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Clinical characteristics of *Chlamydia psittaci* pneumonia

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Psittacosis is a zoonosis caused by *Chlamydia psittaci*, a Gram-negative intracellular bacterium. This condition is caused by the ingestion of contaminated fecal matter and nasal secretions from infected birds. The severity of human psittacosis varies from mild flu-like symptoms to life-threatening severe pneumonia.[1] Given that *C. psittaci* is not a part of the traditional microbiological diagnosis' human psittacosis is often underreported, misdiagnosed, and inadequately diagnosed. In this study, the clinical data of *C. psittaci* pneumonia patients were retrospectively analyzed.

Specifically, we analyzed five consecutive cases of *C. psittaci* pneumonia, who were admitted to The Fourth Affiliated Hospital of Zhejiang University School of Medicine, between December 2019 and May 2020. We screened the hospital's electronic case system and extracted data on demographics, symptoms, signs, laboratory tests, disease severity, dynamic computed tomography, tracheoscopy, and clinical course of each case. We also collected data on treatment prescription, treatment response, and prognosis.

The study was approved by the Ethics Committee of the Fourth Affiliated Hospital of Zhejiang University School of Medicine (Approval No. K2020079). We had obtained written informed consent from all enrolled patients, and concealed their identifiable information as well as relevant images.

Before enrolment, patients diagnosed with *C. psittaci* pneumonia had to meet the following three inclusion criteria: first, they complied with criteria for community-acquired pneumonia[2]; second, metagenomic next-generation sequencing (mNGS) from bronchoalveolar lavage fluid (BALF) revealed a specific deoxyribonucleic acid (DNA) fragment in *C. psittaci*; and third, all routine etiological tests, including blood, sputum, BALF smear, and cultures, were negative, with no other causative organisms present.

We detected *C. psittaci* DNA fragments in all cases. A summary of copy numbers for *C. psittaci* nucleic acid in BALF detected by mNGS is shown in Table 1. *C. psittaci* was the dominant infection across all five cases. However, we simultaneously detected herpes simplex virus type 1 in one severe case, although its immunoglobulin M was negative, suggesting possible colonization or pollution. Two patients (40%) were positive for *Chlamydia abortus*, albeit with low copy numbers, whereas other patients exhibited low copies of *Candida parapsilosis* complex, *Candida albicans*, *Staphylococcus epidermidis*, *Haemophilus influenzae*, *Burkholderia cepacia*, or *Acinetobacter baumannii*, indicating colonization or pollution.

The study group comprised of two (40%) females and three (60%) males, with a median age of 65 (57–71) years. Among the enrolled patients, two (40%) had hypertension, one presented multiple disease states, including hyperlipidemia, hypertension, and pacemaker implantation status, whereas the other three (60%) were healthy. Medical records showed that three (60%) patients had a history of direct contact with domestic poultry before the onset of the disease. Here, one case had been fertilized with pigeon manure, one had newly reared chickens at home, one had reared pigeons, and one had a possible indirect environmental contact because her workplace was located upstairs of a farmers' market (including poultry market areas), consistent with poultry transmissible zoonoses.[3]

The median time from the onset of the first symptoms to admission was 5 (3–7) days. High fever was recorded in five patients. Cough and dyspnea were recorded in three patients, respectively. Fatigue was recorded in two (40%) patients. One patient manifested nausea and vomiting. Relatively slow pulse was recorded in two patients. Mental changes, presented as apathy was recorded in two severe patients. A few moist rales could be heard in three patients (60%). In this group, patients complained of neither headache nor muscle soreness, which was inconsistent with results from the previous reports.[4,5]

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Table 1: Demographical and basic clinical features of the five patients.

Case#	Severity	Age (years)/Sex	Underlying diseases	Poultry exposure	Onset time (days)	mNGS results and specific reads (*n*)	Symptoms	Signs
1	Severe	57/ Female	None	Indirect*	7	*Chlamydia psittaci* (55307); *herpes simplex virus type 1* (17392); *Staphylococcus epidermidis* (126); *Haemophilus influenzae* (9); *Candida parapsilosis* complex (9)	High-fever Cough Dyspnea	40.0°C Apathy Moist rales Relatively slow pulse
2	Severe	69/ Male	None	Pigeon feces	7	*Chlamydia psittaci* (1233); *Chlamydia abortus* (61); *Candida albicans* (12)	High-fever Chills Cough Dyspnea	39.7°C Apathy Moist rales
3	Non-severe	71/ Male	None	None	3	*Chlamydia psittaci* (21); *Haemophilus parainfluenzae* (17)	High-fever chills	40.5°C Moist rales Relatively slow pulse
4	Non-severe	64/ Male	Hypertension	Chicken	3	*Chlamydia psittaci* (362); *Chlamydia abortus* (18)	High-fever Cough Dyspnea	41.5°C
5	Non-severe	65/ Female	Hypertension, hyperlipidemia	Pigeon	5	*Chlamydia psittaci* (73435); *Burkholderia cepacia* (99); *Acinetobacter baumannii* (85)	High-fever Nausea Vomiting Weak	40.0°C

Case#	Arterial blood gas analysis (mmHg)	Inflammatory biomarkers	Biochemistry	Imaging	Antibiotics	Respiratory support	Fever time (d)†	Hospital stays (d)	Outcome
1	FiO_2:221 PCO_2:23.8	WBC:5500/μL NE:91.3% CRP:316.5 mg/L PCT:3.47 ng/L	Lac:1.8 mmol/L LDH:679 U/L CK-MB:18.4 U/L CK:705 U/L	Consolidation air bronchogram	Moxifloxacin tigecycline	Intubation ventilator	10	23	Cured
2	FiO_2: 250 PCO_2:30.6	WBC:11500/μL NE:96.9% CRP:303 mg/L PCT:5.24 ng/L	Lac:1.4 mmol/L LDH:1039 U/L CK-MB:57 U/L CK:1919 U/L	Consolidation air bronchogram	Moxifloxacin tigecycline	Intubation ventilator	5	20	Cured
3	FiO_2: 361 PCO_2:30.2	WBC:5200/μL NE:88.3% CRP:176.7 mg/L PCT:1.58 ng/L	Lac:1.2 mmol/L LDH:265 U/L CK-MB:17.4 U/L CK:472 U/L	Consolidation air bronchogram	Moxifloxacin	Oxygen	1.25	11	Cured
4	FiO_2: 384 PCO_2:30.1	WBC:8700/μL NE:87.7% CRP:191.5 mg/L PCT:0.474 ng/L	Lac:1.5 mmol/L LDH:216 U/L CK-MB:8.2 U/L CK:147 U/L	Consolidation air bronchogram	Moxifloxacin	Oxygen	3	8	Cured
5	FiO_2: 275 PCO_2:29.9	WBC:13200/μL NE:92.7% CRP:278.9 mg/L PCT:1.54 ng/L	Lac:1.2 mmol/L LDH:265 U/L CK-MB:17.4 U/L CK:57 U/L	Consolidation air bronchogram	Moxifloxacin	Oxygen	2	9	Cured

*Workplace of case 1 was located upstairs of a farmers' market (including poultry market areas). †Days from initiation of moxifloxacin therapy until patients' body temperature returns to normal. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CK: Creatine kinase; CK-MB: Creatine kinase isoenzyme; CRP: C-reactive protein; FiO_2: Oxygenation index; Lac: Lactic acid; LDH: Lactate dehydrogenase; mNGS: Metagenomic next-generation sequencing; NE%: Proportion of neutrophils; PCO_2: Partial pressure of carbon dioxide; PCT: Procalcitonin; WBC: White blood cell.

Arterial blood gas analysis revealed type I respiratory failure in three patients (60%). The proportion of neutrophils was increased in five patients, while white blood cell count was increased in two patients. C-reactive protein (CRP) was high in five patients, whereas elevated levels of procalcitonin (PCT) were recorded in four cases. CRP and PCT were significantly higher in severe cases. Lactate dehydrogenase (LDH) and creatine kinase isoenzyme elevated in all five patients. Hyponatremia was recorded in five patients, and hypokalemia and hypocalcemia were recorded in four patients.

Chest CT showed air-containing bronchial shadow consolidation in all five (100%) patients. Specifically, scalloped or oval lesions originated from their pleura or interlobar fissures. As the disease progressed, these lesions incorporated the hilum and other lobes, including the contralateral lung lobe. In addition, the lesions originated from the left lower lung in four patients. Multi-lobe lesions recorded in two severe cases, whereas these lesions were confined to one lobe in three non-severe cases. Two patients had a little pleural effusion. Tracheoscopy revealed that all five patients were clean, with no additional secretions.

All five patients were intravenously injected with 0.4 g moxifloxacin, once a day within 24 h of admission, in combination with β-lactam antibiotics. The three non-severe cases got better within 72 h. Two severe cases had aggravated respiratory failure, at 76 and 88 h after admission. They were intubated for ventilator-assisted breathing and admitted to intensive care unit (ICU). The two severe cases were intravenously injected with tigecycline 50 mg (first dose 100 mg) every 12 h in ICU,

and they were cured at last. This indicated that non-severe cases respond better to moxifloxacin compared with severe ones.

Our study has some limitations. First, we analyzed a small sample size that may not fully represent the clinical features of *C. psittaci* pneumonia. Second, this was a retrospective study. Future studies should analyze prospective clinical cases with larger samples.

We conclude that *C. psittaci* pneumonia is common. History of poultry exposure, high fever, elevated inflammatory biomarkers, elevated LDH, coupled with air-containing bronchial shadow consolidation with little or no secretions may guide early clinical diagnosis of *C. psittaci* pneumonia. Metagenomic sequencing of BALF is an important method for diagnosing this condition.

Conflicts of interest

None.

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