JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Case Report

Severe pneumonia caused by *Chlamydia psittaci*: report of two cases and literature review

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Abstract

Introduction: *Chlamydia psittaci* pneumonia is a zoonotic infectious disease caused by *Chlamydia psittaci*. Its clinical manifestations are nonspecific. Diagnosis of the disease is difficult. In recent years, next-generation sequencing has played an important role in pathogen detection. We report two cases with severe *Chlamydia psittaci* pneumonia confirmed by next-generation sequencing.

Case Study: The first case is that of a 50-year old man who presented with high fever for four days and cough with sputum for two days. The second case is that of a 57-year-old man who was admitted with high fever for one week, dyspnea and cough with sputum for four days. The second man worked at a chicken farm in the last two months. In both cases, the usual laboratory examination for pathogens detection was negative, and the initial anti-infectious therapy had limited effect. The bronchoalveolar lavage fluid of case 1 and the blood and sputum of case 2 were sent for next-generation sequencing which resulted in sequence reads of *Chlamydia psittaci*. Antibiotics were adjusted according to the diagnosis.

Results: The diagnosis of the two cases was confirmed by next-generation sequencing detecting *Chlamydia psittaci*, and the patients had positive results after treatment.

Conclusions: The two cases suggest that next-generation sequencing could be used in early diagnosis of *Chlamydia psittaci* infection to initiate specific anti-infection therapy in time.

Key words: *Chlamydia psittaci*; severe pneumonia; next-generation sequencing (NGS); extracorporeal membrane oxygenation (ECMO).

J Infect Dev Ctries 2022; 16(6):1101-1112. doi:10.3855/jidc.16166

(Received 29 November 2021 – Accepted 09 March 2022)

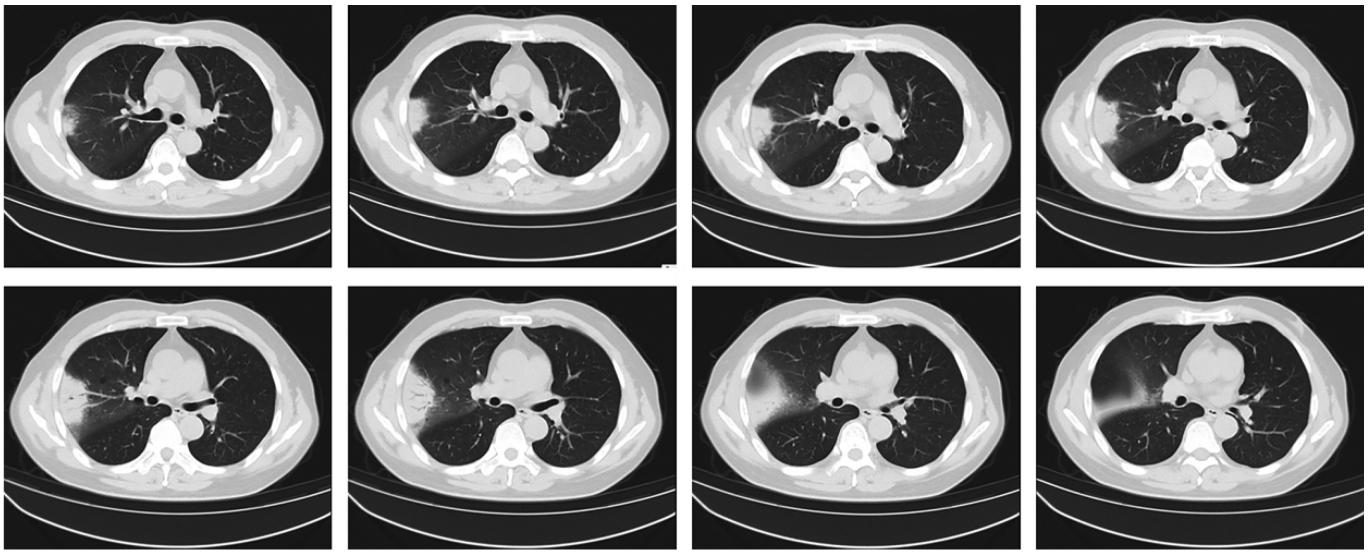
Introduction

Chlamydia psittaci (*C. psittaci*) pneumonia is a zoonotic infectious disease caused by *C. psittaci,* and is estimated to cause approximately 1% of cases of community-acquired pneumonia [1]. *C. psittaci* infection is associated with various clinical manifestations from asymptomatic infection to severe atypical pneumonia and systemic disease. At present, the diagnosis of *C. psittaci* infection mainly depends on laboratory examination, which makes early diagnosis difficult. The next-generation sequencing (NGS) technique enables rapid screening of pathogens and helps with early identification of pathogens to initiate specific anti-infective therapy [2]. In this article, we reported two cases of severe *Chlamydia psittaci* pneumonia, *C. psittaci* was detected in blood, sputum, and bronchoalveolar lavage fluid (BALF) by NGS and was successfully rescued. We have also reviewed relevant literature on *C. psittaci* infection which include a total of 36 cases of infection.

Case 1

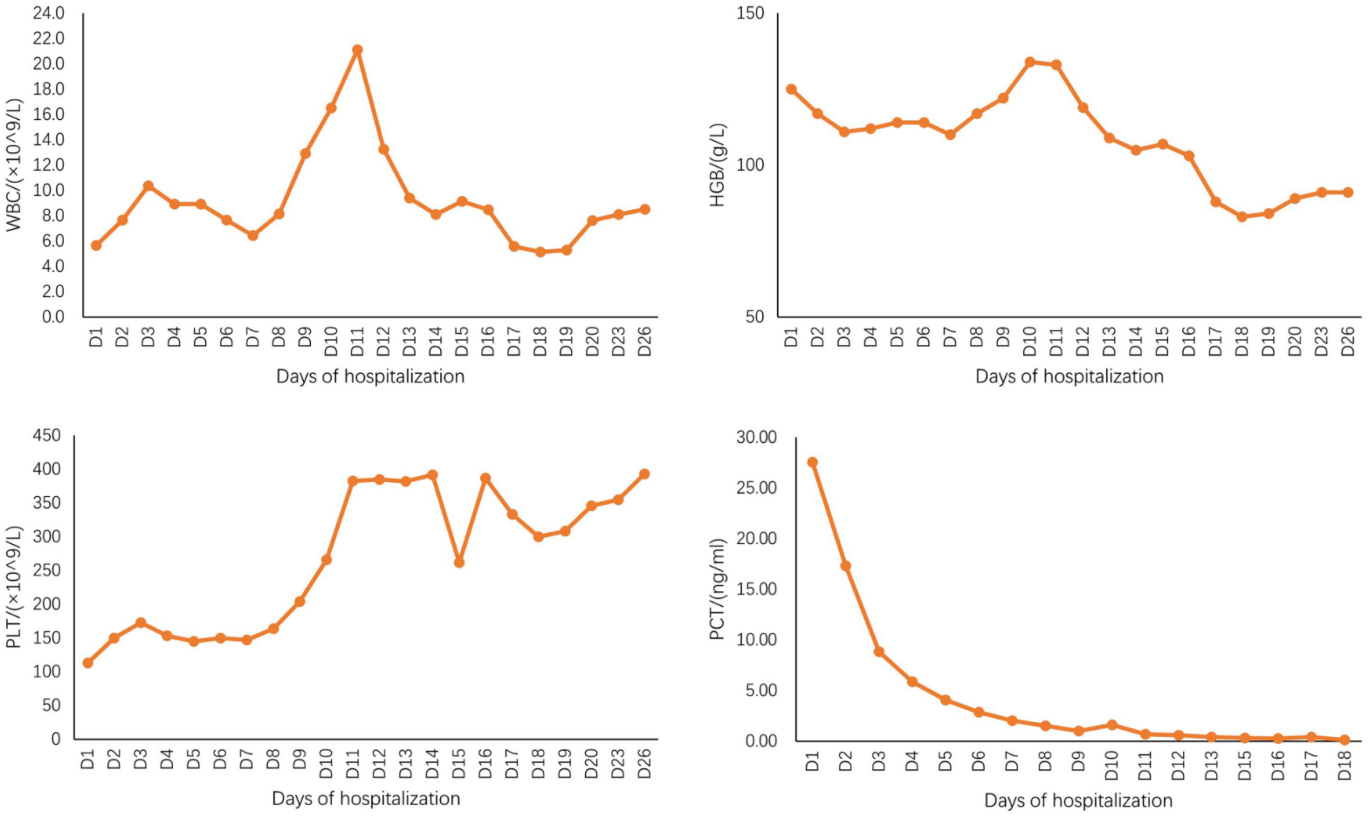
A 50-year-old male was admitted to the hospital on December 2, 2020. The patient had high fever for 4 days, cough with sputum and dyspnea for 2 days. He was an office worker. Four days earlier, the patient had fever after travelling, with a peak body temperature of 40 ℃, along with fatigue, muscle pain, and chills. There was no improvement after self-administered paracetamol and tylenol. Two days later he visited our fever clinic. His blood routine showed the white blood cell (WBC) count was 9.21(*10^9/ L), the neutrophil percentage was 82.9%. The chest CT (Figure 1) showed variegated high-density shadow and abrasive glass density shadow in the upper lobe and middle lobe of the right lung. Considering that the patient was diagnosed with pulmonary infection, he was given moxifloxacin and imipenem and cilastatin sodium, but his condition deteriorated. One day before admission, his oxygenation index fell to 83 and he was sent to the intensive care unit (ICU). Emergency tracheal intubation and ventilator assisted ventilation was applied.

Figure 1. The chest computed tomography CT of case 1 before admission (2020-11-29).



The chest CT showed that the upper lobe and middle lobe of the right lung were stained with high-density shadow and ground glass density shadow, and the bronchus inflation sign was found. The trachea and main bronchi are unobstructed.

Figure 2. Changes in blood routine and procalcitonin (PCT) results of case 1 during hospital stay.



After admission, the white blood cell (WBC) count fluctuated between 5.67*109/L and 21.11*109/L, platelet (PLT) fluctuated between 113*109/L and 393*109/L, hemoglobin (HGB) fluctuated between 83 g/L and 134 g/L. PCT fluctuated between 0.144 ng/mL and 27.59 ng/mL, and it decreased gradually. D: Day.

Table 1. Laboratory test results of the two cases.

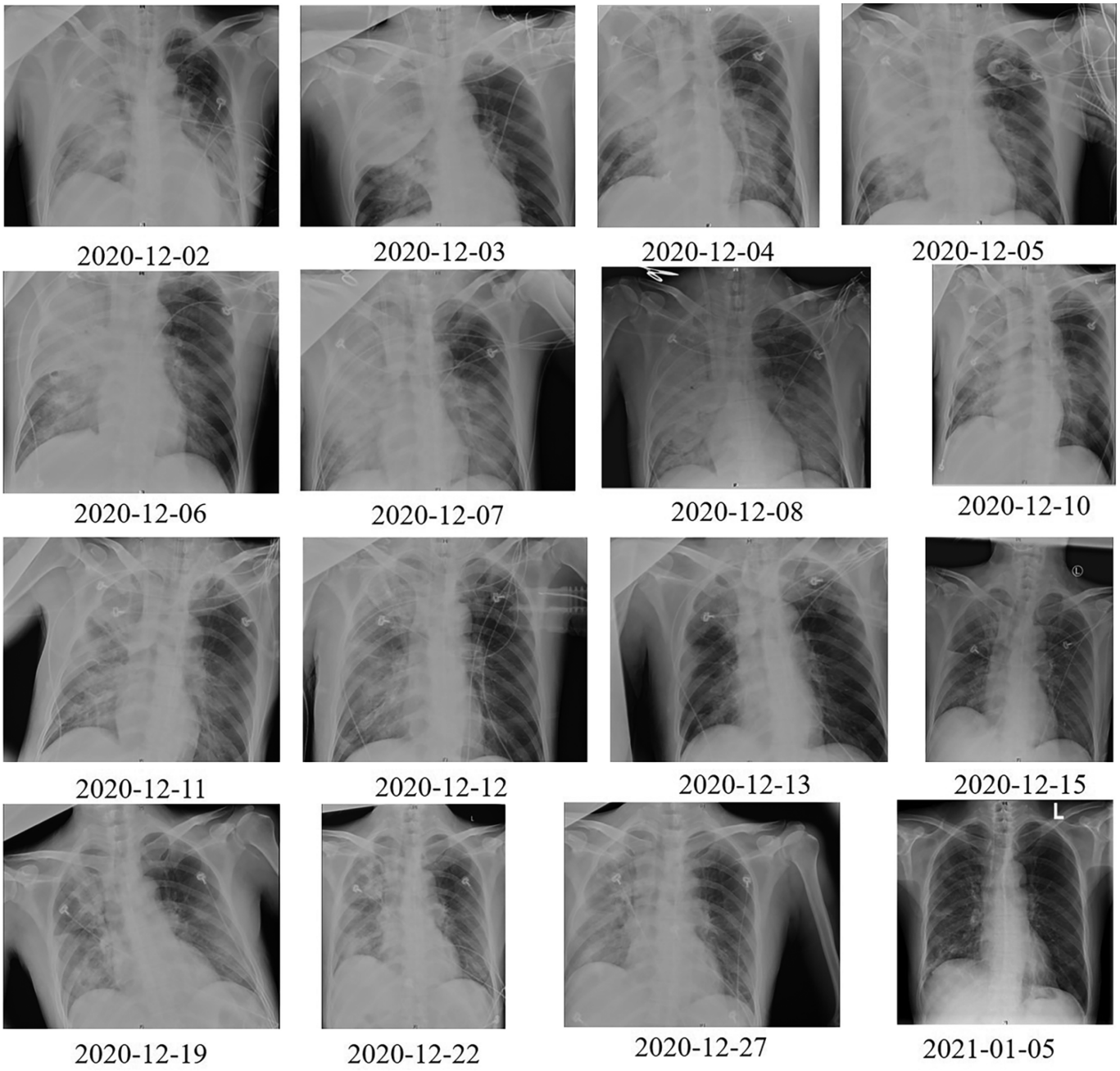
Laboratory test	Case 1	Case 2
Blood routine		
Neut%	95.6%	93.2%
Urine routine	-	U-BLD (+); U-Pro (+)
Blood sodium (mmol/L)	129	133.2
Biochemical indexes		
ALT (U/L)	125	58
AST (U/L)	203	142
LDH (U/L)	606	355
ALB (g/L)	24.6	21.2
CK (U/L)	8368	1248
CK-MB (U/L)	259	8
MYO (ng/mL)	1475	Not found
Scr (μmol/L)	88	93
BUN (mmol/L)	8.49	13.42
TBIL (μmol/L)	24.9	36.9
NT-proBNP (pg/mL)	217	6920
TnI (ng/mL)	< 0.010	< 0.010
Lymphocyte count and classification	-	-
Eight items of preoperative immunity		
HBsAg	-	-
Anti-HBs	-	+
HBeAg	-	-
Anti-HBe	-	-
Anti-HBc	-	+
Anti-HCV	-	-
Anti-TP	-	-
Anti-HIV/P24	-	-
D-dimer (μg/mL)	2.83	7.67
Serum antibody		
IgA (g/L)	9.190	Not found
IgG (g/L)	1.300	Not found
IgM (g/L)	0.328	Not found
IgE (IU/mL)	176.10	Not found
Complement factor 3 (g/L)	1.220	Not found
Complement factor 4 (g/L)	0.384	Not found
Tumor markers		
SCC (ng/mL)	1.6	2.2
bone collagen CYFRA21-1 (ng/mL)	12.56	10.68
NSE (ng/mL)	50.47	24.02
proGRP (pg/mL)	35.7	29.5
CEA (ng/mL)	1.67	8.18
Influenza A virus antigen	-	-
Influenza B virus antigen	-	-
Mycoplasma pneumoniae antibodies	-	-
Streptococcus urois antigen	-	-
Legionella pneumonia antibodies	-	-
Epstein-Barr virus antibodies	-	-
CMV-DNA (copies/mL)	< 500	< 500
Anti-CMV	-	-
Nucleic acid combination of respiratory pathogens		
Streptococcus pneumoniae	-	-
Staphylococcus aureus	-	-
methicillin-resistant *Staphylococcus*	-	-
Klebsiella pneumoniae	-	-
Pseudomonas aeruginosa	-	-
Acinetobacter baumannii	-	-
Stenomonas maltophilia	-	-
Influenza bacillus	-	-
G test	-	-
GM test	-	-
Sputum culture	-	-
Blood culture	-	-

Neut%: percentage of neutrophil; U-BLD: urine occult blood; U-Pro: urine protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; ALB: albumin; CK: creatine kinase; CK-MB: creatine kinase isoenzyme MB; MYO: myoglobin; Scr: serum creatinine concentration; BUN: blood urea nitrogen; TBIL: total bilirubin; NT-proBNP: N-terminal pro-brain natriuretic peptide; TnI: troponin I; HBsAg: hepatitis B virus surface antigen; Anti-HBs: hepatitis B virus surface antibody; HBeAg: hepatitis B virus e antigen; Anti-HBe: hepatitis B virus e antibody; Anti-HBc: hepatitis B virus core antibody; Anti-HCV: hepatitis C virus antibody; Anti-TP: syphilis antibody; Anti-HIV/P24: human immunodeficiency virus antibody/P24 antigen; Ig: immunoglobulin; SCC: squamous cell carcinoma antigen; NSE: neuronspecific enolase; proGRP: pro-gastrin releasing peptide; CEA: carcinoembryonic antigen; CMV: human cytomegalovirus; G test: Fungal (1,3)-β-D-glucan; GM test: detection of aspergillus galactomannan antigen.

The patient had hypertension for more than four years, and he was undergoing treatment with oral nifedipine and benazepril hydrochloride, and he did not monitor blood pressure regularly. The patient had been living abroad recently (Zhucheng to Gaomi, Shandong Province, China).

His body temperature was 38.2 °C, pulse was 128 bpm, blood pressure was 140/88 mmHg, and his respiratory rate was 20 breaths per minute at the time of admission. Following physical examination, the patient was kept under sedation in tracheal intubation and ventilator assisted ventilation. His Glasgow score was 3 and he could not cooperate with physical examination. The skin was stained and the skin temperature of both hands and feet was low. Wet rales could be heard and scattered in both lungs, especially in the right lung. The

Figure 3. The chest images of case 1 after admission.



After active anti-infection treatment, the overall trend of chest image changes is the gradual absorption and reduction of inflammation in both lungs. Among them, chest image (2021-12-19) contrast with 2020-12-15 showed that the double lung texture increased, visible flake shadow can be found, especially in the right lung;. The inflammation in both lungs gradually reduced after adjusting the plan of antibiotics.

patient's laboratory test results for blood routine tests and procalcitonin (PCT) are shown in Figure 2. Other laboratory test results can be found in Table 1.

After admission, diagnosis of type I respiratory failure and severe pneumonia was clear. Based on tracheal intubation assisted ventilation, his oxygen saturation was maintained at about 90% and oxygenation index was 73. The emergency extracorporeal membrane oxygenation (ECMO) was administrated. When using ECMO, simultaneous sedation and analgesia were required, and the use of heparin was adjusted based on the ACT (120-160s) or APTT (60-80s). The parameters of ECMO were adjusted according to the patient's condition. At the same time, the patient was treated with levofloxacin, imipenem and cilastatin sodium, and oseltamivir. Supportive treatment was also given. To identify the pathogen, bronchoalveolar lavage (BAL) was conducted on the second day and bronchoalveolar lavage fluid (BALF) was sent for testing with NGS. On the third day of arrival to our hospital, NGS of BALF and blood reported sequence reads of *Chlamydia psittaci*. Therefore, the antibiotics were adjusted to minocycline, azithromycin, and imipenem and cilastatin sodium. After treatment, the patient was in a stable condition and the lung inflammation was absorbed (Figure 3). Finally, the patient was discharged the twenty sixth day after admission. The patient went for reexamination after 1 week (January 1, 2021) and was in good condition, his chest imaging (Figure 3) showed the double lung inflammation was reduced.

Case 2

A 57-year-old male was admitted to the hospital on October 17, 2020 after suffering from a high fever for 1 week, and cough with sputum and dyspnea for 4 days. His peak body temperature reached 38.9 ℃, accompanied by fatigue, chills, and poor appetite, and there was no improvement after self-administered cephalosporin antibiotics. Four days prior to hospitalization, he started to have cough with white sticky phlegm accompanied with dyspnea. His poor appetite and fatigue were aggravated progressively. Three days prior to hospitalization he went to the local hospital, where his blood pressure was 68/40mmHg; his chest CT (Figure 4) showed double lung inflammation and lung occupation. Considering the diagnosis of severe pneumonia, septic shock, and type I respiratory failure, he was treated with piperacillin sulbactam and oxygen inhalation. He was transferred to the ICU, and the chest CT indicated the progression of pneumonia. Oxygen storage mask and non-invasive ventilation (NIV) were given for assisted breathing. However hypoxemia was difficult to ameliorate and he was treated with emergency tracheal intubation and ventilator assisted ventilation. After the onset of the disease, his mental condition and sleep were poor, stool was normal, urine was dark brown and reduced, and he lost two kilograms in weight.

The patient had a history of splenic tumor resection which happened 40 years ago, and esophageal venous sclerosis treatment owing to cirrhosis and gastrointestinal bleeding 32 years ago. He was diagnosed with "portal vein congenital malformation, cirrhosis" and treated through a surgery. In the previous two months, he worked for a chicken farm. He had a 30-year smoking history and no history of hereditary diseases in the family.

His body temperature was 36.8 °C, pulse 83 bpm, blood pressure 132/85 mmHg, respiratory rate 29 breaths per minute, and his PaO_2 was 75mmHg at the time of admission. Upon physical examination, the patient was kept in tracheal intubation and ventilator assisted ventilation. He appeared acutely ill and and in pain. He was under sedation and could not cooperate. There were liver palms and spider nevus. Wet rales could be heard in both lungs. The heart rate was 94 beats/min, the rhythm was absolutely uneven, and the intensity of the first heart sound was different. The patient's laboratory test results of blood routine and PCT after admission are shown in Figure 5. Other laboratory test results are listed in Table 1. His phlegm was tested negative for tuberculosis and fungus.

After admission, he was diagnosised with type I respiratory failure, severe pneumonia, and adult respiratory distress syndrome (ARDS). Therefore, imipenm, cilastatn sodium and moxifloxacin were used as anti-infective therapy. He was also treated with physical cooling, plasma transfusion, diuretic treatment and other symptomatic therapy. After admission, his blood and sputum were sent for testing for pathogens by using NGS and sequence reads of *Chlamydia psittaci* were reported. This result was in combination with his recent history of poultry exposure. The the antibiotics were adjusted to minocycline, azithromycin, imipenm and cilastatn sodium. The use of antibiotics and parameters of invasive ventilator were adjusted based on parameters such as hospital infection and changes in chest imaging (Figure 6 and Figure 7). As a result of the treatment, the patient was in stable condition, the lung inflammation was absorbed, tracheal intubation was removed on the 17th day after admission.

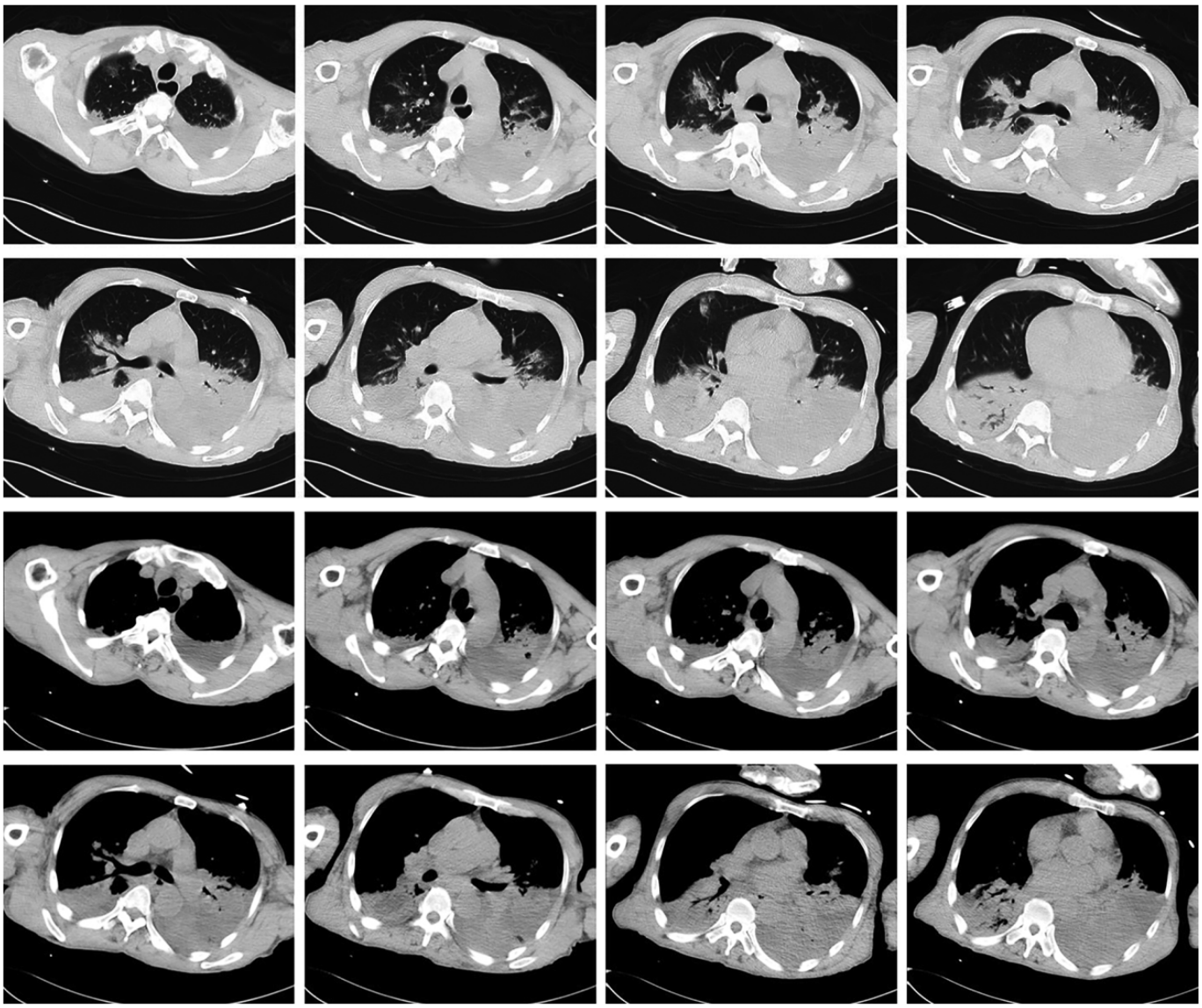
He was also treated for atrial fibrillation during hospitalization. Owing to high levels of BUN, Scr, liver

function, and bilirubin after admission, the protection of essential organs and maintaining water and electrolyte balance were required. Finally, the patient was discharged the 25th day after admission. The patient returned for reexamination after 1 week (November 18, 2020) and was in good condition, his chest imaging showed the double lung inflammation reduced and a small amount of pleural effusion in the left.

Results

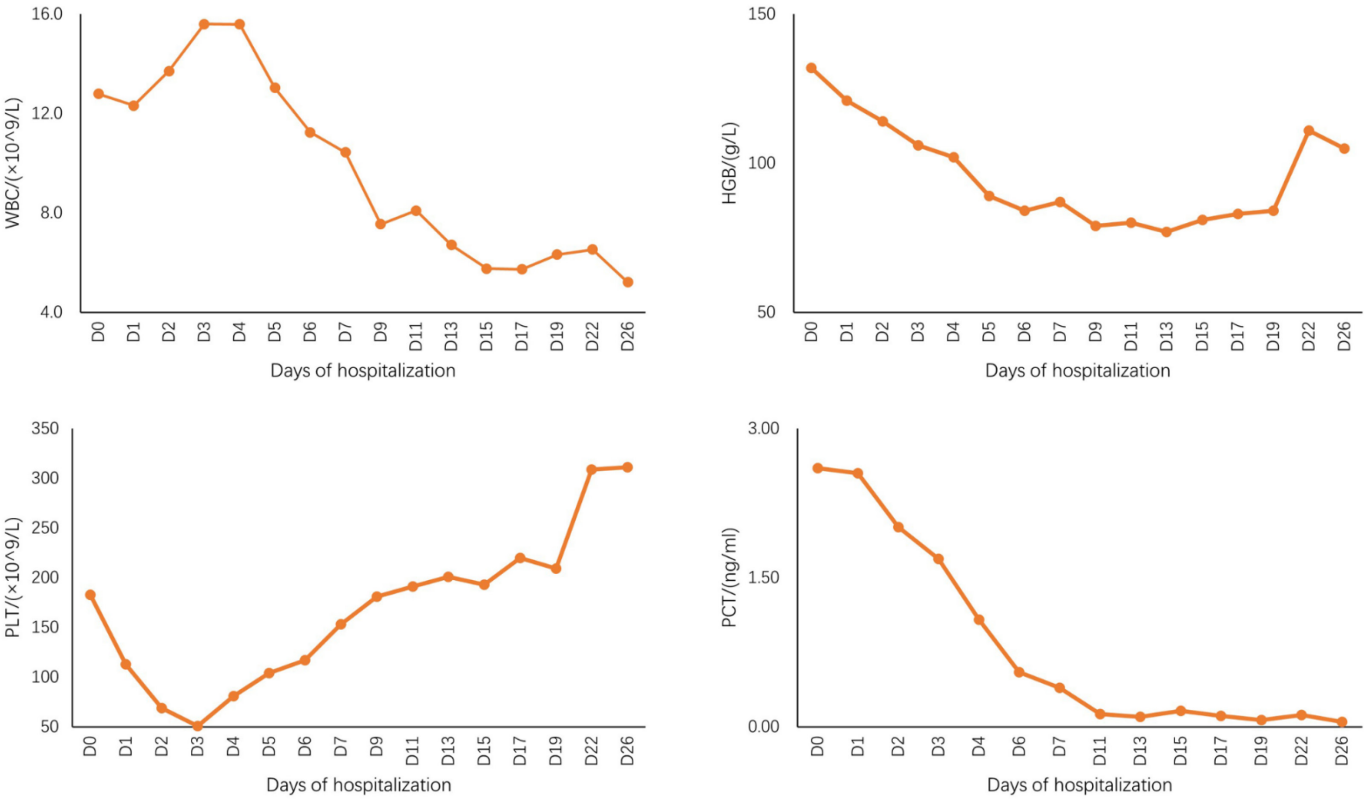
The two cases were diagnosed with *Chlamydia psittaci* though NGS. Antibiotics and other therapies were adjusted according to the result and the patients' condition. The patients improved after treatment and were discharged on the 26th and 25th day, respectively. Reexamination showed good clinical and radiological prognosis.

Figure 4. The chest computed tomography CT before admission of case 2.



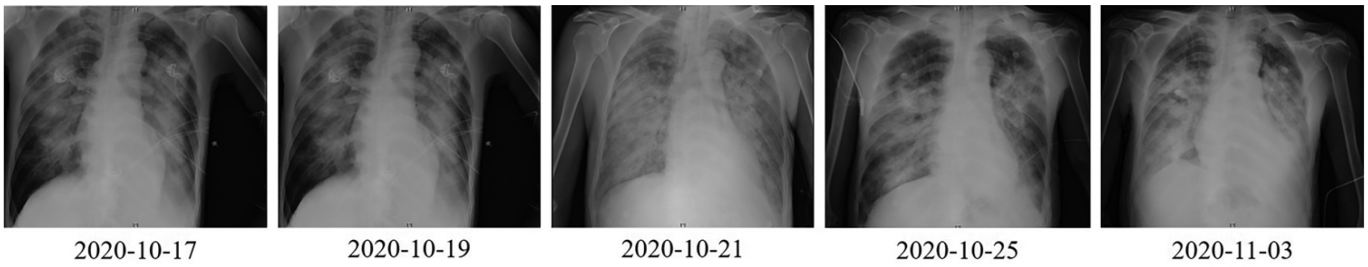
The chest CT showed multiple patchy solid shadows, unclear boundary, air bronchus sign, and obstructed left inferior lobe bronchus. Mediastinal enlarged lymph nodes and bilateral pleural effusion were seen.

Figure 5. Changes in blood routine and procalcitonin (PCT) results during hospital stay of case 2.



After admission, the white blood cell (WBC) count fluctuated between 5.21*109/L and 15.60*109/L, platelet (PLT) fluctuated between 51*109/L and 311*109/L, hemoglobin (HGB) fluctuated between 77 g/L and 132 g/L. PCT fluctuated between 0.053 ng/mL and 2.6 ng/mL, and the overall trend was decreased. D: Day.

Figure 6. The chest images of case 2 after admission.



The chest images of 10-17 showed bilateral lung inflammation and left pleural effusion. The chest images of 10-19 and 10-21 showed that the inflammation of both lungs was more advanced than before; after adjusting antibiotics, the inflammation of both lungs was absorbed and less than that of 10-21; 11-03 compared with 10-25, the inflammation of both lungs was advanced, hence the use of antibiotics was adjusted.

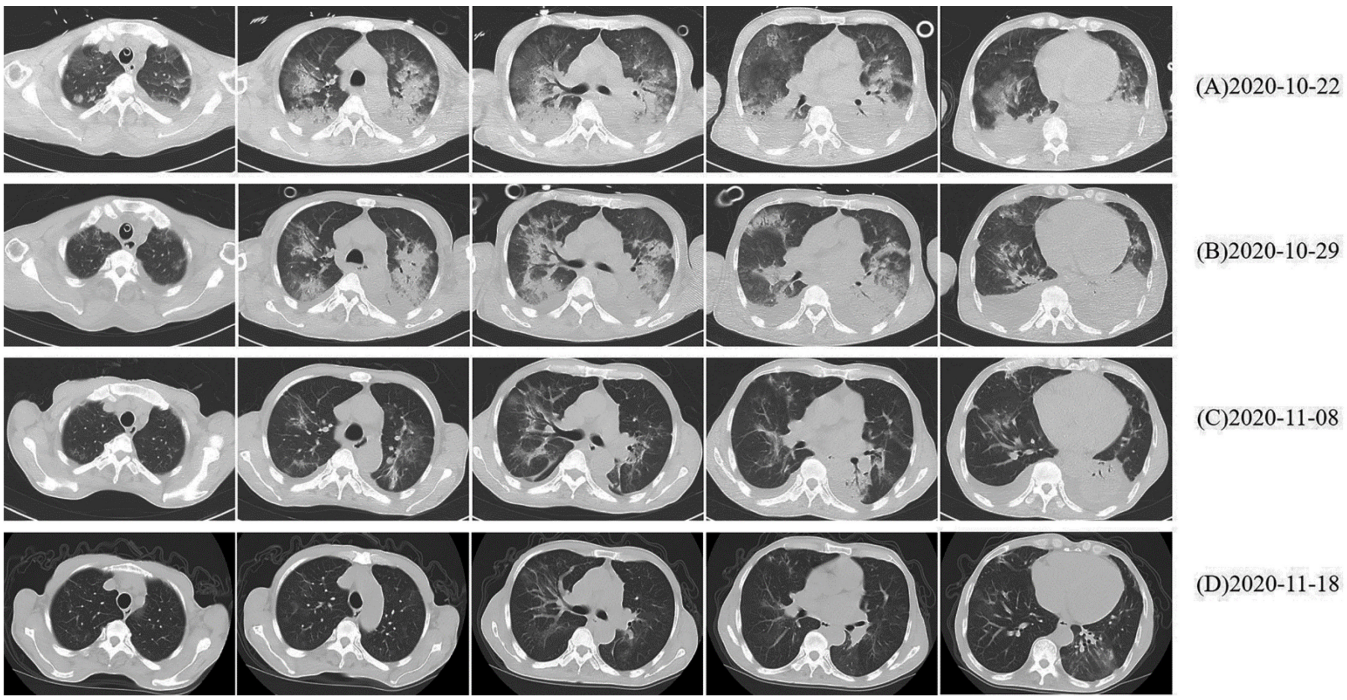
Discussion

Chlamydia psittaci is an obligatory intracellular Gram-negative bacterium, which can be found in the tissues, blood, and fecal material of parrots and other birds. *C. psittaci* mainly infects birds, but can occasionally cause psittacosis in humans when contaminated aerosols from infected birds are inhaled. Based on sequencing of the major outer protein gene (*ompA*), *C. psittaci* can be classified into 10 genotypes, namely A~G, WC, E/B, and M56 [15]. Genotypes A and E can infect humans. The disease usually occurs sporadically, but outbreaks have been described [16,17,18].

C. psittaci pneumonia mainly occurs in young and middle-aged people, and more than half of the patients have a history of contact with birds. As we reviewed in Table 2, most cases (77.8%, 28/36) had a history of contact with birds. The clinical manifestation of *C. psittaci* pneumonia is unspecific. It can appear as high fever, cold, headache, myalgia, cough, pulmonary infiltration, etc. In severe cases, patients can develop severe pneumonia, and even have a poor prognosis [3,19]. As summarized in Table 2 previous studies have identified the symptoms as fever (97.2%, 35/36), cough (75.0%, 27/36), myalgia (36.1%, 13/36), headache (33.3%, 12/36), malaise (25%, 9/36); some cases developed to ARDS; most of the cases were cured, only five cases (13.9%, 5/36) dead. In addition to the respiratory tract, infection with *C. psittaci* has been reported to affect organ systems, resulting in conditions including endocarditis, myocarditis, hepatitis, arthritis, keratoconjunctivitis, encephalitis, and ocular adnexal lymphoma [20]. Some patients may have rhabdomyolysis. Laboratory test results suggest that the WBC count is normal in most patients. If systemic diseases exist, patients may develop liver function abnormalities, hyponatremia, and elevated BUN and Scr. High-level C-reaction protein and low-level ALB can also occur. In the two cases we report here, there were fever, cough, respiratory failure, ARDS, and abnormalities of liver function and ALB; moreover, case 2 presented with abnormal renal function and coagulation.

There is also a lack of specificity in imaging of *C. psittaci* pneumonia. In the review (Table 2), chest imaging of most patients showed consolidation of infiltration, mainly in the lower lobe and unilateral lung, although some involved bilateral lung [21]; hilar lymphadenopathy and pleural effusion (13.9%, 5/36) are rare. In these cases, only two patients had normal chest imaging. High-resolution CT shows that some lesion areas are solid nodular and ground glass [22]. Among the two cases we have reported, there were solid or ground glass pulmonary shadows, and hilar lymphadenopathy and pleural effusion in case 2. Combined with respiratory failure and chest imaging

Figure 7. The chest computed tomography (CT) of case 2 after admission.



The overall trend of chest CT was decreased inflammation and pleural effusion.

findings, severe pneumonia could be diagnosed, but not *C. psittaci* infection.

The diagnosis of *C. psittaci* infection mainly depends on laboratory examination, including cell culture, serological tests, and polymerase chain reaction (PCR). Among them, cell culture is only performed in specialized laboratories (P3 facility), and *C. psittaci* is highly infectious when cultured; *C. psittaci* serological tests show cross-reaction with other chlamydial species, they do not allow source tracing, and the early diagnosis value is low [20,21]. PCR, especially real-time PCR (RT-PCR) is a faster, more sensitive, and more specific way for identification [23]. However, PCR for *C. psittaci* is unavailable in most hospitals in China, including many tertiary hospitals; it is only performed if clinicians have a high suspicion for *C. psittaci* infection. Most of the literature we reviewed were diagnosed by PCR or serological tests.

In recent years, NGS has shown some advantages in pathogen detection. NGS can directly obtain pathogen information from diseased tissues and body fluids [24,25], shorten the detection period significantly, and the high throughput sequencing technology can detect more gene sequences of pathogens simultaneously. NGS is theoretically based on specific nucleic acid sequences, and can realize the unique identification of almost all pathogens, which has obvious advantages for the detection of rare, new and complex pathogens. There are also some limitations of NGS, such as the lack of recognized interpretation standards, unclear relationship between sequencing results and treatment, possible contamination, and high costs, and the results need to be verified by combining with PCR or RT-PCR [26]; However, it plays a role in the diagnosis and treatment of patients with unknown pneumonia. The two cases in this paper were negative for the pathogen detection test which our hospital can perform; their final diagnosis was to detect *C. psittaci* in sputum, blood, and BALF by NGS.

Clinicians need to pay attention to the identification of other infections during treatment. Differential diagnosis is broad and includes infection with *Coxiella burnetii* (Q fever), *Legionella*, *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae*, and respiratory viruses such as influenza. In the context of the novel coronavirus disease 2019 (COVID-19) epidemic since 2020, more attention should be paid to the differential diagnosis between *C. psittaci* pneumonia and COVID-19.

Tetracycline is the first choice in the treatment of *C. psittaci* infection [20]. In Table 2, tetracycline was used on 23 patients and 21 cases were cured, indicating that the efficacy of tetracycline was positive. Macrolides and quinolones could also be considered. The treatment of *C. psittaci* infection must last at least 10-14 days. The two patients in this paper adjusted the antibiotics to tetracycline (minocycline) after identifying *C. psittaci* infection. Their condition improved and they eventually recovered after the adjustment of antibiotics, thus confirming the efficacy of tetracycline in treating *C. psittaci* infection, as reviewed in Table 2.

Table 2. Literature review of case reports on *Chlamydia psittaci* infection.

Reference	Age / Gender	Epidemiological history	Symptoms	Chest imaging	Pathogen detecting tools	Main treatment	Prognosis
Fruzsina Petrovay *et al.* 2008[3]	69/F	Poultry-processing-plant employee	Bad cough, difficulty breathing, general malaise, fever, diarrhoea	Extensive pleuropneumonia in the left lung and right lower lobe infiltrates	Lung tissue PCR (+), *C. psittaci* serology (+)	Mechanical ventilation, levofloxacin	Death
	48/F	Poultry-processing-plant employee	Fever, non-productive cough	A homogeneous left lower lobe infiltrate and an inhomogeneous infiltrate in the whole of the right lobe	Bronchial fluid and lung tissue PCR (+); *C. psittaci* serology (+)	Mechanical ventilation; Doxycycline and clarithromycin	Death
Cesar V. Reyes *et al*. 2010[4]	17/M	Having a parakeet	Mouth pain, fever, sore throat, nausea, vomiting, inability to drink, bilateral conjunctivitis and ulcerative/vesicular orolabial lesions	Normal	Diff-Quik cytologic recognition; *C. psittaci* serology (-)	Doxycycline	Recovery
A. Fraeyman *et al*. 2010[5]	49/F	Veterinary surgeon, and had a history of contact with doves.	General malaise, fever, chills, thoracic tightness, cough	An expansion of the infiltrate and bilateral pneumonia	BALF PCR (+), microbiological culture (-), serology (-)	Moxifloxacin, intravenous steroids	Recovery
	70/F	A history of contact with doves	Fever, non-productive cough, general malaise, weakness, night sweats, chills	An infiltrate compatible with infectious pneumonia	PCR (+), *C. psittaci* serology (-)	Moxifloxacin, mechanically ventilated	Recovery
	18/M	Breeding doves	Fever, night sweats, chills, non-productive cough, nausea, anorexia	Bilateral pneumonia	BALF PCR (+), but *C. psittaci* serology (-)	Moxifloxacin, oxygen therapy	Recovery

Table 2 (continued). Literature review of case reports on *Chlamydia psittaci* infection.

Reference	Age / Gender	Epidemiological history	Symptoms	Chest imaging	Pathogen detecting tools	Main treatment	Prognosis
Ta Thi Dieu Ngan *et al.* 2013[6]	69 (48-78)/2F and 3M		Fever	Right middle and lower lobe consolidation or infiltration (3/5); both middle and lower lobe consolidation (1/5)	PCR (+)	None were given a standard empiric antibiotic regime	One death, four recovery
Yujen Cheng *et al.* 2013[7]	44/M	Keeping two cockatiels at home	Intermittent fever, dyspnea, severe cough without sputum, headache, epigastric pain	Infiltration of the left upper lung with patchy reticular infiltrates radiating from the left hilum, and no pleural effusion	Blood and sputum culture (-); *C. psittaci* serology (+)	Minocycline and ceftriaxone	Recovery
Sandy Chau et al. 2015[8]	62/M	A history of close contact with parrot	Fever, headache, myalgia, cough, and yellowish sputum	Left lower zone consolidation	Sputum PCR (+); *C. psittaci* serology (+)	Ceftriaxone and doxycycline	Recovery
	55/M	Travel history and buying a live chicken	Fever, headache, generalised bone pain, cough	Right upper zone opacities	Sputum PCR (+), sputum culture (-), *C. psittaci* serology (+), nasopharyngeal aspirate PCR (-)	Amoxicillin-clavulanate, doxycycline, and oseltamivir	Recovery
	42/F	Travel history and buying live goose and chicken	Fever, cough, yellowish and blood-stained sputum, breathing difficulty	Right middle and lower zone consolidation, left patchy haziness	Stored sputum PCR (+), sputum culture (-), *C. psittaci* serology (+), nasopharyngeal aspirate PCR (-)	Mechanical ventilation, ECMO; Piperacillin-tazobactam, doxycycline, and oseltamivir	Recovery
Anne-Marie Ionescu et al. 2016[9]	61/M	A pet bird-keeper	Fever, productive cough, malaise, and breathlessness.	Right middle lobe and left lower lobe consolidation; a bilateral pneumonia with small pleural effusions	PCR (+) (sputum), and *C. psittaci* serology (+)	High flow oxygen and intermittent NIV; ceftriaxone, acyclovir and doxycycline	Recovery
Nuria Arenas-Valls *et al.* 2017[10]	47/M	The customer of a store selling birds	Dyspnea, fever, tachypnea	Infiltrate both lower lobes, then progress into ARDS	PCR (+), and *C. psittaci* serology (+)	ECMO, ceftriaxone, levofloxacin and doxycycline	Recovery
	22/M	The employee of a store selling birds	Fever, dry cough, general malaise	Alveolar infiltrate 3 right lobes	*C. psittaci* serology (+), but PCR (-)	High-flow oxygen therapy, ceftriaxone, levofloxacin and doxycycline	Recovery
	20/M	The employee of a store selling birds	Fever, cough with white sputum, general malaise	Alveolar infiltrate right lower lobe	*C. psittaci* serology (+), but PCR (-)	Azithromycin ceftriaxone, and doxycycline	Recovery
	52/F	The employee of a store selling birds	Fever, cough, mucous expectoration, with a tendency toward arterial hypertension	Alveolar infiltrate right upper and middle lobe	*C. psittaci* serology (+), but PCR (-)	Ceftriaxone and azithromycin	Recovery
Stien Vandendriessche *et al.* 2019[11]	57/M	Most probably linked to visit to a South African wildlife reserve	Unilateral swollen eyelid, red right eye, deteriorated vision, arthralgia and myalgia	Normal	PCR (+) (a sample from a crust on the eye), but a serological response couldn't be detected	Doxycycline	Recovery
Daisuke Katsura *et al.* 2020[12]	31/F	Contacting with a parrot at least a year ago.	Fever, headache, malasie and muscle pain	ARDS	PCR (+) (serum)	conventional mechanical ventilation, meropenem	Death, and intrauterine fetal death
Xiancheng Chen et al. 2020[13]	64 (44-83)/3F and 6M	7 (77.8%) patients had a history of exposure to, or close contact with birds or poultry.	Fever and chills (9/9), cough and hypodynamia (9/9), headache (7/9), myalgia (7/9)	Lesion began in superior lobe of lung (8/9), consolidation with air bronchograms (9/9), pleural effusions (4/9)	mNGS (+) (blood and alveolar lavage fluid samples)	Invasive ventilator support (6/9), minocycline; Some severe patients also treated with supplementary carbapenems, linezolid, or tigecycline.	Recovery (8/9); death (1/9)
Lei Gu *et al.* 2020[14]	81/F	Her pet dog had pneumonia	Fever, cough with white sticky sputum, generalized muscle ache and malaise	Alveolar consolidation in the left lower lobe	BALF mNGS (+)	Antibiotics: finally using doxycycline	Recovery
	45/M	A 20-year history of pigeon farming	Fever, productive cough, generalized muscle ache and malaise.	Bilateral diffuse infiltration	BALF mNGS (+)	Doxycycline plus moxifloxacin	Recovery
	85/F	A history of contact with birds	Fever, productive cough, headache, generalized muscle ache and emesis.	Consolidation in the right upper lobe	Lung tissue mNGS (+)	Doxycycline plus moxifloxacin	Recovery
	66/F	A history of close contact with a large poultry farm	Fever, rigor, dry cough, dizziness	Consolidation in the right upper lobe	Lung tissue mNGS (+)	Moxifloxacin	Recovery
	61/F	A history of close contact with a pet parrot	Fever, rigor, weakness, productive coughing, dizziness	Patchy infiltration and consolidation of both lungs	Lung tissue mNGS (+)	Moxifloxacin	Recovery

F: female; M: male; PCR: polymerase chain reaction; ECMO: extracorporeal membrane; BALF: bronchoalveolar lavage fluid; NIV:_ non-invasive ventilation; mNGS: metagenomic next-generation sequencing.

Moreover, both of the patients in this paper had severe pneumonia, respiratory failure, and ARDS, needed respiratory support in treatment to maintain oxygenation saturation and intensive care; and case 1 used ECMO. ECMO is a modified cardiopulmonary bypass circuit that serves as an artificial membrane lung and blood pump to provide gas exchange and systemic perfusion for patient, is a rapidly evolving alternative treatment modality for lung injury in severe acute respiratory distress syndrome and can improve the prognosis [27]. While using ECMO, ECMO operation, oxygenation saturation monitoring, anticoagulant management, pipeline safety, and complication prevention are also important.

Conclusions

Owing to the unspecific clinical features and imaging findings, the diagnosis of *C. psittaci* pneumonia is difficult and it can develop into severe pneumonia. This indicates that relevant epidemiological history and timely pathogen detection are important for the diagnosis. NGS can shorten the time needed for diagnosis and enable earlier initiation of targeted antibiotic therapy, it could be used in early diagnosis of *Chlamydia psittaci* infection. Furthermore, ECMO also showed efficacy in the treatment of severe pneumonia.

Acknowledgements

The authors thank all of the medical staff members involved in treating the patients. Our work is supported by National Natural Science Foundation of China No.81900641, Beijing Natural Science Foundation of China No.7212128, Cross seed funding, by Peking University No. BMU2022MX008 and BMU2021MX020.

Authors' Contributions

Nini Dai and Qiuyu Li contributed equally to this work.

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Conflict of interests: No conflict of interests is declared.