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CASE REPORT

A Case Study of Severe Pneumonia Caused by mixed Infection of *Chlamydia Abortus* and *Influenza a* in a Female Patient

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Background: *Chlamydia abortus* is a zoonotic pathogen that causes miscarriage, stillbirth, and sepsis of pregnancy in pregnant women when it infects humans. However, it rarely causes pneumonia in humans.

Case Presentation: This case reports a case of severe pneumonia characterized by high fever and cough, and the disease rapidly progressed to dyspnea. The patient was treated with moxifloxacin and doxycycline. *Chlamydia abortus was* detected in bronchoscopy examination and bronchoalveolar lavage fluid (BALF) through metagenomic next-generation sequencing (mNGS)-DNA. A weak positive for *influenza A* (*H1N1*) antigen was also found in the throat swab tested. Subsequently, we added mabaloxavir and replaced doxycycline with an intravenous infusion of omadacycline. After effective treatment, the patient developed a urinary tract infection, and the treatment plan was adjusted to meropenem combined with omadacycline. The patient's condition improved, and she was discharged on the 14th day of admission.

Conclusion: This is the first report of cases of non-pregnant female patients with *Chlamydia abortus* infection pneumonia. Consequently, infections with *Chlamydia abortus* can result in severe respiratory distress, disturbance of water and electrolyte balance, and abnormal liver function, which requires timely diagnosis and correct use of antibiotics by clinicians. Consequently, the mixed infection of *H1N1* and *Chlamydia abortus* aggravated the complexity of the condition and treatment. Combining tetracycline and quinolone is effective for treating severe pneumonia with *Chlamydia abortus* infection.

Keywords: chlamydia abortus, severe pneumonia, metagenomics next-generation sequencing, case report

Background

Chlamydia is a family of obligate intracellular Gram-negative bacteria consisting of more than 10 species belonging to the order Chlamydiales and the family Chlamydiaceae.[1] Notably, they are widely distributed worldwide and infect various hosts, including amoebae, insects, aquatic animals, reptiles, birds, and mammals.[2] The most common pathogens that infect humans are *Chlamydia psittaci, Chlamydia trachomatis*, and *Chlamydia pneumoniae*.[3] *Chlamydia abortus* (*C. abortus*) is a zoonotic pathogen that primarily colonizes the placenta of ruminants such as goats, sheep, yaks, pigs, and horses.[4] Human infections with *C. abortus* are infrequent. However, they can result in severe symptoms, such as abortion, stillbirth, gestational sepsis, and rarely pneumonia.[4] Therefore, we report a case of severe pneumonia caused by *C. abortus* infection in a female patient diagnosed using next-generation metagenomic sequencing (mNGS). Further, we discuss the clinical characteristics, signs, laboratory examination, treatment protocol, and prognosis of this case to provide a clinical reference for the future.

Case Presentation

A previously healthy 60-year-old female was admitted to our tertiary academic center for influenza-like illness, headache, dry cough, and fever (40°C) within 14 days. Prior to admission, she sought medical attention at a local clinic. However,

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the effectiveness of antipyretic drugs was not satisfactory. Seven days earlier, she experienced breathing difficulties that gradually worsened.

Upon admission, physical examination showed a temperature of 36.5°C, heart rate of 68/min, respiratory rate of 20/min, and blood pressure of 116/47 mmHg, SPO299% (with high flow humidified oxygen therapy, flow rate 35L/min, oxygen concentration 80%). Auscultation revealed dull percussion in both lungs, thick breathing sounds in both lungs and a few moist rales. Upon questioning the patient's son, we learned she fed chickens and ducks at home and had a history of contact with poultry.

Laboratory investigations revealed type I respiratory failure, disturbance of water and electrolyte balance (hyponatremia, hypokalemia), anemia, hypoproteinemia, abnormal liver function, increased NT-pro BNP, lactate dehydrogenase, procalcitonin, erythrocyte sedimentation rate (ESR), D-dimer, and fibrinogen (Table 1). Other investigations identified urine occult blood, ketone bodies and a negative COVID-19 nucleic acid test. Chest CT showed multiple patchy high-density shadows in both lungs, consolidation shadows in the upper lobes of both lungs, numerous small nodules in both lungs and bilateral pleural effusion (Figure 1).

Table 1 Initial Maternal Laboratory Results

Variable	Result	Reference range
Red blood cell count (10^12/L)	3.36	3.8–5.1
Lymphocyte count (10^9/L)	0.3	1.1–3.2
Hemoglobin (g/L)	99	115–150
Neutrophilic percentage (%)	90.7	40–75
Lymphocyte percentage (%)	7	20–50
Eosinophil count (10^9/L)	0	0.02–0.52
Eosinophil percentage (%)	0	0.4–8
Total protein (g/L)	54.7	65–85
Albumin (g/L)	25.5	40–55
Direct bilirubin (umol/L)	8.1	0–6.8
Alanine aminotransferase (U/L)	104.3	7–40
Aspartate aminotransferase (U/L)	83.4	13–35
Alkaline phosphatase (U/L)	422.9	50–135
Glutamyl transpeptidase (U/L)	356.2	7–45
Lactic dehydrogenase (U/L)	418	120–250
Myoglobin (ug/L)	113.5	<70
D-dimer (mg/L)	2.75	0–0.5
Fibrinogen (g/L)	7.6	2–4
Potassium (mmol/L)	2.78	3.5–5.3
Sodium (mmol/L)	130.6	137–147
Chlorine (mmol/L)	93.1	99–110
Calcium (mmol/L)	1.68	2.11–2.52
Phosphorus (mmol/L)	0.56	0.85–1.51
Erythrocyte sedimentation rate (mm/h)	120	0–38
Procalcitonin (ng/mL)	0.92	0–0.046
NT-pro BNP	1731.1	0–900
Arterial blood gases		
%FiO2	60%	
pH	7.57	7.35–7.45
PCO2 (mm Hg)	30.8	35–45
PO2 (mm Hg)	75	80–105
HCO3- (mmol/L)	28.3	22–26
BE (mmol/L)	6	−2-3

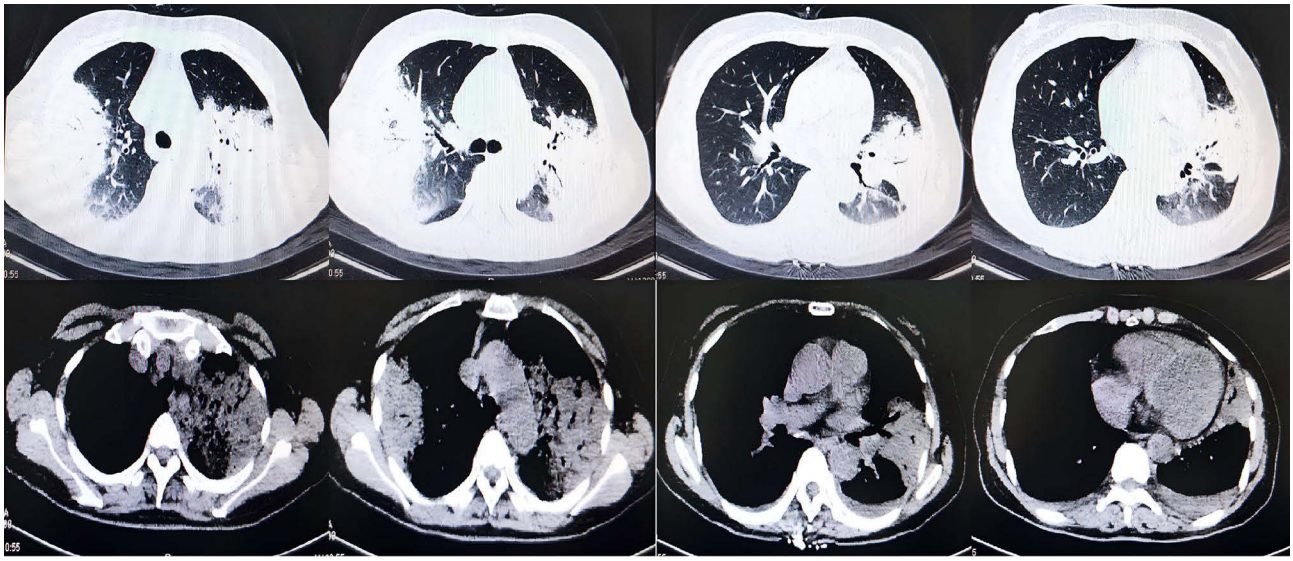

Figure 1 Multiple patchy high-density shadows and consolidation shadows of both lungs (CT image of the chest on 3th day before admission).

The patient was diagnosed with severe pneumonia, type I respiratory failure, hypoproteinemia, electrolyte disturbance (hyponatremia, hypokalemia), abnormal liver function, and mild anemia upon admission. Considering the patient had a history of contact with poultry, preliminary suspicion suggested that the patient may be infected with atypical pathogens. Then, the patient was treated with an intravenous infusion of moxifloxacin (0.4g qd) and oral doxycycline (0.1g q12h), supplemented with protecting gastric mucosa, anticoagulation, resolving phlegm, dilating bronchi, and maintaining water-electrolyte balance by improving the symptom of respiratory failure via oxygen inhalation.

On the second day of admission, the patient experienced a progressive decrease in blood oxygen saturation (oxygenation index of 74). As a result, the patient required intubation and ventilator (PCV, FiO2 70%, PEEP 14.0 cmH2O). Repeated arterial blood-gas analysis showed a pH level of 7.47, PaCO2 at 42mmHg, PaO2 at 87mmHg, PO2/FiO2 at 124 mmHg, and blood lactate at 1.0mmol/L. Laboratory test results indicated a weak positive for *influenza A* (*H1N1*) antigen, and the patient was given oral antiviral treatment with 40mg of mabaloxavir tablets. Bronchoalveolar lavage fluid (BALF) samples were sent for metagenomic next-generation sequencing (mNGS) -DNA detection to obtain more information on the pathogen. Only *C. abortus* was detected with a 1486 sequence number (85.53% of relative abundance) by mNGS-DNA tests of BALF (Figure 2). Thus, we replaced doxycycline with an intravenous infusion of omadacycline (0.1 qd), while the intravenous infusion of moxifloxacin (0.4g qd) treatment was continued.

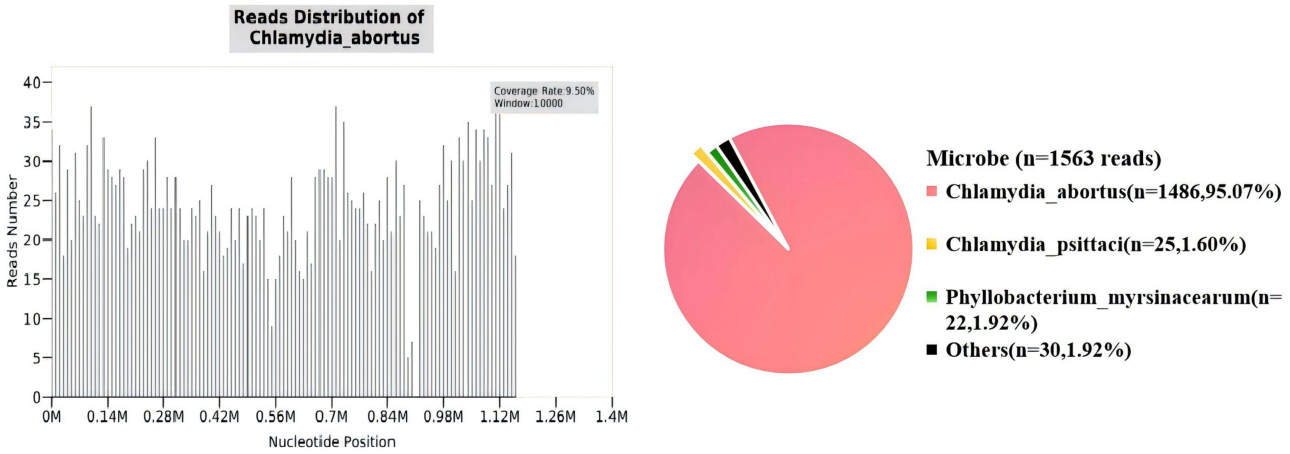

Figure 2 The unique mapping reads of *Chlamydia abortus* was 1486. (Diagnosis of *C. abortus* infection using mNGS test).

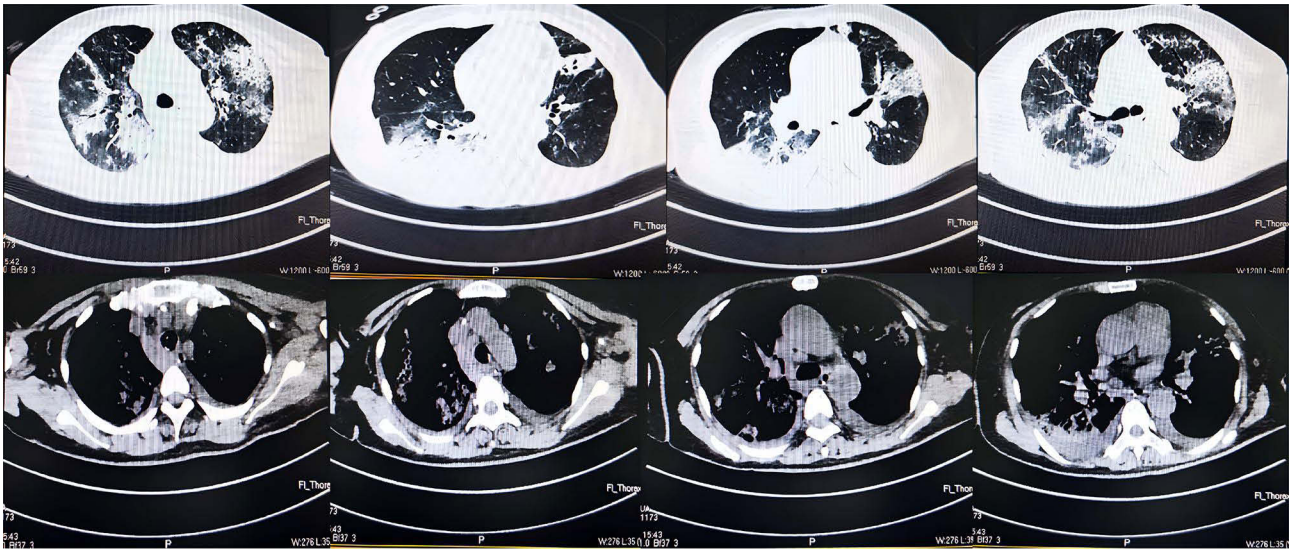

Figure 3 Multiple glass opacities and consolidation shadows were found in both lungs (CT image of the chest on the 7th day of admission).

Delightedly, the temperature and thermal potential of the patient decreased significantly. The oxygenation index increased significantly, the percentage of neutrophilic percentage, and C-reactive protein and procalcitonin continued to decline. However, the patient experienced a high fever (39°C) again on the 7th day of admission. Then, the patient underwent lung CT examination again (Figure 3), indicating that the ground-glass lesions in both lungs were significantly increased. In contrast, the consolidation of both upper lungs was reduced compared to the previous examination. Considering the possibility of other infectious pathogens, the treatment was changed to an intravenous infusion of levofloxacin (0.5g qd) and omadacycline (0.1 qd). Subsequently, the patient's temperature gradually decreased, but a low fever remained. On the 8th day of admission, *Chlamydia* was detected with 9 specific reads (1.07% of relative abundance) by mNGS-DNA tests of BALF.

On the 11th day of admission, the patient was removed from the tracheal intubation and received high-flow sequential oxygen therapy. The patient's urine presented as flocculent material with a slightly cloudy color. A routine urine examination revealed piles of pus cells. Moreover, the urine culture of the patient revealed multi-drug resistant *Escherichia coli* (sensitive to ertapenem, imipenem, meropenem, amikacin, and furantoin, remaining resistant), indicating resistance to levofloxacin (mic≥8). Therefore, levofloxacin was adjusted to an intravenous infusion of meropenem (1g q8h). Consequently, the patient's condition improved, and she was discharged. The patient's condition and laboratory index also improved. The biochemical indicators of the patient's liver function throughout the treatment process showed a slow upward trend. Although hepatoprotective drugs were used, ALT and AST were still at twice the normal upper limit. She was later discharged on the 14th day of admission and transferred to a local hospital for further treatment.

Discussion

To our knowledge, only a few studies reported human pneumonia caused by *C. abortus*. Ortega et al[5] reported the first atypical pneumonia related to *C. abortus* in Spain in 2016. The patient was a 47-year-old male, a veterinarian researcher with a focus on *Chlamydiae*. In 2020, a case of acute respiratory distress syndrome in a pregnant woman infected with *C. abortus* was reported in France.[6] In 2022, a 66-year-old male patient with bloodstream infection and pneumonia caused by *C. abortus* and a 65-year-old male patient with septic shock caused by *C. abortus* infection were reported in China.[7,8] In the same year, a case of severe pneumonia caused by *C. abortus* infection in pregnant women was reported in Switzerland.[9] In 2023, China reported two cases of pneumonia caused by *C. abortus* in men diagnosed through mNGS. One of the patients received extracorporeal membrane oxygenation treatment for respiratory deterioration but unfortunately died.[10,11] According to the reported cases of *C. abortus* infection pneumonia, the majority of patients are male, or

pregnant female patients. There have been no reports of cases of non-pregnant female patients. This case report is a 60-year-old female patient with no underlying diseases.

We should also note that this patient was co-infected with *H1N1*. Mixed infection may have exacerbated the complexity of this patient's condition and treatment. Qiao et al[12] also found that influenza bacterial co-infection was associated with high risk of severe illnesses. Klein et al[13] demonstrated that *Chlamydia* was also an important pathogen in influenza co-infection. Moreover, a study conducted at a tertiary hospital in China, spanning data from 8 influenza seasons, revealed that the incidence of community-acquired influenza with bacterial co-infection was 19.6%, among which the incidence of *Chlamydia* pneumoniae was 4.9%.[14] It was unclear whether the *C. abortus* infection in this patient was secondary to the *H1N1*. Notably, this report also highlights the importance of clinical vigilance for related patients in the future, emphasizing the need for close attention to the possibility of such secondary infections.

There are few reports of human infections caused by *C. abortus*, likely related to difficulties in identification. No serological testing has been approved for diagnosing *C. abortus* infection in humans.[4] Other testing methods for pathogen identification include specimen culture and PCR. Unfortunately, certain limitations exist regarding detection time, rate of positivity, and specificity with these applications. NGS is a technology with high throughput parallel sequencing, which can sequence DNA or RNA fragments simultaneously and independently.[15] Meanwhile, it is little affected by the antibiotics already used by the patient and is especially suitable for diagnosing novel, rare, and atypical etiologies of complicated infectious diseases.[16] Several cases of *C. abortus* infection pneumonia reported in China were confirmed through mNGS.[7,8,10,11] In this case, sputum, BALF, and blood samples were collected for smear and culture, except for a weak positive for *H1N1* antigen, while no pathogenic bacteria and fungi were found. Acid-fast staining of sputum and BALF was negative. However, we detected *C. abortus* in BALF through mNGS, and based on the patient's host factors, clinical symptoms, laboratory test results, imaging, and disease outcomes, we determined that the patient was suffering from severe pneumonia caused by *C. abortus* infection.

Until now, the source of human infection with *C. abortus* is not yet clear, and studies have shown that it may be related to direct or indirect exposure to the urine, milk, feces, and secretions of infected animals.[5,9,17,18] A recent study also showed that infected patients have no apparent history of contact with livestock, indicating the possibility of other undetected infections.[2] A Polish study revealed the occurrence of *C. abortus* in chickens, albeit at a lower detection rate than that of *C. psittaci*.[19] The latest cross-sectional epidemiological study from Belgium found that *C. abortus* was detected in 56.0% of the tested chicken flocks, indicating that *C. abortus* strains can be widespread among chickens.[20] Furthermore, that study also found *C. abortus* DNA from chicken caretakers. Fisher's exact test revealed a significant correlation between the infected backyard chickens and *C. abortus* in humans. In the present case, the patient's son reported a history of contact with poultry. Therefore, we suspect that *C. abortion* could be transmitted through poultry and could cause lung infection in female patients.

However, the specific pathway to human infection with *C. abortus* remains unclear. Likewise, individuals who are not immunocompromised can also be susceptible. In this female patient, the clinical manifestations of *C. abortion*-induced pulmonary infection were non-specific and manifested with fever, cough, and limb weakness as the main symptoms. However, the disease rapidly and quickly progressed to dyspnea. Auxiliary examination exhibited respiratory failure, hyponatremia, hypokalemia, anemia, hypoproteinemia, and abnormal liver function. Chest CT showed multiple patchy high-density shadows, consolidation shadows, and bilateral pleural effusion. Similar to clinical manifestations of *Chlamydia psittaci* infection,[21] human *C. abortus* pneumonia is rare but may have a life-threatening condition. As we reported, the patient rapidly experienced progresses to dyspnea and circulatory instability.

Therefore, clinical physicians must make timely diagnoses and prescribe the correct antibiotic treatment. *Chlamydia* is a gram-negative intracellular bacterium that contains a thin peptidoglycan cell wall and an outer membrane containing lipopolysaccharides. Importantly, beta-lactams are effective on *Chlamydial* elementary bodies. However, they have been linked to the development of aberrant bodies (*Chlamydia* persistence), which is why they are not recommended for treatment.[22] There are no treatment guidelines for *C. abortus* infections in humans, and the current treatment mainly refers to the recommendations for *C. psittaci* infection. Tetracycline antibiotics are considered the most effective treatment for *C. psittaci* infection, with the oral dosage form for mild cases and intravenous injection for severe cases.[23] Moreover, macrolide and quinolone antibiotics are alternative agents.[24,25] Fang et al[26] reported that the new

tetracycline drug, omadacycline, will become a new option for treating severe *C. psittaci* infection due to its safety and the advantage of not requiring dose adjustment in special populations. Importantly, the clinical outcome of this patient showed that the combination of omadacycline and moxifloxacin had a satisfactory therapeutic effect on severe pneumonia with *C. abortus* infection.

Conclusion

Infections of *C. abortus* co-infected with *H1N1* can result in severe respiratory distress, disturbance of water and electrolyte balance, and abnormal liver function, requiring timely diagnosis and correct use of antibiotics by clinicians. Our report also highlights the importance of mNGS as a diagnostic tool for rare pathogens. Combining tetracycline and quinolone is a practical choice for treating severe pneumonia with *C. abortus* infection. Further research is needed to identify the transmission routes of *C. abortus* infection and explore an effective clinical diagnostic model to establish scientific prevention guidelines and precise clinical treatment strategies.

Data Sharing Statement

The dataset supporting the conclusions of this article is included in the article. Specific laboratory or imaging data are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Xiangya Hospital, Central South University (No.ChiCTR2100046040). Written informed consent was obtained from the patient's son for publication of this case report.

Consent for Publication

The patient provided oral informed consent for publication of the clinical details including lung CT images. Written informed consent was provided by the patient's relatives (patient's son) for publication of the case details and images. The patient's verbal informed consent and her son's written informed consent for publication of case-related details were witnessed and documented. Details of the case can be published without institutional approval.

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Disclosure

No conflict of interest exists in the submission of this manuscript, and the manuscript has been approved by all authors for publication.

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