JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Case Report

Pleural effusion caused by *Rickettsia felis* infection

Hong Ren[1 #], Yingying Zhang[1 #], Xue Zhang[1 #], Hanwen Zhang[2], Li Chang[3], Lingyun Gao[1], Lin Li[1], Gaoyang Zhang[1]

[1] *Respiratory Ward 2, Harbin Chest Hospital, Heilongjiang, China*
[2] *Respiratory and Critical Care Medicine Department, Harbin Chest Hospital, Heilongjiang, China*
[3] *Tumor Ward 1, Harbin Chest Hospital, Heilongjiang, China*

# Authors contributed equally to this work.

Abstract

Introduction: *Rickettsia felis*, a Gram-negative obligate intracellular prokaryotic organism, causes human infections with atypical clinical presentations, commonly including fever, fatigue, headache, and maculopapular rash.

Case presentation: This study presents a rare case of pleural effusion (PE) associated with *R. felis* infection, confirmed through targeted next-generation sequencing (tNGS). The patient showed significant clinical improvement and resolution of PE following empirical moxifloxacin followed by pathogen-directed therapy with rifampicin and azithromycin, along with supportive measures for circulation and immune function.

Conclusions: This case report aims to enhance early diagnosis and therapeutic strategies for *R. felis* infections by sharing the diagnostic and management experience.

Key words: *Rickettsia felis*; PE; tNGS; case report.

J Infect Dev Ctries 2026; 20(8):1256-1259. doi:10.3855/jidc.21761

(Received 23 April 2025 – Accepted 06 March 2026)

Introduction

Rickettsia felis belongs to the genus *Rickettsia* and is classified as a Gram-negative prokaryote that obligately infects host cells through the cat fleas which are its primary vector [1]. However, other arthropods, including mosquitoes, ticks, and mites, may also serve as potential vectors [2,3]. Human infections always present with non-specific symptoms, such as fever, fatigue, headache, cough, phlegm production, nausea, vomiting, and maculopapular rash etc. [4,5]; which frequently lead to misdiagnosis and delayed treatment initiation. Serological assays are the most frequently used methods for diagnosing rickettsial infections, and are typically considered the gold standard [6]. However, these methods lack specificity for the diagnosis of *R. felis* infection [7,8]. Targeted next-generation sequencing (tNGS) represents an advanced high-throughput sequencing technology focusing on specific genomic regions that enhance detection sensitivity while minimizing interference from host nucleic acids [9]. Recent evidence supports its superiority over conventional methods in early detection of rickettsial diseases [10]. Notably, *R. felis*-associated pleural effusion (PE) is exceptionally rare [11,12].

Here, we present a confirmed case of *R. felis*-induced PE, diagnosed and managed at Harbin Medical University affiliated Harbin Chest Hospital, aiming to provide a reference for improving clinical recognition and management of similar cases.

Methodology

tNGS is based on multiplex polymerase chain reaction (PCR). The targeted primers for *R. felis* were primer 1, TGCTTATCGTTGTAAGGGCGA (forward) and TTGTCACTTGCTTGACGTGC (reverse); primer 2: GAGACGCTACGCAAACATGC (forward) and ACGCATTTGAATTCTGCCCG (reverse); and primer 3: GGTGAGCGGACGATTCAGTTA (forward) and TGACGCATTTGAATTCTGCCC (reverse). Blood (2–5 mL) was used for nucleic acid extraction with the PathoXtract® basic universal pathogen nucleic acid extraction kit (WYXM03211S, Willingmed, Beijing, China). cDNA synthesis, multiplex PCR pre-amplification of target sites, and library preparation were performed using the pathogen targeted detection kit (Willingmed, Beijing, China). Sequencing was carried out on the MGISEQ-200 platform (MGI, Shenzhen, China), with 0.1M sequencing data for each sample. Sequencing data were trimmed for adapters and filtered for low-quality reads using Fastp v0.20.1 based on default parameters. Species information was obtained by aligning with the reference database (NCBI GenBank/RefSeq/nt database) using Bowtie2 v2.4.1.

Case presentation

A 41-year-old female was admitted to the respiratory ward of Haerbin Chest Hospital on 7 June 2024 with the chief complaint of "left thoracic soreness accompanied by dull shoulder pain persisting over one week". One week prior to that, the patient experienced unexplained left chest and shoulder soreness and dull pain, without other discomforts. She took penicillin V potassium tablets (2 tablets, tid) orally for 2 days without symptomatic improvement. The patient opted for hospitalization due to her history of PE presenting with similar symptoms in the past. Since the onset of the disease, the patient only felt obvious fatigue. The patient had a pet dog, and had a history of left PE for more than one year. She denied any history of smoking and drinking.

Upon admission, the patient's body temperature was 36 °C, pulse rate was 100 beats/min, respiration count was 20 breaths/min, and blood pressure was 112/98 mmHg. The patient's general condition was good, with self-position, clear consciousness, fluent speech, stable breathing, and cooperation in physical examination. Auxiliary examinations conducted included pulmonary function tests demonstrating generally adequate ventilation capacity. Bronchodilation testing yielded negative results. The electrocardiogram results were abnormal, indicating sinus rhythm, left axis deviation, counterclockwise rotation, and ST-T changes. The results of blood routine tests showed normal red blood cell count (3.72×10^{12}/L), hemoglobin (131 g/L), white blood cell count (7.75×10^{9}/L), procalcitonin (PCT, 0.1 ng/mL) and C-reactive protein (CRP, < 3 mg/L). The blood coagulation combination (including prothrombin time, activated partial prothrombin time, thrombin time, fibrinogen, and D-dimer, etc.), various cytokines (including interleukin-2, interleukin-6, interferon γ, tumor necrosis factor α, etc.) and erythrocyte sedimentation rate (ESR, 14 mm/h) were normal. Lung computed tomography (CT) scans illustrated symmetrical bilateral thorax, mediastinal centralization, clarity surrounding bronchovascular bundles, and normal flows. Stripe shadows were seen in the right middle lobe and the left upper lobe, and calcified nodules were seen in the left lower lobe. The trachea and lobar bronchi were patent.

Given the minimal PE, the etiology was considered non-inflammatory. Tuberculous pleurisy was ruled out based on a purified protein derivative (PPD) induration of 8 mm, and malignant effusion was excluded due to normal tumor marker profiles. The initial diagnosis was left-sided PE. Accordingly, anti-infective therapy with piperacillin sodium and tazobactam sodium (4.5 g, q12h) was initiated.

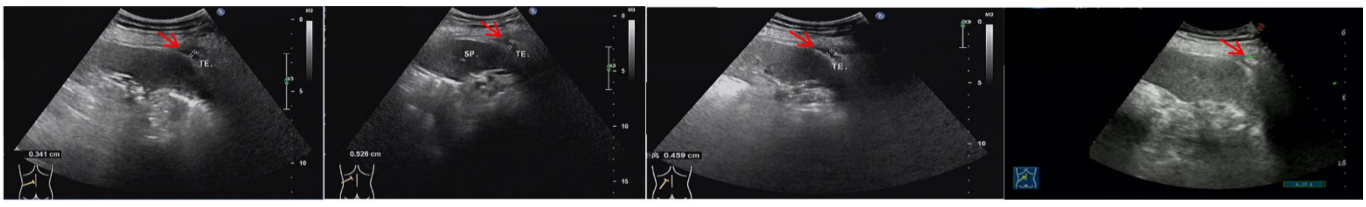
Serial chest ultrasound examinations were performed to monitor the left PE, which demonstrated initial stability (7 June), mild progression after empirical anti-inflammatory therapy for 11 days (17 June), partial absorption following moxifloxacin for 4 days (21 June), and eventual complete resolution after targeted anti-rickettsial treatment (16 July) (Figure 1).

Targeted anti-rickettsial therapy with rifampicin (0.45 g, qd) and azithromycin (Pfizer, Dalian, China) (0.25 g, qd) was initiated based on the definitive etiological evidence provided by blood tNGS, which detected concurrent *Staphylococcus aureus* (reads per ten million (RPTM) = 12) and *Rickettsia felis* (RPTM = 17) infections, along with the patient's history of potential exposure from working in a bathhouse and owning pet dogs.

Clinical improvement was observed within 1 week, with significant alleviation of left chest and shoulder pain. Repeat blood tNGS reported only *Staphylococcus aureus* (RPTM = 3), with no detectable *R. felis*.

This study presents a relatively rare case of PE caused by *R. felis* infection, which may provide a reference for the diagnosis of this pathogen. However, the study has several limitations. First, due to the patient's financial constraints, other etiological tests, including serological assays and PCR, were not performed. Consequently, the validity of the tNGS result was confirmed indirectly by the patient's positive response to subsequent targeted antimicrobial therapy. Second, although the patient's condition improved after

Figure 1. Serial chest ultrasound images demonstrating the dynamic changes of left PE throughout the diagnosis and treatment course.



TE: pleural effusion (red arrow); SP: spleen.

initial treatment with moxifloxacin. The drug regimen was changed to more conventional targeted agents once the etiological diagnosis was established. Therefore, the therapeutic efficacy of moxifloxacin against *R. felis* infection was only partially evaluated in this case and requires further investigation.

Discussion

R. felis is an emerging rickettsial pathogen. The incidence of *R. felis* remains scarce in China [13]. Clinical diagnosis of *R. felis* infections poses significant challenges due to atypical symptoms. A systematic review of PE caused by *Rickettsia infection* in Italy did not find any cases related to *R. felis* infection [11]. Only one study in mainland China identified two female patients who developed *R. felis*-related PE [12]. Unlike the clinical manifestations of the two patients who presented with fever, elevated CRP, and rash; our patient exhibited only chest and shoulder pain with normal inflammatory markers, making the presentation highly atypical. The absence of clear risk factors, such as a history of arthropod bites, further compounded the diagnostic challenge, underscoring the rarity and diagnostic difficulty of this manifestation.

PE can occur in patients with tuberculosis, malignant tumors, rheumatism, or heart failure, etc. Tuberculous PE is typically an exudate with yellow appearance and elevated protein content, often accompanied by systemic symptoms such as fever, fatigue, and night sweats [14]. PE caused by malignant tumors is mostly bloody, grows rapidly, and contains tumor cells [15,16]. Inflammatory PE usually presents with a small volume and tends to resolve with anti-inflammatory therapy [17]. In this case, the patient showed no signs of tuberculous poisoning, and imaging revealed no evidence of tuberculous or malignancy. There was also no history, or manifestations of heart disease or rheumatic conditions. Although the small volume of PE was initially suggestive of an inflammatory etiology, the patient's symptoms did not improve after two weeks of systemic anti-inflammatory treatment, effectively ruling out these common causes. The PE resolved completely after targeted treatment for *R. felis*. Routine pathogen testing could not be performed on pleural fluid or sputum samples due to the minimal amount of PE and absence of sputum. The patient had a long-term occupational history in a bathhouse environment and contact with pet dogs, which are potential hosts for the primary vectors of *R. felis*—cat fleas [18,19]. Considering these factors, the patient was ultimately diagnosed with PE, secondary to *R. felis* infection.

Currently, tetracycline derivatives, primarily doxycycline, are regarded as the most effective antibacterial agents for treating rickettsial infections [20]. Other agents, including rifampin, erythromycin, azithromycin, quinolones, and tigecycline, have also demonstrated effectiveness [21]. Specific quinolones like moxifloxacin and ciprofloxacin are reported to be effective and are considered valuable alternative options [22,23]. In this study, empirical treatment with moxifloxacin for 4 days led to some absorption of the PE, before the infectious etiology was confirmed. Doxycycline was primarily considered after diagnosis of *R. felis* infection; but the patient refused it due to concerns about side-effects including photosensitivity and the potential for sunburn and skin pigmentation [24]. Following empirical treatment with moxifloxacin and subsequent targeted therapy with rifampin and azithromycin, subsequent tNGS tests for *R. felis* returned negative results. This case indicates that moxifloxacin, rifampin, and azithromycin are viable options for anti-rickettsial therapy.

Conclusions

tNGS is an effective method for timely and effective diagnosis of *R. felis* infection. Infection with *R. felis* can cause PE. Moxifloxacin, rifampicin, and azithromycin are viable options for effective treatment strategies.

Acknowledgements

The authors thank all the clinicians, microbiologists, and radiologists who have assisted with this research.

Ethics statement

The studies involving humans were approved by the ethics committee of Harbin Chest Hospital (No. 2025-22). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent was obtained from the patient for the publication of any potentially identifiable images or data included in this article. This manuscript adheres to the CARE checklist for case reports.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions

Conception and design, HR, YZ, XZ: collection and assembly of data; HZ, LC: provision of study materials or patients; LG, LL: data analysis and interpretation; GZ: manuscript writing; all authors: final approval of the manuscript.

Corresponding author
Hong Ren, MM.
No. 417, Xianfeng Road, Dao Wai District,
Harbin 150056, China.
Tel: +86-13946194616
Email: hrbxkyy02@hrbxkyy.org.cn

Conflict of interest
No conflict of interest is declared.

References
1. Adams JR, Schmidtmann ET, Azad AF (1990) Infection of colonized cat fleas, *Ctenocephalides felis* (Bouché), with a rickettsia-like microorganism. Am J Trop Med Hyg 43: 400–409. doi: 10.4269/ajtmh.1990.43.400.
2. Dieme C, Bechah Y, Socolovschi C, Audoly G, Berenger JM, Faye O, Raoult D, Parola P (2015) Transmission potential of *Rickettsia felis* infection by *Anopheles gambiae* mosquitoes. Proc Natl Acad Sci USA 112: 8088–8093. doi: 10.1073/pnas.1413835112.
3. Scarpulla M, Barlozzari G, Marcario A, Salvato L, Blanda V, De Liberato C, D'Agostini C, Torina A, Macrì G (2016) Molecular detection and characterization of spotted fever group rickettsiae in ticks from Central Italy. Ticks Tick Borne Dis 7: 1052–1056. doi: 10.1016/j.ttbdis.2016.06.003.
4. Maina AN, Knobel DL, Jiang J, Halliday J, Feikin DR, Cleaveland S, Ng'ang'a Z, Junghae M, Breiman RF, Richards A L, Njenga MK (2012) *Rickettsia felis* infection in febrile patients, western Kenya, 2007-2010. Emerg Infect Dis 18: 328–331. doi: 10.3201/eid1802.111372.
5. Angelakis E, Mediannikov O, Parola P, Raoult D (2016) *Rickettsia felis*: the complex journey of an emergent human pathogen. Trends Parasitol 32: 554–564. doi: 10.1016/j.pt.2016.04.009.
6. La Scola B, Raoult D (1997) Laboratory diagnosis of rickettsioses: current approaches to diagnosis of old and new rickettsial diseases. J Clin Microbiol 35: 2715–2727. doi: 10.1128/jcm.35.11.2715-2727.1997.
7. Fang R, Raoult D (2003) Antigenic classification of *Rickettsia felis* by using monoclonal and polyclonal antibodies. Clin Diagn Lab Immunol 10: 221–228. doi: 10.1128/CDLI.10.2.221-228.2003.
8. Raoult D, La Scola B, Enea M, Fournier PE, Roux V, Fenollar F, Galvao MA, de Lamballerie X (2001) A flea-associated *Rickettsia* pathogenic for humans. Emerg Infect Dis 7: 73–81. doi: 10.3201/eid0701.010112.
9. Wylie TN, Wylie KM, Herter BN, Storch GA (2015) Enhanced virome sequencing using targeted sequence capture. Genome Res 25: 1910–1920. doi: 10.1101/gr.191049.115.
10. Stewart AG, Stewart AGA (2021) An update on the laboratory diagnosis of *Rickettsia* spp. infection. Pathogens 10: 1319. doi: 10.3390/pathogens10101319.
11. Guccione C, Rubino R, Colomba C, Anastasia A, Caputo V, Iaria C, Cascio A (2022) Rickettsiosis with pleural effusion: a systematic review with a focus on rickettsiosis in Italy. Trop Med Infect Dis 7: 11. doi: 10.3390/tropicalmed7010011.
12. Teng Z, Zhao N, Ren R, Zhang X, Du Z, Wang P, Qin T. (2022) Human *Rickettsia felis* infections in Mainland China. Front Cell Infect Microbiol 12: 997315. doi: 10.3389/fcimb.2022.997315.
13. Lappin MR (2018) Update on flea and tick associated diseases of cats. Vet Parasitol 254: 26–29. doi: 10.1016/j.vetpar.2018.02.022.
14. Chiang SS, Starke JR (2018) 134 - *Mycobacterium tuberculosis*. In Long SS, Prober CG, Fischer M, editors. Principles and Practice of Pediatric Infectious Diseases. Fifth Edition. Elsevier. 790–806.e5. doi: 10.1016/B978-0-323-40181-4.00134-1.
15. Gonnelli F, Hassan W, Bonifazi M, Pinelli V, Bedawi EO, Porcel JM, Rahman NM, Mei F (2024) Malignant pleural effusion: current understanding and therapeutic approach. Respir Res 25: 47. doi: 10.1186/s12931-024-02684-7.
16. Pardessus Otero A, Rafecas-Codern A, Porcel JM, Serra-Mitjà P, Ferreiro L, Botana-Rial M, Ramos-Hernández C, Brenes JM, Canales L, Camacho V, Romero-Romero B, Trujillo JC, Martinez E, Cases E, Barba A, Majem M, Güell E, Pajares V (2024) Malignant pleural effusion: a multidisciplinary approach. Open Respir Arch 6: 100349. doi: 10.1016/j.opresp.2024.100349.
17. Krishna R, Antoine MH, Alahmadi MH, M R (2025) Pleural effusion. Treasure Island (FL): StatPearls Publishing. Available: https://www.ncbi.nlm.nih.gov/books/NBK448189/. Accessed: 28 February 2025.
18. Edouard S, Bhengsri S, Dowell SF, Watt G, Parola P, Raoult D (2014) Two human cases of *Rickettsia felis* infection, Thailand. Emerg Infect Dis 20: 1780–1781. doi: 10.3201/eid2010.140905.
19. Brown LD, Macaluso KR (2016) *Rickettsia felis*, an emerging flea-borne rickettsiosis. Curr Trop Med Rep 3: 27–39. doi: 10.1007/s40475-016-0070-6.
20. Rolain JM, Stuhl L, Maurin M, Raoult D (2002) Evaluation of antibiotic susceptibilities of three rickettsial species including *Rickettsia felis* by a quantitative PCR DNA assay. Antimicrob Agents Chemother 46: 2747–2751. doi: 10.1128/AAC.46.9.2747-2751.2002.
21. Colomba C, Saporito L, Polara VF, Rubino R, Titone L (2006) Mediterranean spotted fever: clinical and laboratory characteristics of 415 Sicilian children. BMC Infect Dis 6: 60. doi: 10.1186/1471-2334-6-60.
22. Schulze MH, Keller C, Müller A, Ziegler U, Langen HJ, Hegasy G, Stich A (2011) *Rickettsia typhi* infection with interstitial pneumonia in a traveler treated with moxifloxacin. J Clin Microbiol 49: 741–743. doi: 10.1128/JCM.01201-10.
23. Alioua Z, Bourazza A, Lamsyah H, Erragragui Y, Boudi O, Karouach K, Ghfir M, Mossedaq R, Sedrati O (2003) [Neurological feature of Mediterranean spotted fever: a study of four cases]. Rev Med Interne 24: 824–829. [Article in French]. doi: 10.1016/j.revmed.2003.08.002.
24. Simman R, Raynolds D (2012) Skin hypersensitivity to sun light due to doxycycline ingestion causing hand partial-thickness burn. J Am Coll Clin Wound Spec 4: 16–17. doi: 10.1016/j.jccw.2013.01.005.