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Case Report

Omadacycline treatment of severe *Chlamydia psittaci* pneumonia with septic shock diagnosed via metagenomic next-generation sequencing

Ping Xu[1], Zhitong Huang[2]

[1] *Department of Pharmacy, Heyuan People's Hospital, Heyuan, Guangdong, China*
[2] *Department of Emergency, Heyuan People's Hospital, Heyuan, Guangdong, China*

Abstract

Introduction: Parrot fever, caused by *Chlamydia psittaci*, is a zoonotic disease typically treated with tetracyclines. Omadacycline, a novel aminomethyl tetracycline, has limited reports on its efficacy in severe *Chlamydia psittaci* pneumonia in the literature.

Case presentation: We present a case of a patient with severe *Chlamydia psittaci* pneumonia showing symptoms of chills, high fever, shock, hepatic and renal insufficiency, and acute respiratory failure with copious yellow watery sputum. *Chlamydia psittaci* was confirmed by metagenomic next-generation sequencing (mNGS). Despite initial treatment with moxifloxacin and doxycycline, the patient did not improve and was subsequently discharged after receiving omadacycline.

Conclusions: Our findings highlight the potential of mNGS for rapid diagnosis of *Chlamydia psittaci* pneumonia and suggest omadacycline as a potential therapeutic option for severe cases that do not respond to conventional treatment.

Key words: *Chlamydia psittaci*; severe pneumonia; metagenomic next-generation sequencing; omadacycline; septic shock.

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Introduction

Chlamydia psittaci pneumonia is a rare but significant cause of community-acquired pneumonia (CAP), accounting for approximately 1% of cases [1]. Recently, it has emerged as a global public health research focus [2]. The clinical presentation of *Chlamydia psittaci* pneumonia is complex and variable, ranging from mild flu-like symptoms such as chills, high fever, headache, myalgia, cough, and pulmonary infiltrative lesions to severe pneumonia with respiratory distress, cyanosis, irritability, coma, and shock, and even fatal outcomes [3,4]. Therefore, prompt and accurate pathogenic diagnosis and the appropriate antibiotic selection are critical for optimal prognosis.

Recent studies have highlighted the potential of mNGS in improving the accuracy and timeliness of diagnosis for *Chlamydia psittaci* pneumonia [5,6]. Tetracyclines are the preferred antibiotics for treatment, with macrolides and quinolones also demonstrating efficacy. Omadacycline, a novel aminomethyltetracycline, has shown in vitro activity against atypical pathogens and has been reported as effective in treating severe *Chlamydia psittaci* pneumonia in some cases [7,8]. Here, we present a severe *Chlamydia psittaci* pneumonia complicated by septic shock that did not respond to moxifloxacin and doxycycline but showed successful resolution with omadacycline treatment. Our report highlights the potential of omadacycline as a therapeutic option in challenging cases of *Chlamydia psittaci* pneumonia and the importance of accurate diagnosis and appropriate antibiotic selection for optimal patient outcomes.

Case Presentation

The patient is a 65-year-old male who previously had good health and worked as a dentist in a rural township. He was admitted to the hospital on August 14, 2022, with a fever that persisted for 3 days. The patient developed chills and a fever with a maximum temperature of 39.8 °C after catching a cold 3 days before admission. He received symptomatic treatment, including anti-infection medication (specific treatment unknown), at the local hospital, but his condition gradually worsened with accompanying symptoms of shortness of breath. As a result, he went to the emergency department of Heyuan People's Hospital, where he was treated with ceftriaxone (2 g Qd intravenous (IV)) and aspirin/lysine (0.9 g Qd IV) and was eventually admitted to the Emergency Intensive Care Unit (EICU).

Physical examination revealed the patient’s body temperature was 37 °C, pulse rate was 102 times/min,

respiration rate was 24 times/min, and blood pressure was 90/46 mmHg (maintained by metaraminol bitartrate 8 mg/h). The patient was fatigued and uncooperative during the physical examination, but provided relevant answers. His bilateral pupils were equally round and large, with a diameter of approximately 2.5 mm, and his reflex to light was sensitive. The patient presented with tachypnea (rapid and shallow breathing) and SpO_2 86%. Coarse breath sounds were audible in both lungs, indicating potential respiratory distress. Additionally, evident wet rales were auscultated in the right lower lung. The heart rate was elevated at 102 beats/min but regular in rhythm and free of murmurs. No other abnormalities were observed during the assessment.

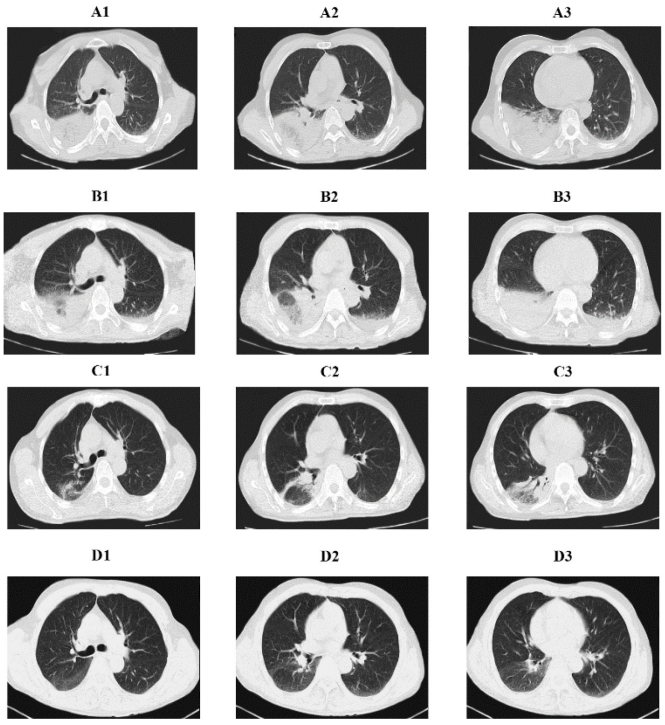
The main laboratory data for this patient are summarized in Table 1. Blood gas analysis (FiO_2: 33%) revealed a pH of 7.54, PO_2 of 58 mmHg, PCO_2 of 32 mmHg, Lac of 1.6 mmol/L, HCO_3^- of 21.8 mmol/L, BE of 5 mmol/L, OI of 176 mmHg. Chest computed tomography (CT) on admission showed inflammation in the lower lobe of the right lung and a small amount of bilateral pleural effusion (Figure 1 A1-A3). Approximately 2 hours after admission, the patient's condition worsened with irritability, shortness of breath, and decreased oxygen saturation to 80%, despite non-invasive ventilator-assisted ventilation. Severe pneumonia, septic shock, and multi-organ dysfunction were diagnosed, and urgent tracheal intubation and ventilator-assisted ventilation were initiated. Fiberoptic bronchoscopy revealed massive yellow watery sputum in the right lung and moderate yellow watery sputum in the left lung. Cefoperazone sulbactam (3 g Q12h IV) and moxifloxacin (0.4 g Qd IV) were given.

Table 1. Main laboratory data.

Laboratory study	Data	Reference values
Hematology		
WBC count	8.5 × 10 ^ 9/L	4.0-10.0 × 10^9/L
Neutrophil (%)	94.6%	50.0-70.0%
Lymphocyte (%)	4.9%	20.0-40.0%
Monocyte count	0.05 × 10^9/L	0.12-0.8 × 10^9/L
PLT count	79 × 10^9/L	100-300 × 10^9/L
Blood Chemistry		
K^+	3.46 mmol/L	3.5-5.1 mmol/L
Glucose	8.92 mmol/L	3.6-6.1 mmol/L
Urea	14.89 mmol/L	1.7-8.3 mmol/L
SCr	130 umol/L	44-115 umol/L
CK	431 U/L	55-170 U/L
LDH	927 U/L	120-246 U/L
Mb	393.9 ng/mL	0-70 ng/mL
Inflammation profile		
PCT	25.57 ng/mL	0-0.1 ng/mL
CRP	26.30 mg/dL	0-1.0 mg/dL
Other		
SARS-CoV-2 RNA	Negative	Negative

WBC: white blood cell; PLT: platelet; K^+: Potassium; SCr: serum creatinine; CK: creatine kinase; LDH: lactate dehydrogenase; Mb: myoglobin; PCT: procalcitonin; CRP: C-reactive protein; SARS-CoV-2 RNA: severe acute respiratory syndrome coronavirus 2 ribonucleic acid.

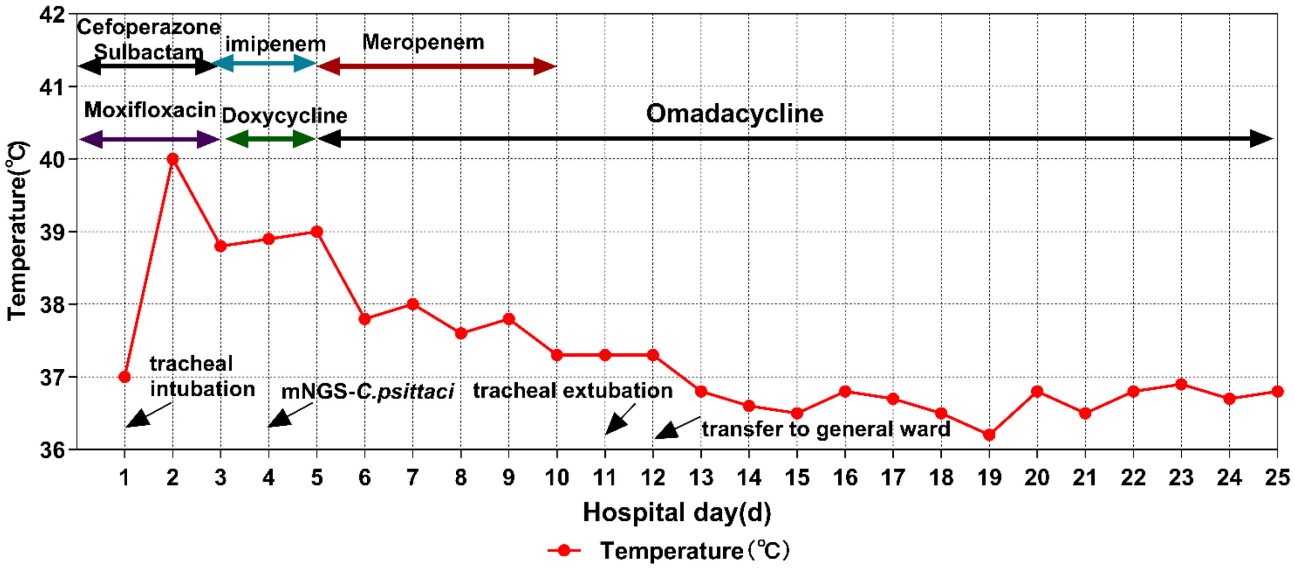
Figure 1. Chest CT presentation of severe *Chlamydia psittaci* pneumonia.



(A1-A3) Day of admission on August 14, 2022. Inflammation in the lower lobe of the right lung with a small bilateral pleural effusion. (B1-B3) Day 12 after admission on August 25, 2022. The right lung lesion is less than before, with a small amount of bilateral pleural effusion and more pleural effusion on the left side. (C1-C3) Day 24 after admission on September 6, 2022. The right lung lesion is significantly reduced compared to the previous one, and bilateral pleural effusion is reduced compared to the previous. (D1-D3) More than 2 months after discharge on November 20, 2022. The right lung lesion was significantly more absorbed, and no pleural effusion was observed.

On day 2 of the initial antibiotic treatment, the patient's condition showed no improvement. He continued to have a fever, with a maximum temperature of 40.0°C, respiration rate of 18 breaths/min, heart rate of 121 beats/min, and blood pressure of 105/76 mmHg (maintained by metaraminol bitartrate 10 mg/h). The patient had a progressive leukocyte decrease, thrombocytopenia, PCT level greater than 50 ng/mL, and increased CRP, blood creatinine, aspartate aminotransferase, and bilirubin levels. Oxygenation remained poor, and large amounts of yellow watery sputum was aspirated between tracheal intubations. Repeated fiberoptic bronchoscopy revealed persistent large amounts of yellow watery sputum in the airways and bronchi of both lungs, which could not be completely removed by aspiration and did not reduce from the previous volume. The dengue virus antigen, as well as Immunoglobulin M antibodies against

Figure 2. Changes in body temperature and antibiotic therapy during hospitalization.



Cefoperazone sulbactam 3 g Q12h IV (day 1-3), moxifloxacin 0.4 g Qd IV (day 1-4), imipenem 1 g Q8h IV (day 3-5), meropenem 2 g Q8h IV (day 5-10), doxycycline 0.2 g Qd IV (day 4-5), omadacycline 0.2 g IV first dose (day 5), 0.1 g Qd IV (day 6-16) and omadacycline 0.3 g Qd po (day 16-25).

respiratory pathogens (*Legionella pneumophila, Mycoplasma pneumoniae, Rickettsia* spp., *Chlamydia pneumoniae,* adenovirus, respiratory syncytial virus, influenza A virus, influenza B virus, and parainfluenza virus), showed all negative results.

On day 3 (August 16, 2022), the patient's condition did not show improvement, with a temperature of 38.8°C, a continued drop in WBC and PLT counts, PCT levels remaining elevated above 50 ng/mL and Empirical adjustment of antibiotics to Imipenem (1 g Q8h IV) and moxifloxacin (0.4 g Qd IV). Considering the severity of the lung infection and uncertainty regarding the pathogen, the patient's family agreed to send the sputum for mNGS to Genskey (Guangzhou Golden Key Medical Laboratory Co., Ltd.).

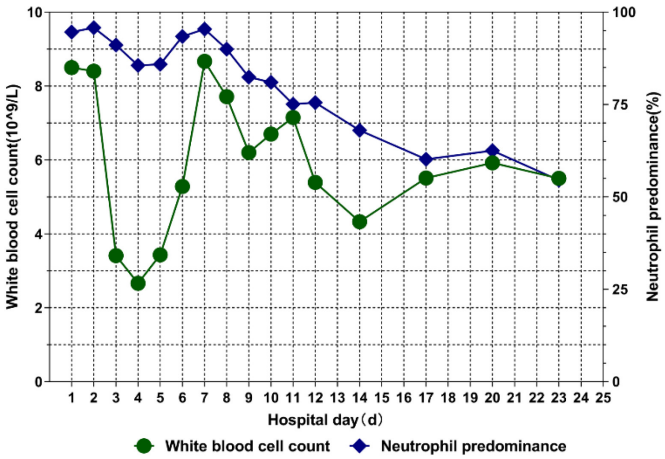
On day 4 (August 17, 2022), the results of sputum mNGS DNA revealed *Chlamydia* spp. with a sequence number of 711864 and a relative abundance of 99.4% and *Chlamydia psittaci* with a sequence number of 473743. Meanwhile, sputum, bacterial blood culture, and (1,3)-β-D-glucan test results were all negative. Based on the clinical manifestations, ancillary examinations, and mNGS results, the diagnosis of severe *Chlamydia psittaci* pneumonia was confirmed, and moxifloxacin was discontinued and replaced with doxycycline (0.2 g Qd IV).

On day 5 (August 18, 2022), after 2 days of doxycycline use, the patient's condition did not improve. The patient continued to have a persistent fever with a maximum temperature of 38.9°C, shortness of breath, poor oxygenation, and fiberoptic bronchoscopy still showed massive yellow sputum in both lungs. There was no reduction in sputum volume. After discussing with the clinical pharmacist, doxycycline was adjusted to omadacycline of 0.2 g IV first dose, followed by 0.1 g Qd IV.

On day 7 (August 20, 2022), after 48 hours of omadacycline, the patient's fever peak decreased compared to the previous day, and the respiratory rate improved. Sputum aspirated at the tracheal intubation was significantly reduced compared to before, and fiberoptic bronchoscopy showed less sputum in the airways and bronchi of both lungs.

On day 9 (August 22, 2022), the patient's circulation

Figure 3. Change in white blood cell count and percentage of neutrophils during hospitalization.



stabilized, vasoactive drugs were discontinued, the fever peak was lower than before (Figure 2), WBC, PCT, and CRP levels showed significant improvement compared to before. Oxygenation was significantly improved as well (Figures 3-5).

On day 11 (August 24, 2022), the patient's condition gradually improved, and indicators such as aspartate aminotransferase and serum creatinine started to recover (Figure 6). The tracheal intubation was successfully removed, and medium-flow oxygen therapy was continued.

On day 12 (August 25, 2022), the patient had no fever, stable respiration, and good oxygenation. Repeat chest CT showed a reduction in the right lung lesion compared to before (Figure 1 B1-B3). The patient was considered stable and transferred to a regular ward.

On day 16 (August 29, 2022), omadacycline was switched from IV to oral administration (tablets, 0.3 g Qd).

On day 24 (September 6, 2022), the chest CT showed a significant reduction in the right lung lesion compared to the previous one (Figure 1 C1-C3). The patient was discharged on day 25 (September 7, 2022). The final diagnosis was severe *Chlamydia psittaci* pneumonia, septic shock, and multiple organ dysfunction. Outpatient follow-up more than 2 months after discharge, the patient had no fever, cough, or sputum. A repeat chest CT showed significant resolution of the right lung lesion with no pleural effusion observed (Figure 1 D1-D3).

Discussion

Chlamydia psittaci is a Gram-negative, strictly intracellular parasitic pathogen that primarily infects birds or poultry. It can be transmitted to humans through respiratory inhalation of aerosols contaminated with *Chlamydia psittaci*, although human-to-human transmission is rare [9]. Although less well-known than other obligate intracellular bacteria, such as *Chlamydia pneumoniae* and *Chlamydia trachomatis*, *Chlamydia psittaci* is a highly pathogenic bacterium [10]. Infection with *Chlamydia psittaci* can range from asymptomatic or mild cases to severe pneumonia, acute respiratory distress syndrome, or even multi-organ failure in severe cases [9,11]. The incubation period of *Chlamydia psittaci* infection typically ranges from 5 to 14 days. The main clinical manifestations include high fever, chills, malaise, headache, myalgia, cough, dyspnea, and occasionally rash or gastrointestinal symptoms such as vomiting and diarrhea. Rare complications may include myocarditis, encephalitis, and hepatitis [12]. In this elderly male patient with no clear history of avian or poultry contact, the main clinical manifestations included high fever, chills, shock, and dyspnea. Laboratory findings showed leukopenia, thrombocytopenia, and lymphocytopenia, alongside significantly elevated aspartate aminotransferase, PCT, and CRP levels. Lung imaging revealed exudate and solid changes in both lungs, particularly in the lower lobe, and fiberoptic bronchoscopy showed bilateral lung airway involvement with yellow watery sputum. The patient's condition rapidly deteriorated after disease onset, with hemodynamic instability, respiratory failure, and multi-organ failure within a short period. However, the prognosis was ultimately

Figure 4. Change in procalcitonin and C-reactive protein during hospitalization.

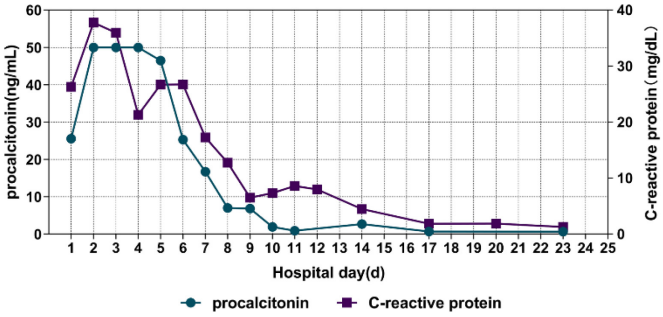


Figure 5. Change in oxygenation index during hospitalization.

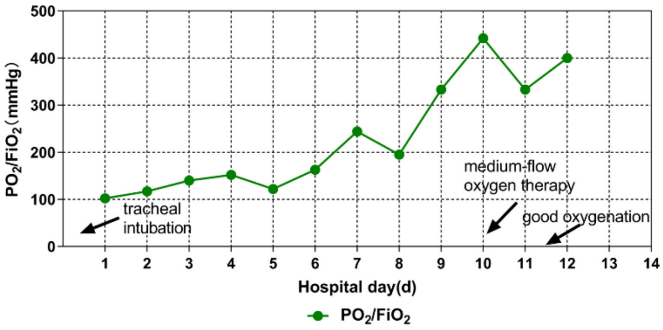
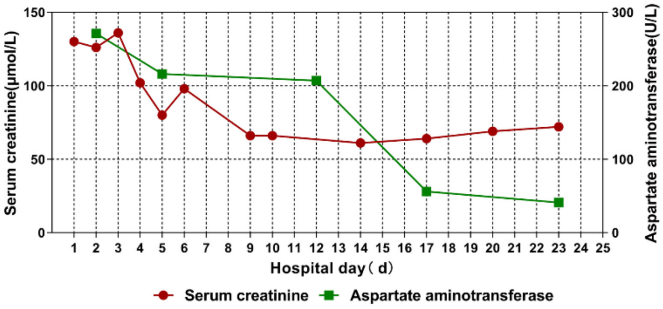


Figure 6. Change in serum creatinine and aspartate aminotransferase during hospitalization.



good with timely diagnosis and treatment, underscoring the importance of early and accurate diagnosis and treatment in improving patient outcomes. Several case reports have corroborated the efficacy of omadacycline treatment. Fang *et al.* reported a severe case of *Chlamydia psittaci* pneumonia complicated by multiple organ failure, with the patient achieving clinical improvement after omadacycline therapy and subsequent discharge from the hospital [8]. Wang *et al.* treated 16 patients with severe *Chlamydia psittaci* pneumonia and acute respiratory distress syndrome (ARDS) using omadacycline, of whom 14 achieved complete recovery and 2 died [13]. Wang *et al.* also described a case of severe *Chlamydia psittaci* pneumonia complicated by Guillain-Barré syndrome, which was successfully managed with omadacycline therapy, resulting in an uneventful recovery and discharge [14]. Li *et al.* demonstrated the clinical efficacy and favorable tolerability of omadacycline in a retrospective analysis of 15 patients with *Chlamydia psittaci* pneumonia [15].

Conventional methods for diagnosing *Chlamydia psittaci* pneumonia include pathogenic bacterial culture, serological tests, and polymerase chain reaction (PCR) [16]. Pathogenic bacterial culture is considered the gold standard for diagnosing *Chlamydia psittaci*. It is time-consuming and requires high biosafety levels, making it impractical for routine use. Serological tests have limited early diagnostic value and are more suitable for retrospective diagnosis [9]. PCR is more sensitive and rapid than pathogen culture and serological tests. Still, there are challenges, such as the limited availability of commercial reagents and the need for increased attention to these pathogens. Underdiagnosis and misdiagnosis of *Chlamydia psittaci* pneumonia can occur due to insufficient knowledge of the disease, atypical clinical symptoms, and limitations of imaging examinations and traditional detection methods [17]. In recent years, mNGS technology has been increasingly used for diagnosing severe pneumonia pathogens, providing evidence for detecting new or rare pathogens [18]. mNGS demonstrates significant clinical utility in infectious disease management through its rapid pathogen identification, short diagnostic turnaround time, high sensitivity and specificity, and minimally invasive sampling techniques that mitigate patient discomfort [6,19-21], thereby establishing itself as a pivotal tool in modern diagnostic and therapeutic workflows. In the case presented, multiple sputum cultures and blood cultures were negative, and mNGS detected *Chlamydia psittaci* in the sputum (sequence number 473743), which was based on clinical manifestations and imaging findings, leading to a diagnosis of severe *Chlamydia psittaci* pneumonia.

Omadacycline, the first aminomethyl tetracycline approved for clinical use, is available in oral and intravenous forms and was FDA approved in October 2018 for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP) in adults [22]. The recommended dosage of omadacycline for the treatment of CABP and ABSSSI is an initial loading dose of 0.2 g via IV on Day 1, or 0.1 g IV twice on Day 1, followed by a maintenance dose of 0.1 g IV once daily or 0.3 g orally once daily, over a treatment course of 7 to 14 days [23]. Omadacycline is associated with common adverse reactions, including nausea, vomiting, diarrhea, elevated liver enzymes, headache, and infusion-site pain. It is contraindicated in patients with known hypersensitivity to tetracycline-class antibiotics. Similar to other tetracyclines, omadacycline may suppress skeletal growth and lead to tooth discoloration or enamel hypoplasia, necessitating avoidance in pregnant individuals and children under 8 years of age. Additionally, concomitant use with metal-containing products (e.g., antacids, iron supplements) should be avoided [23]. It exhibits a broad antibacterial spectrum, effectively targeting Gram-positive and Gram-negative bacteria, including drug-resistant strains like methicillin-resistant *Staphylococcus aureus*, penicillin-resistant *Streptococcus pneumoniae*, Extended Spectrum β-Lactamases (ESBL) -producing *Enterobacteriaceae*, atypical pathogens, and anaerobic bacteria [24,25]. In addition, through modification of the C-7 and C-9 positions of the tetracycline D ring, omadacycline can overcome common tetracycline resistance mechanisms, including tetracycline-specific efflux pumps and ribosomal protection [26,27], making it effective against tetracycline-resistant bacteria, including those resistant to doxycycline and minocycline. Furthermore, omadacycline is well tolerated, undergoes minimal in vivo metabolism, and is excreted as a prototype via feces (81.1%) and urine (14.4%), with few drug interactions [28], making it a suitable choice for patients with hepatic and renal insufficiency.

To treat *Chlamydia psittaci* pneumonia, tetracyclines, particularly doxycycline, are the preferred antibiotics, followed by macrolides and quinolones such as azithromycin and moxifloxacin, for a minimum of 10 to 14 days. Most *Chlamydia psittaci* infections show improvement within 48 hours of initiating effective antibiotic treatment [9]. However,

patients were empirically given moxifloxacin upon admission without significant improvement, which may be related to the low intracellular activity of quinolone against *Chlamydia psittaci* [29]. The diagnosis of *Chlamydia psittaci* pneumonia was later confirmed. Treatment was switched to doxycycline, which also proved ineffective, raising concerns about the severity of pneumonia or doxycycline resistance. Considering the lack of in vitro drug sensitivity data for *Chlamydia psittaci* in China and reports of tetracycline-resistant Chlamydia strains in recent years [30-32], the treatment regimen was ultimately changed to omadacycline. The patient was subsequently discharged and cured with no reported adverse drug reactions.

Conclusions

In conclusion, the diagnosis of *Chlamydia psittaci* pneumonia can be challenging, and emerging diagnostic technologies such as mNGS can provide valuable support for precise clinical treatment. In cases where traditional antibiotics like doxycycline and moxifloxacin have failed, omadacycline may represent a promising new option for treating *Chlamydia psittaci* pneumonia. Its broad antibacterial spectrum and ability to overcome tetracycline resistance mechanisms make it a potential alternative for patients who do not respond to standard treatments. However, further research and clinical experience are needed to better understand the efficacy and safety of omadacycline in the treatment of *Chlamydia psittaci* pneumonia and other bacterial infections. It is important to carefully consider the specific characteristics of the infecting pathogen, potential resistance patterns, and individual patient factors when selecting antibiotics for treatment. Appropriate use, dosing, and monitoring of antibiotics, including omadacycline, are critical to optimize patient outcomes and mitigate the risk of antimicrobial resistance.

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Ethics Approval and Informed Consent

The Ethics Committees of Heyuan People's Hospital (YXYJLL-2023SF31) approved this study.

Authors Contributions

Zhitong Huang. Corresponding author, writing-review and editing. Ping Xu. first author, Conception and design, data curation, writing-review and editing.

Corresponding author

Zhitong Huang, Bachelor of Medicine.
Correspondence: Department of Emergency
Heyuan People's Hospital
Heyuan 517000, Guangdong, China.
Tel: +86 0762 3185865
Email: 13825308575@163.com

Conflict of interest

No conflict of interest is declared.

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