

CASE REPORT

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# Multiple infections secondary to immunosuppression after *Chlamydia psittaci* infection: a case report

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## Abstract

This study presents the clinical profile of a 74-year-old male patient admitted to the hospital due to a 20-day history of coughing, chest tightness, and dyspnea. Upon admission, the patient presented with fever, tachycardia, and tachypnea. Clinical examination revealed evidence of lung infection, sepsis, and multi-organ dysfunction, alongside abnormal blood gas analysis and elevated C-reactive protein (CRP) levels. Pathogen testing confirmed *Chlamydia psittaci* (*C. psittaci*) infection. Throughout the treatment course, the patient developed concurrent fungal and viral infections, necessitating a comprehensive approach involving combined antibiotic and antifungal therapy. Despite encountering treatment-related complications, the patient demonstrated clinical improvement with aggressive management. This case underscores the importance of recognizing immune suppression subsequent to *Chlamydia* infection, emphasizing the critical role of early diagnosis, intervention, and standardized treatment protocols in enhancing patient prognosis.

**Keywords** *Chlamydia psittaci*, Immunosuppression, *Herpesvirus*, Invasive pulmonary *Aspergillus*

## Introduction

*C. psittaci* is a zoonotic pathogen primarily hosted by birds. Human infection can occur through brief contact with feathers, feces, or carcasses of infected birds, or inhalation of aerosolized bacteria. Following infection, patients may exhibit a range of symptoms from asymptomatic to multiple manifestations. The virulence of *C. psittaci* depends on the host's immune response; when the host's immunity is compromised, the chlamydial virulence increases and leads to organ damage. By reviewing

this case's diagnosis and treatment, we aim to emphasize the significance of immune dysfunction following *C. psittaci* infection that can result in severe complications. Early diagnosis, intervention, and standardized treatment are crucial for improving patient prognosis.

## Case report

A 74-year-old male patient was admitted to our hospital due to a 20-day history of productive coughing accompanied by chest tightness and shortness of breath which did not improve significantly after treatment at a local hospital. As a result, he was transferred to our Intensive Care Medicine Department for acute respiratory failure and lung infection. Upon admission physical examination: body temperature 39.6°C, heart rate 112 beats/min, respiratory rate 25 breaths/min, blood pressure 159/79 mmHg. The patient remained conscious but presented profuse sweating along with dyspnea. Auscultation

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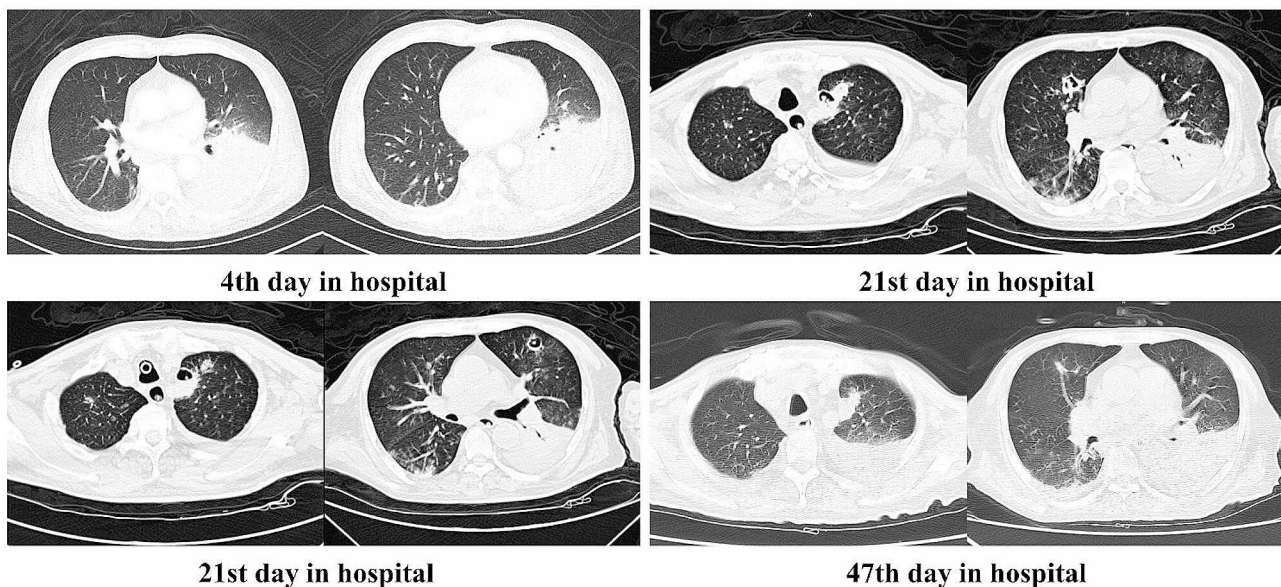
revealed coarse respiratory sounds with audible phlegm and wet rhonchi in both lower lungs, while the heart rhythm was synchronized without any apparent murmurs. Meanwhile, blood gas analysis showed the following results: PaO<sub>2</sub> 48.3 mmHg, PaCO<sub>2</sub> 29.8 mmHg, pH 7.446, blood glucose 8.5 mmol/L, lactate 2.0 mmol/L, and oxygenation index 121. Upon admission, the patient received mask oxygenation, however, adequate oxygen saturation could not be maintained. Therefore, endotracheal intubation was performed followed by mechanical ventilation using a ventilator set to A/C mode with VT of 400 ml and PEEP of 8 cmH<sub>2</sub>O.

The patient's admission test results indicated ultrasensitive CRP levels of 268.21 mg/L, creatinine levels of 340.8 umol/L, leukocyte count of  $16 \times 10^9/L$  with N% at 95.2%. Additionally, tests for calcitoninogen (PCT) and interleukin-6(IL-6) as well as other inflammatory indicators were conducted. Considering the patient's medical history and clinical manifestations, the doctor empirically administered moxifloxacin (0.4 g qd IVgtt) for anti-infection purposes along with gastric protection measures to maintain circulatory function stability, internal environment balance, and nutritional support. The patient had a history of hypertension and hyperlipidemia for over 30 years which had been effectively managed using amlodipine and atorvastatin.

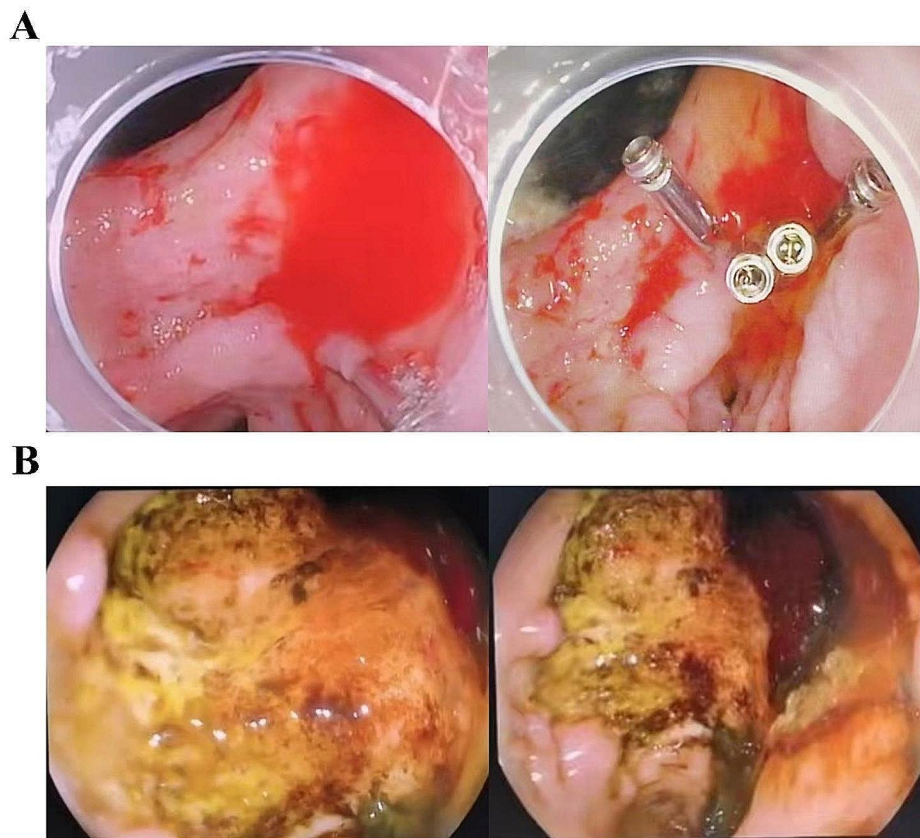
After admission, lung infection rapidly progressed to acute respiratory distress syndrome (ARDS), and chest CT revealed patchy hyperdense images in the left lower lung (Fig. 1 4th day in hospital). In order to improve the patient's condition, a lung-protective ventilation strategy

combined with prone position ventilation therapy was employed. Furthermore, based on information provided by the patient's family, it was discovered that prior to disease onset, the patient had visited flower and bird markets. Therefore, prompt alveolar lavage fluid collection and Metagenome next-generation sequencing (mNGS) of pathogenic microorganisms in both blood samples and lavage fluid were conducted. The diagnosis of *C. psittaci* was ultimately confirmed, and treatment for the patient (4th day in hospital) involved a combination of antibiotics and doxycycline administered at a dosage of 0.1 g q12h. After one week of this treatment, the patient's oxygenation improved; however, intermittent high fever persisted for an additional week after admission. At the same time, the bacterial culture and drug sensitivity results of the patient's sputum suggested ceftazidime sensitivity, so ceftazidime was added to anti-infective treatment. To address this, ceftazidime was added to the anti-infective therapy regimen at a dosage of 2 g q8h IV gtt.

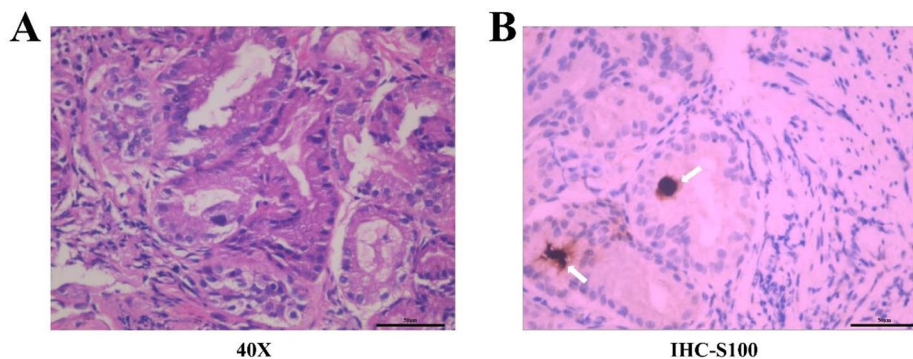
During subsequent treatment, chest CT revealed partial cavity formation with minimal peripheral exudate, indicating invasive pulmonary *Aspergillus* infection (Fig. 1 21st day in hospital). Consequently, voriconazole was introduced as antifungal therapy by administering it intravenously at a dosage of 0.2 g q12h IV gtt. However, despite improved oxygenation after one week in the hospital, the patient experienced recurrent black stools and persistent hematocrit decrease even after hemostasis measures and blood transfusion were implemented. Gastrointestinal endoscopy identified multiple hemorrhages



**Fig. 1** 4th day in hospital shows the patient's chest CT at the time of admission, which showed a patchy dense shadow in the left lower lung, after aggressive anti-infective treatment, a review on 21st day in hospital showed a partial cavity formation with a small amount of peripheral exudate, showing the air crescent sign, which was considered to be an invasive pulmonary *Aspergillus* infection



**Fig. 2** The patient's two gastroscopic images **A**: Gastroscopy was performed to see multiple bleeding points from the gastric antrum to the body of the stomach, and titanium clips were performed to stop the bleeding. **B**: Gastroscopy showed a huge ulcer at the body of the stomach



**Fig. 3** Histopathological biopsies at the time of gastroscopy are reported below: **A**: Pathology suggestive of chronic atrophic gastritis, moderate with activity, enterocytosis and lymphoid follicle formation; **B**: a few intrinsic glands were seen with large nuclei, deeply stained, cytoplasmic vacuolated cells protruding into the lumen, whose immunohistochemical markers showed CMV nuclear positive (white arrow) and chromogenic in situ hybridization (CISH) EBER (-). Cytomegalovirus gastritis was considered

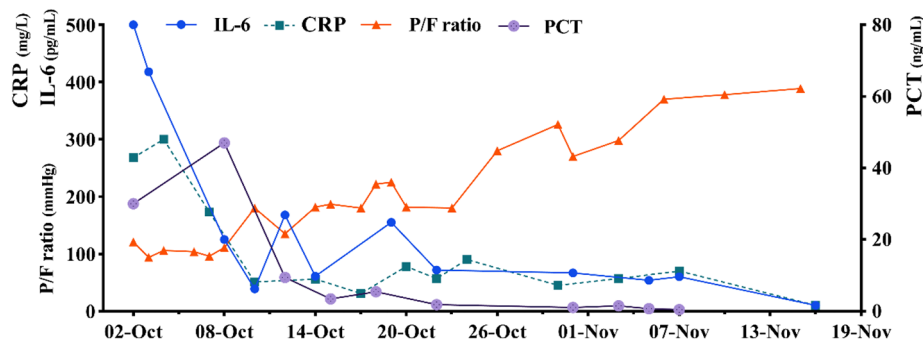
in the gastric sinus area as well as in the angle and body of the stomach necessitating titanium clip application to control bleeding (Fig. 2A); additionally, a large ulcer was observed in the stomach body (Fig. 2B). A tissue biopsy obtained during endoscopy indicated cytomegalovirus gastritis as the primary cause for gastric ulcer development worldwide (Fig. 3). Subsequent administration of

ganciclovir at a dosage of 50 mg qd IV gtt led to improvement in the patient's condition. At a later stage, *Herpesvirus* infection manifested with ulcers around the mouth (Fig. 4), prompting topical application of ganciclovir gel for treatment purposes. After an active treatment period lasting for approximately 50 days, repeat chest CT demonstrated partial absorption within the cavity (Fig. 1 47th





**Fig. 4** Patient with herpes and ulcers around the mouth, considered to be a herpesvirus infection



**Fig. 5** Changes in infection-related indicators and oxygenation index over time after patients' admission to the hospital, as seen in the gradual decrease in infection indicators and the gradual increase in oxygenation index with the overall trend of treatment

day in hospital), signifying improvement in overall condition. The patient was transferred to the rehabilitation department for further treatment after receiving intermittent ventilator-assisted ventilation until withdrawal. Detailed records of changes in relevant infection indicators and specific antimicrobial adjustments throughout the treatment course can be found in Fig. 5; Table 1.

## Discussion

*C. psittaci*, a Gram-negative intracellular bacterium, is known to cause severe psittacosis in humans [1]. Upon invasion of the host, *C. psittaci* primarily affects the lungs and leads to the development of atypical pneumonia. It accounts for approximately 1% of pathogenic microorganisms causing community-acquired pneumonia (CAP) [2]. The difficulty in diagnosing psittacosis due to

diagnostic tests for *C. psittaci* rarely done when patients present with CAP. The patient in this case had a history of exposure to a flower and bird market and the infectious factors were not effectively controlled at the time of admission. After identifying the pathogen as *C. psittaci*, we administered doxycycline [3], leading to gradual control over lung infection. Furthermore, post-admission tests revealed immunosuppression in the patient based on lymphocyte subpopulation counts on 10–22. However, based on the patient's past medical history and test results suggest that the patient has no immune-related diseases. The virulence of *C. psittaci* towards its host depends on host immunity [4], weaker autoimmunity enhances chlamydial virulence and facilitates faster multiplication within the host system while increasing susceptibility to other pathogens [5] and exacerbating

**Table 1** Antibiotic adjustments and treatment of patients at different time points after admission to the hospital

Date (2022)	02-Oct	03-Oct	07-Oct	08-Oct	10-Oct	18-Oct	21-Oct	22-Oct	26-Oct	01-Nov	03-Nov	08-Nov	16-Nov
Hospital	Day1	Day2	Day6	Day7	Day9	Day17	Day20	Day21	Day25	Day31	Day33	Day38	Day46
Prone position													
Antibiotics	Moxifloxacin Doxycycline Ceftazidime Zithromax Voriconazole Voriconazole Ganciclovir	0.4 g qd IVgtt 0.1 g q12h Nasogastric 2 g q8h IVgtt					0.5 g qd IVgtt 0.2 g q12h IVgtt				200 mg bid Oral	50 mg qd IVgtt	
Lymphocyte subpopulation								345 102 31 40		329 212 44 102			
White blood cell (x10 <sup>9</sup> /L)	11.4	30.6	22.6	20.8	13.1		7.6	6.6		9			11.4
Lymphocyte %	3.6	2.7	2.5	2.4	6.3		7.3	10.2		11			3.6

organ damage. In a recent Study, mNGS results indicated that 41.3% of patients with *C.psittaci* infection(19/46) had suspected coinfections. The most common bacterial co-infection was mainly related to *Acinetobacter baumannii*, and the most common co-infection of virus and fungus were *Candida albicans* and EB virus [6]. Heterogeneous immunological responses may occur during psittacosis, including a high-level expression of a variety of chemokines, which promote the rapid proliferation of neutrophils and facilitate the migration to the infection sites within the lung tissue, consistent with the monocyte and lymphocyte infiltrates in the lung tissues of *C. psittaci* patients, hypercytokinemia caused by the combined action of a variety of cytokines led to strong inflammatory responses [7], and a suppression of immune response by inhibiting humoral responses and altering Th1/Th2 balance [5], leading to an increase susceptibility to other pathogens. We detected both *C. psittaci* and *EBV virus* in bronchoalveolar lavage fluid (BALF) and mNGS analysis one day after admission. Additionally, tests conducted 20 days after admission identified sequences related to *Hordeum neoformans bloggeri*, *Anopheles mosquitoes elizabethiae*, *Acinetobacter baumannii bacteria species* along with *human α-herpesvirus type I (HSV-1)*, *EBV virus strain(s)*, *human β-herpesvirus type 5 (human cytomegalovirus or HCMV)*, alongside *C. psittaci* itself. These findings provide compelling evidence that *C. psittaci* is a cause of secondary multiple infections.

The patient presented with papules and ulcers around the mouth on October 23rd, indicating a suspected *herpes virus* infection. Chest X-ray results on October 20th showed improvement in lung infection-related imaging features; however, subsequent review revealed cavity formation in certain areas of both lungs, suggesting a potential fungal infection caused by *Aspergillus spp*. It is worth noting that *Aspergillus spp* are widely distributed in the environment [8]. The risk of infection increases when patients have underlying lung disease, chronic hormone or drug use, and airway endothelial cell damage [9, 10]. ICU patients are particularly susceptible to *Aspergillus spp* infections [11]. Although invasive pulmonary aspergillosis does not exhibit specific pathognomonic features on imaging, the presence of a halo sign strongly suggests the disease [12]. A follow-up chest X-ray conducted on October 20th clearly displayed a cavity resembling a halo sign which eventually resolved completely after appropriate treatment (Fig. 1 47th day in hospital).

However, during the course of treatment, the patient experienced recurrent gastrointestinal bleeding leading to hemorrhagic shock. Initial endoscopy revealed an extensive irregular ulcerated infiltrative lesion located at the gastric sinus and angle to the body of stomach with active bleeding observed at its margins. Subsequent endoscopy demonstrated further development of an

ulcer neoplasm characterized by a white moss-covered hard surface. Biopsy histopathologic findings indicated cytomegalovirus gastritis for this patient. Previous studies have shown that greater immune system suppression significantly increases susceptibility to cytomegalovirus-mediated diseases and clinical presentations can range from transient fever to involvement of multiple organ systems [13, 14].

In clinical practice, when a patient with a history of bird exposure presents symptoms such as cough, sputum production, fever, and hemoptysis without apparent triggers, along with chest imaging indicating lung infection, conventional antibiotic therapy fails to yield significant results. Therefore, it is crucial to remain vigilant about the possibility of *C. psittaci* infection under these circumstances and promptly conduct relevant pathogenicity tests. Metagenomic next-generation sequencing (mNGS) detection has higher accuracy and can effectively detect pathogens that cannot be detected by traditional method [6]. If necessary, mNGS testing can be performed on alveolar lavage fluid and blood samples to accurately identify the pathogen before initiating appropriate medication promptly and precisely. However, patients with confirmed infections may experience secondary viral and fungal infections if immunosuppression occurs during treatment; hence early detection measures should be implemented alongside interventions aimed at improving humoral and cellular immune function to mitigate multiple infections' occurrence. Additionally, active nutritional supportive therapy combined with suitable rehabilitation training can expedite physical recovery while enhancing therapeutic outcomes. In summary, the timely and accurate diagnosis, as well as the correct treatment of potential complications, are crucial strategies for effectively managing immunosuppression following chlamydia infection.

#### Abbreviations

ARDS	Acute respiratory distress syndrome
BALF	Bronchoalveolar lavage fluid
<i>C. psittaci</i>	<i>Chlamydia psittaci</i>
CAP	Community-acquired pneumonia
CRP	C-reactive protein
IL-6	Interleukin-6
mNGS	Metagenome next-generation sequencing
PCT	Calcitoninogen

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Not applicable.

#### Author contributions

MZ, QX and WL designed this study and protocol development; YC, HZ, and WL were responsible for the data collection; MZ and QX conducted the manuscript writing; YC and WL revised the manuscript; WL provided final approval for this version to be published; All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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#### Data availability

All data supporting the results of this study can be found in the paper and its Supplementary Information. Data related to metagenomic next-generation sequencing (mNGS) of pathogenic microorganisms in blood samples and lavage fluids are available at the following links: <http://www.ncbi.nlm.nih.gov/bioproject/1113407>.

#### Declarations

##### Ethics approval and consent to participate

The study was conducted under ethical principles (Declaration of Helsinki). Written consent was obtained from her authorized representatives.

##### Consent for publication

Written informed consent was obtained from the patient for publication of this report and any accompanying images.

##### Competing interests

The authors declare no competing interests.

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