Clin. Lab. 2026;72:XXX-XXX


## CASE REPORT

# Tropheryma whipplei Infection Presenting Initially with Chest Pain

Siran Xu [1], Yuting Fan [1, 2], Zhao Chen [1], Zhi Ping Deng [1]

[1] *Zigong First People's Hospital, Zigong, Sichuan, China*
[2] *North Sichuan Medical College, Nanchong, Sichuan, China*

### SUMMARY

***Background:*** **Tropheryma whipplei is a rare pathogenic bacterium, a Gram-positive actinomycete widely distributed in the natural environment. It mainly infects individuals with immunodeficiency, but is rarely observed in individuals with normal immune function. Most patients present with non-specific symptoms, and since it is not feasible to culture the bacteria using conventional methods, diagnosing this infection is very difficult. In this case, next-generation sequencing (NGS) detection via bronchoscopy confirmed the final diagnosis of Tropheryma whipplei infection.**
***Methods:*** **Bronchoscopy and next-generation sequencing were used.**
***Results:*** **Through bronchoscopy, NGS of bronchoalveolar lavage fluid indicated the presence of Tropheryma whipplei. Therefore, anti-infective treatment was administered.**
***Conclusions:*** **For cases of long-standing chest pain of unknown origin with abnormal findings on chest imaging, it is crucial to stabilize the patient's condition while identifying the underlying cause. Prompt implementation of relevant diagnostic procedures, such as bronchoscopy, is essential for establishing a diagnosis.**
**(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250521)**

**Correspondence:**
Zhi P. Deng
Zigong First People's Hospital, Zigong
Sichuan
China
Phone: +86 13608158051
Email: dengzp1016@163.com

Case Report accepted May 13, 2025

### KEYWORDS

Tropheryma whipplei, bronchoscopy examination, next-generation sequencing

### CASE REPORT

A 75-year-old elderly man was admitted to the hospital mainly due to chest pain for more than 10 years, which had worsened in the past 3 days. He stated that he had experienced chest pain on the left side, mainly dull pain, accompanied by palpitations and shortness of breath after activity, which could be relieved after rest, since more than 10 years ago due to trauma. A chest DR examination in an external hospital at that time showed no rib fractures. The above-mentioned symptoms worsened 3 days ago, presenting as stabbing pain, which could be aggravated by activity and deep breathing. There was no cough, expectoration, fever, fatigue, night sweats or other discomforts. A chest CT examination in our hospital showed scattered inflammation in both lungs. The patient had a long-term smoking history and denied a history of tuberculosis. On admission, hypopnea was

heard during pulmonary auscultation, and no dry or moist rales were heard in both lungs. No obvious abnormalities were found in the rest of the physical examination. After admission, the blood routine test showed: RBC 4.49 x $10^{12}$/L (reference range: 4 x $10^{12}$/L - 5.5 x $10^{12}$/L), HGB 107 g/L (reference range: 115 g/L - 150 g/L), WBC 4.12 x $10^{9}$/L (reference range: 4 x $10^{9}$/L - 10 x $10^{9}$/L), NEU 2.69 x $10^{9}$/L (reference range: 1.8 x $10^{9}$/L - 6.3 x $10^{9}$/L), LYM 0.66 x $10^{9}$/L (reference range: 1.1 x $10^{9}$/L - 3.2 x $10^{9}$/L), MON 0.50 x $10^{9}$/L (reference range: 0.1 x $10^{9}$/L - 0.6 x $10^{9}$/L). Meanwhile, the infection - related indicators were as follows: hs-CRP 30.9 mg/L (reference range: 0 mg/L - 5 mg/L), PCT 0.037 ng/mL (reference range: 0 ng/mL - 0.05 ng/mL), fibrinogen 1.32 g/L (reference range: 2 g/L - 4 g/L). There were no obvious abnormalities in biochemical tests, myocardial enzyme tests, tumor markers, and detection of Mycobacterium tuberculosis complex DNA. Sputum culture indicated the presence of Pseudomonas aeruginosa (4+). Chest CT scan showed scattered small patchy and nodular increased density shadows in both lungs, bronchiectasis in the middle and upper lobes of the right lung and the lower lobe of the left lung, and thickening and adhesion of bilateral pleura. Initially, we considered pulmonary infection and gave piperacillin-tazobactam sodium 4.5 g q12 hours for anti-infective treatment, but the treatment effect was poor. Therefore, we performed bronchoscopy. The NGS test result showed Tropheryma whipplei. Finally, we diagnosed the patient with Tropheryma whipplei pneumonia and gave ceftriaxone 2 g qd for anti-infective treatment. Currently, the patient's condition has improved and he was discharged from the hospital. After discharge, he was regularly given compound sulfamethoxazole tablets, 0.96 g bid, for anti-infective treatment.

## DISCUSSION

Tropheryma whipplei is the bacterium associated with Whipple's disease, described by George H. Whipple in 1907 [1]. T. whipplei is a rod-shaped Gram-positive bacterium belonging to the Actinomycetes. T. whipplei is a rare pathogen, with only a small number of case reports. It is a Gram-positive actinomycete widely distributed in the natural environment. It is unlikely to cause disease in healthy people, but it can cause a chronic and multisystem infectious disease called Whipple's disease, which mainly affects middle-aged white men [2-4]. Recent epidemiological estimates suggest that the annual incidence is 3 per million population, the ratio of male to female patients is 8:1, and there are also strong geographical differences [5,6]. Typical Whipple's disease often presents with extremely complex clinical manifestations due to the involvement of multiple aspects of multiple physiological systems [7]. Due to the lack of specific clinical manifestations and insufficient understanding of T. whipplei, it is often misdiagnosed or missed in clinical practice. With the development of molecular biology techniques, in 1991, bacterial 16S ribosomal DNA was first discovered in the small intestine biopsy specimens of patients with typical Whipple's disease through nucleotide sequencing and PCR amplification [8]. Subsequently, PCR technology was used to detect T. whipplei DNA in various samples such as feces, saliva, urine, blood, cerebrospinal fluid, and BALF [9]. In some studies, T. whipplei has been proven to be an etiological pathogen of pneumonia. Additionally, T. whipplei is more commonly found in the bronchoalveolar lavage fluid of HIV-positive individuals, which is considered a potential factor for pulmonary complications. This further suggests that T. whipplei may be involved in the development of certain lung diseases.

Pneumonia is a common clinical disease, and there are significant challenges in its diagnosis and treatment, especially when it is caused by infections of rare or unfamiliar pathogens [5]. After infection with T. whipplei, most infected individuals show asymptomatic or self-limited infections through the development of protective humoral and cellular immunity, while only a small number of cases develop Whipple's disease [10]. Typical symptoms of Whipple's disease include joint pain, diarrhea, steatorrhea, weight loss, lymphadenopathy, abdominal pain, hypoalbuminemia, and anemia. It affects the gastrointestinal tract, bones and joints, cardiovascular system, and nervous system, and is rarely associated with pulmonary infections [3,4]. Recently, studies have shown the role of T. whipplei as a pathogen of community-acquired pneumonia [5]. Researchers have also found T. whipplei in the saliva of asymptomatic individuals. T. whipplei can be inhaled from the oral flora, potentially leading to community-acquired and aspiration pneumonia [1]. Lin et al. analyzed 1,725 BALF samples using NGS. T. whipplei was detectable in the BALF of 70 patients, but only 9 of these patients had immunodeficiency [1]. Therefore, attention should also be paid to non-immunocompromised patients. The spectrum of the pathogenic effects of T. whipplei in BALF is quite broad [11]. T. whipplei infection may initially cause fever and idiopathic or migratory arthritis, and progress to result in steatorrhea, weight loss, hepatosplenomegaly, and ascites. Notably, approximately 30% of T. whipplei infections affect the lungs, leading to respiratory symptoms, including dry cough, chest pain, shortness of breath, and pleural adhesions [12]. Zhang et al. retrospectively analyzed the case data of 20 patients with pulmonary infections caused by T. whipplei and reported different imaging findings. Among them, 10 patients presented with pulmonary nodules, 5 with interstitial changes, and 5 with patchy shadows. A small number showed cavities, mediastinal lymphadenopathy, and pleural effusion [13]. The patient initially presented with unexplained chest pain, and the chest imaging showed scattered small patchy and nodular increased-density shadows in both lungs. Eventually, T. whipplei was detected by NGS.

To date, the treatment of Whipple's disease with pulmo-

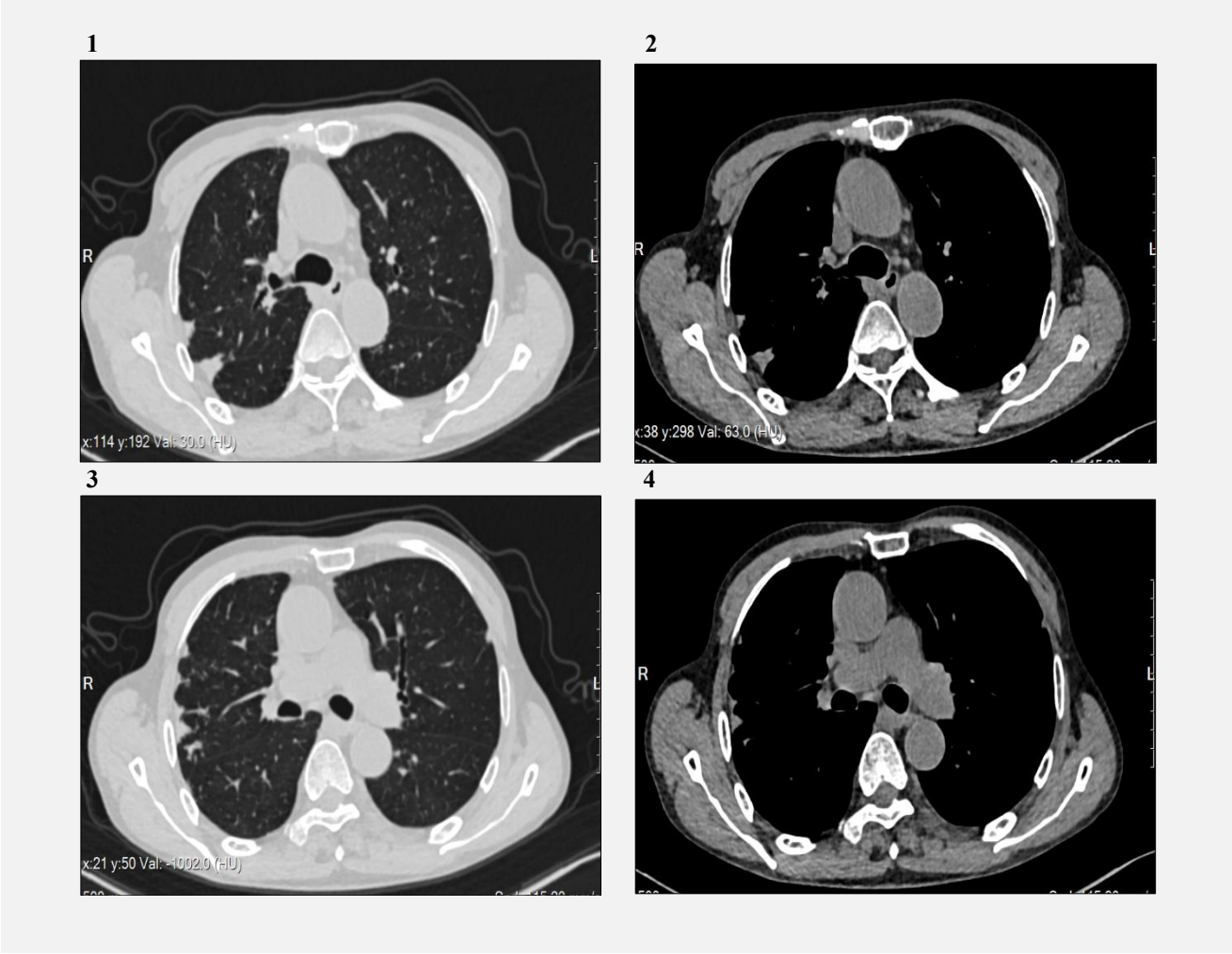


**Figure 1 - 4. Chest CT scan showed scattered small patchy and nodular increased density shadows in both lungs, partial bronchiectasis in the middle and upper lobes of the right lung and the lower lobe of the left lung, and thickening and adhesion of the bilateral pleura.**

**NGS reported**

| Detection index | RPTM * | Positive reference range | Qualitative results |
|---|---|---|---|
| Tropheryma whipplei | 125,003 | ≥ 1 | bacterial positive |

*** RPTM - the number of sequences that are aligned with the target sequence of the pathogen. A higher value of this parameter indicates a stronger detection signal for the pathogen.**

nary symptoms as the main complaint is still in its early stages and not standardized. In our case, based on the NGS test results, we promptly changed the treatment plan, and the patient's condition improved. The most common anti-infective regimen for the treatment of Whipple's disease includes intravenous ceftriaxone (2 g qd) or meropenem (1 g q 8 hours, if ceftriaxone is not tolerated) for 2 weeks, followed by cotrimoxazole for 1 year, or doxycycline if cotrimoxazole is not tolerated. Another alternative regimen that has been used by some specialists is hydroxychloroquine (600 mg qd) and doxycycline (200 mg qd) for 12 months. In addition, considering the high recurrence rate of Whipple's disease, some experts recommend using doxycycline for lifelong maintenance treatment after 12 months of alternative treatment with doxycycline (200 mg once daily) and hydroxychloroquine (600 mg once daily) to prevent reinfection [14]. In our patient, after sequential administration of ceftriaxone and trimethoprim-sulfamethoxazole, substantial improvements in symptoms and imaging findings were noted. The prognosis of Whipple's disease depends on several factors, including the disease

stage at diagnosis and the effectiveness of treatment. Early recognition and treatment usually lead to better outcomes. With appropriate and timely treatment, the symptoms of most patients are significantly improved and the prognosis is favorable. Regular follow-up and monitoring are necessary to manage the disease and prevent recurrence.

## CONCLUSION

Our case indicates that for patients with long-term unexplained chest pain and abnormal chest imaging findings, attention should be paid to the possibility of T. whipplei infection. If necessary, bronchoscopy and NGS testing should be performed to clarify the diagnosis. Developing an appropriate treatment plan in the early stage of the disease can provide optimal treatment at the initial phase, thereby improving the patient's prognosis.

**Acknowledgment:**
We would like to thank other members of the Department of Respiratory Medicine, Zigong First People's Hospital of Technology, for their constructive criticism.

**Ethical Approval:**
This study was approved by the ethics committee of Zigong First People's Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

**Declaration of Interest:**
No conflicts of interest.

**References:**

1. Lin M, Wang K, Qiu L, et al. Tropheryma whipplei detection by metagenomic next-generation sequencing in bronchoalveolar lavage fluid: A cross-sectional study. Front Cell Infect Microbiol 2022;12:961297. (PMID: 36061864)

2. Fenollar F, Lagier JC, Raoult D. Tropheryma whipplei and Whipple's disease. J Infect 2014;69(2):103-12. (PMID: 24877762)

3. Lagier JC, Lepidi H, Raoult D, Fenollar F. Systemic Tropheryma whipplei: clinical presentation of 142 patients with infections diagnosed or confirmed in a reference center. Medicine (Baltimore) 2010;89(5):337-45. (PMID: 20827111)

4. Lu Z, Zhang A, Guo J, Ni H. An unusual case of severe pneumonia caused by Tropheryma whipplei combined with Legionella pneumophila. World J Emerg. Med 2023;14(6):492-4. (PMID: 37969216)

5. Marth T, Moos V, Muller C, Biagi F, Schneider T. Tropheryma whipplei infection and Whipple's disease. Lancet Infect Dis 2016; 16(3):e13-22. (PMID: 26856775)

6. Wang S, Xia D, Wu J, Jia D, Li L, Xu S. Severe Pneumonia Caused by Infection With Tropheryma whipplei Complicated With Acinetobacter baumannii Infection: A Case Report Involving a Young Woman. Front Public Health 2021;9:729595. (PMID: 34760862)

7. Fang Z, Liu Q, Tang W, et al. Experience in the diagnosis and treatment of pneumonia caused by infection with Tropheryma whipplei: A case series. Heliyon 2023;9(6):e17132. (PMID: 37484369)

8. Relman DA, Schmidt TM, MacDermott RP, Falkow S. Identification of the uncultured bacillus of Whipple's disease. N Engl J Med 1992;327(5):293-301. (PMID: 1377787)

9. Fenollar F, Ponge T, La Scola B, Lagier JC, Lefebvre M, Raoult D. First isolation of Tropheryma whipplei from bronchoalveolar fluid and clinical implications. J Infect 2012;65(3):275-8. (PMID: 22172770)

10. Fenollar F, Perreal C, Raoult D. Tropheryma whipplei natural resistance to trimethoprim and sulphonamides *in vitro*. Int J Antimicrob Agents 2014;43(4):388-90. (PMID: 24613421)

11. Boumaza A, Ben Azzouz E, Arrindell J, Lepidi H, Mezouar S, Desnues B. Whipple's disease and Tropheryma whipplei infections: from bench to bedside. Lancet Infect Dis 2022;22(10): e280-e291. (PMID: 35427488)

12. Zhu B, Tang J, Fang R, et al. Pulmonary coinfection of Mycobacterium tuberculosis and Tropheryma whipplei: a case report. J Med Case Rep 2021;15(1):359. (PMID: 34243811)

13. Zhang WM, Xu L. Pulmonary parenchymal involvement caused by Tropheryma whipplei. Open Med (Wars) 2021;16(1):843-6. (PMID: 34131590)

14. Lagier JC, Fenollar F, Lepidi H, Giorgi R, Million M, Raoult D. Treatment of classic Whipple's disease: from *in vitro* results to clinical outcome. J Antimicrob Chemother 2014;69(1):219-27. (PMID: 23946319)