Infection and Drug Resistance

Dovepress
open access to scientific and medical research

Open Access Full Text Article

CASE REPORT

Omadacycline for the Treatment of Severe *Chlamydia psittaci* Pneumonia Complicated with Multiple Organ Failure: A Case Report

Changquan Fang[1,*], Limin Xu[2,*], Jiarong Tan[1], Hongyi Tan[1], Junhong Lin[1], Ziwen Zhao[3]

[1]Department of Pulmonary and Critical Care Medicine, Huizhou Central People's Hospital, Huizhou, Guangdong Province, Peoples' Republic of China; [2]Department of Geriatrics, Huizhou First People's Hospital, Huizhou, Guangdong Province, Peoples' Republic of China; [3]Department of Pulmonary and Critical Care Medicine, Guangzhou First People's Hospital Affiliated to South China University of Technology, Guangzhou, Guangdong Province, Peoples' Republic of China

*These authors contributed equally to this work

Correspondence: Junhong Lin, Department of Pulmonary and Critical Care Medicine, Huizhou Central People's Hospital, No. 41 Eling North Road, Huicheng District, Huizhou City, Guangdong Province, 516000, Peoples' Republic of China, Tel +86 130-7528-2839, Email hz_ljh@163.com; Ziwen Zhao, Department of Pulmonary and Critical Care Medicine, Guangzhou First People's Hospital Affiliated to South China University of Technology, No. 1 Panfu Road, Yuexiu District, Guangzhou City, Guangdong Province, 510180, Peoples' Republic of China, Tel +86 130-0687-2260, Email zhaozw@yeah.net

Abstract: Psittacosis is a rare zoonotic disease caused by *Chlamydia psittaci* infection, and tetracyclines are the preferred treatment. Omadacycline is a novel tetracycline that has a strong in vitro antibacterial activity against atypical pathogens, including *C. psittaci*; however, clinical data for its usage are lacking. We report a patient with severe *C. psittaci*-induced pneumonia presenting with a high fever, muscle aches, severe hepatic and renal insufficiency, and acute respiratory failure requiring tracheal intubation and mechanical ventilation. The condition was diagnosed using metagenomic next-generation sequencing. The patient was discharged after treatment with omadacycline. The findings of this study suggest that metagenomic next-generation sequencing is valuable for the rapid and accurate diagnosis of psittacosis. With its good safety profile and no requirement for dose adjustment in special populations, omadacycline is a new option for the treatment of severe *C. psittaci* pneumonia. However, additional case reports are needed to support this conclusion.

Keywords: *Chlamydia psittaci*, pneumonia, omadacycline, multiple organ failure, metagenomic next-generation sequencing

Introduction

Chlamydia psittaci pneumonia is a rare clinical condition that accounts for approximately 1% of cases of community-acquired pneumonia.[1] It has a variable clinical presentation and usually progresses to critical illness and multiple extrapulmonary complications, including acute liver injury, acute kidney injury, rhabdomyolysis, and even multiple organ system failure.[2,3] Thus, the use of conventional effective antibiotics, including minocycline, doxycycline, levofloxacin, moxifloxacin, azithromycin, and erythromycin, is limited.

Omadacycline is a novel tetracycline derivative available in both intravenous and oral dosage forms, and it was approved by the United States Food and Drug Administration (FDA) in 2018 for the treatment of community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections.[4] It exhibits a strong in vitro antibacterial activity against atypical pathogens,[4,5] although the relevant clinical data are lacking. Herein, we report a case of severe *C. psittaci* pneumonia combined with multiple organ system failure that was successfully treated with omadacycline.

Case Presentation

The case involved a 62-year-old male farmer with a history of alcoholic liver disease. He was admitted to the hospital on March 2, 2022, and the chief complaint was "fever and cough with difficult breathing for 4 d". Four days before

Received: 2 August 2022
Accepted: 28 September 2022
Published: 4 October 2022

admission, the patient had a fever with no obvious cause, a maximum temperature of 41.0°C, chills, poor appetite, fatigue, headache and generalised muscle aches, intermittent disordered speech, cough, expectoration, and gradually worsening dyspnoea, for which he visited a local hospital. Chest computed tomography (CT) suggested infection and partial consolidation of the right lung. The patient was diagnosed to have "severe pneumonia" and administered the antibiotics piperacillin sulbactam, meropenem, and levofloxacin, and antiviral agent oseltamivir; however, a recurrent persistent fever and worsening dyspnoea were observed. The patient was admitted to the RICU of Huizhou Central People's Hospital for further treatment.

Physical examination presented the following findings: body temperature: 39.2°C, pulse: 93 beats/min, respiratory rate: 35 breaths/min, blood pressure: 113/76 mmHg, pulse oximetry: 90% (5 L/min oxygen by face mask). The patient was conscious and lethargic and had no yellowing of the skin, mucosa, or sclera and no enlargement of superficial lymph nodes. He was tachypnoeic with coarse breath sounds in both lungs, and wet rales could be heard in the bilateral lower lungs. The heart rate was 93 beats/min and regular; no pathological murmurs were heard in any of the valve auscultation areas and no other significant abnormalities were observed.

Laboratory examination presented the following findings: negative for novel coronavirus RNA and influenza A and B virus antigens; blood gas analysis (FiO_2: 41%): pH: 7.445, PO_2: 49.0 mmHg, PCO_2: 25.4 mmHg, HCO_3: 18.7 mmol/L, base excess: –4 mmol/L, oxygen saturation index: 119.5. Complete blood count was as follows: white blood cell (WBC): 3.7×10^9/L, neutrophil percentage: 86.1%, lymphocyte count: 0.24×10^9/L, haemoglobin: 105 g/L, platelets: 69×10^9/L; high-sensitivity C-reactive protein (hs-CRP): 320.25 mg/L, procalcitonin (PCT): 47.86 ng/mL. The liver function test results were as follows: alanine aminotransferase (ALT): 116 U/L, aspartate aminotransferase (AST): 696 U/L, total bilirubin: 32.3 μmol/L, albumin: 23.5 g/L. The kidney function test results were as follows: urea: 11.8 mmol/L, serum creatinine: 119 μmol/L, lactate: 1.22 mmol/L, plasma ammonia: 42.3 μmol/L, blood potassium: 3.53 mmol/L, blood sodium: 130 mmol/L. Coagulation function: fibrinogen: 9.95 g/L, D-dimer: 12,500 ng/mL; creatine kinase (CK): 8454 U/L, lactate dehydrogenase (LDH): 785 U/L. Brain natriuretic peptide precursor: 1470 pg/mL and high-sensitivity troponin T: 35.73 ng/L. Chest CT at the time of admission (Figure 1A–C) showed multiple patchy exudative opacities in the right lung and a large consolidated shadow in the right lower lung. Six hours after admission, the patient's condition worsened, obvious respiratory distress was observed, and the oxygen saturation index dropped to 95 mmHg. A diagnosis of severe community-acquired pneumonia (SCAP) with acute respiratory distress syndrome (ARDS) was considered, and the patient was administered tracheal intubation with invasive mechanical ventilation, methylprednisolone (40 mg) as an anti-inflammatory and liver protective drug, and an antibiotic regimen of meropenem injection (1.0 g q. 8 h), moxifloxacin injection (0.4 g q.d.), and oseltamivir capsules (75 mg q. 12 h). The patient had a severe infection with rapidly progressing pulmonary lesions, the efficacy of conventional antibiotics was poor, and the causative pathogen was not obvious. After obtaining written consent from his family members, 10 mL of bronchoalveolar fluid (BALF) collected via fibreoptic bronchoscopy was sent to the Daan Gene sequencing platform (Daan Gene Co., Ltd. of Sun Yat-sen University) for metagenomic next-generation sequencing (mNGS). During this period, the Widal test, Weil–Felix test, tuberculosis antibodies, anti-neutrophil cytoplasmic antibodies, and IgM antibodies for respiratory pathogens (*Legionella pneumophila, Chlamydia pneumoniae, Mycoplasma pneumoniae*, Q fever *Rickettsia*, adenovirus, respiratory syncytial virus, influenza A virus, influenza B virus, and parainfluenza virus) were all negative. The bacterial and fungal cultures of blood, phlegm, and BALF were negative. After the initial antibiotic treatment, the patient's condition did not improve; he still had a persistent fever and showed limited improvement in oxygenation, decreased platelets, and progressive increase in liver enzymes and blood creatinine. On March 4 (day 3), laboratory re-examination showed the following: platelets: 52×10^9/L, ALT: 559 U/L, AST: 1548 U/L, and serum creatinine: 341 μmol/L. On the same day, the DNA mNGS results indicated the presence of *C. psittaci*, with a sequence number of 14940, coverage of 97%, and relative abundance of 74.2%. Follow-up based on the patient's medical history indicated that he raised chickens, ducks, and other fowl at home. Taking together, the patient's clinical presentation and mNGS results led to a diagnosis of severe *C. psittaci* pneumonia. The patient had severe hepatic and renal insufficiency, and treatment with respiratory quinolones, macrolides, and antibiotics, such as doxycycline and minocycline, was not appropriate. After consultation with the hospital clinical pharmacist, the antibiotic regimen was adjusted to omadacycline injection (first dose: 100 mg IV q. 12 h, followed by: 100 mg IV q.d.). After 72 h of treatment, the patient's temperature gradually decreased to a normal level (Figure 2), and a complete blood count re-examination on

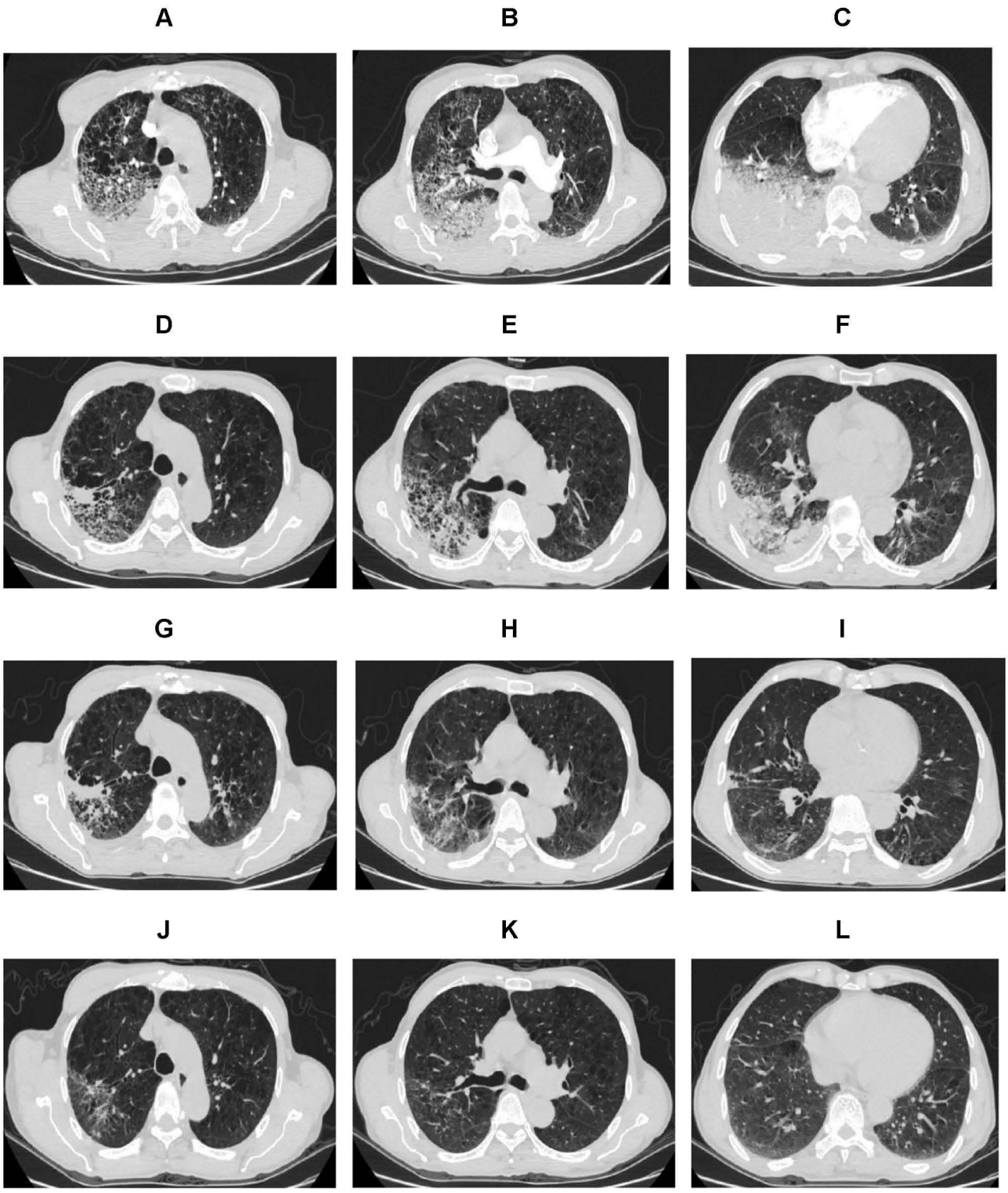

Figure 1 Chest CT findings of Severe *Chlamydia psittaci* pneumonia. (**A**–**C**) March 2, 2022: The day of admission. Large exudative foci in the right lung and a large consolidation shadow in the right lower lung. (**D**–**F**) Thirteen day after admission on March 15, 2022. Exudative foci and consolidation shadow in the right lung were less pronounced than those before. (**G**–**I**) Twenty-two day after admission on March 24, 2022. Further resorption of the right lung lesion than before. (**J**–**L**) April 24, 2022: 1 month after discharge. The lung lesions were largely resorbed, leaving only a small number of fibrous linear opacities.

March 7 (day 6) showed the following: WBC: 6.3×10^9/L, neutrophil percentage: 85.1%, lymphocyte count: 0.64×10^9/L, haemoglobin: 85 g/L, platelets: 116×10^9/L, hs-CRP: 127.14 mg/L, PCT: 5.53 ng, ALT: 228 U/L, AST: 430 U/L, serum creatinine: 202 μmol/L. The patient's condition gradually improved; inflammation indices decreased significantly; and liver

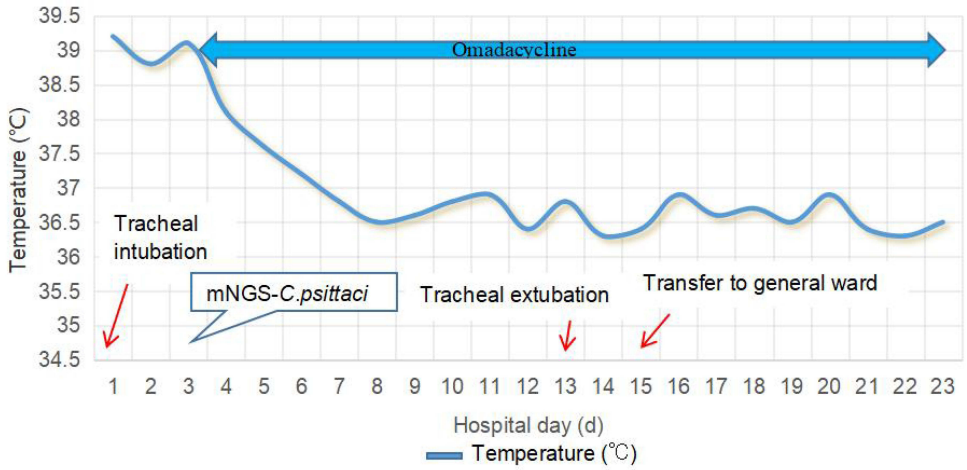

Figure 2 Body temperature and antimicrobial treatment during hospitalisation with meropenem at 1.0 g ivgtt Q8h (days 1–3), moxifloxacin at 0.4 g ivgtt Qd (days 1–3), oseltamivir at 75 mg po Q12h (days 1–3), and omadacycline at 100 mg ivgtt Q12 h (day 3), 100 mg ivgtt Qd (days 4–14), and 300 mg po Qd (days 15–23).

enzymes, creatinine, CK, and LDH gradually returned to normal levels (Figures 3–7). On March 14 (day 13), the patient was successfully extubated and high-flow oxygen therapy was continued. Chest CT re-examination indicated significant resorption of the right lung lesion (Figure 1D–F). The patient's condition was considered stable and his gastrointestinal function improved. On March 16 (day 15), the omadacycline injection was changed to an oral preparation (300 mg p.o. q. d.), and the patient was administered low-flow oxygen therapy and transferred to the general ward. On March 23 (day 22), chest CT re-examination indicated further resorption of the right lung lesion (Figure 1G–I), and the patient was discharged the following day. The final diagnosis was psittacosis, severe community-acquired pneumonia, ARDS, multiple organ system failure (type I respiratory failure, liver failure, and renal failure), rhabdomyolysis, and alcoholic liver disease. Outpatient follow-up at 1 month after discharge indicated no significant abnormalities in inflammation indices (hs-CRP and PCT) and liver and kidney functions, and chest CT indicated that the lung lesions were largely resorbed, leaving only a small number of fibrous linear opacities (Figure 1J–L).

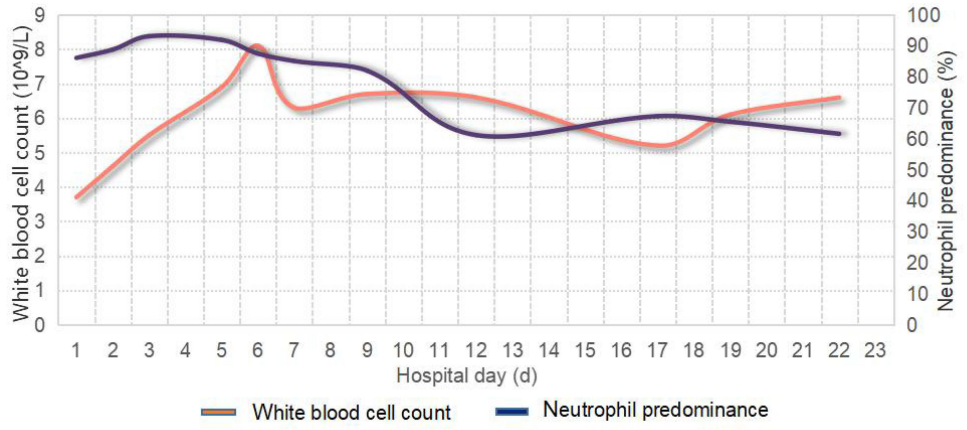

Figure 3 Change in white blood cell count and neutrophil predominance during hospitalisation.

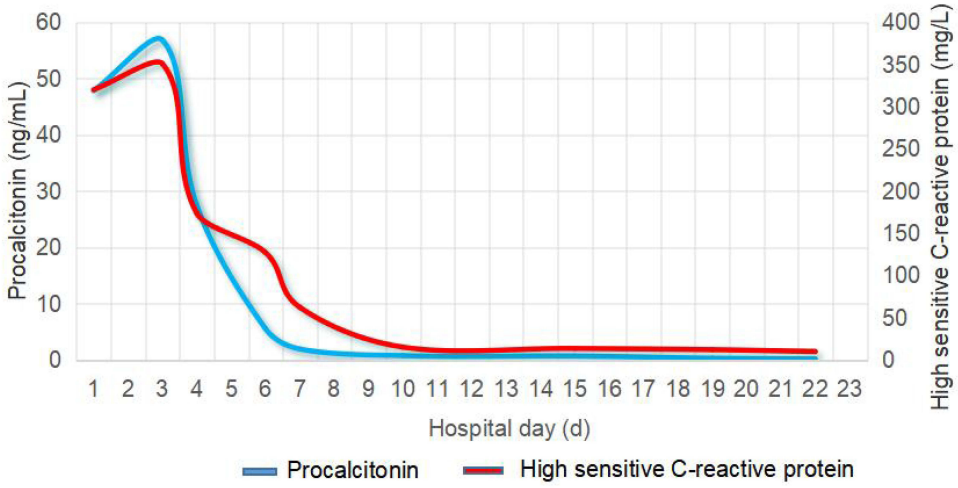

Figure 4 Change in C-reactive protein and procalcitonin during hospitalisation.

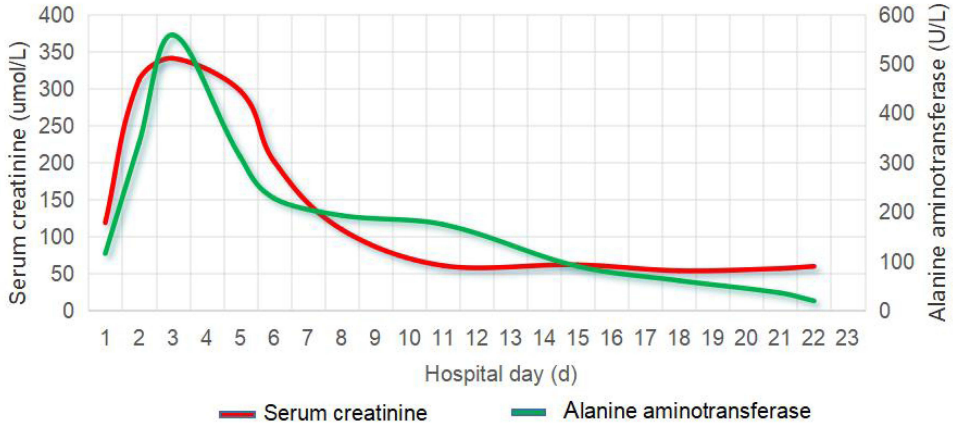

Figure 5 Change in alanine aminotransferase and serum creatinine during hospitalisation.

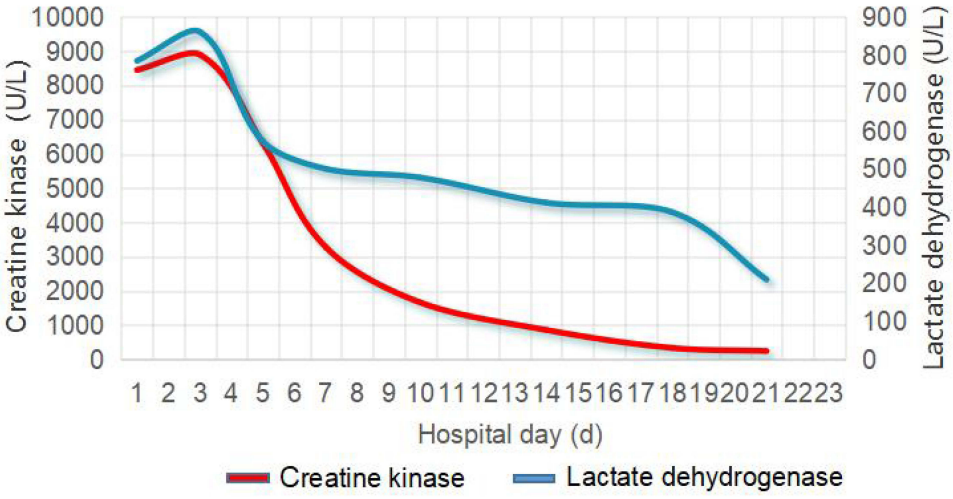

Figure 6 Change in creatine kinase and lactate dehydrogenase during hospitalisation.

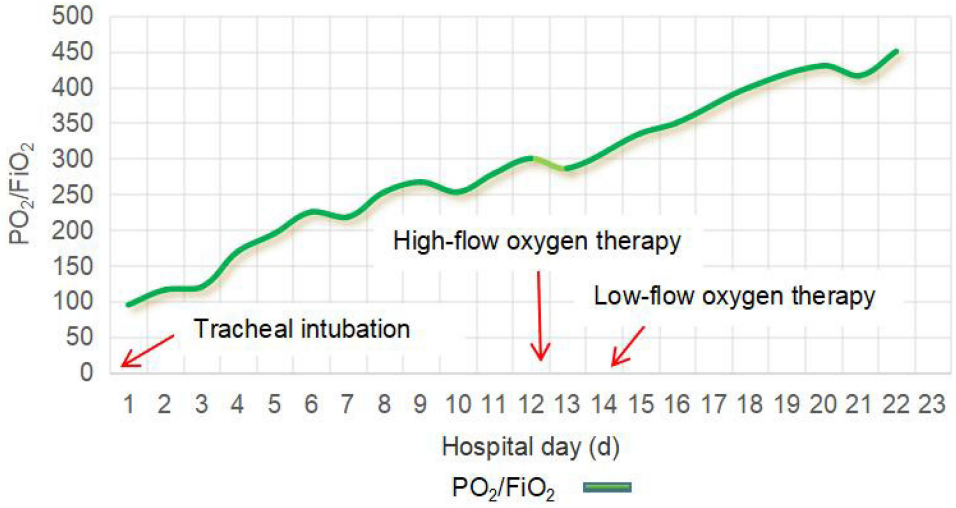

Figure 7 Change in the oxygenation index during hospitalisation.

Discussion

Chlamydia psittaci is a gram-negative, strictly intracellular parasitic pathogen that can cause zoonotic disease. Birds or poultry are common hosts, and inhalation or contact with the secretions or excretions of these hosts is the primary route of human infection. Human-to-human transmission has also been reported but is relatively rare.[6] Compared to other species of *Chlamydia, C. psittaci* is highly pathogenic and likely to cause severe systemic inflammatory reactions.[7] After infection, it first proliferates in the local monocyte-macrophage system in the respiratory tract. Thereafter, it spreads through the bloodstream to the lungs and other organs of the body, including the liver and kidney, circulatory system, and neuromuscular system. The pathogen causes inflammatory lesions in the lungs and damage the liver, kidney, and heart, of which lung injury is the primary manifestation and often results in severe pneumonia.[2,7] Common clinical manifestations include fever, chills, headache, and muscle aches; low sputum volume; relatively slow pulse; and generally normal or mildly elevated white blood cell count. Chest imaging indicates predominantly consolidated lung lesions, and respiratory distress and respiratory failure can develop rapidly in most severely ill patients, with some patients presenting ARDS and even multiple organ system failure.[8,9] In the present case, the disease progressed rapidly after onset, and respiratory failure, ARDS, and severe liver and kidney failure developed within a short period. However, the patient had a good prognosis after timely and accurate diagnosis and treatment, suggesting that early and accurate treatment is essential for improving prognosis.

Previously, diagnosis of psittacosis relied on serological tests, polymerase chain reaction (PCR), or pathogenic culture. However, serological tests are time-consuming and unsuitable for the diagnosis of acute-phase infections, PCR detects single types of pathogens and is prone to missed diagnosis, and pathogenic culture caries the risk of specimen contamination and low positive rates.[10,11] mNGS is a next-generation technology for precise pathogen detection that is not based on pathogenic culture and can be used for rapid and efficient high-throughput sequencing of nucleic acids in clinical samples. If intracellular bacteria or rare pathogens are detected, they should be considered as possible pathogens even if the sequence number is low.[12,13] Our patient presented with severe pneumonia and a poor response to conventional antibiotics, and *C. psittaci* was detected using mNGS of BALF as an intracellular bacterium and rare pathogen with a high sequence number of 14940. Along with the clinical manifestations, a clear diagnosis of severe *C. psittaci* pneumonia was made because of the combination of clinical manifestations, imaging features, and rapid improvement of the disease after targeted treatment. However, as the conditions for PCR and serological detection of *C. psittaci* were not available, the disease was not confirmed using the above diagnostic methods.

Omadacycline is a novel tetracycline obtained by adding an aminomethyl group to minocycline. It is effective against a variety of pathogens including methicillin-resistant *Staphylococcus aureus*, drug-resistant *Streptococcus pneumoniae*, extended-spectrum β-lactamase-producing gram-negative bacteria, anaerobic bacteria, and atypical pathogens. As it can

overcome resistance mechanisms, such as bacterial ribosomal protection proteins and drug efflux, it still has a strong antibacterial activity against bacteria resistant to doxycycline and minocycline.[14,15] It is not metabolised in the body, with 81.1% excreted via the faeces and 14.4% excreted via the kidneys;[16] therefore, it is more suitable for use in patients with hepatic and renal insufficiency. High concentrations of omadacycline have been found in alveolar cells, and omadacycline is not inferior to moxifloxacin as a potential antibiotic for the treatment of community-acquired pneumonia.[17,18]

Tetracyclines are the preferred treatment for *C. psittaci* pneumonia, with the oral dosage form for mild cases and intravenous injection recommended for severe cases. Other effective therapeutic agents include azithromycin, moxifloxacin, and levofloxacin for at least 10–14 d.[19,20] Our patient was treated with quinolones prior to diagnosis, although the efficacy was poor, which may be related to the low intracellular activity of quinolones in *C. psittaci*.[21] Doxycycline, minocycline, and macrolides are metabolised by the liver, which is prone to drug-induced injury and further deterioration of function.[22,23] Psittacosis is essentially a systemic infectious disease that can easily lead to multiple organ system failure.[2,7] Our patient developed severe hepatic and renal insufficiency rapidly after the onset of disease, which prevented the use of quinolones, macrolides, and conventional tetracycline antibiotic treatments. Studies have shown that omadacycline is not metabolised in the body and is primarily eliminated via faeces, and no dose adjustment is required for its application in special populations, such as the elderly individuals and patients with hepatic and renal insufficiency.[24,25] In the present study, the patient was treated with omadacycline promptly after diagnosis, and his condition improved rapidly, with all organ functions gradually returning to normal levels.

Conclusion

Psittacosis is a rare infectious disease, and it is not easily diagnosed through conventional pathogenic testing methods. mNGS is valuable for rapid and accurate diagnosis of this disease. Omadacycline has a good safety profile, does not require dose adjustment for special populations, and results in a good prognosis with timely use.

Ethics Approval and Informed Consent

The Ethics Committees of Huizhou Central People's Hospital (LLBA201946A) approved this study. Informed consent was obtained from the patient and guardians.

Consent for Publication

Signed consent was obtained for the publication of the case details from the participant.

Author Contributions

All authors made a substantial contribution to the work reported, including study conception, design, and execution; data acquisition, analysis, and interpretation. All authors were involved in drafting, revising, or critically reviewing the article. All author provided the final approval of the version to be published in the journal and agree to be accountable for all aspects of the work. All authors have read and approved the manuscript.

Funding

This study was supported by the Science and Technology Special Project of Huizhou (Grant no. 2020Y105).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Hogerwerf L, De Gier B, Baan B, et al. *Chlamydia psittaci* (psittacosis) as a cause of community-acquired pneumonia: a systematic review and meta-analysis. *Epidemiol Infect*. 2017;145(15):3096–3105. doi:10.1017/S0950268817002060
2. Zhang H, Zhan D, Chen D, et al. Next-generation sequencing diagnosis of severe pneumonia from fulminant psittacosis with multiple organ failure: a case report and literature review. *Ann Transl Med*. 2020;8(6):401. doi:10.21037/atm.2020.03.17
3. Zhang A, Xia X, Yuan X, et al. Severe *Chlamydia psittaci* pneumonia complicated by rhabdomyolysis: a case series. *Infect Drug Resist*. 2022;15:873–881. doi:10.2147/IDR.S355024

4. Zhanel GG, Esquivel J, Zelenitsky S, et al. Omadacycline: a novel oral and intravenous aminomethylcycline antibiotic agent. *Drugs*. 2020;80(3):285–313. doi:10.1007/s40265-020-01257-4
5. Kohlhoff SA, Huerta N, Hammerschlag MR. In vitro activity of omadacycline against *Chlamydia pneumoniae*. *Antimicrob Agents Chemother*. 2019;63(2):e01907–18. doi:10.1128/AAC.01907-18
6. Zhang Z, Zhou H, Cao H, et al. Human-to-human transmission of *Chlamydia psittaci* in China, 2020: an epidemiological and aetiological investigation. *Lancet Microbe*. 2022;3(7):e512–e520. doi:10.1016/S2666-5247(22)00064-7
7. Knittler MR, Sachse K. *Chlamydia psittaci*: update on an underestimated zoonotic agent. *Pathog Dis*. 2015;73(1):1–15. doi:10.1093/femspd/ftu007
8. Xiao Q, Shen W, Zou Y, et al. Sixteen cases of severe pneumonia caused by *Chlamydia psittaci* in South China investigated via metagenomic next-generation sequencing. *J Med Microbiol*. 2021;70(11). doi:10.1099/jmm.0.001456
9. Teng XQ, Gong WC, Qi TT, et al. Clinical analysis of metagenomic next-generation sequencing confirmed *Chlamydia psittaci* pneumonia: a case series and literature review. *Infect Drug Resist*. 2021;14:1481–1492. doi:10.2147/IDR.S305790
10. Li N, Li S, Tan W, et al. Metagenomic next-generation sequencing in the family outbreak of psittacosis: the first reported family outbreak of psittacosis in China under COVID-19. *Emerg Microbes Infect*. 2021;10(1):1418–1428. doi:10.1080/22221751.2021.1948358
11. Chen X, Cao K, Wei Y, et al. Metagenomic next-generation sequencing in the diagnosis of severe pneumonias caused by *Chlamydia psittaci*. *Infection*. 2020;48(4):535–542. doi:10.1007/s15010-020-01429-0
12. Li N, Cai Q, Miao Q, et al. High- throughput metagenomics for identification of pathogens in the clinical settings. *Small Methods*. 2021;5(1):2000792. doi:10.1002/smtd.202000792
13. Wu X, Li Y, Zhang M, et al. Etiology of severe community-acquired pneumonia in adults based on metagenomic next-generation sequencing: a prospective multicenter study. *Infect Dis Ther*. 2020;9(4):1003–1015. doi:10.1007/s40121-020-00353-y
14. Karlowsky JA, Steenbergen J, Zhanel GG. Microbiology and preclinical review of omadacycline. *Clin Infect Dis*. 2019;69(Suppl 1):S6–S15. doi:10.1093/cid/ciz395
15. Burgos RM, Rodvold KA. Omadacycline: a novel aminomethylcycline. *Infect Drug Resist*. 2019;12:1895–1915. doi:10.2147/IDR.S171352
16. Flarakos J, Du Y, Gu H, et al. Clinical disposition, metabolism and in vitro drug-drug interaction properties of omadacycline. *Xenobiotica*. 2017;47(8):682–696. doi:10.1080/00498254.2016.1213465
17. Gotfried MH, Horn K, Garrity-Ryan L, et al. Comparison of omadacycline and tigecycline pharmacokinetics in the plasma, epithelial lining fluid, and alveolar cells of healthy adult subjects. *Antimicrob Agents Chemother*. 2017;61(9):e01135–17. doi:10.1128/AAC.01135-17
18. Stets R, Popescu M, Gonong JR, et al. Omadacycline for community-acquired bacterial pneumonia. *N Engl J Med*. 2019;380(6):517–527. doi:10.1056/NEJMoa1800201
19. Balsamo G, Maxted AM, Midla JW, et al. Compendium of measures to control *Chlamydia psittaci* infection among humans (psittacosis) and pet birds (avian chlamydiosis), 2017. *J Avian Med Surg*. 2017;31(3):262–282. doi:10.1647/217-265
20. Cao B, Huang Y, She DY, et al. Diagnosis and treatment of community-acquired pneumonia in adults: 2016 clinical practice guidelines by the Chinese Thoracic Society, Chinese Medical Association. *Clin Respir J*. 2018;12(4):1320–1360. doi:10.1111/crj.12674
21. Cillóniz C, Torres A, Niederman M, et al. Community-acquired pneumonia related to intracellular pathogens. *Intensive Care Med*. 2016;42(9):1374–1386. doi:10.1007/s00134-016-4394-4
22. Wei C, Liu Y, Jiang A, et al. A pharmacovigilance study of the association between tetracyclines and hepatotoxicity based on Food and Drug Administration adverse event reporting system data. *Int J Clin Pharm*. 2022;44(3):709–716. doi:10.1007/s11096-022-01397-5
23. Ferrer P, Amelio J, Ballarín E, et al. Systematic review and meta-analysis: macrolides- and amoxicillin/clavulanate-induced acute liver injury. *Basic Clin Pharmacol Toxicol*. 2016;119(1):3–9. doi:10.1111/bcpt.12550
24. Rodvold KA, Burgos RM, Tan X, et al. Omadacycline: a review of the clinical pharmacokinetics and pharmacodynamics. *Clin Pharmacokinet*. 2020;59(4):409–425. doi:10.1007/s40262-019-00843-4
25. Yang H, Huang Z, Chen Y, et al. Pharmacokinetics, safety and pharmacokinetics/pharmacodynamics analysis of omadacycline in Chinese healthy subjects. *Front Pharmacol*. 2022;13:869237. doi:10.3389/fphar.2022.869237