Comparative analysis of clinical presentation of community-acquired pneumonia induced by *Chlamydia psittaci* and *Legionella* Diagnosed through Metagenomic Next-Generation Sequencing

Shanshan Su  
Wenzhou Medical University First Affiliated Hospital

Jiahao Zeng  
Wenzhou Medical University First Affiliated Hospital

Yunlei Li  
Wenzhou Medical College Affiliated Yueqing Hospital

Pengcheng Lin  
Wenzhou Medical University First Affiliated Hospital

Junjie Chen  
Wenzhou Medical University First Affiliated Hospital

Chengshui Chen  
Wenzhou Medical University First Affiliated Hospital

Ying Zhou  
Wenzhou Medical University First Affiliated Hospital

Yuping Li (✉ wzliyp@163.com)  
Department of Pulmonary and Critical Care Medicine, The First Affiliated Hospital of Wenzhou Medical University  
https://orcid.org/0000-0002-5833-931X

Research article

**Keywords:** Pneumonia, Psittacosis, Chlamydia psittaci, Legionella, Next-generation sequencing

**Posted Date:** July 24th, 2020

**DOI:** https://doi.org/10.21203/rs.3.rs-45675/v1

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Abstract

Background

*Legionella* and *Chlamydia psittaci* cause atypical community-acquired pneumonia, which mimic each other. Our aim was to compare the clinical characteristics of *Legionella* pneumonia (LP) and psittacosis and assess whether metagenomic next-generation sequencing (mNGS) is an effective method for early diagnosis.

Methods

We conducted a retrospective study and compared seventeen patients with *Chlamydia psittaci* pneumonia and nine patients with LP, diagnosed by mNGS. This study was carried out in the First Affiliated Hospital of Wenzhou Medical University, China, from July 2018 to May 2020. mNGS was carried out from bronchial alveolar lavage fluid (BALF) and/or lung tissues.

Results

76.5% of psittacosis cases and 0% of legionellosis cases had an avian exposure history (*p* < 0.001). Compared with LP patients, psittacosis patients had significantly higher hemoglobin (118.9 ± 20.2 vs. 93.2 ± 23.2 g/L, *p* = 0.007), serum sodium (138.9 ± 5.4 vs. 133.9 ± 6.5 mmol/L, *p* = 0.047), and higher proportion of elevated aspartate aminotransferase levels (88.2 vs. 44.4%, *p* = 0.028). Other clinical parameters were similar in psittacosis and LP patients: normal or slightly elevated leucocytes (10.5 vs. 9.5 x 10^9/L, *p* > 0.05), neutrophils (9.4 vs. 8.3 x 10^9/L, *p* > 0.05), and procalcitonin (0.8 vs 5.1 ng/mL, *p* > 0.05); highly increased C-reactive protein levels (205.1 vs. 234.9 mg/L, *p* > 0.05); and decreased lymphocytes (0.7 vs. 0.6 x 10^9/L, *p* > 0.05). Extra-pulmonary manifestations and mortality (11.8% in psittacosis vs. 22.2% in LP group, *p* = 0.591) were also similar in both the groups. mNGS detected *Chlamydia psittaci* in 17/17 BALF samples, and *Legionella* in 8/8 BALF samples and 1/1 lung tissue sample.

Conclusions

Apart from sharing many features with legionellosis, psittacosis is a vital differential diagnosis for LP, especially in patients with avian exposure history. mNGS is a sensitive and promising method for early diagnosis of both psittacosis and LP.

Background
Community-acquired pneumonia (CAP) is associated with high morbidity and mortality worldwide[1]. Atypical pathogens such as *Legionella, Mycoplasma pneumoniae, Chlamydia pneumoniae,* and *Chlamydia psittaci* are the common causes (15–28%) of CAP[2].

*Chlamydia psittaci* is an obligatory, intra-cellular gram-negative bacterium that may infect humans and cause zoonotic infection named psittacosis or parrot fever[3]. Usually, transmission occurs through inhalation of contaminated aerosols originating from the excretions of infected birds. Psittacosis can be asymptomatic or acute symptomatic infection characterized by mild influenza-like illness to severe pneumonia and extra-pulmonary systemic disease, which can be fatal. *Chlamydia psittaci* leads to CAP in rare cases (1.03%, range: 0–6.7%)[4]. Because of the low disease awareness, nonspecific clinical manifestations, and lack of rapid and accurate diagnostic methods, psittacosis is easy to be underdiagnosed. Metagenomic next generation sequencing (mNGS) has been increasingly applied to diagnose many infectious diseases especially when traditional diagnostic methods have limitations[5]. With the widespread application of mNGS in clinical settings, psittacosis cases are getting reported frequently in recent years[6–8].

*Legionella spp.* are gram-negative intracellular bacteria that frequently leads to severe CAP (SCAP) requiring admission in intensive care unit (ICU). *Legionella pneumonia* (LP) is most likely caused by *Legionella pneumophila*. The most common bacterial mimics of legionnaire's disease (LD) are *Streptococcus pneumoniae* and psittacosis[9]. Studies have been conducted to determine whether LP can be distinguished from pneumonia caused by *S. pneumoniae*[10]. However, few studies describe the problem of differentiating LP from *C. psittaci* pneumonia in clinical settings.

We performed a retrospective study of 17 cases of *C. psittaci* pneumonia diagnosed by mNGS and compared them with 9 cases of LP. This comparison was carried out to find whether the cases differ in clinical manifestations and to demonstrate whether mNGS is an effective diagnostic method. We present the following article in accordance with the STROBE reporting checklist.

**Methods**

**Study design**

This was a retrospective study. The study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. The requirement for informed consent was waived due to the retrospective nature of the study.

**Diagnostic criteria**

Cases of *C. psittaci* pneumonia met the following three criteria: (1) Fulfilled the diagnostic criteria for CAP[11]; (2) A specific DNA fragment of *C. psittaci* identified by mNGS; and (3) Negative routine etiological tests, including blood, sputum, and bronchial alveolar lavage fluid (BALF) culture.
Cases of LP fulfilled the criteria for CAP and met at least one of the following criteria: (1) *Legionella* successfully isolated from a respiratory sample or lung tissue sample and cultured on buffered charcoal yeast extract (BCYE) media; (2) Positive urine test for *Legionella* antigen; (3) A specific DNA fragment of *Legionella* identified by mNGS and negative routine etiological tests.

### Study participants

A total of seventeen cases with *C. psittaci* pneumonia and nine cases with LP who were admitted to the First Affiliated Hospital of Wenzhou Medical University, a tertiary hospital in Zhejiang, China, between July 2018 and May 2020. For each case, we extracted the demographic data, comorbidities, illness severity, clinical manifestations, laboratory and imaging data, treatment, and outcomes from electronic medical records.

### mNGS

The procedures such as sample processing, DNA extraction, construction of DNA libraries, sequencing, and bioinformatic analysis were completed by BGI-Huada Genomics Institute (Shenzhen, China), according to the previously described procedures by Miao et al.[12].

### Statistical analysis

Continuous variables were expressed as means ± standard deviation (SD), or medians (25th, 75th percentiles), depending on whether the variables were normally distributed or not. Categorical variables were expressed as percentages. *T*-test or the Mann-Whitney *U*-test were used to compare continuous variables. Categorical variables were compared using chi-square or Fisher’s exact test. A p value of less than 0.05 was considered as statistically significant. All analyses were performed using the SPSS software (version 26.0, SPSS Inc., Chicago, Illinois).

### Results

### Psittacosis and LP diagnosis

During the study period, 17 patients were diagnosed with psittacosis, and 9 patients with LP. *C. psittaci* was detected in BALF samples of 17 psittacosis patients by mNGS. Blood and BALF cultures were negative for all the 17 patients. We detected *Legionella pneumophila* in BALF samples of 8 LP patients using mNGS and *Legionella bozemanii* in lung tissue sample through percutaneous lung biopsy of 1 patient using mNGS. Blood and BALF cultures were conducted for all LP patients; BALF samples of 3 out of 8 patients were found positive for *Legionella pneumophila*. Tissue culture conducted in 1 patient through percutaneous lung biopsy revealed *Legionella bozemanii* growth. The mean time when the culture turned positive was 9.5 days. Urine *Legionella* antigen test were found positive in 3 out of 9 patients.

### General characteristics
The demographic and general characteristics of the patients are shown in Table 1. 13 of the 17 patients of psittacosis group (76.5%) and no patient of the LP group (0%) had a history of avian or poultry exposure ($p < 0.001$). The median time from onset of illness to admission was 5 days in both the groups. Psittacosis patients were admitted at all seasons while no LP patients were admitted in the winter. 41.2% of the psittacosis patients (7/17) were admitted in the spring, while 44.4% of the LP patients (4/9) were admitted in the autumn.

**Clinical characteristics**

All the patients infected with psittacosis and LP were febrile with a mean temperature of 39.8 °C. Majority of the patients in both the groups had similar symptoms (no significant difference): non-specific rigors, fatigue, cough, sputum, and dyspnoea. Also, many extra-pulmonary manifestations were similar between both the two groups: relative bradycardia, neurological symptoms (such as headache, dizziness), and gastrointestinal symptoms (vomiting and diarrhea). Meanwhile, 5 patients in the psittacosis group and 1 in the LP group were complicated with rhabdomyolysis. The diagnosis of rhabdomyolysis was confirmed when the level of serum creatine kinase (CK) was found higher than 1000 U/L[13]. Clinical manifestations of the patients are shown in Table 2.

The laboratory and radiological tests results are shown in Table 3. The psittacosis patients had a mean white blood cell counts, neutrophils and lymphocyte of $10.5 \times 10^9/L$, $9.4 \times 10^9/L$, and $0.7 \times 10^9/L$, respectively, while the corresponding counts in LP patients were $9.5 \times 10^9/L$, $8.3 \times 10^9/L$, and $0.6 \times 10^9/L$ respectively. Similarly, C-reactive protein (CRP) and procalcitonin (PCT) levels were 205.1 mg/L and 0.8 ng/mL, respectively, in psittacosis patients whereas the corresponding levels in the LP patients were 234.9 mg/L and 5.1 ng/mL. As compared with LP patients, psittacosis patients had significantly higher levels of hemoglobin, serum sodium, and higher proportion of elevated aspartate aminotransferase (AST). Both the groups had elevated levels of IL-6. Moreover, consolidation, inflammatory exudation, and pleural effusions were frequently observed in computed tomography (CT) scans in both psittacosis and LP patients (Fig. 1, 2).

**Treatment and outcomes**

All antimicrobial treatments received by the patients are listed in Table 4. 23.5% of psittacosis and 44.4% of LP patients did not receive active antibiotics against *C. psittaci* or *Legionella* on admission. Reporting of the mNGS results took 48–72 h from the time of receipt of the samples. One psittacosis patient refused hemodialysis and one LP patient refused invasive mechanical ventilation; both the patients received carbapenem as initial empirical antibiotic and died before receiving their mNGS reports. Quinolone (moxifloxacin, 0.4 g intravenously q.d.) was frequently administered to patients of both the groups. The median fever clearance time in psittacosis patients (6 days) did not significantly differ from that in LP patients (5 days). 58.8% (10/17) of psittacosis and 44.4% (4/9) of LP patients fulfilled the criteria for SCAP. The final prognosis was similar in both the groups; hospital mortality rate was 11.8% (2/17) in psittacosis patients and 22.2% (2/9) in LP patients ($p = 0.591$).
Discussion

*Legionella* accounts for approximately 1 to 10% of CAP and is the second most common cause of SCAP, which requires ICU admission[14]. Although *C. psittaci* is documented as an uncommon cause of CAP, CAP cases induced by *C. psittaci* may be underdiagnosed. A French study on distinctive features of pneumonia caused by *C. psittaci* and *L. pneumophila* showed that severe psittacosis and severe legionellosis share many common characteristics in ICU patients[15]. However, the recommended first line antibiotics are different for psittacosis and LP. For *Legionella* species, fluoroquinolone and azithromycin are the preferred antimicrobials, while for *C. psittaci* tetracycline is recommended[11, 16]. Consequently, to an optimal initial administration of empirical antibiotics, the differentiation of psittacosis from LP is frequently concerned in clinical practice.

Our results suggest that psittacosis and LP indeed share many similarities consistent with reported findings[6, 15, 17]. They both manifest as hyperpyrexia with a mean temperature of 39.8 °C. In addition, they have similar extra-pulmonary symptoms: neurological symptoms, gastrointestinal symptoms, relative bradycardia and rhabdomyolysis. *Legionella*-associated rhabdomyolysis has been frequently reported in literature[18, 19]. Rhabdomyolysis is not usually caused by pathogens, but most pathogen-induced rhabdomyolysis in the patients is due to an infection by *Legionella* species[18]. The exact mechanism is unclear, but it involves either the release of endotoxin in the circulation, resulting in muscle and kidney damage, or the direct invasion of *Legionella* into the muscle tissues[20]. Meanwhile, case reports suggest that rhabdomyolysis also occurs in psittacosis[21, 22]. Our study reveals that psittacosis-associated rhabdomyolysis is not rare, and even more common than *Legionella* (no significant difference). But the mechanism behind the complication of psittacosis by rhabdomyolysis is unknown.

The laboratory findings of psittacosis and LP groups generally showed normal or slightly increased white blood cell counts, neutrophils, and PCT level, highly elevated CRP, and decreased lymphocytes. Gacouin et al. reported that the outcome of patients with psittacosis is similar to that of LP patients[15]. Our study also reveals that psittacosis and LP groups share similar proportion of SCAP and outcomes.

However, there are some differences between psittacosis and LP. We observed that 76.5% of the patients with psittacosis and 0% of the patients with LP had a contact with birds. Studies report that about 70% of psittacosis cases have a known source of infection as a result of contact with birds[23]. A study reported that 100% of the psittacosis cases had a bird exposure history while the corresponding percentage for LP cases is only 5.9%[15]. Therefore, a history of avian or poultry contact is an important diagnostic feature of psittacosis.

This study also shows that psittacosis patients are admitted at all seasons, and LP patients are not admitted in the winter season. Moreover, 41.2% of the psittacosis patients were admitted in the spring, while 44.4% of the LP patients were admitted in the autumn. In a Britain study, no seasonal variation was observed in psittacosis[24]. Furthermore, a higher portion of pigeons were found positive for *C. psittaci* IgG antibodies in the spring season. This observation suggests that pigeons may act as a significant source of human infection during the spring season[25]. Furthermore, raising poultry in all the seasons is
quite common in China, which adds to the problem. Legionnaires' disease is more common in the late summer and early autumn, seasons that are associated with wet and humid weather[26]. In our study, 44.4% of LP patients were admitted in the autumn and 0% in the winter season. This trend might be due to the fact that the weather in Wenzhou, China is wet throughout the year except winters. However, due to a limited sample size, the correlation between the admission of psittacosis or LP patients and the seasons could not be elucidated.

In *Legionella* CAP and psittacosis, hepatic involvement is common and generally manifested by mildly increased serum transaminases[9, 23]. It is reported that abnormal liver function tests occurs in some cases of psittacosis, and occurs in many cases in LP[17]. However, in our study, a significant number of patients with psittacosis had a higher proportion of elevated AST. We hypothesize that this observation might be attributed to the co-involvement of rhabdomyolysis. In addition, compared to psittacosis patients, LP patients have lower levels of serum sodium and hemoglobin. LP is frequently associated with hyponatremia[23], which may in turn be associated with the syndrome of inappropriate antidiuretic hormone secretion[27]. There is some anecdotal evidence associating hemolytic anemia to legionellosis, but the underlying mechanism is unknown[28, 29]. However, in our study, the bilirubin levels in both LP and psittacosis patients were found to be in the normal range, suggesting no evidence of hemolytic anemia. 2 LP patients out of 9 had comorbidities of chronic renal failure; another 2 patients had hematologic diseases (1 patient had myeloproliferative neoplastic disease and the other one had leukemia) (no significant difference as compared with psittacosis, data not shown). The comorbidities may be the cause of the lower hemoglobin levels in LP patients. As compared with severe legionellosis patients, patients with severe psittacosis are reported to be younger and less frequent smokers, having fewer chronic diseases and longer duration of pre-hospital symptoms[15]. However, in our study both legionellosis and psittacosis patients shared similar such features. The differences between our study and the reported studies might be due to variations in study population.

Although certain clinical features may suggest *Legionella* or *C. psittaci* infection, microbiological tests are required to confirm the diagnosis. Available diagnostic methods for *C. psittaci* infection are not ideal. Culture methods are time consuming and requires at least biosafety level III facility[30]. Serological tests are suitable for retrospective diagnosis as sera are required in both acute and convalescent phases[31]. Also, cross-reactivity with other *Chlamydia spp.* also poses problems[3]. Polymerase chain reaction (PCR) based testing is a more specific and rapid detecting method but has high sensitivity only in the acute stage[32]. For diagnosis of legionnaire's disease, *in vitro* culture is the gold standard, requiring a specific BCYE agar media. However, the prolonged incubation time of \( \geq 3 \) days limits its utility for early diagnosis[3]. Also, prior antibiotic exposure in the patient may decrease the culture positivity. The urinary antigen test, of good sensitivity and specificity[33], can detect the pathogen early and the antigen persists for several weeks despite the antibacterial therapy[3]. But such tests can only detect *L. pneumophila* serogroup I. PCR assays can rapidly detect most *Legionella* species, but its sensitivity and specificity varies[34, 35]. Moreover, PCR is available only in a few hospitals in China.
mNGS has emerged as a high-throughput method for pathogen identification and is superior to the currently available microbiological diagnostic methods for the identification of hard-to-culture pathogens. Because of its potential to use non-specific primers and a short turnaround time, mNGS can detect etiologic pathogens rapidly, leading to early diagnosis and a better prognosis[36]. Furthermore, mNGS is less affected by prior antibiotic exposure[12]. Several studies have discussed the potential of mNGS in diagnosing psittacosis or legionnaire's disease[6–8, 37]. In our study, all 17 psittacosis patients and 9 LP patients were diagnosed with the help of mNGS. Only 44.4% (4/9) patients tested positive for *Legionella* using culture methods, with a mean time to positivity as 9.5 days. Urine *Legionella* antigen test was positive only in 33.3% (3/9) patients. Therefore, mNGS may be a promising and rapid method for diagnosing psittacosis or legionnaire's disease.

The tetracyclines are the preferred antibiotics for the treatment of psittacosis[11, 16]. Macrolides are considered as alternatives for patients who are contraindicated for tetracyclines[16]. Studies are needed to establish the utility of quinolones in treating these diseases. A few fluoroquinolones were found to be active against *C. psittaci* in experimental models[17]. In the present study, quinolones were administered to 10 psittacosis patients, and on one out of 10 died, indicating that quinolones may be effective against *C. psittaci*. The unavailability of doxycycline in the hospital might be a reason why quinolones were frequently administered in our study. Besides, the use of tigecycline is restricted because of the high price and high incidence of hepatic side effects.

This study has several limitations. Sample size of this study is limited, and the diagnosis of psittacosis was made solely through mNGS, with no confirmation by other methods. However, clinical manifestations are consistent with literature and BALF in all cases showed *C. psittaci* reads with mNGS. Further, direct comparison between psittacosis and LP provides important information on the differential diagnosis of the two diseases based on clinical parameters.

**Conclusions**

There are many similarities between psittacosis and LP, including extra-pulmonary manifestations, biological features, and prognosis. Psittacosis is a vital differential diagnosis of LP, especially in patients with prior avian exposure. mNGS is a sensitive tool and has potential for the early detection of *C. psittaci* and *Legionella*. These preliminary findings should be correlated with diagnostic trials in the future studies.

**Abbreviations**

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BALF: Bronchial alveolar lavage fluid; BCYE: Buffered charcoal yeast extract; BNP: B natriuretic peptide; CAP: Community-acquired pneumonia; CK: Creatine kinase; CRP: C-reactive protein; CT: Computed tomography; ICU: Intensive care unit; LD: Legionnaire's disease; LDH: Lactate dehydrogenase; LP: *Legionella* pneumonia; mNGS: Metagenomic
next generation sequencing; PCR: Polymerase chain reaction; PCT: Procalcitonin; SCAP: Severe CAP; SD: Standard deviation; WBC: White blood cell

Declarations

Acknowledgments

Not Applicable.

Authors’ contributions

YZ and YPL participated in study conception and design. SSS, JHZ, YLL and PCL collected and assembled the data. JJC and CSC participated in data analysis and interpretation. All authors read and approved the final manuscript.

Funding

This work was supported by the Project of National Natural Science Foundation of China [Grant number 81970066]. The funding body had no role in the study design, the collection, analysis or interpretation of the data.

Availability of data and materials

The dataset used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. The requirement for informed consent was waived due to the retrospective nature of the study. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not Applicable.

Competing interests

The authors have no conflicts of interest to declare.

Author details

1Department of Pulmonary and Critical Care Medicine, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China. 2Department of Pulmonary and Critical Care Medicine, Yueqing City People’s Hospital, Yueqing, China.
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**Tables**

Table.1 General characteristics of patients with psittacosis versus *Legionella* pneumonia
| Characteristics                                      | C. psittaci pneumonia (n=17) | Legionella pneumonia (n=9) | p-value |
|------------------------------------------------------|------------------------------|----------------------------|---------|
| Ages, years                                          | 62.1±9.7                     | 56.6±20.8                  | 0.465   |
| Male, n(%)                                           | 9 (52.9)                     | 7 (77.8)                   | 0.399   |
| Current smoker, Current drinker, n (%)               | 5 (29.4)                     | 3 (33.3)                   | 1.000   |
| History of contact with avian or poultry, n (%)      | 13 (76.5)                    | 0 (0)                      | <0.001  |
| Chronic underlying diseases, n (%)                   | 10 (58.8)                    | 8 (88.9)                   | 0.190   |
| Symptoms duration before admission, days             | 5.0 (3.0,7.5)                | 5.0 (3.0, 7.0)             | 0.634   |
| Season of admission, n (%)                           |                              |                            | 0.910   |
| Spring                                               | 7 (41.2)                     | 3 (33.3)                   |         |
| Summer                                               | 4 (23.5)                     | 2 (22.2)                   |         |
| Autumn                                               | 3 (17.6)                     | 4 (44.4)                   |         |
| Winter                                               | 3 (17.6)                     | 0 (0)                      |         |

Table 2. Clinical manifestations of patients with psittacosis versus *Legionella* pneumonia
| Characteristics                        | C. psittaci pneumonia (n=17) | Legionella pneumonia (n=9) | p-value |
|---------------------------------------|-----------------------------|---------------------------|---------|
| Fever, n(%)                           | 17 (100)                    | 9 (100)                   | -       |
| Temperature                           | 39.8±0.5                    | 39.8±0.3                  | 0.974   |
| Rigors, n(%)                          | 12 (70.6)                   | 3 (33.3)                  | 0.103   |
| Fatigue, n(%)                         | 8 (47.1)                    | 6 (66.7)                  | 0.429   |
| Myalgia, n(%)                         | 4 (23.5)                    | 0 (0)                     | 0.263   |
| Cough, n(%)                           | 14 (82.4)                   | 8 (88.9)                  | 1.000   |
| Sputum, n(%)                          | 12 (70.6)                   | 6 (66.7)                  | 1.000   |
| Dyspnoea, n(%)                        | 13 (76.5)                   | 7 (77.8)                  | 1.000   |
| Extrapulmonary findings, n (%)        |                             |                           |         |
| Relative bradycardia                  | 11 (64.7)                   | 5 (55.6)                  | 0.692   |
| Neurological symptoms                 | 8 (47.1)                    | 1 (11.1)                  | 0.098   |
| Gastrointestinal symptoms             | 3 (17.6)                    | 1 (11.1)                  | 1.000   |
| Rhabdomyolysis                        | 5 (29.4)                    | 1 (11.1)                  | 0.380   |

Table 3: Laboratory and radiological findings of patients with psittacosis versus Legionella pneumonia
| Characteristics             | C. psittaci pneumonia (n=17) | Legionella pneumonia (n=9) | p-value |
|-----------------------------|------------------------------|---------------------------|---------|
| WBC, ×10⁹/L                 | 10.5±6.3                     | 9.5±5.3                   | 0.672   |
| Elevated WBC                | 8 (47.1)                     | 3 (33.3)                  | 0.683   |
| Neutrophils, ×10⁹/L         | 9.4±5.9                      | 8.3±5.4                   | 0.647   |
| Lymphocyte, ×10⁹/L          | 0.7±0.4                      | 0.6±0.2                   | 0.390   |
| Decreased lymphocyte        | 16 (94.1)                    | 9 (100)                   | 1.000   |
| Hemoglobin, g/L             | 118.9±20.2                   | 93.2±23.2                 | 0.007   |
| CRP, mg/L                   | 205.1±90.0                   | 234.9±114.0               | 0.471   |
| PCT, ng/mL                  | 0.8 (0.3, 6.0)               | 5.1 (1.2, 27.9)           | 0.063   |
| ALT, U/L                    | 78.0 (37.0, 125.5)           | 24.0 (10.5, 101.5)        | 0.112   |
| AST, U/L                    | 140.0 (48.0, 271.5)          | 31.0 (20.0, 170.5)        | 0.071   |
| Elevated AST                | 15 (88.2)                    | 4 (44.4)                  | 0.028   |
| Urea, mmol/L                | 10.1±8.6                     | 11.2±7.6                  | 0.757   |
| Creatinine, μmol/l          | 64.0 (53.0, 213.5)           | 78.0 (71.5, 154.0)        | 0.403   |
| Serum sodium, mmol/L        | 138.9±5.4                    | 133.9±6.5                 | 0.047   |
| LDH, U/L                    | 481.5 (359.3, 725.5)         | 430.0 (316.3, 597.8)      | 0.327   |
| CK, U/L                     | 456.0 (91.5, 2270.0)         | 104.0 (32.5, 263.0)       | 0.063   |
| BNP, pg/mL                  | 185.0 (54.0, 256.0)          | 377.0 (84.0, 624.0)       | 0.456   |
| CD4+ T cell                 | 305.8±185.8                  | 167.9±93.8                | 0.082   |
| CD8+ T cell                 | 99.0 (70.3, 129.0)           | 112.0 (78.0, 161.0)       | 0.601   |
| IL-6, pg/mL                 | 307.3 (89.4, 1141.8)         | 314.9 (115.2, 1908.1)     | 0.934   |
| IL-10, pg/mL                | 8.3 (4.2, 20.2)              | 6.5 (3.2, 64.3)           | 0.934   |
| IFN-γ, pg/mL                | 31.9 (9.7, 198.0)            | 17.8 (6.4, 57.7)          | 0.284   |
| Pao2/Fio2 ratio, mmHg        | 218.3±114.2                  | 244.2±78.4                | 0.552   |
| Imaging                     |                              |                           |         |
| Consolidation               | 14 (82.4)                    | 8 (88.9)                  | 1.000   |
| Inflammatory                | 8 (47.1)                     | 6 (66.7)                  | 0.429   |
exudation

| Pleural effusions | 13 (76.5) | 6 (66.7) | 0.661 |

WBC white blood cell, CRP C-reactive protein, PCT procalcitonin, ALT Alanine aminotransferase, AST Aspartate aminotransferase, LDH lactate dehydrogenase, CK creatine kinase, BNP B natriuretic peptide

Table 4: Treatment and outcomes of patients with psittacosis versus *Legionella* pneumonia
|                              | C. psittaci pneumonia (n=17) | Legionella pneumonia (n=9) | \(p\)-value |
|------------------------------|-----------------------------|-----------------------------|-------------|
| Empirical antibiotics not covered | 4 (23.5)                   | 4 (44.4)                    | 0.382       |
| Antimicrobial therapy        |                             |                             | 0.305       |
| Tetracycline                 | 1 (6.3)\(^\dagger\)        | 0 (0)\(^\ddagger\)         |             |
| Macrolides                   | 3 (18.8)\(^\dagger\)       | 0 (0)\(^\ddagger\)         |             |
| Quinolones                   | 10 (62.5)\(^\dagger\)      | 6 (75.0)\(^\ddagger\)      |             |
| Combination of above antibiotics | 2 (12.5)\(^\dagger\)      | 2 (25.0)\(^\ddagger\)      |             |
| Fever clearance time, days   | 6.0 (4.3, 7.0)              | 5.0 (2.0, 7.0)              | 0.311       |
| SCAP, n(%)                   | 10 (58.8)                   | 4 (44.4)                    | 0.683       |
| Respiratory support, n(%)    |                             |                             | 0.782       |
| Invasive ventilation         | 7 (41.2)                    | 2 (22.2)                    |             |
| Non-invasive ventilation     | 0 (0)                       | 2 (22.2)                    |             |
| No mechanical ventilation    | 10 (58.8)                   | 5 (55.6)                    |             |
| Septic shock, n(%)           | 11 (64.7)                   | 4 (44.4)                    | 0.419       |
| Hemodialysis, n(%)           | 3 (17.6)                    | 1 (11.1)                    | 1.000       |
| Median length of hospital stay, days | 12.0 (10.0, 16.5) | 13.0 (8.0, 30.0)            | 0.865       |
| Death, n(%)                  | 2 (11.8)                    | 2 (22.2)                    | 0.591       |

\(^\dagger\) n=16, \(^\ddagger\) n=8

**Figures**
Figure 1

Chest computed tomography (CT) scan of a 71-year-old man with psittacosis on the day of admission (2 days after onset). It shows air-space consolidation in left lower lobe. A, lung window; B, mediastinum window.

Figure 2

Chest computed tomography (CT) scan of a 45-year-old woman with Legionella pneumonia on the day of admission (3 days after onset). It shows air-space consolidation and inflammatory exudation in right middle lobe, with small interlobar effusion. A, lung window; B, mediastinum window.