A VV-ECMO supported severe pneumonia caused by Chlamydia abortus: a case report

wahkwong Yip
The third hospital of Xiamen

bin wu (michaellyjl@163.com)
The third hospital of Xiamen

baohua ye
The third hospital of Xiamen

chengyi ji
The third hospital of Xiamen

ziyao wu
The third hospital of Xiamen

minli chen
The third hospital of Xiamen

chunmiao lin
The third hospital of Xiamen

Jialiang Ye
The third hospital of Xiamen

wenzhi ke
The third hospital of Xiamen

qiuyan chen
The third hospital of Xiamen

shumin xu
The third hospital of Xiamen

huimin chen
The third hospital of Xiamen

Case Report

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Abstract

Background:

Human infection with Chlamydia abortus is very rare, mainly described as septicemia and abortion in pregnant women with previous Chlamydia abortus exposure. Though there is a case of atypical pneumonia caused by Chlamydia abortus in 2016, none of the reported infections manifested primarily as severe hypoxemia.

Case Presentation:

A 69-year-old male farmer admitted to our ICU for pneumonia caused severe hypoxemia, with PaO2/FiO2 ratio dropped to 53.1 mmHg when under mechanical ventilation. Bronchoalveolar lavage fluid (BALF) for untargeted metagenomic NGS was taken soon after VV-ECMO support. Sequencing results indicate Chlamydia abortus is the pathogen. The patient operated a farm raising more than a hundred pigs and some poultry before the disease, with no ruminant in the farm, and the possibility of contact was denied. Two weeks later, the patient was weaned from ECMO, recovered, and was discharged a month later.

Conclusion:

Chlamydia abortus infection in humans may as well cause severe pneumonia with hypoxemia and need ECMO support. Clinician veterinarians and public health officials should be aware of possible severe pulmonary infection due to Chlamydia abortus.

Background

Chlamydia abortus is recognized as a common cause of reproductive failure in small ruminants and other domestic animals (1). However human infection with Chlamydia abortus is very rare, mainly described as septicemia, organ dysfunction, thrombocytopenia, and abortion in pregnant women with previous Chlamydia abortus exposure (2–7). In 2016, Ortega et al reported the first case of human atypical pneumonia caused by Chlamydia abortus (8), in which a veterinarian researcher developed symptoms after exposure to artificial pathogenic aerosols. In Pinchon et al case, though the pregnant woman developed ARDS secondary to septicemia and intubated for mechanical ventilation (7), none of the cases primarily present with obvious hypoxemia. We report a case of severe pneumonia presented as hypoxemia that needs ECMO support caused by Chlamydia abortus and diagnosed by bronchoalveolar lavage fluid (BALF) metagenomic next-generation sequencing (mNGS).

Case Presentation

A 69-year-old male pig farmer presented to our hospital with seven days of general malaise, dry cough, and deteriorating dyspnea for a day, without obvious chills or fever. In the emergency ward, digital oxygen saturation fluctuated below 80% even with support by HFNC at fractional inspired oxygen (FiO2) of 60%,
immediate CT scan showed full consolidation of the left lung and areas of the right lung (g:1), indicating severe pneumonia and admitted to ICU. As arterial blood-gas analysis confirmed the severe hypoxemia with PaO2/FiO2 ratio at 90.8 mmHg, we intubated the patient. No airway exudation was gained from the initial suction. We ventilated the patient in prone position, and empirically used meropenem and moxifloxacin to cover gram-negative rods and atypical bacteria. Even ventilated with pure oxygen and PEEP 18cmH2O, digital oxygen saturation fluctuated below 96%, and arterial blood-gas analysis two hours after intubation showed oxygen partial pressure (PaO2) at 53.1mmHg, obliging us to start VV ECMO. Circulation is surprisingly stable as under sedation and in such MV condition little vasopressor was required.

As digital oxygen saturation stabilized, we took bronchoalveolar lavage fluid (BALF) for metagenomic NGS (Genskey, Beijing, China), smear microscopy, and culture. Neutrophilia raised C-reactive protein levels and elevated procalcitonin levels supported the diagnosis of infective pneumonia (table 1). Nasal swab multiplex PCR for 13 respiratory pathogens (Healthgenetech, Ningbo, China) showed Chlamydia (genus-specific) positive but negative for all other items including Mycoplasma pneumonia and virus (Human coronavirus, Influenza A B C, Parainfluenza, HRSV, etc.) Both serum detection for (1-3)-β-D-Glucan and Galactomannan were negative. No bacteria nor fungal hypha was found under smear microscopy.

Within 72h after BALF was taken, Metagenomic sequencing gained 3313067 DNA reads with Q30 at 93.67% after subtraction of human host sequence, of which 2571199 reads matched genus Chlamydia with relative abundance at 95.02%, and 1071733 reads were further identified as Chlamydia abortus. No other bacteria DNA was sequenced with a relative abundance of more than 0.1%. For fungi, 229 reads of DNA matched Aspergillus Terreus with relative abundance at 61.68% and 7 reads met Candida parapsilosis. No DNA sequence read was gained matched to viruses, parasites, or mycobacteria. Metagenomic Transcriptome Sequencing yielded 484298 RNA reads with Q30 at 92.45% after subtracting background message, of which 25081 reads matched genus Chlamydia with relative abundance at 99.61%, 9769 reads were further identified as from Chlamydia abortus. Only 4 reads of RNA matched Burkholderia contaminans. No RNA sequence read was gained matched to the virus, parasites, mycobacteria, or fungi. (table 2).

Synchronized reduction of neutrophils, PCT, and CRP level indicating the effectiveness of antibiotic treatment, result for BALF culture was negative. Two weeks later, the patient was weaned from ECMO, and a month later the patient improved clinically and biologically and was discharged from the hospital.

The patient operated a farm raising more than a hundred pigs and some poultry before the disease. There was no ruminant on the farm and the possibility of contact was denied, in addition, no animal abortion nor weight loss was noticed by the family.

Discussion

Metagenomic next-generation sequencing is capable of generating large-scale sequence data sets that unbiasedly describe the genomic content of entire microbial communities (bacterial, viral, and eukaryotic
organisms)(9). According to reported research, when mNGS identified a microbe (species level) whose relative abundance is more than 30% at the genus level in bacteria or fungi, it can potentially be regarded as a causative pathogen(10). In this mNGS report, both Aspergillus terreus and Chlamydia abortus met the Criteria.

Aspergillus terreus produces spores that disperse efficiently in the air and are prevalent in tropical and subtropical regions(11). Aspergillus terreus causes invasive aspergillosis (IA) in immunocompromised patients, especially those who suffer from neutropenia and are under high-dose steroid treatment(12). This previously healthy patient did not possess these risk factors, we considered it as contamination and did not start anti-fungal treatment. As human infection with Chlamydia abortus is very rare, the possibility of contamination should be excluded(13). After checking the lab record, the technician of Genskey denied Chlamydia abortus detected before this case, excluding the possibility of contamination in the laboratory environment. Nasal swab multiplex PCR for 13 respiratory pathogens indicating positive for genus Chlamydia as well consistent with the sequencing result. The positive metagenomic transcriptome sequencing result implies that the organism was “active”, as well supporting the diagnosis. As the patient was improving and recovered, we believe it is Chlamydia abortus causing this severe pneumonia and hypoxemia.

Chlamydiaceae is of the order Chlamydiales, which is a family of obligate intracellular Gram-negative bacteria. Underwent a number of taxonomic reclassifications, the genus Chlamydia (which is under the family Chlamydiaceae) currently includes 14 species((Chlamydia abortus, Chlamydia avium, Chlamydia buttons, Chlamydia caviae, Chlamydia felis, Chlamydia gallinacean, Chlamydia muridarum, Chlamydia pecorum, Chlamydia pneumonia, Chlamydia poikilothermic, Chlamydia psittaci, Chlamydia serpents, Chlamydia suis and Chlamydia trachomatis)) and four Candidatus species(14).

Before 1990, Chlamydia psittaci encompassed a huge group of strains been grouped by a number of methods. Andersen grouped strains of Chlamydia psittaci into serotype I by Serovar-Specific Monoclonal Antibodies, which latterly been grouped as Chlamydia abortus (15).

Besides being associated with enzootic abortion in small ruminants, Chlamydia abortus causes pig abortion in both intensive and extensive production systems(16.17). In this case, it seems possible that pigs from the farm are transmitters of this zoonotic agent to the farmer. There is published research involving experimental infections with Chlamydia abortus that has identified the ability of this pathogen to cause pulmonary disease in animal species(18.19). In Ortega et al case, the veterinary researcher developed pan-lobar pneumonia ten days after operating the suspension of Chlamydia abortus sprayed on animals, through serological and molecular analysis the microorganism was confirmed. Interestingly, two asymptomatic colleagues of the patient showed antibody production against Chlamydia abortus(8). In another case, the patient did not directly contact the animals but just handled contaminated clothing of her husband and developed Chlamydia abortus infection and abortion(7). From these cases, we can see that Chlamydia abortus can be highly transmissible, and conditionally may cause fatal conditions as it is in our case.
Admittedly, there are some pitfalls in this case. According to the mNGS result, the possibility of co-infection with Aspergillus terreus should not have been ruled out arbitrarily, and anti-fungal treatment may be reasonable. Considering the rarity of human Chlamydia abortus infection, an alternative method should be obtained to confirm the pathogen diagnosis. A seroepidemiological study of the animals on that farm could have revealed more information. Unfortunately, it was more than a month later when we realized the issues above, the patient is recovered and discharged, and the family had already sold all the animals on the farm to meat factories when they were informed the patient’s severe disease was caused by a zoonotic pathogen.

From this case, we can see that Chlamydia abortus infection in human may as well cause severe pneumonia with hypoxemia and need ECMO support. Thus, veterinarians and public health officials should be aware of possible severe pulmonary infection due to Chlamydia abortus.

**Abbreviations**

<table>
<thead>
<tr>
<th>Term</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchoalveolar lavage fluid</td>
<td>BALF</td>
</tr>
<tr>
<td>metagenomic next generation sequencing</td>
<td>mNGS</td>
</tr>
<tr>
<td>DeoxyriboNucleic Acid</td>
<td>DNA</td>
</tr>
<tr>
<td>Ribonucleic Acid</td>
<td>RNA</td>
</tr>
<tr>
<td>Veno-Venous Extracorporeal Membrane Oxygenation VV ECMO</td>
<td>VV ECMO</td>
</tr>
<tr>
<td>High-flow Nasal Cannula</td>
<td>HFNC</td>
</tr>
<tr>
<td>Fractional inspired oxygen</td>
<td>FIO2</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome</td>
<td>ARDS</td>
</tr>
<tr>
<td>Human respiratory syncytial virus</td>
<td>HRSV</td>
</tr>
<tr>
<td>Computer tomography</td>
<td>CT</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>PCT</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>CRP</td>
</tr>
<tr>
<td>Polymerase chain reaction</td>
<td>PCR</td>
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</table>

**Declarations**

**Ethics approval and consent to participate**
We obtained written permission from the patient to publish this case report. This study was approved by the ethics committee of The Third Hospital of Xiamen.

**Consent for publication**

The patient of this case has given consent in written form for his personal detail and identifying images to be published in this case report.

**Availability of data and material**

The Sequence file supporting this case is deposited in SRA (Sequence Read Archive) database with access numbers SRA: PRJNA813338; BioProject: PRJNA813338.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors' contributions**

Wah Kwong YIP, ZiYao Wu, Jialiang Ye, and Baohua Ye contributed to writing the manuscript. Bin Wu, Chengyi Ji, Huimin Chen, Minli Chen, Wenzhi Ke, Qiuyan Chen, Chunmiao Lin, and Shumin Xu are members of our ECMO team, contributing significantly to the treatment of patients. All authors have read and approved the final manuscript.

**Acknowledgements**

We thank Genskey, Beijing, China for the genetic sequencing work of this case.

**References**


Tables

Table 1: Relevant laboratory data on admission day.
<table>
<thead>
<tr>
<th>Item name</th>
<th>Reference range</th>
<th>Actual value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total leukocyte counting</td>
<td>3.5-9.5×10⁹/L</td>
<td>8.3</td>
</tr>
<tr>
<td>Neutrophil counting</td>
<td>1.8-6.3×10⁹/L</td>
<td>8.0</td>
</tr>
<tr>
<td>Lymphocyte counting</td>
<td>1.1-3.2×10⁹/L</td>
<td>0.2</td>
</tr>
<tr>
<td>Eosinophils counting</td>
<td>0.02-0.52×10⁹/L</td>
<td>0.0</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>130-175g/L</td>
<td>136.0</td>
</tr>
<tr>
<td>Platelet counting</td>
<td>125-350×10⁹/L</td>
<td>151.0</td>
</tr>
<tr>
<td>C-reactive protein level</td>
<td>0.4-5.2 mg/dl</td>
<td>260.85</td>
</tr>
<tr>
<td>Procalcitonin (PCT)</td>
<td>&lt;0.5ug/L</td>
<td>20.94</td>
</tr>
<tr>
<td>NT-pro-BNP</td>
<td>0.0-300pg/mL</td>
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</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>2.9-8.2mmol/L</td>
<td>12.4</td>
</tr>
<tr>
<td>Creatinine</td>
<td>62-115μmol/L</td>
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<tr>
<td>Aspartate aminotransferase</td>
<td>0 40U/L</td>
<td>312</td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
<td>0 40U/L</td>
<td>201</td>
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</table>

Table 2: BALF mNGS result for DNA and RNA sequencing.

<table>
<thead>
<tr>
<th>genera</th>
<th>Amount of reads</th>
<th>Relative abundance</th>
<th>specie</th>
<th>Amount of reads</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>2571199</td>
<td>95.02%</td>
<td>Chlamydia abortus</td>
<td>1071733</td>
</tr>
<tr>
<td>Burkholderia</td>
<td>116833</td>
<td>4.32%</td>
<td>Burkholderia contaminans</td>
<td>24228</td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>132</td>
<td>&lt; 0.01%</td>
<td>Staphylococcus aureus</td>
<td>46</td>
</tr>
<tr>
<td>Aspergillus</td>
<td>330</td>
<td>61.68%</td>
<td>Aspergillus terreus</td>
<td>299</td>
</tr>
</tbody>
</table>

mNGS result for RNA sequencing.

<table>
<thead>
<tr>
<th>genera</th>
<th>Amount of reads</th>
<th>Relative abundance</th>
<th>specie</th>
<th>Amount of reads</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>25081</td>
<td>99.61%</td>
<td>Chlamydia abortus</td>
<td>9769</td>
</tr>
<tr>
<td>Burkholderia</td>
<td>50</td>
<td>0.20%</td>
<td>Burkholderia contaminans</td>
<td>4</td>
</tr>
</tbody>
</table>

Figures
Figure 1

CT scan on admission day.