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Case Report

A case report of healthcare-associated psittacosis

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Abstract

Introduction: Psittacosis is a well-recognized zoonotic infectious disorder caused by *Chlamydia psittaci* (*C. psittaci*). Human-to-human transmission of *C. psittaci* has rarely been reported previously, especially in the case of healthcare-associated infections.

Case report: A 32-year-old man was admitted to the intensive care unit with severe pneumonia. An intensive care unit healthcare worker contracted pneumonia 7 days after performing endotracheal intubation on the patient. The first patient, a duck feeder, had been closely exposed to ducks, while the second patient had not been exposed to any birds, mammals or poultry. *C. psittaci* sequences were obtained by metagenomic next-generation sequencing analyses of bronchial alveolar lavage fluid of both the patients, and they were diagnosed with psittacosis. Therefore, healthcare-associated human-to-human transmission between both cases took place.

Conclusions: Our findings have implications for managing patients with suspected psittacosis. stringent protective measures are needed to prevent healthcare-associated human-to-human transmission of *C. psittaci*.

Key words: psittacosis; healthcare-associated psittacosis; human-to-human transmission; endotracheal intubation.

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Introduction

Infection with *Chlamydia psittaci* (*C. psittaci*) in humans mainly results from exposure to dried contaminated secretions, dried-out droppings or feather dust from infected birds, such as parrots and pigeons, as well as from mammals and poultry [1,2]. *C. psittaci* infection, called psittacosis, mainly results in respiratory tract infections and bacteremia in humans. Pneumonia caused by *C. psittaci* comprises approximately 1% of all community-acquired pneumonia cases [1]. The infection has an incubation period of five to fourteen days [3]. The common symptoms of psittacosis include fever, chills, myalgia, cough, headache, and dyspnea. *C. psittaci* can manifest as severe pneumonia, resulting in systemic multiple-organ dysfunction and even death [4-6]. Human-to-human transmission of *C. psittaci* infection, including healthcare-associated infections (HAIs), has been reported, but it is believed to be extremely rare [7-11]. Here, we report the cases of a duck feeder admitted to the intensive care unit (ICU) with severe pneumonia, and an ICU worker who had no exposure to any birds, mammals, and poultry, but also contracted pneumonia 7 days after performing endotracheal intubation on the first patient. Both the patients were diagnosed with psittacosis by metagenomic next-generation sequencing (mNGS) analyses of bronchial alveolar lavage fluid (BALF). It was concluded that healthcare-associated human-to-human transmission between the two patients had taken place.

Case report

Case 1

The first patient is a 32-year-old man who is a farmer and breeds ducks. He was admitted to the ICU in Hanchuan Hospital of Renmin Hospital of Wuhan University (Hanchuan, China) on December 18, 2021, because of recurrent cough, expectoration, fever for ten days, wheezing, chest tightness, and dyspnea for four days. The patient had no history of such symptoms. The fever spiked to over 40 °C four days before admission. The patient was tested for SARS-CoV-2 with a nucleic acid test, which was negative. The patient had a clear consciousness at admission. His blood pressure was

96/68 mmHg, body temperature 35 °C, heart rate 85 beats/min, respiratory rate 22 beats/min, and his oxygen (SpO_2) was 82% when the inhaled oxygen flow was 2 L/min (inhaled oxygen concentration 29%; normal level of inhaled oxygen concentration 21%). Auscultation revealed wet rales over both lungs. No other specific signs were detected during the physical examination.

Laboratory findings require special attention, and the results are presented in Table 1. Serological tests for *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, adenovirus, influenza virus, parainfluenza virus, and respiratory syncytial virus were negative. The hepatitis B surface antigen, syphilis antibody, human immunodeficiency virus (HIV) antibody, and hepatitis C antibody tests were also negative. Three blood and sputum cultures were sterile for pathogenic microorganisms, and the Xpert *Mycobacterium tuberculosis* and rifampicin resistance (Xpert MTB/RIF) test of the patient's sputum were negative. Rheumatoid factor (RF), antistreptolysin O (ASO), anti-neutrophil cytoplasmic antibody (ANCA), antinuclear antibody (ANA), and tumor markers were also negative. Ultrasound scans of the abdomen and lower extremity deep veins showed normal results. Echocardiography showed depressed left ventricular function (ejection fraction = 46%) and right ventricular dilatation (transverse diameter of right ventricle = 45 mm). His chest computed tomography (CT) imaging showed diffuse consolidation of both lungs with a bronchial inflation sign and pneumomediastinum (Figures 1A and B).

The patient was diagnosed with severe community-acquired pneumonia [12], severe acute respiratory distress syndrome [13], hypoxic respiratory failure [13], sepsis [14], and multiple-organ dysfunction [15,14,16-18]. Thus, the patient received empirical intravenous teicoplanin (800 mg/day) and imipenem/cilastatin (3 g/day) to treat severe community-acquired pneumonia and sepsis after admission. Due to severe acute respiratory distress syndrome and hypoxic respiratory failure, he received noninvasive mechanical ventilation treatment. Seven hours after admission, the patient's blood oxygen saturation was reduced to 60%, and he presented in a coma. He required endotracheal intubation and invasive mechanical ventilation. Two days later, the patient had no improvement in his symptoms and signs. Given the history of contact with ducks and the chest CT imaging characteristics, it was suspected that *C. psittaci* might be the pathogen. Therefore, we suspended teicoplanin and started intravenous moxifloxacin (0.4 g/day) and doxycycline via nasal feeding (0.2 g/day) [3,12].

Table 1. Routine laboratory findings for cases 1 and 2.

	Case 1		Case 2		Normal values
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	
Leukocytes ($\times10^9$/L)	2.41	5.49	10.24	4.92	3.97-9.15
Percentage of neutrophils (%)	74.6	58.7	80.9	52.4	50-70
Platelets ($\times10^9$/L)	45	321	158	119	85-303
Hemoglobin (g/L)	126	100	142	135	131-172
CRP (mg/L)	241.20	10.23	43.62	4.72	0-10
PCT (ng/mL)	16.80	0.15	0.14	-	0.00-0.50
Bilirubin (μmol/L)	30.9	6.8	11.3	-	2-20.4
ALT (U/L)	63	98	16	-	5-40
AST (U/L)	141	44	20	-	8-40
ESR (mm/h)	76	8	59.00	-	Male: 0-15 Female: 0-20
Serum amyloid A (mg/L)	-	-	473.51	-	0-10
Creatinine (μmol/L)	124	45	69	-	53-123
Urea nitrogen (mmol/L)	10.45	5.25	3.38	-	2.86-8.20
Prothrombin time (S)	16.40	12.50	13.10	-	10-14
Fibrinogen (g/L)	4.92	3.44	3.2	-	2-4
D-Dimer (ng/mL)	17220	2720	420	-	0-1000
NT-proBNP (pg/mL)	2146	1133	74.9	-	0-96.5
Arterial blood gas analysis					
pH	7.409	7.447	7.411	-	7.350-7.450
PaO_2 (mmHg)	51.2	96.7	92.7	-	83-108
$PaCO_2$ (mmHg)	36.5	42.8	39.9	-	35.0-45.0
Lactate (mmol/L)	1.5	1.3	1.1	-	0.5-1.6
SO_2 (%)	81.7	97.6	96.6	-	93.0-98.0

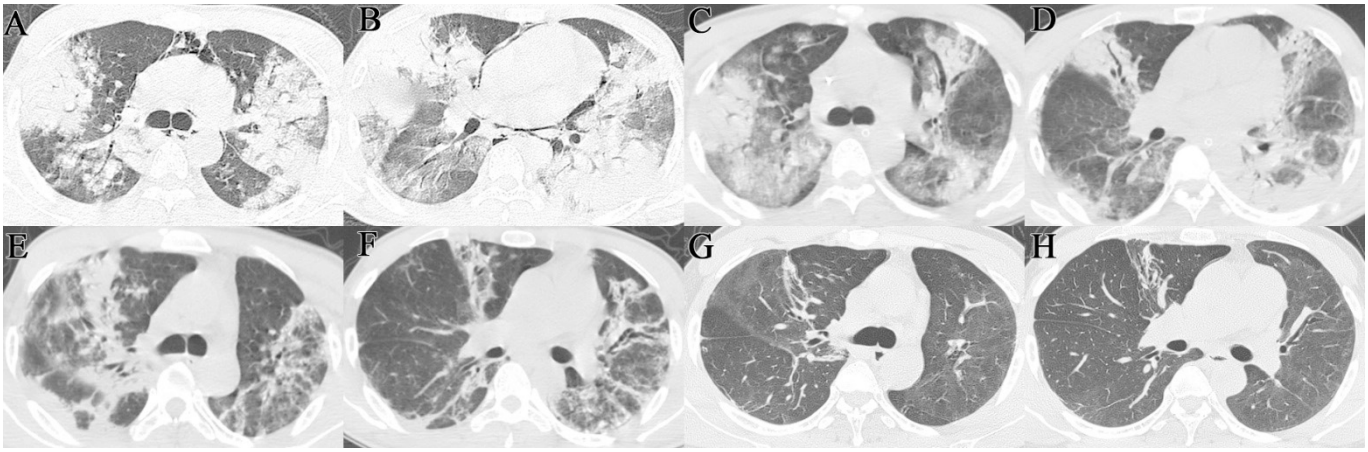
CRP: C-reactive protein; PCT: Procalcitonin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; NT-proBNP: N-terminal pro-brain natriuretic peptide; $PaCO_2$: partial pressure of arterial blood carbon dioxide; PaO_2: partial pressure of arterial blood oxygen; SO_2: oxygen saturation; FiO_2, fraction of inspiration oxygen; -: item was not tested.

Meanwhile, he was subjected to a bronchoscopy examination, and BALF was collected for mNGS analysis. After 48 hours, the mNGS analysis showed that 7299 sequences of *C. psittaci* were present in the BALF, confirming psittacosis. Meropenem was discontinued on the third day after admission because the antimicrobial spectrum did not cover *C. psittaci*. Thus, combination therapy of intravenous moxifloxacin (0.4 g/day) and doxycycline via nasal feeding (0.2 g/day) was chosen to treat severe community-acquired psittacosis pneumonia according to study recommendations [19-21]. On the fifth day after admission, his chest CT scans showed that the consolidations were smaller than before, and his pneumomediastinum had resolved following effective anti-infective therapy (Figure 1C and D). The reviewed echocardiogram showed normal results. On the eighth day after admission, his arterial blood gas analysis was significantly improved; thus, he was removed from tracheal intubation and weaned off mechanical ventilation. On the tenth day after admission, his body temperature changed from repeated fever to normal, and he was transferred to our hospital's Department of Respiratory and Critical Care Medicine for further therapy. On the seventeenth day after admission, his chest CT scans showed that the consolidations were significantly smaller than before (Figure 1E and F). The blood examinations were significantly improved (Table 1). The patient was discharged on the eighteenth day after admission and was prescribed oral doxycycline (0.2 g/day) for a week. A follow-up chest CT examination was performed within 40 days after discharge, and the chest CT scans showed that the consolidation was absorbed entirely (Figure 1G and H).

Case 2

This patient is a 32-year-old man. He was the ICU physician who performed the endotracheal intubation for the patient in case 1. The patient in case 2 had been in good health and had no recent close contact with any bird, animal, or domestic poultry. The patients in cases 1 and 2 lived in different communities and had no prior history of exposure to the same environment. In addition, the patient in case 2 had no contact history with the patient in case 1 other than at the time of the endotracheal intubation. During endotracheal intubation, patient 2 wore a general medical mask and gloves for protection. Seven days after the endotracheal intubation for the patient in case 1, the patient in case 2 presented with fever, chills without cough, apparent expectoration, myalgia, headache, and dyspnea. He was initially diagnosed with infectious fever, and empirical intravenous amoxicillin-clavulanate (1.3 g/8 hours) was administered. Six days later, there was no relief from his symptoms. So, he was admitted to the Department of Respiratory and Critical Care Medicine of Hanchuan Hospital of Renmin Hospital of Wuhan University (Hanchuan, China) for further treatment. On admission, his blood pressure was 120/84 mmHg, body temperature was 38.8 °C, heart rate was 124 beats/min, and respiratory rate was 21 beats/min. Auscultation revealed wet rales in the left lower lobe. No other specific signs were detected during the physical examination.

Figure 1. Chest computed tomography (CT) imaging of case 1.



A-B: Initial chest CT scan (2 days after admission) shows diffuse consolidation of both lungs with bronchial inflation sign and pneumomediastinum; **C-D**: Chest CT scan (5 days after admission) shows that the consolidation area gradually decreased following treatment; **E-F**: Chest CT scan (17 days after admission) shows that the consolidation area significantly decreased following targeted treatment; **G-H**: chest CT scan (40 days after discharge) shows that the consolidation was completely absorbed (G and H).

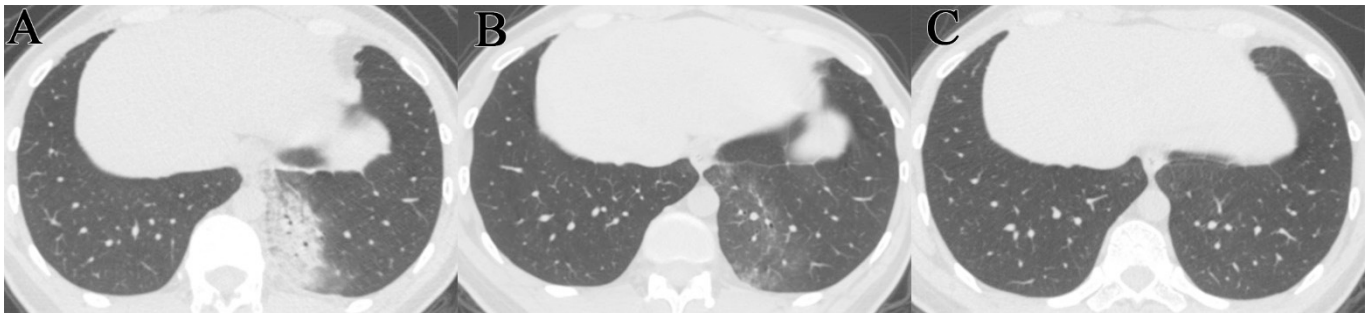
Laboratory study findings require special attention, and the results are presented in Table 1. Serological tests for *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, adenovirus, influenza virus, parainfluenza virus, and respiratory syncytial virus were all negative. The hepatitis B surface antigen, syphilis antibody, HIV antibody, and hepatitis C antibody were within normal limits. Two blood cultures were sterile, and sputum culture was not performed because he did not produce any sputum. Abdominal ultrasonography and echocardiography showed normal results. Chest CT imaging showed consolidations in the left lower lobe. (Figure 2A). Combined with the leukocyte counts, the erythrocyte sedimentation rate and serum amyloid A levels being significantly increased, he was diagnosed with non-severe pneumonia [12]. Considering the ineffectiveness of empirical amoxicillin-clavulanate treatment and since the patient had a history of close contact with the patient in case 1 during endotracheal intubation, he was suspected to have psittacosis. He received empirical oral doxycycline (0.2 g/day) and intravenous moxifloxacin (0.4 g/day) treatment [16,18]. Shortly after the first dose of doxycycline, the patient complained about nausea and stomach discomfort. Therefore, we did not use doxycycline in the subsequent treatments. At the same time, he underwent a bronchoscopic examination, and BALF was collected for mNGS analysis. On the second day after admission, his body temperature returned to normal. The results of the mNGS test indicated that 174 sequences of *C. psittaci* were present in the BALF after 48 hours; this confirmed the diagnosis of *C. psittaci* pneumonia. The patient was discharged on the third day after admission and was prescribed oral moxifloxacin (0.4 g/day) for a week. A follow-up chest CT was performed 6 days after discharge, which showed that the consolidations had gradually decreased (Figure 2B). Finally, his follow-up chest CT showed that his consolidations had wholly disappeared by 31 days after discharge (Figure 2C).

Discussion

Psittacosis is a well-recognized zoonotic infectious disorder caused by *C. psittaci*, a Gram-negative, strictly intracellular bacterial pathogen sporadically occurring worldwide. The primary hosts of *C. psittaci* are diverse birds, including parrots and pigeons. Additionally, mammals and domestic poultry have been reported to be potential hosts of *C. psittaci* [2,22]. It has been reported that *C. psittaci* infections in ducks existed previously in Europe, Australia, and the USA [23-25]. A previous study also showed that *C. psittaci* infections are present in market-sold ducks in northwestern China [26]. These data have indicated that ducks are essential hosts of *C. psittaci*. Laroucau *et al*. reported five severe cases of psittacosis in individuals in France who were associated with duck farms and who were diagnosed by serology and/or molecular detection by polymerase chain reaction (PCR) from respiratory samples [25]. Another study found that 38.9% of the ducks slaughtered in the surrounding slaughterhouses possessed anti-*C. psittaci* antibodies in their serum [27]. These findings suggested that *C. psittaci* infection can be transmitted to human beings through exposure to ducks.

In our case, the primary patient had been involved in duck breeding activities at his farm for many years. Therefore, it was probable that the primary patient in this study had contracted psittacosis from direct contact with ducks. The patient in case 2 suffered from psittacosis within the incubation period after having been closely exposed to the primary patient while he was performing endotracheal intubation, and no other likely transmission pathways were determined. Therefore, it was probable that the patient in case 2 had contracted psittacosis from direct contact with the

Figure 2. Chest computed tomography (CT) imaging of case 2.



A: Initial chest CT scan (on the day of admission) shows consolidations in the left lower lobe; **B**: Chest CT scan (9 days after admission) shows that the consolidation area significantly decreased following treatment; **C**: Chest CT scan (31 days after discharge) shows that the consolidation had completely disappeared.

patient in case 1. Surprisingly, the other healthcare workers in the same intensive care unit did not fall ill.

Hogerwerf *et al*. evaluated inhalation of contaminated aerosols as an important cause of human psittacosis in their systematic review [1]. Dhillon *et al.* revealed that tracheal intubation can produce massive aerosols and droplets, which contain a large number of pathogens [28,29]. Healthcare workers are in close contact with the patient's respiratory tract during tracheal intubation procedures and are exposed to large amounts of infectious aerosols [30]. As such, the patient in case 2 developed *C. psittaci* pneumonia after performing endotracheal intubation in the primary patient. This study supported that healthcare-associated human-to-human transmission of *C. psittaci* infection had occurred, while human-to-human transmission had not previously been considered an important transmission route.

A meta-analysis published in 2017 indicated that pneumonia caused by *C. psittaci* accounts for approximately 1% of all community-acquired pneumonia cases worldwide [1]. The main clinical manifestations of psittacosis include fever, chills, myalgia, cough, headache, and dyspnea. Upon transmission to human beings, *C. psittaci* infection mainly manifests as a nonspecific flu-like illness or community-acquired pneumonia [31]. In this study, our data showed that the primary patient presented severely ill and with pneumonia, whereas the second presented with non-severe pneumonia.

Therefore, diagnosing psittacosis is challenging owing to its atypical clinical features. Diagnostic procedures that are presently used for *C. psittaci* infection include microbiological culture, serological examination, and molecular biology techniques such as PCR. Notably, the low sensitivity and complex, time-consuming method of *C. psittaci* culture makes it difficult to routinely perform in most diagnostic laboratories [3]. Furthermore, the serological examination method is hampered by cross-reactivity with other *Chlamydia* strains and is usually used for retrospective diagnosis and epidemiological investigation of *C. psittaci* infections [32]. In addition, in the early stage of disease, the serological tests could be negative [32,33]. While PCR is applied to diagnose early and asymptomatic patients and helps determine the source of *C. psittaci* infection through genotyping, this method has questionable sensitivity and specificity [33,34]. The mNGS method can examine diverse pathogenic microorganisms with no bias by sequencing and analyzing the pathogens in clinical specimens. Notably, quick screening of pathogenic microorganisms promotes the timely and accurate identification of pathogens so that targeted antibiotic treatment can be started in clinical practice. Therefore, the mNGS method has been gradually incorporated in clinical settings [3,35,36]. In our present cases, two patients were diagnosed with pneumonia caused by *C. psittaci* through the mNGS method within 48 h of displaying no improvement after starting empirical antibiotic therapeutic approach. Thus, the mNGS method effectively and accurately facilitates the diagnosis of pneumonia caused by *C. psittaci* and has obvious diagnostic value.

Several limitations were present in this study. First, the existence of *C. psittaci* in the ducks could not be investigated, although this was supposed to be the probable source of the suspected *C. psittaci* infections. The primary patient did not consent to having samples collected from the ducks and the surroundings of the duck sheds to determine whether *C. psittaci* was present. Second, as we did not isolate *C. psittaci* and because the main purpose of mNGS in our cases did not include the detection of drug resistance genes, we did not perform antibiotic sensitivity tests and resistance gene detection. Finally, avian strains of *C. psittaci* include at least six serotypes from A to F, as determined by serovar-specific monoclonal antibodies [10]. It has been assumed that different serotypes are linked with particular categories of host species of *C. psittaci*. In this study, genotyping of *C. psittaci* from human samples and duck isolates was not measured to assess the epidemiological link between our patients with *C. psittaci* pneumonia and ducks more accurately.

Conclusions

In conclusion, the findings of this observation suggest that *C. psittaci* has been transmitted from human to human during endotracheal intubation in hospital surroundings and caused pneumonia. Thus, when health care workers need to perform high-risk aerosol generation procedures (such as endotracheal intubation) to care for severely ill patients with atypical pneumonia, personal protection may be required to prevent healthcare-associated transmission from patients with psittacosis. These protection strategies include the use of filtering facepiece masks and the treatment of patients in an isolation ward. Meanwhile, the mNGS method allows timely and accurate detection of unknown pathogenic microorganisms related to patients with severe pneumonia; thus, it is recommended to determine the presence of *C. psittaci.*

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