Clustering cases of Chlamydia psittaci pneumonia in COVID-19 screening ward staff

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ABSTRACT

Four medical staff cases of Chlamydia psittaci pneumonia in a COVID-19 screening ward, as well as the experience in dealing with such a nosocomial infection event, were described. It reminds that atypical pneumonia except for COVID-19 should also be considered when clustering cases occurred even during a COVID-19 pneumonia pandemic.

Keywords: Chlamydia psittaci; COVID-19; Nosocomial infection; Differential diagnosis; Epidemic prevention and control

The coronavirus disease 2019 (COVID-19) pandemic is spreading globally [1]. When clustering pneumonia occurred in the medical staff, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection should be excluded. Meanwhile, other atypical pneumonia should also be considered [2-3]. Although most of the common or atypical pathogens related to respiratory infection can be confirmed by popular etiological detection methods, etiological detection of Chlamydia psittaci can't be carried out in most hospitals and physicians are not vigilant enough about its infection [2, 4-5]. Facing worldwide pandemic of COVID-19, misdiagnosis of Chlamydia psittaci pneumonia for COVID-19 is possible.

In May 2020, clustering Chlamydia psittaci pneumonia occurred in 4 medical staff in the COVID-19 screening ward of the 2nd Xiangya Hospital. Two doctors and two nurses were attacked almost simultaneously. Their symptoms and lung computed tomography (CT) changes were very similar to those of COVID-19 cases. Metagenomic next-generation sequencing (mNGS) revealed presence of Chlamydia psittacis in their bronchoalveolar lavage fluids (BALF).

METHODS

The clinical courses, diagnosis and treatment of the four cases, as well as the experience in dealing with such a nosocomial infection event, were reported. The study was approved by the Ethics Committee of the hospital.

RESULTS

1. Clinical features of the cases

The first case was a 29-year-old female doctor. She had continuous fever and mild cough with a little white phlegm since May 24, 2020, accompanied with headache, fatigue, myalgia, and loss of appetite. Thereafter, a 36-year-old male doctor, a 26-year-old male nurse and a

32-year-old female nurse developed similar symptoms on May 27, May 28 and May 29, respectively. Lung CT scan examinations revealed similar inflammatory infiltration and consolidation in their lower lung lobes.

They were quarantined and were started on empirical antibiotic therapy with ceftriaxone, piperacillin, amoxicillin or cefoperazone, respectively. However, their symptoms were not alleviated, then moxifloxacin therapy was combined, and their fever subsided within 2-4 days, with the other symptoms disappearing gradually. On June 3, Chlamydia psittaci pneumonia was confirmed by presence of sequence reads of Chlamydia psittaci in all of their BALF specimens by mNGS. Their antibiotic therapeutic regimes were adjusted to combination therapy by doxycycline and moxifloxacin.

By June 4, all patients had maintained normal body temperature for more than 3 days, and the lung CT examinations showed markable infiltrate absorption and consolidation remission. Then they were allowed to be back home with continuous oral moxifloxacin and doxycycline treatments, strict quarantine in single rooms and wearing masks to keep respiratory tract isolation from their families. The follow-up lung CT scans on June 18 showed disappearance of pulmonary consolidation and almost thorough absorption of inflammation. Then moxifloxacin treatment was discontinued while doxycycline was kept till the fourth week to prevent recurrence. Till July 31, no similar cases had been found in their family members, in their hospital colleagues and other close contacts.

Their routine laboratory test results were shown in Table 1. It could be found that many examination results were similar to those of COVID-19 patients, except that their peripheral blood lymphocyte counts were within the reference ranges throughout, without hypolymphocytemia.

2. Etiological examinations

Nucleic acid of SARS-CoV-2 in throat swab and BALF specimens were repeatedly detected by real time RT-PCR assay in each patient. Plasma IgM or IgG antibodies against SARS-CoV-2 were repeatedly tested by ELISA at admission and two weeks later. Besides, routine cultures of BALF, blood and sputum samples, indirect immunofluorescence tests of serum specific IgM antibodies against common respiratory pathogens (Table 1), isothermal amplifying tests on gene chips of nucleic acids of common pathogens in BALF (Table 1), galactomannan tests and 1-3-β-D Glucosamine tests in blood were carried out. None of the above tests reported positive results.

On June 3, BALF mNGS etiologic analysis in Shenzhen Huada Gene Research Institute reported that considerable number of sequence reads of Chlamydia psittaci were found in all of their BALF specimens (Table 1).

3. Epidemiological investigation

Although the four staff had been working in the emergency COVID-19 screening ward for several months, all of them and their family members definitely had not contacted with confirmed cases of COVID-19 within half a month before the onset of the disease， nor had they closely contacted with symptomatic patients coming from the COVID-19 epidemic areas since April 15.

None of them and their family members admitted any recent close contact with birds and live poultry within one month before the onset of the disease. However, the male doctor told that there were several pet parrots in his neighbor's house, and he couldn't rule out the possibility that the droppings and feathers of the parrots might fall into his house unawares.

The CDC (Center for Disease Control and Prevention) staff investigated the pet parrots' owner and his family members and other neighbors, as well as the family members of the male doctor. None of them had symptoms similar to the four Chlamydia psittaci infected cases. Although the parrots looked healthy, the owner isolated the parrots to an independent space according to the CDC staff's guidance.

4. Contingency plans in dealing with the suspected nosocomial infection event

Although the patient's access to the COVID-19 screening ward was independently set on the other side of the medical building away from the staff's access, and the fresh-air air conditioning system in the isolation area had been closed since January 18, 2020, and all the medical staff working in the building were requested to wear masks and other protective tools in strict accordance with the requirements, the possibility of clustering cases of nosocomial infection in the medical staff still could not be entirely excluded.

Therefore, the following measures were promptly taken. 1. To shut down the whole fresh-air air conditioning system of the building. 2. To collect air and environmental specimens for SARS-CoV-2 and other pathogens testing around the working rooms of the staff, especially around the fresh-air outlets, and then to clean and disinfect the air and suspected contaminated facilities. 3. To isolate each of the four cases in a single room for treatments. 4. To make a plan to manage the close contacts, especially the colleagues in the same ward and their family members. People with similar symptoms were isolated immediately, screened for SARS-CoV-2 infection and CT features of pulmonary infection. Those without symptoms were examined voluntarily, and were required to reduce or avoid outdoor activities as much as possible until being informed that the isolation measures were removed. 5. To make more detailed epidemiological investigations on the four cases. 6. To implement more strict

disinfection and isolation measures in the medical building, especially to emphasize the measures and necessary screening examinations to protect the medical staff from nosocomial infections.

Until July 31, no similar cases were found in all the staff in the screening ward and their family members, nor did nosocomial infection related to the four cases occur in the patients and their accompanies who had been to the medical building.

DISCUSSION

It is a noticeable nosocomial infection event which reminds that atypical pneumonia besides COVID-19 should be considered when clustering cases occur in the medical staff even during a COVID-19 pneumonia pandemic despite that many clinical features of the four patients were similar to those of COVID-19 patients.

Etiological test is essential for differential diagnosis. Due to false positive and false negative in detecting nucleic acid of and serum antibodies against SARS-CoV-2 virus in COVID-19 cases [6-7] and difficulty in identifying psittacosis by routine culture and serological methods [2, 4-5], mNGS for detecting unknown pathogen in pneumonia patients is recommended [8-10]. It discovered sequence reads of Chlamydia psittaci present in all their BALF specimens. Although Chlamydia psittaci infection was not confirmed by a second test, 4 identical cases all positive for Chlamydia psittaci was hard to discount. Their peripheral blood lymphocyte count and percentage kept normal throughout, consistent with the results reported previously [5, 8-9] and different from common decrease in COVID-19[11-12], which can be of great value in clinical differential diagnosis.

Human got infected with Chlamydia psittaci mainly by inhaling ornithic secretions or contaminated aerosols when being in close contact with infected birds or poultry [4-5]. Person-to-person transmission of psittacosis is possible but rare [5]. The four medical staff working in the same ward got infected almost simultaneously. In view of no similar infection in their family closest contacts and no accompanying activities outside hospital for them, there was little possibility that they were individually infected at home or outside the hospital. It was more likely that the Chlamydia psittaci infection source existed in the environment where they worked together.

The various pipelines of the medical building, especially the fresh-air air conditioning system, might be the possible routes from which the Chlamydia psittaci contaminated pollutants came. In fact, when the conditioning system had been closed, cleaned and disinfected, no more similar cases appeared. No evidence of contact with birds or poultry was found in a large proportion of the reported Chlamydia psittaci pneumonia patients [5].

Notes:

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Potential conflicts of interest. The authors declare no conflict of interest.

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Figure 1 The dynamic changes of lung CT images of the 4 cases.

Note: The initial CT scans on the day of admission showed peripheral focal lesions in the lower lung of inflammatory infiltration, ground-glass opacities, lobular air-space consolidation, traction bronchiectasis and vascular enlargement in the lesion (a). Gradual infiltrate absorptions and disappearances of the pulmonary consolidations were found after the treatments of moxifloxacin and doxycycline were initiated (b and c).

Table 1 The results of laboratory tests of the 4 Chlamydia psittaci pneumonia cases

Detection index	Unit	Reference range	CASE 1. female, 29y.		CASE 2. male, 36y.		CASE 3. male, 26y.		CASE 4. female, 32y.	
			Date	Result	Date	Result	Date	Result	Date	Result
CRP	mg/L	<10.00	5-26	31.87	5-31	12.17	5-30	58.01	5-30	50.55
			5-28	89.50			6-1	52.27	6-1	40.03
			6-22	1.81	6-22	<0.5	6-18	<0.5	6-18	<0.5
PCT	ng/ml	0-0.050			6-1	0.087	5-30	0.136	5-31	0.127
BR.WBC	10^9/L	3.50-9.50	5-26	10.07	6-1	10.43	5-29	10.53	5-30	11.70
			5-28	7.55	6-18	6.70	6-1	6.22	5-31	10.69
			6-1	5.58			6-18	6.36	6-1	13.11
			6-22	7.84					6-18	8.47
BR.NEUT	10^9/L	1.80-6.30	5-26	6.61	6-1	7.57	5-29	8.41	5-30	8.66
			5-28	5.02	6-18	2.95	6-1	4.37	5-31	8.37
			6-1	2.82			6-18	3.96	6-1	11.00
			6-22	4.29					6-18	4.45

BR.NEUT%	%	40.00-75.00	5-26	65.70	6-1	72.50	5-29	79.90	5-30	74.00
			5-28	66.50	6-18	44.00	6-1	70.20	5-31	78.30
			6-1	50.60			6-18	62.20	6-1	83.80
			6-22	54.60					6-18	52.60
BR.LYMPH	10^9/L	1.10-3.20	5-26	2.33	6-1	2.04	5-29	1.11	5-30	2.21
			5-28	1.73	6-18	3.14	6-1	1.21	5-31	1.50
			6-1	2.35			6-18	1.94	6-1	1.57
			6-22	2.93					6-18	3.51
BR.LYMPH%	%	20.00-50.00	5-26	23.10	6-1	19.60	5-29	10.50	5-30	18.90
			5-28	22.9	6-18	46.90	6-1	19.50	5-31	14.00
			6-1	42.10			6-18	30.50	6-1	12.00
			6-22	37.40					6-18	41.40
BR.PLT	10^9/L	125-350	5-26	249	6-1	369	5-29	193	5-30	241
			5-28	213	6-18	255	6-1	141	5-31	242
			6-1	287			6-18	232	6-1	231
			6-22	236					6-18	353
ALT	U/L	7.0-40.0	5-29	14.8	6-1	30.1	5-30	8.3		

			6-22	16.6	6-22	54.8	6-22	22.6	6-22	24.3
AST	U/L	13.0-35.0	5-29	25.6	6-1	23.0	5-30	19.7		
			6-22	19.7	6-22	30.7	6-22	21.6	6-22	24.3
ALB	g/L	40.0-55.0	5-29	35.7	6-1	38.1	5-30	38.0		
			6-22	45.2	6-22	44.4	6-22	45.2	6-22	42.6
GLO	g/l	20.0-40.0	5-29	30.0	6-1	34.4	5-30	28.3		
			6-22	32.4	6-22	33.1	6-22	30.0	6-22	34.9
TBIL	μmol/L	3.4-17.1	5-29	6.8	6-1	13.0	5-30	11.1		
			6-22	10.4	6-22	13.6	6-22	18.9	6-22	5.3
DBIL	μmol/L	0-6.0	5-29	2.9	6-1	5.1	5-30	4.6		
			6-22	3.8	6-22	5.3	6-22	7.2	6-22	2.1
TBA	μmol/L	0-10.0	5-29	5.0	6-1	2.7	5-30	4.0		
			6-22	3.8	6-22	7.1	6-22	1.0	6-22	7.7
CK	U/L	40.0-200.0	5-29	179.9	6-1	57.0	5-30	231.9		
CK-MB	U/L	0-24.0	5-29	9.7	6-1	8.0	5-30	15.4		
UREA	mmol/L	2.90-7.14	5-29	1.47	6-1	4.68	5-30	3.16		
			6-22	3.29	6-22	3.93	6-22	3.62	6-22	2.90

CREA	μmol/L	44.0-133.0	5-29	55.2	6-1	89.7	5-30	91.4		
			6-22	56.1	6-22	83.5	6-22	75.2	6-22	51.1
UA	μmol/L	155.0-357.0	5-29	274.4	6-1	262.1	5-30	224.0		
			6-22	262.6	6-22	335.3	6-22	360.5	6-22	183.7
Serum IgM antibodies against nine common respiratory pathogens [1]			6-1	Neg	6-1	Neg	6-1	Neg	5-31	Neg
Isothermal amplifying tests on gene chips of nucleic acids of 13 respiratory pathogens in BALF [2]			5-31	Neg	5-31	Neg	5-31	Neg	5-31	Neg
Chlamydia psittaci sequence reads reported by BALF mNGS [3]		DNA reads	5-31	2 [4]	5-31	274	5-31	254	5-31	82
		RNA reads	5-31	3 [4]	5-31	249	5-31	99	5-31	80

Note:

1. Indirect immunofluorescence tests of serum specific IgM antibodies against nine common respiratory pathogens (*Adenovirus, Parainfluenza virus, Respiratory syncytial virus, Influenza A virus, Influenza B virus, Legionella pneumophila, Mycoplasma pneumoniae, Chlamydophila pneumoniae, Rickettsia of Q fever*) (Autobio Diagnostics Co. Ltd, China).

2. Isothermal amplifying tests on gene chips of nucleic acids of pathogens (*Streptococcus pneumoniae, Staphylococcus aureus, methicillin-resistant Staphylococcus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas*

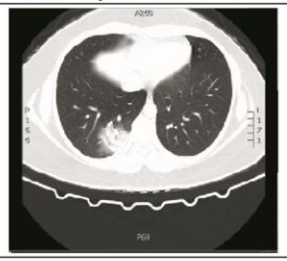
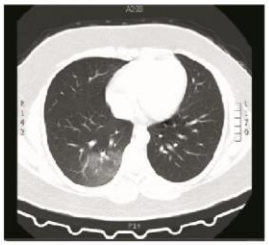
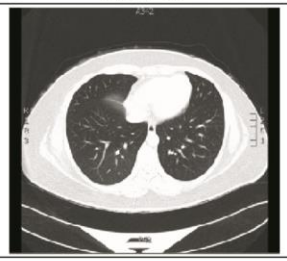
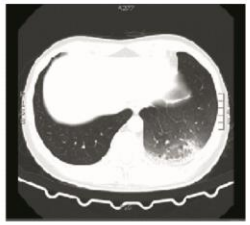
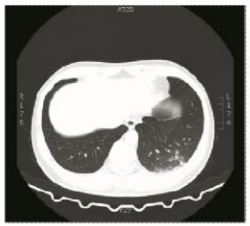
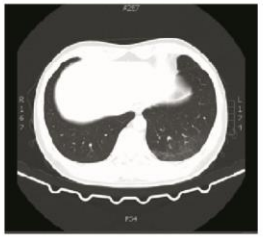
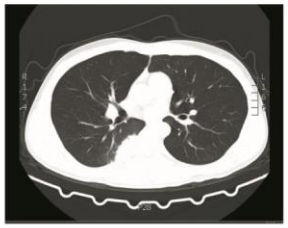
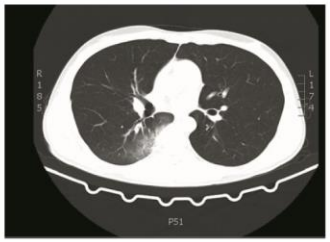
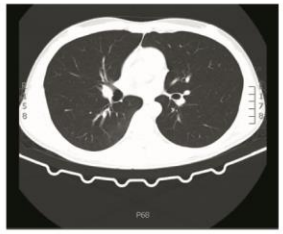
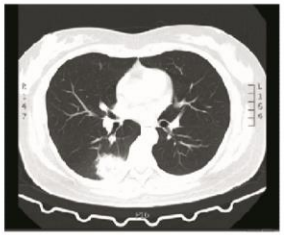
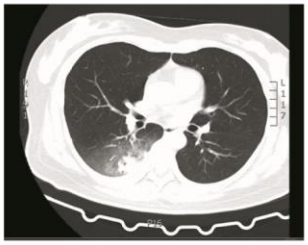
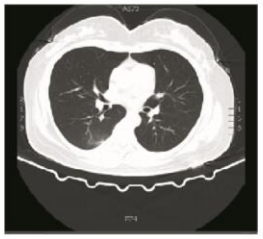
maltophilia, Haemophilus influenzae, Legionella pneumophila, Mycobacterium tuberculosis, Mycoplasma pneumoniae and Chlamydia pneumoniae) in BALF (Boao Crystal Core Biological Technology Co., Ltd, China).

3. BALF specimen was collected on May 31 in the separate quarantine room of each patient. A separate aseptic bronchoscope was used for each patient in order to avoid cross contamination.

4. By the time BALF was collected on the night of May 31, case 1 had been treated with moxifloxacin for three days and her body temperature had been normal for one and a half days.

5. Abbreviations：ALB, serum albumin; ALT, serum alanine aminotransferase; AST, serum aspartate aminotransferase; BALF, bronchoalveolar lavage fluids; BR, routine blood test; CK, serum creatine kinase; CK-MB, serum creatine kinase isoenzyme MB; CREA, serum creatinine; CRP, C-reactive protein; DBIL, serum direct bilirubin; DNA, deoxyribonucleic acid; GLO, serum globulin; LYMPH, lymphocyte; mNGS, metagenomic next-generation sequencing; Negative, Neg; NEUT, neutrophils; %, percent; PLT, platelet; PCT, procalcitonin; RNA, ribonucleic acid; TBA, serum total bile acids; TBIL, serum total bilirubin; UA, serum uric acid; UREA, serum urea nitrogen; WBC, white blood cell, leukocyte;

Figure 1

case	The day of admission	June 4	June 18
1			
2			
3			
4			
Fig	a	b	c