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Case report

A case of acute community-acquired pneumonia caused by *Tropheryma whipplei* in pregnant woman without predisposing medical conditions

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ABSTRACT

Tropheryma whipplei (*T. whipplei*) is extensively known as the etiological bacterium of Whipple's disease (WD). Here, we reported a case of community-acquired pneumonia caused by *T. whipplei* in a young pregnant woman without predisposing medical conditions. This case indicated that *T. whipplei* might be also transmitted via respiratory droplet.

Introduction

Tropheryma whipplei (*T. whipplei*), as a rod-shaped, Gram-positive bacterium, 2 mm long and 0.25–0.5 mm diameter, was for the first time identified in 1990 by sequencing of 16s ribosomal RNA genes and successfully cultured in 1997. It is the etiological pathogenic bacterium of Whipple's disease (WD). In recent years, more and more extra-intestinal infections caused by *T. whipplei* were confirmed or described, which included other chronic infections (endocarditis, neurological infections, uveitis, arthritis and osteoarticular infections and isolated adenopathies) and acute infections (gastroenteritis, pneumonia and bacteremia) ever since the advances in molecular diagnostic tools[1]. But these infections caused by *T. whipplei*[2] mostly occurred to middle-aged man with some risk factors, including smoke, immunosuppressed diseases, HIV-infected individuals, sewer workers and contact with the patients with WD, poor living conditions of homeless people in shelters. Here, we reported a case of community-acquired pneumonia (CAP) with acute respiratory distress syndrome (ARDS) caused by *T. whipplei* in a young pregnant woman without any risk factors.

Case presentation

A 25-year-old woman without any medical history came to Qilu hospital of Shandong University at her 32 weeks pregnant and complained for progressive dyspnea, chest distress and short of breath accompany with edema of both lower extremities for 2 weeks. She denied any recent travel and exposure to chemicals. The emergent chest computer tomography (CT) showed local consolidation in the lower lobe of the right lung and multiple diffuse bilateral pneumonia (Fig. 1). She immediately received cesarean section because of rapidly deteriorated hypoxic (oxygen saturation 80 % on 6 liters oxygen by nasal cannula). After operation, she was immediately transferred to intensive care unit (ICU) with endotracheal intubation. The arterial blood gas analysis showed PO_2 57 mmHg, PCO_2 80 mmHg, FiO_2 0.7, and PH 7.17. The parameters of mechanical ventilation included high positive end-expiratory pressure (PEEP, 12cmH_2O) and FiO_2 70 %.

On her admission to ICU, her vital signs were stable and physical examination showed bilateral scattered crepitations. The lab examinations demonstrated WBC (white blood cell) 8.3×10^9/l (3.5–9.5 $\times 10^9$/l), neutrophils 7.1×10^9/l (1.8–6.5 $\times 10^9$/l), and lymphocytes 0.43×10^9/l (1.1–3.2 $\times 10^9$/l), procalcitonin (PCT) 0.468 ng/ml (<0.1 ng/ml). The empirical antibiotic (piperacillin-tazobactam and moxifloxacin) and antiviral (peramivir) treatments were initiated, which covered most possible pathogen of CAP. The routine culture and smear of sputum as well as bronchoalveolar lavage fluid (BALF) did not detect any bacterium and fungi. The blood culture was also negative. In addition, the nucleotide analysis of current respiratory viruses, including influenza A, influenza B, parainfluenza 1,2,3, respiratory syncytial, adenovirus and coronavirus, were negative. Thus, we send BALF to perform metagenomics next-generation sequencing (mNGS) for rapidly detecting possible pathogenic microorganism. mNGS results of BALF revealed 127 unique sequencing reads of *T. whipplei,* covering

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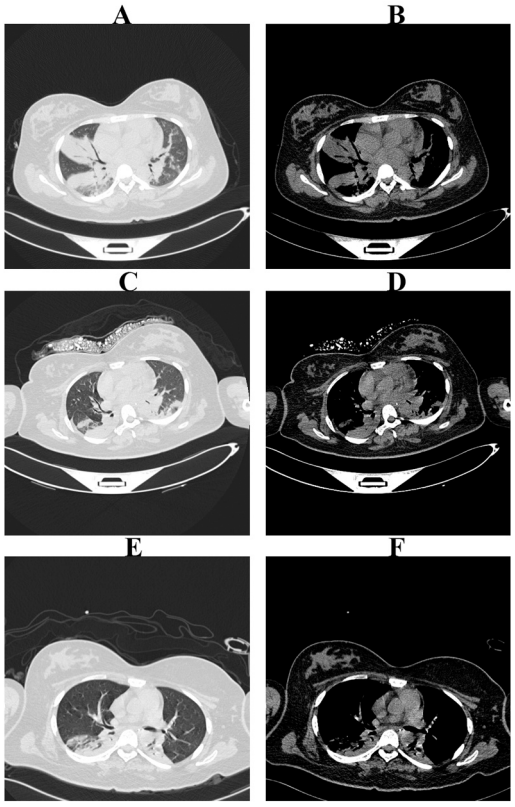

Fig. 1. The chest CT imagines at different times: A, C&E indicated lung windows of lung CT at 1st, 14th, 28th day. B, D&F indicated mediastinum windows of lung CT at 1st, 14th, 28th day.

0.7168 % of the nucleotide sequences (Fig. 2A). More importantly, *T. whipplei* was also the only microorganism detected by NGS. Thus, moxifloxacin and peramivir were discontinued. The regular polymerase chain reaction (PCR) analysis was also performed to confirm the presence of *T. whipplei* in BALF by sequencing of 16S ribosomal DNA (rDNA)

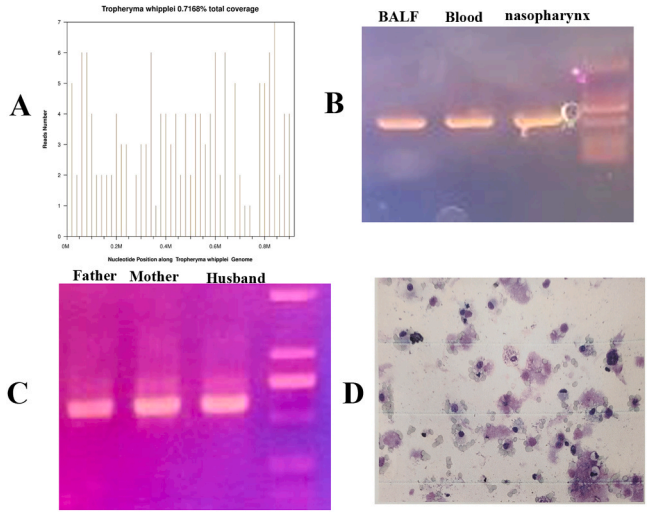

Fig. 2. The data from mNGS, regular PCR and cell phenotype. The location of detected nucleic acid sequences in T. whipplei, which yielded a total coverage of 0.7168 %. B.The bright bands were *T. whipplei* amplified products in BALF, blood and nasopharynx. C. The bright bands were *T. whipplei* amplified products in nasopharynx from the patient's husband and parents. D.The cell phenotype of BALF: neutrophils and alveolar macrophage respectively account for 45 % and 5 %.

(Fig. 2B). In addition, the presence of *T. whipplei* was also confirmed in blood, and nasopharynx via regular PCR technology, but was not detected in stomach, duodenum as well as stool (data not shown). *T. whipplei* was also detected in the nasopharynx from her husband and parents (Fig. 2C) via regular PCR, but not in stool (Fig. 2C). The cell phenotype analysis of BALF showed neutrophils 45 % and alveolar macrophage 5 % (Fig. 2D).

Her temperature maintained 37.2–37.8℃at the first 5 days of admission to the hospital. Later, her temperature maintained higher level (38.2–39 ℃) for the next two weeks. The count of WBC maintained normal level during the whole course of the disease while PCT rapidly decreased to the normal level at the 6th day and maintained normal level during the left course. However, the parameters of mechanical ventilation maintained higher PEEP (8–10cmH_2O) and FiO_2 (50–70 %) for 3 weeks. Tracheostomy was performed at the 8th day of admission to the hospital. At the 14th day of admission to the hospital, the chest CT showed bilateral infiltration was more extended than the initial chest CT findings (Fig. 1A &B). In total, piperacillin-tazobactam lasted for 5 weeks, followed by trimethoprim-sulfamethoazole at 480 mg fourth daily for 2 weeks. After 7 weeks of treatment, she was successfully extubated and discharged.

Discussion

In the current case report, we described a young female patient at late stage pregnancy suffering from severe CAP with ARDS caused by *T. whipplei.* Although it was not the first case presentation of pneumonia caused by *T. whipplei* in China, there were new characteristics different from the previously reported cases[3], including the sole causative bacterium detected in BALF, the severity of disease (higher mechanical ventilation parameters, long duration, high temperature) inconsistent with lab examinations as well as no predisposing medical conditions.

According to the clinical symptoms, lab examinations and chest CT imaging (Fig. 1 C&D), it was consistent with the diagnosis of CAP with ARDS. The common causative microorganisms of severe CAP included Streptococcus pneumonia, enteric gram-negative bacilli, Pseudomonas aeruginosa, Haemophilus influenzae and seasonal respiratory virus[4]. However, we did not detect any bacterium and respiratory virus via routine diagnostic tools. *T. whipplei* was the sole bacterium detected in BALF via mNGS although the nucleotide sequencing reads was 127 (Fig. 2A). Although *T. whipplei* is considered to be the pathogen of Whipple's disease (WD) [1], the mono-microbial detection of *T. whipplei* DNA in BALF strongly supported the link between *T. whipplei* and CAP. PCT (procalcitonin) as a serum protein is used to discriminating viral and bacterial infection. Neutrophils accounted for less than 1 % in BALF of healthy adults while increased percent of neutrophils in BALF supported bacterial infection. Our data showed that PCT was mildly elevated and the percent of neutrophils in BALF was significantly increased. Thus, the elevated PCT level as well as the increased percent of neutrophils in BALF further confirmed the causative effect of *T. whipplei* on pneumonia. The symptoms of classical WD include abdominal pain, diarrhea, weight loss and arthralgia[1]. However, the patient denied all of the above those manifestations. More importantly, *T. whipplei* was not detected in stomach, duodenum as well as stool. Thus, we concluded that CAP with ARDS might be the independent clinical manifestation caused by *T. whipplei*, not the extra-intestinal manifestation of WD.

T. whipplei existed ubiquitously in the environment, especially in sewage water, fecal material and sewage plant workers[5]. However, this patient denied above any risk factors. In addition, Fig. 2C also showed that *T. whipplei* was positive in the nasopharynx from her husband and parents while negative in stool. But, they were all asymptomatic. A study in France revealed that the prevalence of *T. whipplei* in fecal samples from the relatives of patients with classical Whipple disease was more high than general population and up to 24 %[6], which indicated intra-familial circulation of *T. whipplei*. It is well accepted that

T. whipplei is able to be transmitted between humans via oral-oral or feco-oral transmission[6]. Although these current evidences did not support the diagnosis of WD, they still indicated the possibility of intra-familial circulation of *T. whipplei* via respiratory droplet. Unfortunately, further genotypic analysis on the bacterial strain from the family members, in order to compare for similarities to the patient's strain of T. whipplei was not done. But, we could not rule out the intra-familial circulation via respiratory droplet or oral-oral transmission. Thus, it is still necessary for the family members to do personal hygiene practices good and self-protection, such as hand washing.

Conclusion

T. whipplei is the unusual opportunistic and intra-familial circulation pathogenic microorganism of CAP. It might be also transmitted via respiratory droplet except for oral-oral or feco-oral route. In addition, *T. whipplei* still should be considered in the differential diagnosis of severe CAP in pregnant women although pneumonia caused by *T. whipplei* relatively rarely occur and difficult to diagnose.

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CRediT authorship contribution statement

Hongna Yang collected the clinical data and wrote the manuscript. Hao Wang a helped to collect the data. All authors reviewed the manuscript.

CRediT authorship contribution statement

Hongna Yang: Writing – review & editing, Writing – original draft. **Hao Wang:** Data curation.

Declaration of Competing Interest

All the authors declared there was no competing interest.

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References

[1] Marth T, Moos V, Müller C, Biagi F, Schneider T. Tropheryma whipplei infection and Whipple's disease. Lancet Infect Dis 2016;16:e13–22.
[2] Bousbia S, Papazian L, Auffray J-P, Fenollar F, Martin C, et al. Tropheryma whippleiin patients with pneumonia. Emerg Infect Dis 2010;16:258–63.
[3] Li W, Zhang Q, Xu Y, Zhang X, Huang Q, et al. Severe pneumonia in adults caused by Tropheryma whipplei and Candida sp. infection: a 2019 case series. BMC Pulm Med 2021;21.
[4] Lanks CW, Musani AI, Hsia DW. Community-acquired pneumonia and hospital-acquired pneumonia. Med Clin North Am 2019;103:487–501.
[5] Freeman HJ. Tropheryma whipplei infection. World J Gastroenterol 2009;15:2078.
[6] Fenollar F, Keita AK, Buffet S, Raoult D. Intrafamilial circulation of tropheryma whipplei, France. Emerg Infect Dis 2012;18.