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ARTICLE

Omadacycline in the Treatment of *Chlamydia psittaci* Pneumonia: A Retrospective Study on Efficacy and Safety

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Abstract

Aims/Background *Chlamydia psittaci* is an obligate intracellular bacterium that primarily infects birds, but can cause respiratory infections in humans. Clinical evidence supporting the use of omadacycline for the treatment of *Chlamydia psittaci* pneumonia remains limited; therefore, this study aimed to evaluate the potential of omadacycline in treating *Chlamydia psittaci* pneumonia by analyzing the patients' clinical outcomes and the drug safety profile.

Methods We retrospectively reviewed the medical records of 15 patients with *Chlamydia psittaci* pneumonia treated at the First Affiliated Hospital, Zhejiang University School of Medicine between January and December 2023. Following diagnosis with the aid of metagenomic next-generation sequencing, the patients received omadacycline for treatment, and their clinical outcomes and laboratory marker profiles were monitored to assess the treatment efficacy and safety.

Results Significant improvements were observed in clinical symptoms and laboratory markers, including C-reactive protein ($p < 0.001$), procalcitonin ($p = 0.001$), neutrophil percentage ($p < 0.001$), and the SpO_2/FiO_2 ratio ($p < 0.001$), after treatment with omadacycline. A 100% cure rate was reported within 28 days of treatment initiation, with gastrointestinal disturbances being the most common side effect.

Conclusion Omadacycline shows promise in treating *Chlamydia psittaci* pneumonia and is well tolerated by the users. However, further controlled trials involving larger samples are required to confirm the efficacy and safety of the drug.

Key words: *Chlamydia psittaci*; pneumonia; omadacycline; metagenomic next-generation sequencing

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Introduction

Chlamydia psittaci (*C. psittaci*), a gram-negative obligate intracellular bacterium, has long been recognized for its zoonotic potential, predominantly affecting avian species, and also posing a significant threat to human health (Kong et al, 2021; Kohn et al, 2021). In humans, this pathogen can cause a spectrum of respiratory conditions ranging from mild flu-like symptoms to severe pneumonia, which in some instances can lead to substantial morbidity or even mortality (Balsamo et al, 2017). Epidemiological studies indicate that *C. psittaci* accounts for approximately 1% of all community-acquired pneumonia (CAP) cases, highlighting its significant

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relevance to respiratory infections despite its relatively low prevalence compared to other pathogens (Hogerwerf et al, 2017).

Recent advancements in diagnostic technologies, particularly metagenomic next-generation sequencing (mNGS), have significantly improved our ability to detect and accurately diagnose infections caused by this bacterium (Gu et al, 2019; Schlaberg et al, 2017; Zhou et al, 2021). mNGS allows for the comprehensive analysis of genetic material from a clinical sample, enabling the identification of a wide range of pathogens, including those that are difficult to culture or identify using traditional methods. This paradigm shift in diagnostic approach has led to an increased detection rate of *C. psittaci* pneumonia, implying frequent instances of underdiagnosis or misdiagnosis of *C. psittaci* pneumonia in the past (Nieuwenhuizen et al, 2018; Gu et al, 2020).

Tetracyclines have been the mainstay of therapy for *C. psittaci* infections, evidenced by the broad recommendation in a range of guidelines to prescribe this class of antibiotics for CAP (Cillóniz et al, 2016). Among these, omadacycline, a next-generation tetracycline derivative, has garnered attention owing to its potential use in CAP (Zhanel et al, 2020; Stets et al, 2019). However, clinical evidence supporting the specific application of omadacycline in the treatment of *C. psittaci* pneumonia remains limited, creating a gap in our comprehensive understanding of its efficacy and safety profile.

This study aimed to bridge this knowledge gap by evaluating the potential efficacy and safety of omadacycline in treating *C. psittaci* pneumonia as diagnosed using mNGS, offering preliminary clinical evidence that could inform practice and guide future therapeutic strategies for managing this zoonotic infection. Through this study, we hope to contribute to broader efforts to combat respiratory infections caused by zoonotic pathogens, improve patient outcomes, and advance public health initiatives.

Methods

In this retrospective study, the medical records of 15 patients with *C. psittaci* pneumonia diagnosed using mNGS were reviewed. These patients were hospitalized and treated at the First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China, from January 2023 to December 2023.

Inclusion and Exclusion Criteria

Patients who met the inclusion criteria in the following were included in this study: (1) patients aged 18 years or older; (2) patients diagnosed with *C. psittaci* pneumonia confirmed through chest computed tomography (CT) and mNGS of bronchoalveolar lavage fluid (BALF); and (3) patients treated with omadacycline to combat the *C. psittaci* infection after mNGS-based diagnosis. The exclusion criteria set for this investigation are as follows: (1) patients who had received omadacycline for other anti-infective purposes prior to the omadacycline treatment under study; (2) patients who were found to have coinfection with other microorganisms based on the mNGS-based diagnosis; and (3) patients who had been treated with multiple antibiotics following the mNGS-based diagnosis.

Treatments

After confirming the diagnosis of *C. psittaci* pneumonia using mNGS, 100 mg omadacycline (XJ01AAA367B001010104641, Zhejiang Hisun Pharmaceutical Co., Ltd., Taizhou, China) was administered intravenously once a day (initial dose, 200 mg). In addition, according to the recommendations of the acute respiratory distress syndrome (ARDS) guidelines, mechanical ventilation and prone positioning treatment measures were implemented as per the severity of ARDS (Grasselli et al, 2023).

Clinical Outcomes

Clinical cure was defined as: (1) notable alleviation of clinical symptoms associated with pneumonia; (2) significant improvement in inflammatory markers, including white blood cell (WBC) count, C-reactive protein (CRP), and procalcitonin (PCT); and (3) fulfillment of established standards for patient discharge.

Data Collection

For each case, the collected data encompassed a range of clinical characteristics including patient age, sex, body mass index (BMI), primary symptoms, number of days before hospital admission, any coexisting conditions, smoking history, exposure to birds, pneumonia severity index (PSI) score, PSI risk class, and SpO_2/FiO_2 ratio. In addition, information on the severity of ARDS was documented. Diagnostic and treatment strategies were detailed, covering aspects such as chest CT imaging, microbial identification through mNGS, including the number of species-specific reads, antibiotic regimens before and after mNGS-based diagnosis, duration of omadacycline treatment, duration of ventilation support, length of stay in the intensive care unit (ICU), and overall hospital stay.

Laboratory data for each patient were meticulously recorded, including WBC count, neutrophil percentage (N%), hemoglobin (HB) concentration, hematocrit (HCT) percentage, platelet (PLT) count, PCT levels, CRP levels, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, total bilirubin (TBIL), creatinine, blood urea nitrogen (BUN), and the SpO_2/FiO_2 ratio.

Clinical outcomes and complications experienced by the included patients, including gastrointestinal symptoms, elevated alanine aminotransferase and aspartate aminotransferase levels, diarrhea or constipation, and headache, were documented. Adverse events associated with omadacycline treatment were evaluated and categorized based on the Common Toxicity Criteria for Adverse Events (CTCAE), version 5.0. This comprehensive methodology allows for a detailed assessment of each patient's status, therapy, and outcomes, facilitating a nuanced understanding of the efficacy and safety of the interventions implemented.

Data Analysis

Statistical analyses were performed using R software (http://www.R-project.org; Version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria). Normal distribution was tested using the Shapiro–Wilk test. Continuous data with a normal distribution were expressed as mean ± standard deviation, and a paired *t*-test was

conducted to compare pre- and post-treatment variables. Non-normally distributed data were presented as medians with interquartile ranges, and were analyzed using the Wilcoxon test. A $p < 0.05$ was considered statistically significant.

Results

Patient Characteristics

The patients included in this study had a median age of 58 years (27–80 years), with a high proportion of male presentation (60%) in the sample. The patients had a median BMI of 24 kg/m^2, which suggests a generally healthy weight range. The main symptoms reported by the patients included fever (100%), cough (73%), chills (27%), headache (13%), myalgia (13%), and dyspnea (13%), whereas the prevalent comorbidities encompassed hypertension (47%), chronic heart disease (20%), and diabetes (6%). The median number of days before admission was 7 (4–15 days), indicating variable disease progression among the patients leading to eventually seeking hospital care. The findings revealed that 94% of patients had no smoking history, whereas 6% were former smokers. Additionally, bird exposure was reported by 47% of the cases. The PSI score presented variability, reflecting the spectrum of disease severity among the patients. The patients were also classified on the basis of ARDS severity, such as none (33%), mild (20%), moderate (33%), or severe (13%) (Table 1).

Chest CT, mNGS Findings, and Treatment Strategies

Chest CT findings revealed that all patients were affected by pneumonia, with bilateral involvement noted in 47% of the cases. Combining the results of bronchoscopy and the mNGS conducted on alveolar lavage fluid samples, we identified *C. psittaci* as the causative agent. Prior to obtaining these results, the patients were variably treated with cefuroxime, ceftriaxone, levofloxacin, moxifloxacin, piperacillin/tazobactam, cefoperazone/sulbactam, or meropenem, but none of these antibiotics resulted in an improvement of their condition. Following the identification of *C. psittaci* as the prime pathogen, antibiotic therapy was adjusted to omadacycline, which was applied to these patients for a median duration of 6 days, ranging from 4 to 19 days. Twenty percent of the patients were admitted to the ICU and required mechanical ventilation. The median length of hospital stay was 6 days (4–21 days; Table 2).

Laboratory Data

Table 3 displays laboratory data obtained before and after the administration of omadacycline. The median CRP level of the 15 patients exhibited a statistically significant decrease following treatment with omadacycline (171.00 mg/L pre-treatment compared to 22.64 mg/L post-treatment, $p < 0.001$). PCT levels (0.34 vs. 0.12 ng/mL, $p = 0.001$) and N% (86.1 vs. 73.7, $p < 0.001$) also demonstrated marked reductions post-omadacycline treatment. Additionally, the ratio of SpO_2/FiO_2 significantly increased after treatment, as compared to pre-treatment values (243 vs. 467, $p < 0.001$). Furthermore, the median PLT levels exhibited a significant increase (184.33 ± 97.49 vs. $286.87 \pm 91.94 \times 10^9$/L, $p = 0.008$).

Table 1. Clinical characteristics of study participants.

Cases (n = 15)	Age (years)	Gender	BMI	Main symptoms	Days before admission	Coexisting conditions	Smoking history	Bird exposure	PSI score	PSI risk class	SpO_2/FiO_2 ratio	ARDS severity
1	48	Male	30	Fever, headache	4	Hypertension	No	No	153	V	119	Severe
2	67	Male	22	Fever, dyspnea	15	Hypertension	No	Yes	152	V	118	Severe
3	67	Male	20	Fever, chills, myalgia	7	None	No	No	107	IV	188	Moderate
4	27	Male	27	Fever, cough	6	None	No	Yes	37	II	338	No
5	53	Female	23	Fever, cough, headache, myalgia	5	Hypertension, chronic heart disease	No	Yes	53	II	220	Moderate
6	64	Female	24	Fever, cough	7	Hypertension	No	Yes	89	III	334	No
7	53	Female	27	Fever, cough	7	Chronic heart disease	No	No	108	IV	234	Moderate
8	68	Male	25	Fever, chills	7	Hypertension	No	No	118	IV	243	Mild
9	43	Male	27	Fever, cough, chills	6	None	No	Yes	63	II	288	Mild
10	80	Male	22	Fever, cough	10	Hypertension, chronic heart disease, diabetes	No	Yes	130	IV	235	Moderate
11	58	Male	22	Fever, cough, chills	10	None	Yes	Yes	78	III	232	Moderate
12	52	Female	20	Fever, cough, dyspnea	5	None	No	No	82	III	345	No
13	47	Male	28	Fever, cough,	7	None	No	No	67	II	328	No
14	60	Female	22	Fever, cough	7	None	No	No	70	II	328	No
15	71	Female	24	Fever, cough	7	Hypertension	No	No	71	III	279	Mild

Abbreviations: BMI, body mass index; PSI, pneumonia severity index; ARDS, acute respiratory distress syndrome.

Table 2. Chest CT, mNGS findings, and treatment strategies for each patient.

Cases (n = 15)	Chest CT	mNGS (no. of species-specific reads)	Antibiotics before mNGS	Antibiotics after mNGS	Duration of omadacycline (days)	Duration of ventilation (days)	Length of stay in ICU (days)	Length of stay in hospital (days)
1	Bilateral	*Chlamydia psittaci* (6113)	Piperacillin/tazobactam + levofloxacin	Omadacycline	19	10	15	21
2	Bilateral	*Chlamydia psittaci* (810)	Piperacillin/tazobactam + meropenem + levofloxacin	Omadacycline	19	10	14	21
3	Bilateral	*Chlamydia psittaci* (2)	Piperacillin/tazobactam	Omadacycline	12	5	6	13
4	Unilateral	*Chlamydia psittaci* (10)	Cefuroxime + levofloxacin	Omadacycline	5	0	0	5
5	Unilateral	*Chlamydia psittaci* (4)	Cefoperazone/sulbactam	Omadacycline	11	0	0	16
6	Unilateral	*Chlamydia psittaci* (3)	Cefuroxime + cefoperazone/sulbactam	Omadacycline	4	0	0	4
7	Bilateral	*Chlamydia psittaci* (114)	Cefuroxime + meropenem	Omadacycline	12	0	0	14
8	Unilateral	*Chlamydia psittaci* (229)	Cefoperazone/sulbactam	Omadacycline	4	0	0	6
9	Bilateral	*Chlamydia psittaci* (13)	Cefuroxime + cefoperazone/sulbactam	Omadacycline	5	0	0	5
10	Unilateral	*Chlamydia psittaci* (22)	Piperacillin/tazobactam + levofloxacin	Omadacycline	6	0	0	6
11	Bilateral	*Chlamydia psittaci* (49)	Ceftriaxone + cefoperazone/sulbactam	Omadacycline	5	0	0	5
12	Bilateral	*Chlamydia psittaci* (163)	Cefuroxime + moxifloxacin	Omadacycline	8	0	0	8
13	Unilateral	*Chlamydia psittaci* (13)	Cefuroxime + cefoperazone/sulbactam	Omadacycline	6	0	0	6
14	Unilateral	*Chlamydia psittaci* (7)	Piperacillin/tazobactam + levofloxacin	Omadacycline	6	0	0	6
15	Unilateral	*Chlamydia psittaci* (18)	Cefuroxime + levofloxacin	Omadacycline	5	0	0	8

Abbreviations: CT, computed tomography; mNGS, metagenomic next-generation sequencing; ICU, intensive care unit.

Table 3. Laboratory data of patients.

Laboratory parameters	Before treatment with omadacycline (n = 15)	After treatment with omadacycline (n = 15)	*p*-value	*t*/z value
WBC count ($\times 10^9$/L)	8.42 (4.89, 10.00)	6.67 (5.43, 7.39)	0.361	–1.21
N% (%)	86.10 (80.30, 89.85)	73.70 (56.50, 77.10)	<0.001	–3.87
HB (g/L)	123.27 ± 15.47	116.47 ± 19.18	0.295	–1.06
HCT (%)	36.18 ± 4.95	34.96 ± 5.54	0.530	–0.63
PLT ($\times 10^9$/L)	184.33 ± 97.49	286.87 ± 91.94	0.008	–2.69
PCT (ng/mL)	0.34 (0.20, 2.38)	0.12 (0.08, 0.17)	0.001	–3.45
CRP (mg/L)	171.00 (103.91, 223.34)	22.64 (13.68, 28.12)	<0.001	–3.91
ALT (U/L)	61.00 (29.50, 110.00)	96.00 (47.50, 123.50)	0.361	0.92
AST (U/L)	74.00 (37.50, 107.50)	44.00 (36.50, 71.00)	0.299	–1.05
TBIL (μmol/L)	10.80 (7.05, 17.15)	8.10 (5.40, 10.95)	0.101	–1.64
Creatinine (μmol/L)	79.00 (62.50, 85.00)	64.00 (57.00, 69.00)	0.078	–1.75
BUN (mmol/L)	5.29 (4.72, 6.72)	5.35 (3.69, 6.94)	0.983	0.02
SpO_2/FiO_2 ratio	243.00 (226.00, 328.00)	467.00 (454.50, 469.00)	<0.001	–3.83

Abbreviations: WBC, white blood cell; N%, neutrophil percentage; HB, hemoglobin; HCT, hematocrit; PLT, platelet; PCT, procalcitonin; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; BUN, blood urea nitrogen.

Table 4. Clinical outcomes and complications.

Outcome/complication	Number of cases (%)	Number of adverse events (%)	
	n = 15	Grade 1–2	Grade 3 or higher
Number of cured cases	15 (100)	—	—
28-day mortality	0 (0)	—	—
Adverse events			
Gastrointestinal symptoms (nausea and vomiting)	3 (20)	3 (20)	0 (0)
Elevated ALT	3 (20)	3 (20)	0 (0)
Elevated AST	0 (0)	0 (0)	0 (0)
Diarrhea or constipation	1 (6)	1 (6)	0 (0)
Headache	0 (0)	0 (0)	0 (0)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Clinical Outcomes and Complications

A 100% cure rate was attained at the end of the study, with no fatalities reported within 28 days post-treatment. Throughout the treatment and subsequent monitoring, gastrointestinal symptoms were reported in three patients (20%), elevated alanine aminotransferase levels were detected in three patients (20%), and diarrhea and constipation were reported by one patient (6.7%). No instances of drug-induced elevation in the aspartate aminotransferase levels or other adverse effects were documented. Furthermore, no adverse events of grade 3 severity or higher were identified (Table 4).

Discussion

A retrospective analysis was performed on 15 patients with CAP who had been symptomatic for a minimum of four days and had failed initial empirical antibiotic therapy. The severity of the cases ranged from mild (not developing to ARDS) to severe (developing into severe ARDS) (Matthay et al, 2024; Wu et al, 2023). Upon admission, the key intervention involved the use of mNGS to rapidly identify the causative pathogen and promptly adjust antibiotic therapy, contributing to successful prevention of disease progression (Evans et al, 2021). Omadacycline was the antibiotic treatment prescribed to all the patients in this study.

As a novel therapeutic option for respiratory infections including *C. psittaci* pneumonia, omadacycline has shown promising results in terms of efficacy, as evidenced by significant improvements in laboratory markers, including N%, CRP, PCT, and SpO_2/FiO_2 ratio following treatment. After implementing of omadacycline treatment, all patients were successfully transitioned to take oral medication, recovered, and were discharged, demonstrating the omadacycline's efficacy in *C. psittaci* pneumonia treatment. These outcomes are consistent with the expected pharmacological effects of omadacycline and are supported by data from broader studies on CAP management, indicating its potential as a potent agent against *C. psittaci* (Stets et al, 2019; Ramirez et al, 2021).

Gastrointestinal symptoms were identified as the predominant side effects, manifesting at an expected rate and not necessitating treatment cessation (Bax et al, 2019). A slight elevation in ALT levels was observed in three subjects after treatment, but a causal relationship attributed to omadacycline remains unclear. These findings are consistent with those of previous studies, and suggest that the adverse effects of omadacycline do not compromise its therapeutic utility (Burgos and Rodvold, 2019). The absence of significant drug-induced toxicities in the current patient cohort further underscores its suitability for diverse patient populations, including those at an elevated risk of adverse reactions to traditional antibiotics. It is worthy to note that patients in this study received other antibiotics before the initiation of omadacycline treatment, potentially influencing the study outcomes.

Literature on the use of omadacycline in the treatment of *C. psittaci* pneumonia is limited. Several case reports have corroborated the efficacy of omadacycline treatment but additionally highlighted the challenges posed by complex patient presentations (Fang et al, 2022; Chen et al, 2024). In a prominent investigation, a cohort of 16 individuals with severe pneumonia attributed to *C. psittaci* was examined, and two mortality cases were reported (Wang et al, 2024). In contrast to their methodology, which predominantly incorporated varied mNGS findings and a combination of antibiotic protocols, our study focused exclusively on patients with confirmed *C. psittaci* infections who were treated with omadacycline, in order to facilitate a more precise evaluation of the drug's therapeutic efficacy. Similarly, however, both studies acknowledged the limited effectiveness of quinolones in combating *C. psittaci* pneumonia, underscoring the importance of investigating drug resistance mechanisms in this regard (Benamri et al, 2021).

Tetracyclines have long been recognized for their efficacy against *C. psittaci* (He et al, 2023; Wu et al, 2021); however, the emergence of omadacycline contributes to a notable stride in the management of this infection. Our research indicates that omadacycline has the potential to transform the therapeutic paradigm for *C. psittaci* pneumonia by providing a superior and safer option that overcomes the limitations of existing antibiotics.

Nevertheless, it is important to acknowledge the limitations of the present study, such as the small sample size, retrospective research design, lack of a control group, and the inability to monitor drug concentrations, which may have affected the interpretation of the results. Future research should focus on validating these findings by conducting randomized controlled trials in larger and more diverse populations, as well as longitudinal studies to investigate the long-term efficacy and resistance patterns of omadacycline.

Conclusion

The current study provides preliminary evidence supporting the efficacy and safety of omadacycline in *C. psittaci* pneumonia treatment. Our results depict promising improvements in patients' condition, evaluated in terms of clinical symptoms and laboratory markers, indicating that omadacycline may be a viable treatment option. These findings warrant further investigation to confirm the potential benefits of omadacycline in larger controlled studies.

Key Points

- Omadacycline significantly improved clinical symptoms and laboratory markers, such as C-reactive protein, procalcitonin, neutrophil percentage, and SpO_2/FiO_2 ratio in patients with *Chlamydia psittaci* pneumonia.
- This study reported a 100% cure rate within 28 days after omadacycline treatment initiation, indicating its potential as an effective treatment option.
- Gastrointestinal disturbances were the most commonly reported side effects, and no severe adverse events were documented, suggesting that omadacycline was well tolerated by patients.
- These findings provide preliminary evidence for the use of omadacycline as a treatment option and highlight the need for further research in larger controlled trials.

Availability of Data and Materials

All the data of this study are included in this article.

Author Contributions

HL and WY designed the research study. HL, ZW and WY performed the research. XM analyzed the data. HL and ZW drafted the manuscript. All authors

contributed to important editorial changes of important content in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the principles of the Declaration of Helsinki. This study was approved by the Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine (IIT20240280A). Written informed consent for participation was not required for this study according to national legislation and institutional requirements by the Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine.

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Conflict of Interest

The authors declare no conflict of interest.

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