

# New Detection and Treatment for Chlamydia Psittaci: A Case Report

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## Case Study

**Keywords:** Chlamydia psittaci, severe community-acquired pneumonia, gestational psittacosis, next-generation sequencing, tigecycline

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## Abstract

**Background:** The presentation of psittacosis can vary from subclinical infection to fatal pneumonia with a high mortality rate. *Chlamydia psittaci* infection during pregnancy is rare and might result in placental involvement, premature delivery or miscarriage. Herein, we report a case of severe pneumonia in a pregnant woman caused by *C. psittaci*.

**Case presentation:** A 27-year-old female with a pregnancy at 22 weeks was admitted with hyperpyrexia, dry cough and dyspnea. Laboratory tests showed increased white blood cell count and slightly-elevated procalcitonin. Chest computed tomography scan revealed consolidation in the lingual and inferior lobe of the left lung. She suffered rapidly progressing respiratory failure and required mechanical ventilation and extracorporeal membrane oxygenation (ECMO). Her sample of bronchoalveolar lavage fluid (BALF) was collected, from which *C. psittaci* was detected using next-generation sequencing (NGS). The pathogen was further confirmed by polymerase chain reaction (PCR) with the primers specific for the microorganism. Moreover, paired serum tests showed elevated *C. psittaci* group titer in both IgG and IgM. She was treated with azithromycin and tigecycline. After 24-day hospitalization, the patient was clinically well and discharged home.

**Conclusion:** We report a case of severe pneumonia in a pregnant woman caused by *C. psittaci*, which diagnosed by NGS, and was cured without adverse effects on infant with tigecycline. The introduction of NGS and other effective assays might increase the detection rate. *C. psittaci* infection in pregnant women is very rare, but critical. Early diagnosis and correct treatment may save the mother and fetus. New tetracycline agent, tigecycline, may also be an effective alternative and should be further evaluated in psittacosis.

## Background

*Chlamydia psittaci*, an intracellular bacterium, can infect birds and other animals, such as livestock, and can cause zoonotic infection in human psittacosis[1]. The symptoms of pneumonia due to *C. psittaci* were usually mild, including fever, headache, and general discomfort[2]. However, the organism can also lead to fatal pneumonia with high morbidity and appreciable mortality[3]. The main imaging features are single lobe exudation or consolidation, and the lower lobes are more commonly observed[4]. Definitive diagnosis can be established by culture, serology test, or polymerase chain reaction (PCR) specifically targeting at *C. psittaci*. Infections during pregnancy by *C. psittaci* are rare, but might result in placental involvement, premature delivery or miscarriage[5, 6]. Herein, we report a case of severe pneumonia and respiratory failure due to the microorganism in a pregnant woman, requiring mechanical ventilation and extracorporeal membrane oxygenation (ECMO). Next-generation sequencing (NGS) of bronchoalveolar lavage fluid (BALF) was used and *C. psittaci* was identified, and later confirmed by PCR and sera test. To the best of our knowledge, this is the first report of *C. psittaci* as the causative agent of severe community acquired pneumonia (CAP) in pregnant woman which was diagnosed by NGS in China.

## Case Presentation

A 27-year-old female was admitted to China-Japan Friendship hospital on 7th October 2018, with hyperpyrexia, dry cough and dyspnea. On admission, she was fully conscious. On examination, the patient was febrile (39.5°C), with a respiratory rate of 25 breaths/minute, a pulse rate of 110 beats/minute and a blood pressure of 101/55 mmHg. Her breathing sound of the left lower lung was low. In addition, history taking revealed that she was pregnant at 22 weeks and physically fit. Laboratory tests showed a white blood cell count of  $7.69 \times 10^9/L$ , comprising 90.7% neutrophils, 5.6% lymphocytes and 2.2% monocytes, a hemoglobin of 70 g/L and a platelet count of  $138 \times 10^9/L$ . Besides, hyponatremia and hypokalemia were found, and no abnormalities in liver or renal function tests were observed. Blood gas analysis suggested type I respiratory failure. Chest computed tomography (CT) scan revealed consolidation in lingual and inferior lobe of her left lung (Fig. 1). Hypoxic dyspnea progressed rapidly after admission and she was transferred to the intensive care unit (ICU) after tracheal intubation on the same day. With the support of invasive ventilation, her oxygenation index still remained below 70 mmHg, therefore, the venous-venous extracorporeal membrane oxygenation (VV-ECMO) was given as adjuvant supportive therapy. The severe circulatory failure occurred rapidly after VV-ECMO was established. Echocardiography showed that ejection fraction dropped from 71% on the previous day to 30%, and the apex expanded globally and contraction weakened. Stress cardiomyopathy was considered.

She was empirically treated with azithromycin, ceftriaxone and oseltamivir as a case of severe community-acquired pneumonia. Tracheoscopy revealed congestion and edema of bilateral bronchial mucosa, with white and thin secretions in each lumen. Furthermore, her urine was negative for *Legionella pneumophila* serogroup 1 and pneumococcal antigens, and her sputum and BALF were negative for respiratory viruses and atypical pathogens identified by PCR, too. Moreover, the culture of bacteria and fungi remained negative after 2–7 day incubation. Then, we got another BALF and NGS was used to identify the possible pathogen. BALF was lysed and subjected to nucleic acid extraction with nucleic acid mini kit (Qiagen) following the manufacturer's instruction. The concentration of DNA was determined by Qubit 4 (Thermo). Then library construction was completed by DNA library construction kit (Vision medicals), which including fragmentation, the synthesis of 1st and 2nd strand, end repairment and adaptor ligation. The amplified libraries of each sample were pooled together and

sequenced on an Illumina Nextseq sequencer for clinical metagenomic analysis. A minimum of 10M single-end 75 bp reads was obtained per sample. Sequence analysis was performed through Vision Medicals' IDseq™ commercial bioinformatic pipeline. Briefly, low-quality and short (length < 35 bp) reads and reads that mapped to human genome and plasmids were removed. The remaining reads were taxonomically classified by aligning curated microbial database consisting of viruses, bacteria, fungi, and parasites. The taxonomic references were downloaded from National Center Biotechnology Information (NCBI). Upon identification of critical pathogen, the identified species-specific sequences were further confirmed by Blastn for further accuracy validation. At last, 18 reads of *C. psittaci* were detected (1 read is equal to approximately 1 fragment of 75 ~ 150 bp). The antibiotics were changed to azithromycin and tigecycline. Four days later, her pulmonary imaging improved (Fig. 2), and cardiac function gradually restored after one week. After 11 days, the ventilator and ECMO were both evacuated. Paired serum drawn two weeks apart showed rising *C. psittaci* group titer both in IgG and IgM (Table 1). PCR for *C. psittaci* with the primers specific the microorganism by Cp2-F, Cp2-R, Cp-1, Cp-2 and Cp-3[7] was also positive in her BALF. The region of gene ompA was targeted. And a 131-bp specific sequence was amplified and sequenced with the primers (3'-TGTGATTCACAAACCAAGAGGCTATA - 5' and 3'-CGAGGCCTACTTGCCATTCA-5'). Re-examination of medical history revealed that the woman once played with the parrots for about 15 minutes five days before the onset of psittacosis.

Table 1  
*Chlamydophila psittaci* group titre in IgG and IgM

	2018-10-9	2018-10-22	2018-10-24
Parrot chlamydia antibody IgG	1:64	1:1024	1:1024
Parrot chlamydia antibody IgM	negative	1:128	1:256

Table 2  
Case series of psittacosis during pregnancy in literature

Author	Year	Country	Gestational Age	Symptoms	X-ray	Diagnosis	Experience and outcome of mother	Outcome of fetal
Our Case.	2018	China	22 weeks	fever, dry cough and dyspnea	consolidation in lingual and inferior lobe of her left lung	NGS on BALF	severe hypoxemia, stress cardiomyopathy	health
Litty et al <sup>6</sup>	2018	America	21 weeks	fever, headache, neck pain, nausea and fatigue		NGS on lung tissue of the infant	mild symptoms and healed	premature and died
Janssen et al <sup>5</sup>	2006	Netherlands	31 weeks	fever, headache and abdominal pain	pulmonary edema and diffuse infiltrates	maternal serum for antibody titres	severe hypoxemia, septic shock, AKI, and healed	emergency termination
Hyde et al <sup>14</sup> and Jorgensen <sup>21</sup>	1997	American	22 weeks	fever, headache, myalgia, dry cough and abdominal pain	diffuse bilateral infiltrates	genus-specific fluorescein-tagged monoclonal antibody staining on placenta	hypoxemia, thrombocytopenia, and healed	emergency termination and died
Khatib et al <sup>15</sup>	1995	American	31 weeks	fever, headache, backache, dry cough, pleuritic chest pain and nausea	patchy infiltrates in both upper lobes and in left lower lobe	maternal serum for antibody titres	severe hypoxemia and healed	emergency termination
Gherman et al <sup>13</sup>	1995	American	32weeks	fever, headache, sore throat, dry cough nausea and abdominal pain	right lower lobe infiltrate, left basilar opacification with pleural effusion	maternal serum for antibody titres	severe hypoxemia, septic shock, DIC and healed	emergency termination
Helm et al <sup>16</sup>	1989	England	27weeks	fever, headache, sore-throat, mulse pain and rigors		monoclonal antibody staining on placenta and maternal serum for antibody titres	jaundice, DIC, renal failure and healed	premature and died
Johnson et al <sup>17</sup>	1985	England	28weeks	fever, headache, nausea, vomiting	bilateral pulmonary edema	maternal serum for antibody titres	severe hypoxemia, septic shock, AKI, DIC and healed	premature and died
McKinlay et al <sup>18</sup>	1985	England	28 weeks	fever, headache, chest pain and sore throat		maternal serum for antibody titres	DIC, cardiac insufficiency and healed	premature and died
McKinlay et al <sup>18</sup>	1985	England	25weeks	fever, headache, nausea, photophobia and rigors		maternal serum for antibody titres	DIC, septic shock, jaundice, renal failure and healed	premature and died

NGS: next-generation sequencing; AKI: acute renal injury; DIC: disseminated intravascular coagulation

Author	Year	Country	Gestational Age	Symptoms	X-ray	Diagnosis	Experience and outcome of mother	Outcome of fetal
RJ Beer et al <sup>19</sup>	1982	England	34 weeks	fever, headache and neck, chest and abdominal pain		maternal serum for antibody titres	septic shock, severe hypoxemia, DIC, and healed	emergency termination
NGS: next-generation sequencing; AKI: acute renal injury; DIC: disseminated intravascular coagulation								

After 24-day hospitalization, the patient recovered well and discharged from the hospital. Throughout the whole course, the fetus was stable and there was no sign of threatened premature delivery.

## Discussion And Conclusions

Psittacosis is a zoonotic disease, and animal-to-human transmission might occur through direct contact with golden bird, parrot, pigeon, turkey and other birds, or inhalation of aerosols from their excrement dust [8, 9]. Recently, it has been reported that peacock, duck and chicken can also carry pathogens and result in transmission[10, 11]. *C. psittaci* is rarely documented as the pathogen in hospitalized CAP. The reported incidence by the organism, ranging from 0–2.1%, might be underestimated, because the detection of psittacosis is rarely incorporated in the routine microbiological diagnostics in CAP, and serological method is also rarely available[12]. Reviewing the history of travel, occupation, contact, and cluster, revealed that most of these patients had family clusters or pet bird contact history. This is confirmed in our case, and the patient had a parrot contact history before the onset of the disease.

Diagnosis of psittacosis is often based on the clinical examination, epidemiological history, and laboratory tests, including direct (culture or PCR) or indirect (serology) methods. It is a challenge to identify *C. psittaci* as the pathogen due to the lack of effective diagnostic methods and its elusiveness. Given the complexity and slow-growth nature, the culture of *C. psittaci* (biosafety level 3) is almost unavailable, and the clinical criteria for a diagnosis of psittacosis is a positive PCR result or a four-fold rise of antibody titer in complement fixation test (CFT) confirmed by micro-immunofluorescence[3]. However, to date, with the wide application of NGS[13], the detection rate of *C. psittaci* may be increased[6]. However, there is no uniform standard for the interpretation of NGS results, and to date, it can only be used as a clinical clue and needs further confirmation.

Psittacosis during pregnancy is very rare and can lead to numbers of maternal and fetal mortality[14]. Most mothers suffered multiple organ failure, including severe hypoxemia, hepatic dysfunction, renal dysfunction and disseminated intravascular coagulation(DIC). Moreover, more than half of the fetuses died and, if alive, they would be born prematurely[15]. In our case, although the mother had multiple organ failure (severe respiratory failure, acute kidney injury, cardiogenic shock, liver function injury and coagulation dysfunction), the baby had been relatively healthy, and there was no sign of threatened premature delivery throughout the course of the disease. Therefore, early recognition and proper management may improve the prognosis of mother and fetus.

Tetracycline, especially doxycycline, is the first-line medicine, and may show significant improvement after 3 day administration[3]. Macrolides can be used as an alternative antibiotic agent, but are less effective in severe pregnant cases[16]. In the present case, we chose another tetracycline agent. The woman in our case had the regimen of the combination of azithromycin and tigecycline, which was remarkably effective. The patient recovered well and discharged home. No recurrence of symptoms and signs was reported in a two-month of outpatient follow-up.

In summary, psittacosis may not be underestimated due to limited diagnostical methods. *C. psittaci* infection in pregnant women is very rare, but critical. Early diagnosis and correct treatment may save the mother and fetus. The introduction of NGS and other effective assays might increase the detection rate. The new tetracycline agent, tigecycline, may also be an effective alternative and should be further evaluated in psittacosis.

## Abbreviations

ECMO: extracorporeal membrane oxygenation; BALF: bronchoalveolar lavage fluid; NGS: next-generation sequencing; PCR: polymerase chain reaction; CAP: community acquired pneumonia; CT: computed tomography; ICU: intensive care unit; VV-ECMO: venous-venous extracorporeal membrane oxygenation; CFT: complement fixation test; DIC: disseminated intravascular coagulation

## Declarations

## Ethics approval and consent to participate

Not applicable.

## Consent for publication

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor of this journal.

## Availability of data and materials

Not applicable.

## Competing Interests

The authors declare that they have no competing interests.

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## Authors' contributions

XJW: Study design, Data collection, Data analysis, Writing

TL, YFF, ML, YT and QLW: Data collection

BHL and QYZ: Study design, Data collection, Data analysis.

All authors read and approved the final manuscript.

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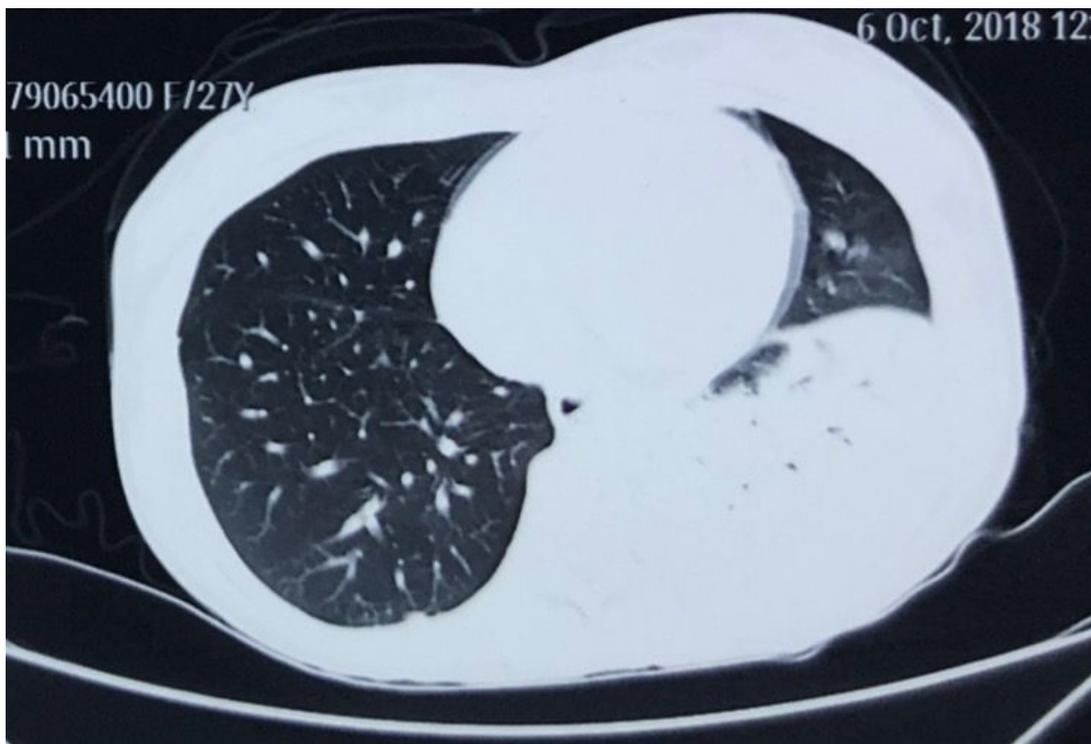
Not applicable.

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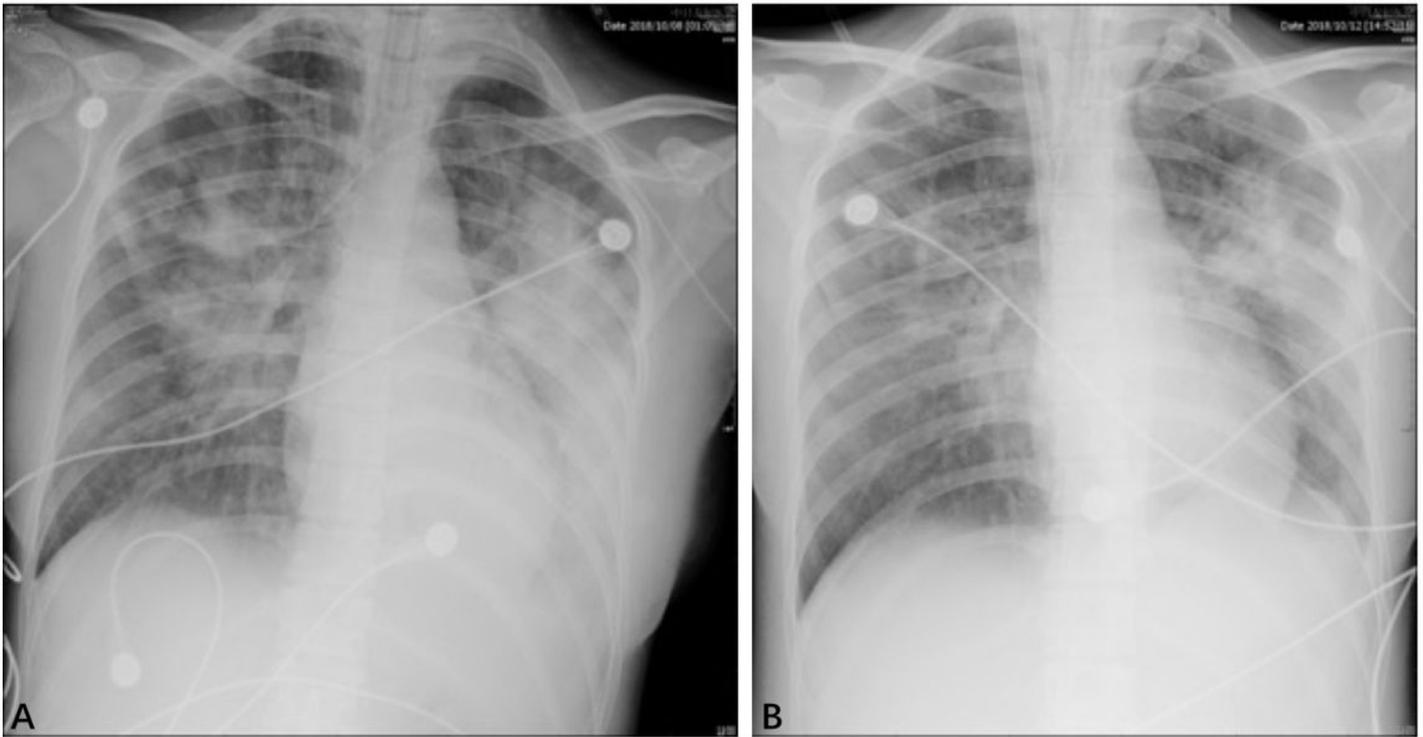
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## Figures



**Figure 1**

Chest computed tomography (CT) scan revealed consolidation in lingual and inferior lobe of the left lung



**Figure 2**

A: X-Ray on the 9th October; B: X-Ray on 13th October, which revealed significant improvement