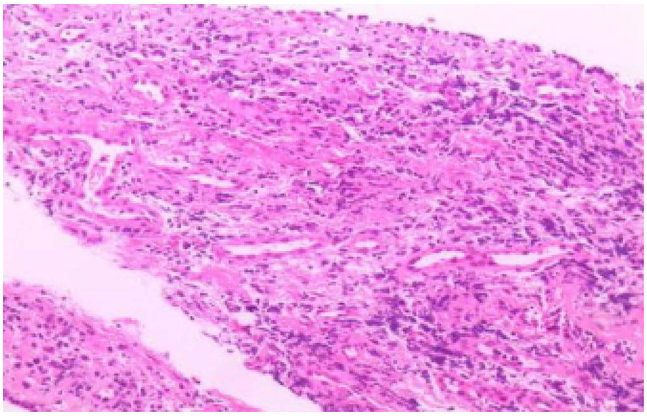

Figure 4 Pathological findings from a bronchoscopic biopsy of the left upper lobe revealed small bronchial mucosal fragments with extensive infiltration of lymphocytes, plasma cells, and a few eosinophils in the lamina propria. Immunohistochemical staining results were as follows: Ki-67 (5%+), P53 (5%+/wild-type), TTF-1 (-), CK7 (epithelial+), P40 (basal cell+), CD3 (T lymphocytes+), CD20 (B lymphocytes+), CD138 (plasma cells+), Kappa (+), Lambda (+), CMV (-). In situ hybridization for EBER was negative.

NGS of BAL fluid identified *C. pneumoniae* as the sole pathogen. Given the patient's lack of response to quinolone therapy, treatment was switched to intravenous omadacycline (200 mg loading dose, followed by 100 mg once daily) on November 30.

Discharge and Follow-Up

The patient was discharged on December 4 with a prescription for oral omadacycline (300 mg once daily for one week). At discharge, her fever had resolved, and her cough and sputum production had significantly improved. A follow-up CT scan on January 17, 2025, showed residual lesions in the left upper lobe (≤25%, score: 2), with no abnormalities in other lobes (score: 0), bringing the total CTSS to 2.

Discussion

Chlamydia pneumoniae (*C. pneumoniae*) is an atypical pneumonia pathogen that is often overlooked in clinical practice despite its significance.[13] The infection typically presents with an insidious onset, with symptoms resembling those of viral or mycoplasma infections. In most cases, *C. pneumoniae* pneumonia is mild and self-limiting.[14] Recent evidence suggests that although *Chlamydia pneumoniae* is traditionally considered an opportunistic pathogen, its impact on immunocompetent hosts may be significantly underappreciated. Delayed diagnosis in these patients can lead to severe clinical deterioration. For instance, Miyashita highlighted that even in patients without underlying diseases, a delayed recognition of *C. pneumoniae* infection could result in rapidly progressive lung damage, particularly in the context of emerging antibiotic resistance.[9] This observation underscores the urgent need for early and precise diagnostic measures in managing atypical pneumonia.

Additionally, due to its intracellular nature and difficulty in cultivation, *C. pneumoniae* presents challenges in clinical diagnostics.[15] In pneumonia cases unresponsive to empirical treatment, bronchoscopy combined with bronchoalveolar lavage (BAL) plays a crucial diagnostic role.[16] In this case, bronchoscopy revealed significant mucus obstruction and bronchial mucosal swelling, while BAL findings showed a decreased proportion of alveolar macrophages, morphological changes, and increased neutrophil and eosinophil proportions. These findings suggest immune dysregulation or epithelial damage caused by the pathogen, supporting the diagnosis of atypical pneumonia.[17] Furthermore, BAL ruled out tuberculosis, fungal infections, and other opportunistic pathogens, providing a basis for precisely adjusting the treatment strategy.

Traditional microbiological methods, such as sputum culture, serological testing, have low sensitivity and prolonged turnaround times in detecting *C. pneumoniae*.[18] In contrast, NGS of BAL fluid allows for rapid and comprehensive pathogen identification with high molecular diagnostic accuracy.[19,20] In this case, NGS confirmed *C. pneumoniae* as the sole pathogen, excluding bacterial co-infection and avoiding unnecessary combination antibiotic therapy, thus optimizing the anti-infective strategy. This case further validates the critical role of NGS in pneumonia diagnostics, emphasizing its potential in reducing antibiotic overuse and improving antimicrobial stewardship (AMS).

In our case, the clinical improvement following the switch to omadacycline was marked and timely. The patient's fever began to resolve within 48 hours of initiating intravenous omadacycline, accompanied by a reduction in sputum production and gradual improvement on serial CT scans, evidenced by a decline in the CT Severity Score (CTSS). These findings are consistent with the data reported by Stets et al, who demonstrated rapid clinical efficacy of omadacycline in community-acquired bacterial pneumonia.[21]

A systematic review and meta-analysis compared the efficacy and safety of omadacycline versus moxifloxacin in the treatment of community-acquired bacterial pneumonia (CABP). The results demonstrated that omadacycline achieved comparable clinical cure and bacterial eradication rates to moxifloxacin, while exhibiting a lower incidence of adverse events—particularly gastrointestinal disturbances and QT interval prolongation. These findings suggest that omadacycline is an effective alternative for treating infections caused by resistant pathogens, especially in patients with moxifloxacin resistance or an elevated risk of QT prolongation.[21] Furthermore, the integration of NGS into the clinical workflow significantly reduced the use of unnecessary broad-spectrum antibiotics in our case, in line with antimicrobial stewardship goals.[22] However, as a single case study, our findings need to be validated with a larger cohort to determine the efficacy of omadacycline against quinolone-resistant *Chlamydia pneumoniae* pneumonia.

Although quinolones such as moxifloxacin are commonly used for atypical pneumonia,[23] this patient's condition worsened despite treatment. Possible reasons include the intracellular survival capability of *C. pneumoniae*, quinolone resistance, and the lack of precise targeting of the pathogen in initial treatment.[24] The switch to omadacycline led to marked clinical improvement, highlighting its efficacy in treating intracellular infections. As a next-generation tetracycline, omadacycline exhibits superior intracellular penetration, broad-spectrum antimicrobial activity, and fewer adverse effects such as QT interval prolongation.[25] This case supports the use of omadacycline as a preferred option for quinolone-refractory pneumonia.

The accurate diagnosis of pneumonia typically relies on a combination of clinical symptoms, imaging, and laboratory tests. Chest computed tomography (CT) has become an essential tool for evaluating the extent and severity of lung lesions.[26] However, the lack of standardized and widely accepted quantitative methods limits its application in precise disease assessment and treatment monitoring.[27] The CT Severity Score (CTSS) system used in this case provided a more objective and quantitative approach to evaluating lung involvement, potentially enhancing the understanding of disease progression and therapeutic response.

Conclusion

This case underscores three critical lessons: (1) Bronchoscopy with BAL and NGS should be prioritized in antibiotic-refractory pneumonia; (2) CTSS provides a quantifiable tool for monitoring disease progression; (3) Omadacycline is a viable alternative for quinolone-resistant intracellular pathogens, warranting further clinical trials.

Ethical Approval

The specimens analyzed in this study were obtained through routine hospital laboratory procedures. The research adhered strictly to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Zhejiang Provincial Hospital of Traditional Chinese Medicine (Approval No. 2024-KS-406-01). Written informed consent was obtained from the patient on December 29, 2024, including permission for the publication of case details. Institutional approval was not required specifically for publication of the case details, as this was covered under the general ethics approval and informed consent process.

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Disclosure

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