Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

A Case of Tropheryma whipplei Pneumonia with Recurrent ARDS and Literature Review

Juan Zhang
Deyang People's Hospital
Ying-mei Xiao
1334021063@163.com

Deyang People's Hospital
Xiao-ling Zhu
Deyang People's Hospital
Mao-Juan Wang
Deyang People's Hospital

Case Report

Keywords: Tropheryma whipplei, Severe community-acquired pneumonia, Immune reconstitution inflammatory syndrome, Secondary infection, Literature Review

Posted Date: November 23rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11500054/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations:
No competing interests reported.

Table 1 is available in the Supplementary Files section.

A Case of Tropheryma whipplei Pneumonia with Recurrent ARDS and Literature Review

Juan Zhang[1], Ying-mei Xiao[1]*, Xiao-ling Zhu[1], and Mao-Juan Wang[1]

* Correspondence: 13340210634@163.com

[1] Intensive Care Unit, Deyang People's Hospital, No 173, North Taishan Road, Deyang 618000, Sichuan Province, People’s Republic of China.

Abstract

Background: Tropheryma whipplei is a rare Gram-positive bacillus that can cause chronic multisystem infections. Respiratory involvement is uncommon and presents with diverse clinical manifestations, often leading to misdiagnosis. Disease relapse or progression is associated with complex mechanisms, including potential pathogen reactivation due to immune compromise, antibiotic-triggered immune reconstitution inflammatory syndrome causing lung injury, and predisposition to secondary infections.

Case presentation: A 55-year-old male patient with a history of diabetes mellitus, smoking, and psittacine exposure was admitted with Acute Respiratory Distress Syndrome (ARDS).Pathogen identification was confirmed via metagenomic next-generation sequencing of bronchoalveolar lavage fluid, revealing a rare infection with Tropheryma whipplei. Despite aggressive anti-infective therapy combined with comprehensive anti-inflammatory and anti-fibrotic treatment, the clinical course was characterized by three distinct recurrent episodes of ARDS. The patient ultimately succumbed to progressive respiratory failure and multiple organ dysfunction syndrome. We conducted a literature review of case reports, summarizing clinical features, imaging manifestations, diagnostic methods, and management strategies of T. whipplei pneumonia.

Conclusions: As a rare and clinically complex infectious disease, Tropheryma whipplei pneumonia is difficult to diagnose, prone to relapse, and carries a poor prognosis. In the clinical management of pneumonia caused by this particular

pathogen, in addition to early and precise identification and anti-infective therapy, great importance should be attached to the regulation of immune-inflammatory responses, along with dynamic assessment of the possibility of secondary infections.

Keywords: Tropheryma whipplei; Severe community-acquired pneumonia; Immune reconstitution inflammatory syndrome; Secondary infection; Literature Review.

Background

Tropheryma whipplei is an opportunistic pathogen commonly found in the environment, with primary transmission occurring through the fecal-oral or oral-oral routes[1]. Infection predominantly affects the gastrointestinal tract, typically manifesting as malabsorption syndrome, though it can also involve multiple systems such as the cardiovascular and central nervous systems, as well as the joints[2-3]. Pulmonary involvement occurs in approximately 30%–40% of patients, presenting with often subtle symptoms including chronic cough, chest pain, and dyspnea, which can be easily mistaken for other respiratory infections[4]. On chest Computed Tomography(CT), pulmonary nodules are the most frequent finding, while other presentations may include interstitial changes, patchy infiltrates, or pleural effusion[5]. Diagnosis is established through detection of the pathogen's nucleic acid in bronchoalveolar lavage fluid via metagenomic next-generation sequencing (mNGS) or Polymerase Chain Reaction(PCR)[6]. Currently, no consensus treatment guidelines exist. Empirical regimens commonly consist of intravenous ceftriaxone or meropenem followed by oral trimethoprim-sulfamethoxazole[2-5, 7].

Despite the increasing recognition of T. whipplei as a cause of pneumonia, severe cases requiring mechanical ventilation remain exceedingly rare, and the mechanisms underlying disease recurrence—whether due to pathogen relapse, secondary infection, or immune reconstitution inflammatory syndrome (IRIS)—are poorly understood. Herein, we present a case of recurrent severe T. whipplei pneumonia with three episodes of ARDS, ultimately resulting in death, and we provide a systematic review of the literature. The aim of this report is to highlight the diagnostic and therapeutic challenges of severe T. whipplei pulmonary infection, particularly the risks of recurrence and secondary infection, and to summarize the existing evidence to guide clinical management.

Case presentation

A 55-year-old male patient was admitted on July 25, 2025, due to recurrent fever and shortness of breath lasting for 3 days with aggravation over the preceding day. An outpatient chest CT scan demonstrated bilateral pulmonary opacities.Medical history is significant for type 2 diabetes mellitus, with non-adherence to medications and irregular blood glucose monitoring. A 40-year history of smoking at 20 cigarettes per day and keeping parrots as household pets. Admission physical examination: Temperature 37°C, heart rate 101 beats per minute, respiratory rate 23 breaths per minute, arterial blood pressure 117/81 mmHg, oxygen saturation 79%. The patient was alert and oriented with cyanosis of the lips and rales audible over both lungs.Complete blood count revealed a mild increase in white blood cell (WBC) count to 10.20×10^{9}/L, with neutrophil percentage (NEUT%) slightly elevated at 87.3%

and lymphocyte percentage (LYM%) decreased to 6.7%. Procalcitonin (PCT) was significantly elevated at 8.117 ng/ml. Liver function tests indicated elevated alanine aminotransferase (ALT) at 97 U/L and aspartate aminotransferase (AST) at 155 U/L. Arterial blood gas analysis showed pH 7.452, partial pressure of carbon dioxide (PCO_2) at 30.8 mmHg, and partial pressure of oxygen (PO_2) at 46.5 mmHg.Chest CT revealed diffuse ground-glass opacities, consolidations, and reticular patterns in both lungs, along with mediastinal lymphadenopathy (Figure 1). After admission, high-flow nasal cannula oxygen was administered, but maintaining oxygen saturation proved difficult. Intubation was performed.Mechanical ventilation was set to A/C mode with a tidal volume of 420 mL (6 mL/kg predicted body weight), PEEP of 12 cmH_2O, and FiO_2 of 1.0. Arterial blood gas analysis revealed a PaO_2 of 83mmHg, corresponding to a PaO_2/FiO_2 ratio of 83mmHg. The Sequential Organ Failure Assessment (SOFA) score was 7(respiratory 4, cardiovascular 3).

Methylprednisolone 40 mg once daily was given for 5 days for anti-inflammatory purposes. Metagenomic next-generation sequencing (mNGS) of bronchoalveolar lavage fluid was performed using the IDseq™ Ultra platform (Captive Bioscience), a capture-based metagenomic assay designed for high-sensitivity pathogen detection. The sample was processed using the full workflow protocol. Tropheryma whipplei was identified with 10,581 reads and a relative abundance of 64.1%. The anti-infective regimen was adjusted to meropenem, combined with nintedanib for anti-fibrotic therapy. Follow-up chest imaging showed improvement (Figure 1). On Day 10, extubation was performed, and

meropenem was de-escalated to ceftriaxone. On Day 18, the patient was transferred to the respiratory medicine department. On day 23, the patient developed fever (maximum 38.5°C). By day 25, shortness of breath worsened with oxygen saturation dropping to 65%, prompting readmission to the ICU, where invasive mechanical ventilation was initiated. Mechanical ventilation was set to A/C mode with a tidal volume of 420 mL, respiratory rate of 14 breaths/min, PEEP of 14 cmH_2O, and FiO_2 of 1.0. Arterial blood gas analysis revealed a PaO_2/FiO_2 ratio of 78 mmHg, meeting the Berlin criteria for severe ARDS.The SOFA score was 8(respiratory 4, cardiovascular 4). Considering the possibility of Tropheryma whipplei relapse and co-infection with other pathogens, the anti-infective regimen was adjusted to meropenem, voriconazole, and sulfonamide. The patient developed severe hypercapnia, with the highest recorded carbon dioxide level reaching 141 mmHg. Management included optimization of ventilator settings, measures to reduce carbon dioxide production and oxygen consumption, and administration of methylprednisolone 200 mg daily for 5 days, followed by a gradual taper. Bronchoalveolar lavage fluid culture identified Aspergillus. Following treatment, the patient's condition gradually improved. Repeat chest CT showed resolution of the pulmonary lesions (Figure 1). Extubation was performed on day 38. The patient was transferred to the respiratory medicine department on day 46 and discharged on day 60. Oral therapy with faropenem, sulfonamide, voriconazole, corticosteroids, and nintedanib was continued at outpatient follow-up.

On day 82, the patient presented to a local hospital with abdominal pain and was diagnosed with cholecystolithiasis, for which medical management was initiated. On day 84, he developed shortness of breath without accompanying cough or fever, prompting transfer to the local Hospital. Chest CT performed at the local hospital revealed severe pneumonia (Figure 1), and the patient was subsequently transferred to ICU. He presented with tachypnea and a peripheral oxygen saturation of 66%, necessitating reintubation.Mechanical ventilation was set to A/C mode with a tidal volume of 420 mL, PEEP of 14 cmH_2O, and FiO_2 of 1.0. Arterial blood gas analysis revealed a PaO_2 of 68 mmHg, resulting in a PaO_2/FiO_2 ratio of 68 mmHg. Laboratory findings included: WBC12.99×10^9/L, NEUT% 89.4%, LYM% 7%, procalcitonin 2.686 ng/mL; liver function tests showed ALT 71 U/L and AST 130 U/L; renal function, coagulation profile, myocardial injury markers, and urinalysis were unremarkable. Arterial blood gas analysis revealed pH 7.195, PCO_2 58.6 mmHg, PO_2 58.1 mmHg, sodium 142 mmol/L, potassium 4.1 mmol/L, lactate 0.7 mmol/L, bicarbonate 22.7 mmol/L, and base excess -6.1 mmol/L. Echocardiography demonstrated mildly enlarged left atrium, mild mitral regurgitation, mild tricuspid regurgitation, trace pericardial effusion, and ejection fraction of 64%. Treatment was reinitiated with meropenem, voriconazole, sulfonamide antimicrobials, methylprednisolone 80 mg daily for anti-inflammatory effects, prone positioning ventilation, and lung recruitment maneuvers. Bronchoscopic examination revealed minimal white sputum and mNGS of bronchoalveolar lavage fluid returned negative, as did blood cultures. Despite interventions, the patient's condition deteriorated

progressively, with arterial blood gas analysis indicating severe hypoxemia, hypercapnia, and anuria, complicated by malignant arrhythmias. The family declined blood purification and extracorporeal membrane oxygenation therapy.

The patient died on day 86. The clinical course is summarized in Figure 2.

Literature Review

We conducted a systematic search of PubMed using the term “Tropheryma whipplei pneumonia” , which yielded approximately 86 results. After screening, we identified and carefully reviewed all case reports and case series with sufficient clinical data on pulmonary involvement. The key clinical characteristics, diagnostic approaches, treatments, and outcomes of these cases are now summarized in a structured Table 1, which has been incorporated into the revised manuscript.

As shown in Table 1 , among the 27 reviewed cases, the majority presented with pulmonary nodules or focal ground-glass opacities, and most patients survived with appropriate antibiotic therapy. However, severe cases requiring invasive mechanical ventilation were rare (only 4 cases, 14.8%), and recurrent episodes were documented in only 4 cases (14.8%), mostly attributed to inadequate treatment or secondary infections. Notably, none of the previously reported cases described three distinct episodes of ARDS with recurrent need for mechanical ventilation, as observed in our case.

Epidemiological Characteristics

Tropheryma whipplei (TW) is a Gram-positive bacterium and the primary causative agent of Whipple’s disease. Whipple’s disease is a rare disease worldwide. A marked gender disparity is observed in Whipple’s disease, with incidence significantly higher in males than in females[6-7]. This difference may be related to higher occupational or environmental exposure opportunities in males, as well as potential gender-based differences in immune function [9，20]. The age of onset is typically between 50 and

60 years, with an average age of approximately 52.6 years[13]. Disease manifestation in younger patients is often associated with immune dysfunction or a clear history of occupational or environmental exposure. Elderly individuals, users of immunosuppressive agents, and patients with tumors are commonly identified as susceptible populations [17]. TW is primarily transmitted via the fecal-oral route, and contact with contaminated soil or sewage represents a significant exposure risk factor[10]. Following infection, individuals may remain asymptomatic carriers, develop acute infections (such as pneumonia or gastroenteritis), or progress to chronic localized infection or even systemic Whipple's disease[8].

Clinical Manifestations

The clinical manifestations of Tropheryma whipplei infection are non-specific. The infection most frequently involves the gastrointestinal system, typically presenting with malabsorption-like symptoms such as abdominal pain, diarrhea, and weight loss[15-16]. Furthermore, the infection can affect multiple other organ systems, leading to systemic manifestations including arthralgia, lymphadenopathy, fever, and mental confusion[17].When the lungs are involved, patients may experience symptoms such as cough, dyspnea, and chest tightness[18-19]. Severe cases can rapidly progress to respiratory failure, often accompanied by systemic inflammatory responses like fever[18-20]. Notably, some patients may present with isolated pulmonary nodules on imaging, with cough and chest tightness being the predominant clinical features[15-16]. This presentation is easily mistaken for lung cancer, increasing the complexity of differential diagnosis.It is particularly important to note

that immunocompromised individuals often experience more severe disease, with more pronounced symptoms and a significantly higher risk of co-infection with other pathogens[22].

Imaging manifestations

The imaging manifestations of Tropheryma whipplei pneumonia are complex, diverse, and non-specific, making its diagnosis highly challenging[28]. Among these, pulmonary nodules are the most common imaging finding. They are typically solitary, measuring approximately 0.8 to 4.5 cm in diameter, often with ill-defined borders[29-30]. Some nodules may be accompanied by surrounding ground-glass opacity or internal calcification[30]. Notably, these nodules frequently exhibit increased metabolic activity on PET/CT, which can easily lead to a clinical misdiagnosis of malignancy[31].Other imaging presentations include patchy areas of pulmonary consolidation and ground-glass opacities. Some patients may present with small to moderate amounts of pleural effusion, as well as mediastinal and hilar lymphadenopathy—findings that are also readily mistaken for tumor metastasis[32]. In severe cases, imaging may reveal extensive bilateral pulmonary consolidation or even lung abscess formation. Furthermore, when co-infection with other pathogens is present, the imaging presentation can become even more complex and varied.

Diagnostic methods

The diagnosis of TW pneumonia requires a comprehensive evaluation based on clinical manifestations, imaging features, and etiologic evidence, with particular attention paid to the differentiation of atypical pneumonia. Clinically, the possibility

of this disease should be considered in the following scenarios: community-acquired pneumonia showing poor response to standard antibiotic therapy; pneumonia accompanied by multi-system manifestations such as arthralgia and diarrhea; recurrent or persistent pneumonia in immunocompromised patients; or a clear history of TW exposure[33]. Etiologic diagnosis primarily relies on PCR testing, which can amplify the 16S rRNA gene from bronchoalveolar lavage fluid, sputum, or blood samples, demonstrating high sensitivity and specificity[24]. Metagenomic next-generation sequencing is suitable for severe, complex, or mixed infection cases, as it can simultaneously identify pathogens and their antibiotic resistance genes[29]. Tissue immunohistochemistry and bacterial culture can serve as auxiliary diagnostic methods, although the long cultivation period limits their clinical utility. Differential diagnosis should focus on ruling out tuberculosis, non-tuberculous mycobacterial infections, fungal pneumonia, other bacterial pneumonias, and pulmonary involvement associated with rheumatic diseases[34-35].

Treatment and Management Strategies

Metagenomic next-generation sequencing has emerged as a powerful tool for diagnosing T. whipplei pneumonia, particularly in severe or immunocompromised cases, with reported sensitivity of 95.2% and specificity of 98.7% in respiratory specimens [25，35]. However, false-positive results may occur due to contamination, necessitating cautious interpretation. Currently, no standardized treatment guidelines exist, and therapy remains empirical. The core regimen consists of intravenous induction (meropenem or ceftriaxone for 14 days) followed by oral sequential therapy

with co-trimoxazole (0.96–1.92 g/day for 3–12 months) [36-37]. For patients intolerant to co-trimoxazole, tetracycline plus hydroxychloroquine may be used, with treatment extended to 12 months in immunocompromised or severe cases [38]. Therapeutic drug monitoring is recommended due to co-trimoxazole's narrow therapeutic window.

Discussion

We present a rare case of recurrent severe Tropheryma whipplei pneumonia in a 55-year-old male with type 2 diabetes mellitus, characterized by three distinct episodes of ARDS, secondary Aspergillus infection, and fatal outcome. This case offers several insights into the clinical spectrum of this uncommon pathogen.

Host factors

The patient's age, male sex, and history of diabetes align with the known epidemiology of T. whipplei infection, which predominantly affects middle-aged men and immunocompromised individuals . Diabetes-associated immune dysfunction likely contributed to impaired pathogen clearance and increased susceptibility to both primary infection and secondary opportunistic infections, such as the Aspergillus superinfection observed here [22, 39]. His 40-year smoking history may have caused chronic airway inflammation, potentially facilitating pathogen persistence.Although the patient had a history of psittacine exposure, testing for Chlamydia psittaci was negative, ruling out this important differential diagnosis in community-acquired pneumonia.

Severity and need for invasive mechanical ventilation

Unlike most reported cases of T. whipplei pneumonia, which typically follow an indolent course and do not require intensive care [9-10], our patient developed severe ARDS requiring invasive mechanical ventilation on three separate occasions. As summarized in Table 1, only a few of the reviewed cases necessitated invasive mechanical ventilation, all of which occurred in immunocompromised hosts (diabetes, myelodysplastic syndrome, or AIDS). Notably, none of the previously reported cases described a recurrent need for mechanical ventilation. Our case therefore represents an extreme phenotype of T. whipplei pneumonia, characterized by repeated episodes of respiratory failure requiring ICU admission and ultimately resulting in death.

Imaging findings and prognosis

The radiographic presentation in this case is strikingly unusual. While most reported cases present with solitary or multiple pulmonary nodules [4，26], our patient exhibited diffuse bilateral opacities meeting ARDS criteria on three separate occasions. As shown in Table 1, this pattern of diffuse bilateral opacities is exceedingly rare. Notably, nearly all patients with such severe pulmonary involvement died, suggesting that this severe radiographic phenotype may portend a poor prognosis. Our case is unique in that diffuse opacities recurred three times, a phenomenon not previously documented in the literature.

Recurrence mechanisms

The recurrent episodes in this case illustrate different underlying mechanisms. During the initial admission, the patient was hospitalized due to Tropheryma whipplei infection, and after anti-infective therapy, both clinical manifestations and

imaging findings improved significantly. The first recurrence on day 25 was considered to be caused by secondary Aspergillus infection, as confirmed by BALF culture, highlighting the increased risk of fungal coinfection in immunocompromised hosts receiving broad-spectrum antibiotics and corticosteroids.The second recurrence on day 84 warrants further analysis. After discharge, the patient had been taking antibacterial and antifungal medications regularly, and infection-related biomarkers were not significantly elevated. Although no definitive pathogen was detected, active infection was considered unlikely. While persistent T. whipplei infection cannot be entirely excluded, we consider IRIS following T. whipplei infection to be the more likely mechanism. This inference is based on the following observations. First, clinical deterioration occurred after effective pathogen clearance, which aligns with the typical temporal profile of IRIS. Second, both BALF and blood cultures at the time of recurrent dyspnea were negative for pathogens. Third, imaging findings showed non-specific diffuse opacities rather than focal recurrent infection. Additionally, the patient's underlying immunocompromised status—specifically diabetes—also increased the likelihood of IRIS. However, due to the lack of direct immunological data such as CD4 counts or cytokine profiling, this mechanism remains speculative, and further studies on IRIS following T. whipplei infection are warranted in the future.

Diagnostic and therapeutic challenges

Diagnosing T. whipplei pneumonia is difficult due to its non-specific presentation and rarity [13，20]. Conventional microbiological tests often fail to identify the

pathogen. In our patient, mNGS of BALF established the diagnosis, highlighting its value in atypical severe pneumonia. However, interpretation requires caution, as detection does not always distinguish infection from colonization].The high read count (10,581) and relative abundance (64.1%) in our case supported true infection.Therapeutically, no standardized guidelines exist [26]. Our patient initially responded to meropenem, but relapses underscore the difficulty of achieving sustained clearance in immunocompromised hosts. The use of faropenem as oral continuation therapy lacks robust evidence and may have been insufficient . Corticosteroids, while beneficial for ARDS, likely contributed to secondary Aspergillus infection—a known risk in immunocompromised patients receiving broad-spectrum antibiotics and steroids [31]. This case emphasizes the need for careful risk-benefit assessment and vigilant monitoring for secondary infections.

Conclusions

We report a case of T. whipplei pneumonia with three episodes of recurrent ARDS, secondary Aspergillus infection, and fatal outcome. These findings highlight the importance of considering this pathogen in severe community-acquired pneumonia, the diagnostic value of mNGS, and the need for vigilance against secondary fungal infections as well as careful corticosteroid use.

Ethical Approval and Consent to participate

This study was approved by the De Yang Peope’s Hospital (Approval Number: 2024-03-054-H01). This case report was conducted in accordance with the ethical standards of the institutional and national research committee and with the Helsinki

Declaration. Written informed consent for participation in clinical management and data collection was obtained from the patient's next of kin.

Consent for publication

Written informed consent for publication of the case details and any accompanying images was obtained from the patient's next of kin.

Availability of supporting data

The datasets generated and/or analysed during the current study are available in the NGDC BioProject database under the reference number PRJCA055098(https://ngdc.cncb.ac.cn/gsa/).

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by the 2026 Social Development Field Key Research and Development Guidance Project of the Deyang Municipal Science and Technology Bureau (Grant No. 2026SYCX015).

Clinical trial number

Not applicable.

Authors' contributions

JZ contributed to the clinical management, data collection, and drafting of the manuscript. YMX supervised the clinical care, revised the manuscript critically, and approved the final version. XLZ and MJW participated in the patient's management

and assisted in manuscript preparation. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References

1.Shan X, Li Z, Dong L. A case of pneumonia caused by infection with Tropheryma whipplei complicated by cryptococcus during treatment with a Janus kinase inhibitor: a case report. BMC Pulm Med. 2024 Dec 20;24(1):625.
2.Mottola G, Boucherit N, Trouplin V, et al. Tropheryma whipplei, the agent of Whipple's disease, affects the early to late phagosome transition and survives in a Rab5- and Rab7-positive compartment. PLoS One. 2014 Feb 24;9(2):e89367.
3.Huo Y, Wu C, Ma D. Application of metagenomic next-generation sequencing in the diagnosis and treatment of acute pneumonia caused by Tropheryma whipplei. BMC Pulm Med. 2025 Apr 30;25(1):207.
4.Shi J, Liu R, Qiu J, et al. Pulmonary infection caused by Tropheryma whipplei: a case report and review of the literature. J Med Case Rep. 2024 Dec 28;18(1):613.
5.Dolmans RA, Boel CH, Lacle MM, et al. Clinical Manifestations, Treatment, and Diagnosis of Tropheryma whipplei Infections. Clin Microbiol Rev. 2017 Apr;30(2):529-555.
6.Goyo D, Camacho A, Gómez C, et al. False-positive PCR detection of Tropheryma whipplei in cerebrospinal fluid and biopsy samples from a child with chronic lymphocytic meningitis. J Clin Microbiol. 2009 Nov;47(11):3783-4.
7.Algin A, Wegdam-Blans M, Verduin K, et al. Tropheryma whipplei aortic valve endocarditis, cured without surgical treatment. BMC Res Notes. 2012 Oct 30;5:600.
8.Bousbia S, Papazian L, Auffray JP, et al. Tropheryma whipplei in patients with pneumonia. Emerg Infect Dis. 2010 Feb;16(2):258-63.
9.Stein A, Doutchi M, Fenollar F, et al. Tropheryma whipplei pneumonia in a patient with HIV-2 infection. Am J Respir Crit Care Med. 2013 Oct 15;188(8):1036-7.
10.Wang H, Yang H. A case of acute community-acquired pneumonia caused by Tropheryma whipplei in pregnant woman without predisposing medical conditions. IDCases. 2024 Dec 6;39:e02123.
11.Zhang WM, Xu L. Pulmonary parenchymal involvement caused by Tropheryma whipplei. Open Medicine. 2021;16(1):843-846.
12.Lu Z, Zhang A, Guo J, Ni H. An unusual case of severe pneumonia caused by Tropheryma whipplei combined with Legionella pneumophila. World Journal of Emergency Medicine. 2023;14(6):492-494.
13.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.
14.Shen Y, Cui S, Teng X, et al. Acute pneumonia due to Tropheryma whipplei diagnosed by metagenomic next-generation sequencing and pathology: A case report. Heliyon. 2024;10:e26747.

15.Liu F, Yang X, He Z, et al. Using Targeted Next-Generation Sequencing to Diagnose Severe Pneumonia Due to Tropheryma Whipple and Human Metapneumovirus: A Case Report and Literature Review[J]. Infection and Drug Resistance, 2024, 17: 1863-1868.
16.Chen H, Zhao B, Yang J, et al. Case report: A patient with HHV-6 and HHV-7 combined with Whipple's trophoblast infection and streptococcal pneumonia. Frontiers in Medicine. 2024;11:1375325.
17.Li X, Feng Q, Yu H. A Rare Case of Concurrent Tropheryma Whipplei and Pneumocystis Jirovecii Pneumonia in a Patient During Endocrine Therapy for Breast Cancer. Infect Drug Resist. 2026 Feb 25;19:580235.
18.Yu M, Wang W, Chen W, et al. Diagnosis of Tropheryma whipplei pneumonia using targeted nanopore sequencing: a rare case report and literature review. Frontiers in Medicine. 2025;12:1556735.
19.Jin D, Li F, Fang J, et al. Severe pneumonia caused by Legionella pneumophila associated with Tropheryma whipplei: A case report. Medicine. 2025;104(28):e43121.
20.Li J, Guo B, Zhao G, et al. Protheryma whipplei in interstitial lung disease: A case series. Respiratory Medicine Case Reports. 2025;57:102279.
21.Fu Y, Zhou J, He P, et al. A Rare Case Report of Tropheryma Whipplei-Induced Acute Respiratory Distress Syndrome in an Immunocompetent Patient. Infection and Drug Resistance. 2025;18:1-6.
22.Sun X, Zhu H. Case Report: Whipple's disease pneumonia caused by inhalation of gas or liquid. Frontiers in Medicine. 2025;12:1664867.
23.Lv Y, Jiang G, Gao S, et al. Severe and Rapid Progression of Tropheryma whipplei-Related Pneumonia With Septic Shock: A Case Report. Respirol Case Rep. 2025 Jun 9;13(6):e70231.
24.Hu Y, Zhang J, Wang T, et al. Acute eosinophilic pneumonia with detection of pure Tropheryma whipplei in bronchoalveolar lavage fluid: a case report. Frontiers in Medicine. 2025;12:168384.
25.Sun X, Gong Q. A case report of AIDS complicated by Pneumocystis jirovecii and Tropheryma whipplei mixed pulmonary infection identified via metagenomic next-generation sequencing. Frontiers in Medicine. 2025;12:1599261.
26.Luo Y, Ding H, Pan J, et al. Use of metagenomic next-generation sequencing to diagnose Tropheryma whippleiinfection-related pneumonia: A case report. Exp Ther Med. 2026 Jan 21;31(3):75.
27.Chen J, Yang J, Zhang Y. Case Report: Rare pulmonary infection and cytomegalovirus retinitis revealed a case of lymphoma. Frontiers in Medicine. 2026;13:1732360.
28.Friebel J, Schinnerling K, Weigt K, et al. Uptake of Tropheryma whipplei by Intestinal Epithelia. Int J Mol Sci. 2023 Mar 24;24(7):6197.
29.Xu L, Li D. Lymphoma combined with Tropheryma whipplei infection: A case report and literature review. Medicine (Baltimore). 2025 Sep 19;104(38):e44611.
30.Du ZM, Chen P. Co-infection of Chlamydia psittaci and Tropheryma whipplei: A case report. World J Clin Cases. 2023 Oct 16;11(29):7144-7149.
31.Song X, Duan R, Duan L, et al. Current knowledge of the immune reconstitution inflammatory syndrome in Whipple disease: a review. Front Immunol. 2023 Oct 13;14:1265414.

32.Hofmann P, Durisch N, Buetikofer C, et al. Granulomatous lung disease and immune reconstitution inflammatory syndrome in Whipple's disease. BMJ Case Rep. 2021 Jun 18;14(6):e243633.
33.Yan J, Zhang B, Zhang Z, et al. Case Report: Tropheryma whipplei Hide in an AIDS Patient With Pneumocystis Pneumonia. Front Public Health. 2021 Aug 13;9:663093.
34.Zhu B, Tang J, Fang R, et al. Pulmonary coinfection of Mycobacterium tuberculosis and Tropheryma whipplei: a case report. J Med Case Rep. 2021 Jul 9;15(1):359.
35.Moter A, Schmiedel D, Petrich A, et al. Validation of an rpoB gene PCR assay for detection of Tropheryma whipplei: 10 years' experience in a National Reference Laboratory. J Clin Microbiol. 2013 Nov;51(11):3858-61.
36.Freeman HJ. Tropheryma whipplei infection. World J Gastroenterol. 2009 May 7;15(17):2078-80.
37.Gabus V, Grenak-Degoumois Z, Jeanneret S, et al. Tropheryma whipplei tricuspid endocarditis: a case report and review of the literature. J Med Case Rep. 2010 Aug 4;4:245.
38.Stojan G, Melia MT, Khandhar SJ, et al. Constrictive pleuropericarditis: a dominant clinical manifestation in Whipple's disease. BMC Infect Dis. 2013 Dec 9;13:579. doi: 10.1186/1471-2334-13-579.
39.Yoon S, Hong ME, Hong SA, et al. Prevalence estimation of Tropheryma whipplei in duodenal biopsy tissues of Koreans. Ann Clin Microbiol Antimicrob. 2024 Jan 3;23(1):2.

Figure 1 Serial chest CT findings over the clinical course.

Day 1(A1-A2):A1–A2 (lung window) show diffuse ground-glass opacities, consolidations, and reticular patterns(red arrows).A3 (mediastinal window) shows enlarged mediastinal lymph nodes (red arrows).

Day 10(B1-B3):Marked resolution of pulmonary opacities.

Day 25(C1-C3):Diffuse bilateral opacities reappear(red arrows).

Day48(D1-D3):Post-treatment CT demonstrated marked improvement.

Day84(E1-E3):Progression of bilateral pulmonary lesions(red arrows).

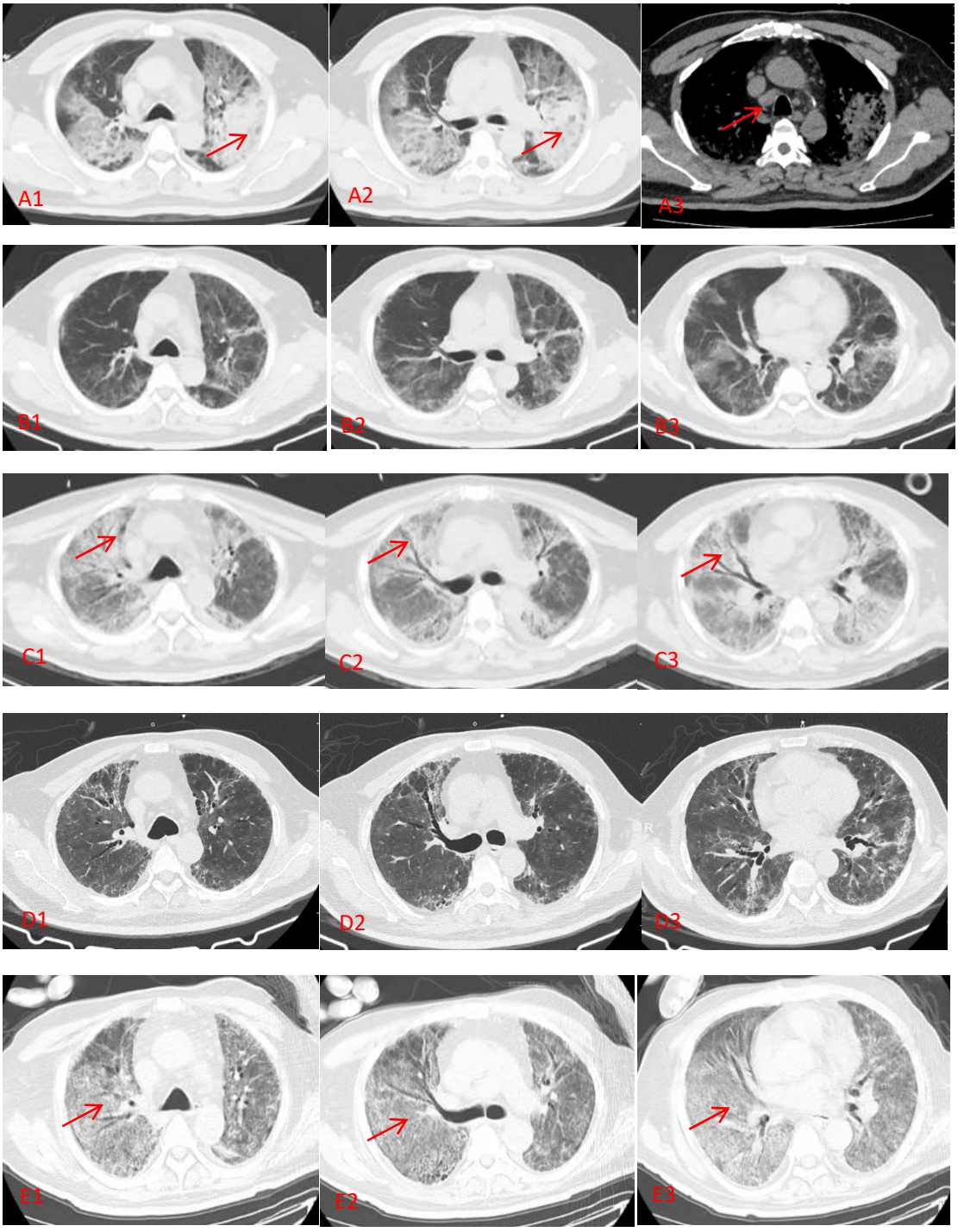
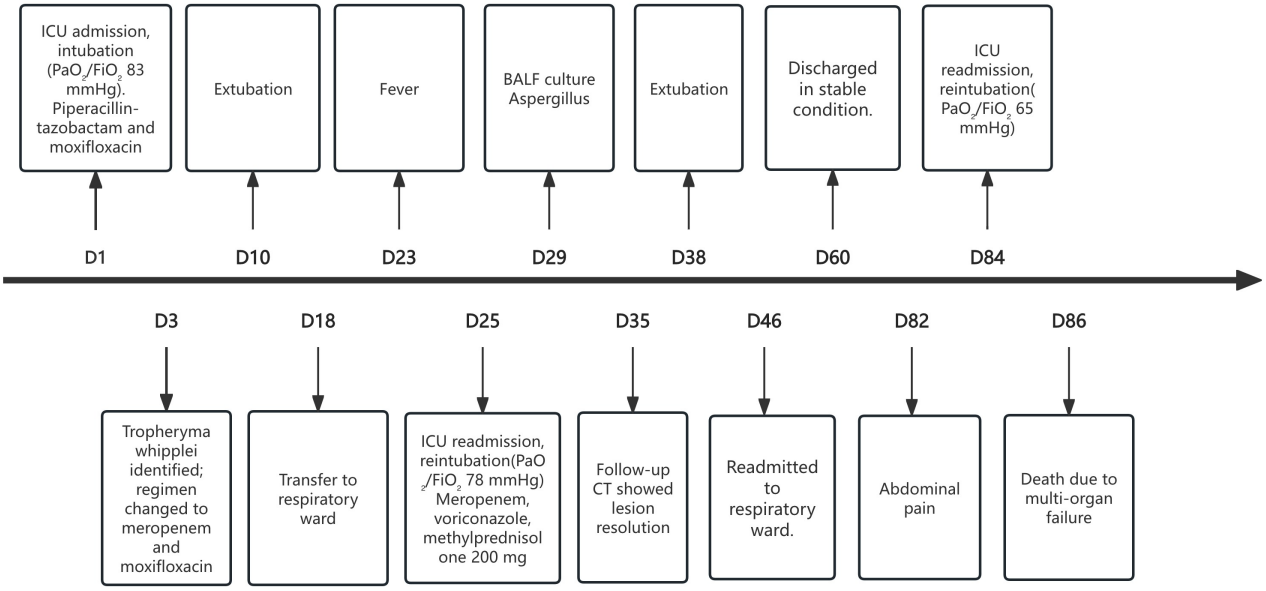


Figure 2 Clinical course and treatment timeline



Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1SummaryofreportedcasesofTropherymawh.docx