Clin. Lab. 2023;69:XXX-XXX

CASE REPORT

Organizing Pneumonia Secondary to Infection with *Coxiella Burnetii*: a Case Report

Jing S. Bai, Qin Zhang, Jing X. Liu, Jing M. Wang, Qian C. Chen, Xin Y. Zhou, Rong X. Liu, Shan Gao, Ai S. Fu, Yan L. Ge

Department of Respiratory Medicine, North China University of Science and Technology Affiliated Hospital, Tangshan, Hebei, China

SUMMARY

Background: **Organizing pneumonia is a non-specific inflammatory response to various types of damage to the lungs. It is usually considered bacterial pneumonia that has not been absorbed for more than 4 weeks, accompanied by granulomas and fibrosis. Lung lesions in patients with organizing pneumonia are usually irreversible and the prognosis is relatively poor. *Coxiella burnetii* can cause Q fever. Acute Q fever usually presents as a self-limiting febrile illness with a good prognosis, but there are few cases of coexisting organizing pneumonia. We report a case of organizing pneumonia secondary to *Coxiella burnetii* infection.**
Methods: **Percutaneous lung biopsy, Next-generation sequencing (NGS).**
Results: **Percutaneous lung biopsy showed the existence of organizing pneumonia, and external examination of NGS showed the existence of *Coxiella burnetii* infection. After symptomatic treatment with azithromycin and glucocorticoids, the patient improved and was discharged from the hospital.**
Conclusions: **For lesions with obvious heterogeneous enhancement on chest CT imaging, percutaneous lung biopsy or bronchoscopy should be performed promptly to obtain pathological tissue, and NGS should be used for definite diagnosis if necessary.**
(Clin. Lab. 2023;69:xx-xx. DOI: 10.7754/Clin.Lab.2022.220721)

Correspondence:
Yan L. Ge
North China University of Science and Technology Affiliated Hospital
Tangshan, Hebei
China
Phone: +86 15932081296
Email: 495732196@qq.com

Case Report accepted July 29, 2022

KEYWORDS

organizing pneumonia, Q fever, *Coxiella burnetii*, percutaneous lung aspiration, next-generation sequencing

CASE REPORT

A 70-year-old man was admitted to the hospital mainly due to fever for 3 days after catching a cold. He privately complained that he developed a fever after having caught cold 3 days before admission with a body temperature of up to 38.9°C, accompanied by abdominal distension, no chills, chills, no muscle pain in limbs, no obvious cough, expectoration, no abdominal pain, no frequent urination, urgency, or dysuria, etc. Bladder irritation symptoms, take "ibuprofen sustained-release capsules 0.3 g bid" by himself, the body temperature can drop, but it is not normal, and high fever occurs repeatedly after that. The patient initially denied a history of

drug allergy, but during subsequent treatment, we found him to be allergic to "Piperacillin Sodium and Tazobactam Sodium". On admission, pulmonary auscultation was audible and the breath sounds were rough, and there was no obvious abnormality in the rest of the examination. Relevant laboratory examinations such as infection indicators after admission: CRP 89.5 mg/L (reference value 0 mg/L - 8 mg/L), SAA 253.09 mg/L (reference value 0 mg/L - 10 mg/L), PCT 0.51 ng/mL (reference value 0 ng/mL - 0.05 ng/mL), ESR 47 mm/hours (reference value 0 mm/h - 15 mm/hours), fibrinogen 4.88 g/L (reference value 2 g/L - 4 g/L). Simultaneous blood routine prompts: WBC 3.3 x 10^9/L (reference value 4 x 10^9/L -10 x 10^9/L), LYM 0.75 x 10^9/L (reference value 0.8 x 10^9/L - 4 x 10^9/L), and no obvious abnormality was found in biochemical tests. A chest CT scan showed a patchy high-density shadow in the lower lobe of the left lung, with obvious inhomogeneous enhancement, blurred borders, and surrounding halo signs (Figure 1, 2). Inflammatory lesions should be considered, and space-occupying lesions should be excluded after anti-inflammatory treatment. We initially diagnosed community-acquired pneumonia, so until the test results were reported, the patient was given empiric antibiotic therapy: intravenous (IV) moxifloxacin with a dose of 0.4 g once daily. After 48 hours of anti-infection treatment, the patient still had repeated fever. During the period, the virus series, G test, GM test, sputum smear, sputum culture, blood culture, and other related tests were all negative, and no pathogen was finally detected. We prepared to adjust the antibiotic but found that the patient was allergic to "Piperacillin Sodium and Tazobactam Sodium", and finally added intravenous (IV) etimicin with a dose of 300 mg once daily based on moxifloxacin. The patient underwent 72 hours of anti-infection treatment again. Although the body temperature did not rise again, the infection indicators were rechecked: CRP 8.9 mg/L (reference value 0 mg/L - 8 mg/L), SAA 50.1 mg/L (reference value 0 mg/L - 10 mg/L), PCT 0.14 ng/mL (reference value 0 ng/mL - 0.05 ng/mL), ESR 59 mm/hours (reference value 0 mm/hours - 15 mm/hours). We consider that the patient's symptoms such as fever have improved compared with before, but he is still in an infected state. The cryptococcal antigen analysis is negative, and we have not been able to identify the pathogenic bacteria. To further identify the pathogenic bacteria, CT-guided percutaneous lung puncture and biopsy of the lower lobe of the left lung showed alveolar epithelial cell hyperplasia, interstitial fibrosis with carbon deposition, and organized pneumonia (Figure 3, 4). At the same time, the external inspection NGS reported that there was a sequence number of 3 (reference range ≥ 1) of *Coxiella burnetii*, and the qualitative result was positive. Finally, it was confirmed that the patient was diagnosed with organizing pneumonia combined with Q fever infection, and the patient was treated with azithromycin 0.5 g orally 1/day combined with glucocorticoids. After one week of treatment, the patient's current infection index dropped to the normal range. Three weeks later, the patient's chest CT scan showed that the patchy high-density shadow in the left lower lung was smaller than before, and the surrounding halo sign disappeared, showing moderate enhancement (Figure 5, 6). Subsequently, the patient improved and was discharged from the hospital and adhered to glucocorticoid maintenance therapy.

DISCUSSION

Organizing pneumonia (OP) is a rare interstitial lung disease affecting distal bronchioles and alveoli and is considered a nonspecific response to lung injury [1]. OP is a clinical-radiologic-pathologic (CRP) diagnosis [2] characterized by the presence of granulation tissue within the terminal or respiratory bronchioles, alveolar ducts, and surrounding alveoli, associated with chronic inflammation of the remaining lung parenchyma [3]. OP may be associated with connective tissue diseases, drugs, malignancies, and bacterial or viral infections [4]. Early studies found that the incidence of OP was 6 - 7 cases per 100,000 people [5], with secondary OP accounting for the majority. A recent retrospective study of 1,346 cases of OP by Yuan Zhang et al. showed that 1,170 cases were secondary OP, accounting for 86.9% of the total sample [6]. Pathological biopsies are infrequently performed in patients with OP and are often misdiagnosed as pulmonary infection, tuberculosis, or cancer [7]. No unique pattern was found in the clinical presentation of OP patients. In addition, OP secondary to infectious factors often has a subacute course, which is the main reason for early misdiagnosis. At the same time, the chest imaging manifestations of patients with secondary OP are polymorphic and diverse, which makes it difficult for early diagnosis of OP. This patient had an acute course of the disease, and chest CT only showed patchy high-density shadows in the lower lobe of the left lung, so we misdiagnosed it as community-acquired pneumonia in the early stage.

OP secondary to infectious factors is not uncommon, but *Coxiella burnetii* infection is rarely associated with secondary OP. *Coxiella burnetii* infection is the typical pathogen causing Q fever [8], an obligate Gram-negative bacterium that infects humans, and various animals, and is found in labor products (e.g., placenta), urine. It is excreted in liquid, milk, and feces [9], and the main route of transmission is the inhalation of contaminated aerosols [10]. Q fever can present in acute or chronic forms, and many people with acute Q fever are asymptomatic, but some develop fever, pneumonia, or hepatitis. Chronic infection is rare, occurring in less than 5% of contacts. A recent national surveillance study of Q fever in the United States showed that the 10-year average annual incidence for acute Q fever was 0.36 cases per million persons, and the average annual incidence for chronic Q fever was 0.09 cases per million persons [11]. Q fever has a low incidence, no specific clinical manifestations, and is often overlooked clinically. In re-

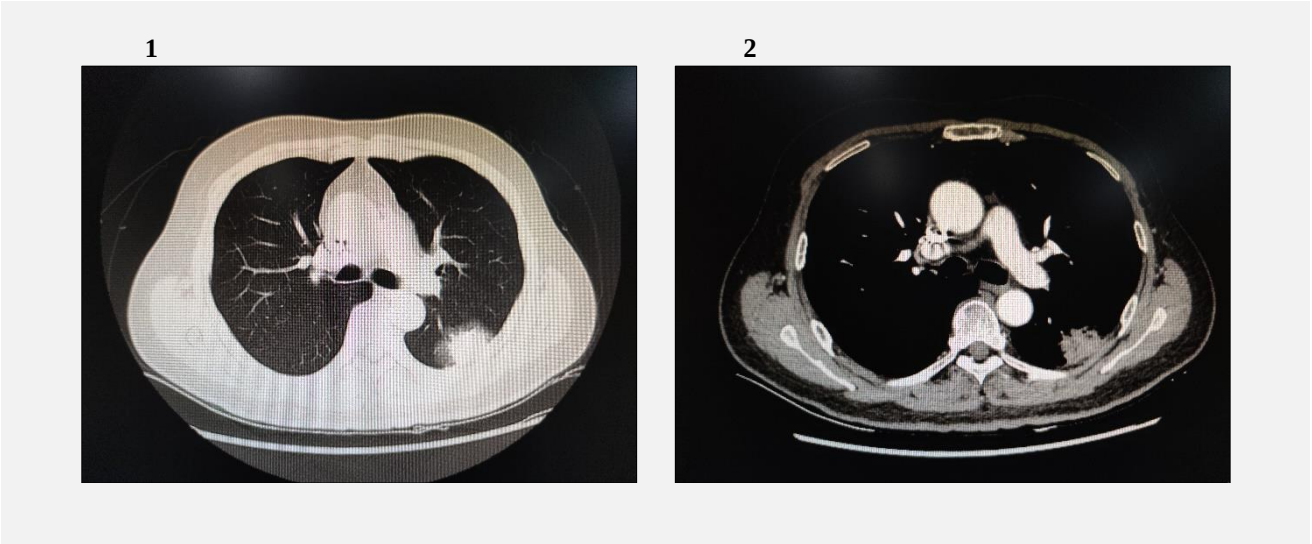

Figure 1 and 2. A patchy high-density shadow can be seen in the lower lobe of the left lung, with moderate enhancement, blurred borders, and a halo sign around it. It is considered that there is an inflammatory lesion in the lower lobe of the left lung.

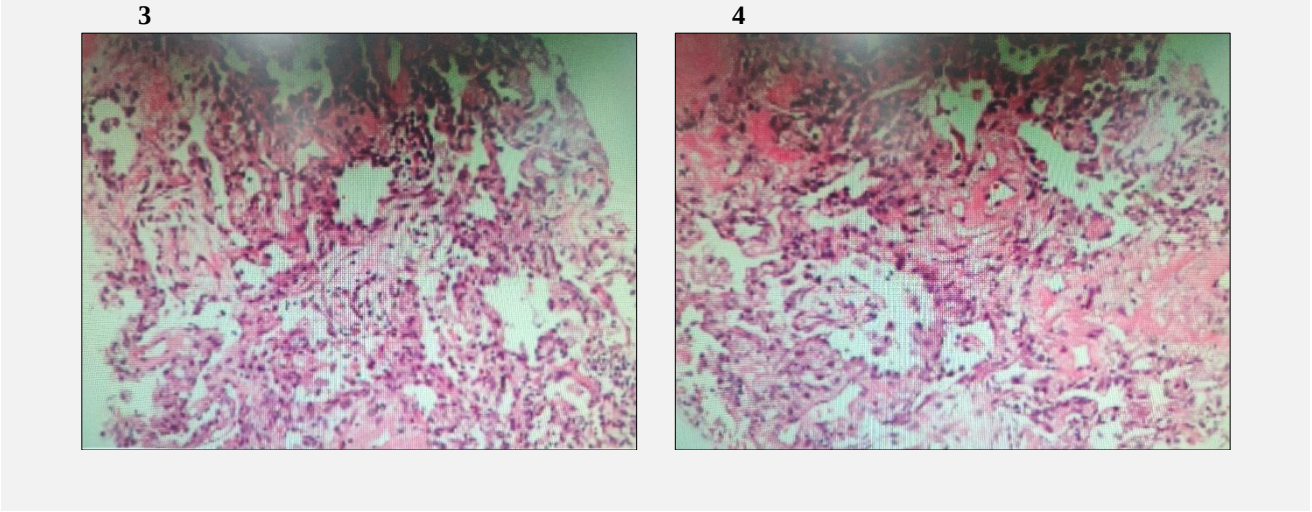

Figure 3. and 4. Needle biopsy of the left lower lobe showed hyperplasia of alveolar epithelial cells, interstitial fibrosis with carbon deposits, and organizing pneumonia.

The results of immunohistochemistry and special staining supported the diagnosis of organizing pneumonia. TTF-1(+), CK(+), P63(-), P53(+, 1%), Ki-67 hot spot index 1%, PAS(-), silver hexamine (-).

NGS reported.

Detection index	RPTM *	Positive reference range	Qualitative results
Coxiella burnetii	3	≥ 1	Bacterial positive

*** RPTM - The number of positive sequences contained in every 10 million detected sequences.**

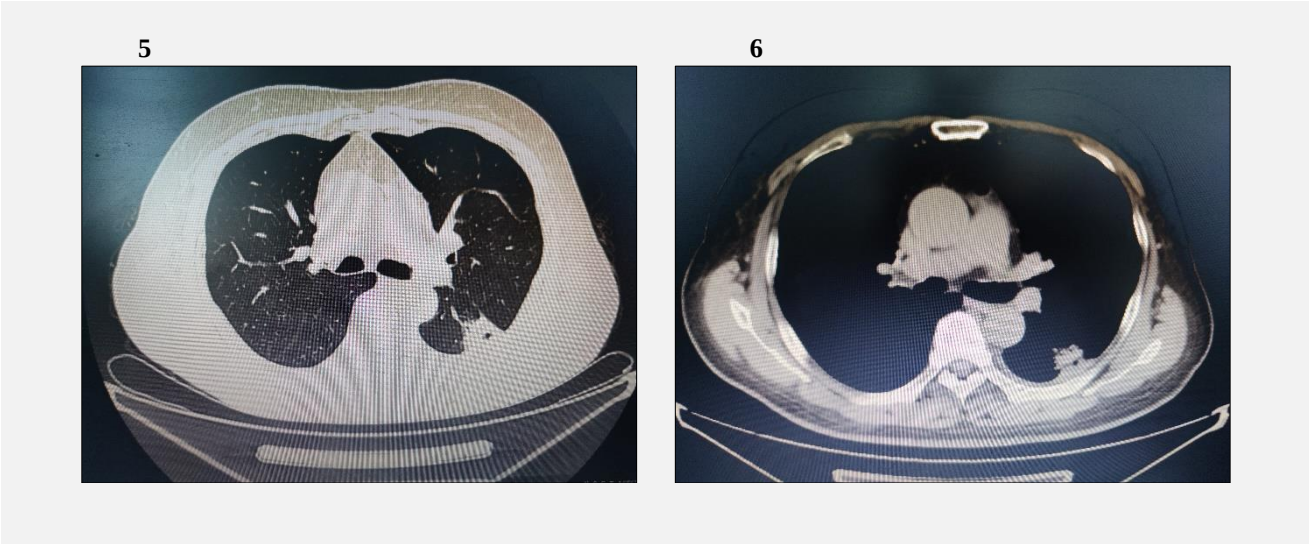

Figure 5. and 6. After three weeks of azithromycin combined with glucocorticoid treatment, the patchy high-density shadow in the left lower lung shrunk compared with the previous one, and the surrounding halo sign disappeared, showing moderate enhancement.

cent years, clinical metagenomic next-generation sequencing (NGS), a new molecular method that can characterize all DNA or RNA and identify various microorganisms in a sample [12], has been used to identify pathogens, including shellfish Cox's body [13]. For this patient, we used NGS to identify the presence of *Coxiella burnetii* infection in the early stage and gave early drug treatment to avoid serious complications such as endocarditis in the patient.

OP secondary to *Coxiella burnetii* infection has a good response to glucocorticoids. In this case, after the application of macrolide antibiotics and glucocorticoids, the fever symptoms and infection indicators were well controlled. Although, short-term chest imaging left lower lung hyperdensity was not significantly relieved, which may be due to imaging lag, and the patient was older and had a longer recovery period.

CONCLUSION

Our case shows that for suspected pneumonia patients who have not significantly improved by antibiotic treatment, early examinations such as bronchoscopy or percutaneous lung biopsy are required to make a definite diagnosis and customize steroid therapy early in the disease process, which will ultimately reduce the incidence of disease rate, length of hospital stay, and improved quality of life.

Acknowledgment:
We would like to thank the other members of the Department of Respiratory Medicine, Affiliated Hospital of the North China University of Technology for their constructive criticism.

Source of Support:
This work was supported by the Notice of Hebei Medical applicable technology tracking project plan in 2021 (gz2021057).

Ethical Approval:
This study was approved by the ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:
No conflicts of interest to declare.

References:

1. Khatib S, Al-Shyoukh A, Abdalla K, Jaber FS, Salzman G. Organizing Pneumonia Secondary to Pulmonary Actinomycosis: A Case Report and Literature Review. Cureus 2022 Jan 11;14(1): e21133. (PMID: 35165586)

2. King TE Jr, Lee JS. Cryptogenic Organizing Pneumonia. N Engl J Med 2022 Mar 17;386(11):1058-69. (PMID: 35294814)

3. Tiralongo F, Palermo M, Distefano G, et al. Cryptogenic Organizing Pneumonia: Evolution of Morphological Patterns Assessed by HRCT. Diagnostics (Basel) 2020 Apr 29;10(5):262. (PMID: 32365469)

4. Fujita J, Bandoh S, Yamaguchi M, Higa F, Tateyama M. Chest CT findings of influenza virus-associated pneumonia in 12 adult patients. Influenza Other Respir Viruses 2007 Sep-Nov;1(5-6): 183-7. (PMID: 19453425)

5. Zhou X, Chen Y, Zhao L. Organizing pneumonia: a rare pulmonary manifestation of well-controlled ulcerative colitis. J Thorac Dis 2018 Aug;10(8):E634-E638. (PMID: 30233901)

6. Zhang Y, Li N, Li Q, et al. Analysis of the clinical characteristics of 176 patients with pathologically confirmed cryptogenic organizing pneumonia. Ann Transl Med 2020 Jun;8(12):763. (PMID: 32647688)

7. Murofushi KN, Oguchi M, Gosho M, Kozuka T, Sakurai H. Radiation-induced bronchiolitis obliterans organizing pneumonia (BOOP) syndrome in breast cancer patients is associated with age. Radiat Oncol 2015 Apr 26;10:103. (PMID: 25924810)

8. Espana PP, Uranga A, Cilloniz C, Torres A. Q Fever (Coxiella Burnetii). Semin Respir Crit Care Med 2020 Aug;41(4):509-21. (PMID: 32629489)

9. Eldin C, Melenotte C, Mediannikov O, et al. From Q Fever to Coxiella burnetii Infection: a Paradigm Change. Clin Microbiol Rev 2017 Jan;30(1):115-90. (PMID: 27856520)

10. Farooq M, Khan AU, El-Adawy H, et al. Research Trends and Hotspots of Q Fever Research: A Bibliometric Analysis 1990-2019. Biomed Res Int. 2022 Jan 15;2022:9324471. (PMID: 35075431).

11. Cherry CC, Nichols Heitman K, Bestul NC, Kersh GJ. Acute and chronic Q fever national surveillance - United States, 2008 - 2017. Zoonoses Public Health 2022 Mar;69(2):73-82. (PMID: 34626097)

12. Chiu CY, Miller SA. Clinical metagenomics. Nat Rev Genet 2019 Jun;20(6):341-55. (PMID: 30918369)

13. Kondo M, Dalai SC, Venkatasubrahmanyam S, et al. Diagnosis and Genotyping of *Coxiella burnetii* Endocarditis in a Patient with Prosthetic Pulmonary Valve Replacement Using Next-Generation Sequencing of Plasma Microbial Cell-Free DNA. Open Forum Infect Dis 2019 Jun 1;6(6):ofz242. (PMID: 31249846)