Tropical Biomedicine 43(2): 219-222 (2026)
https://doi.org/10.47665/tb.43.2.012

CASE REPORT

Unmasking *Bartonella henselae*: A forgotten cause of hepatosplenic and marrow involvement

Zainulabid, U.A.[1], Cheong, X.K.[2*], Kori, N.[2], Kueh, J.W.T.[3], Mohamed Rose, I.[3], Ramli, R.[4], Abdul Muien, M.Z.[2,5], Periyasamy, P.[2], Ramli, S.R.[6]

[1]Department of Internal Medicine, Kulliyyah of Medicine, International Islamic University Malaysia, 25200 Kuantan, Pahang, Malaysia
[2]Department of Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia, 56000 Cheras, Kuala Lumpur, Malaysia
[3]Histopathology Unit, Department of Laboratory Diagnostic Services, Hospital Canselor Tuanku Muhriz, 56000 Cheras, Kuala Lumpur, Malaysia
[4]Bacteriology Unit, Department of Laboratory Diagnostic Services, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia, 56000 Cheras, Kuala Lumpur, Malaysia
[5]Department of Radiology, Faculty of Medicine and Health Science, Universiti Malaysia Sabah, 88400 Kota Kinabalu, Sabah, Malaysia
[6]Bacteriology Unit, Infectious Disease Research Centre (IDRC), National Institutes of Health (NIH), 40170 Shah Alam, Selangor, Malaysia
*Corresponding author: cheongxk@gmail.com

ARTICLE HISTORY

Received: 31 October 2025
Revised: 27 May 2026
Accepted: 27 May 2026
Published: 30 June 2026

ABSTRACT

Bartonella henselae is an uncommon but important cause of prolonged pyrexia of unknown origin (PUO) and hepatosplenomegaly. Conventional diagnostic tools often fail in disseminated disease, leading to delayed or missed diagnoses. We report a 60-year-old man with PUO, progressive weight loss, and hepatosplenomegaly. Clinical suspicion, guided by significant cat exposure, led to molecular confirmation of *B. henselae* infection after conventional workup proved inconclusive. Liver biopsy revealed pleomorphic rod-shaped organisms on Warthin-Starry staining, while real-time PCR targeting the *rpoB* gene and conventional PCR targeting the *gltA* gene performed on bone marrow aspirate confirmed disseminated bartonellosis. The patient responded well to prolonged doxycycline and rifampicin therapy, achieving near-complete recovery. This case underscores the importance of clinical vigilance, histological clues, and molecular diagnostics in identifying rare but treatable infections.

Keywords: *Bartonella henselae*; cats; bacillary peliosis; hepatosplenomegaly; pyrexia of unknown origin.

INTRODUCTION

Bartonella henselae is a fastidious, facultative intracellular Gram-negative bacillus transmitted primarily through scratches or bites from cats and occasionally via the cat flea (*Ctenocephalides felis*) (Okaro *et al*., 2021). Although most commonly linked to cat scratch disease (CSD), it can cause severe disseminated infections in both immunocompromised and immunocompetent hosts. Hepatosplenic involvement with bone marrow infiltration, including the vasculoproliferative entity known as bacillary peliosis, may mimic other systemic conditions such as tuberculosis, lymphoma, or histoplasmosis (Steed *et al*., 2022).

In Malaysia, CSD is an under-recognised but nationally distributed zoonosis. A five-year retrospective serosurvey by Zabari *et al*. examining 3,525 samples from suspected CSD patients across government and private hospitals between 2015 and 2019 reported *B. henselae* seropositivity by indirect immunofluorescence assay, with the highest rates in Selangor (23%), Sabah (12%), and Johor (11%) (Zabari *et al*., 2025). Axillary or inguinal lymphadenopathy and fever were identified as significant risk factors for seropositivity. Notably, these figures likely underestimate the true burden, as serological assays have variable sensitivity, particularly in disseminated disease, where low antibody titres or immune complex formation may yield false-negative results.

Despite its clinical significance, *B. henselae* remains under-recognised in practice. Routine cultures are frequently negative due to the organism's slow growth and fastidious nutritional requirements, while histopathological staining with Warthin-Starry can suggest the diagnosis but lacks specificity. Advanced molecular diagnostics, including polymerase chain reaction (PCR) with optional Sanger sequencing of the amplified product and metagenomic next-generation sequencing (mNGS), have therefore become essential tools for definitive confirmation (Li *et al*., 2022; Peng *et al*., 2020).

We report a case of disseminated *B. henselae* infection in an immunocompetent adult presenting with prolonged fever and massive hepatosplenomegaly, in which molecular diagnostics established the diagnosis after conventional methods failed.

CASE REPORT

A 60-year-old Malay man with a background history of hypertension, hyperlipidemia, and gout presented with a two-month history of intermittent fever and progressive abdominal distension. The fever episodes were mostly nocturnal, occurring around 7.30 pm, and were documented at 38°C. He also described an intermittent dry cough and a sensation of abdominal bloatedness.

On physical examination, he appeared ill but was afebrile at the time of review. Cardiovascular assessment revealed a systolic

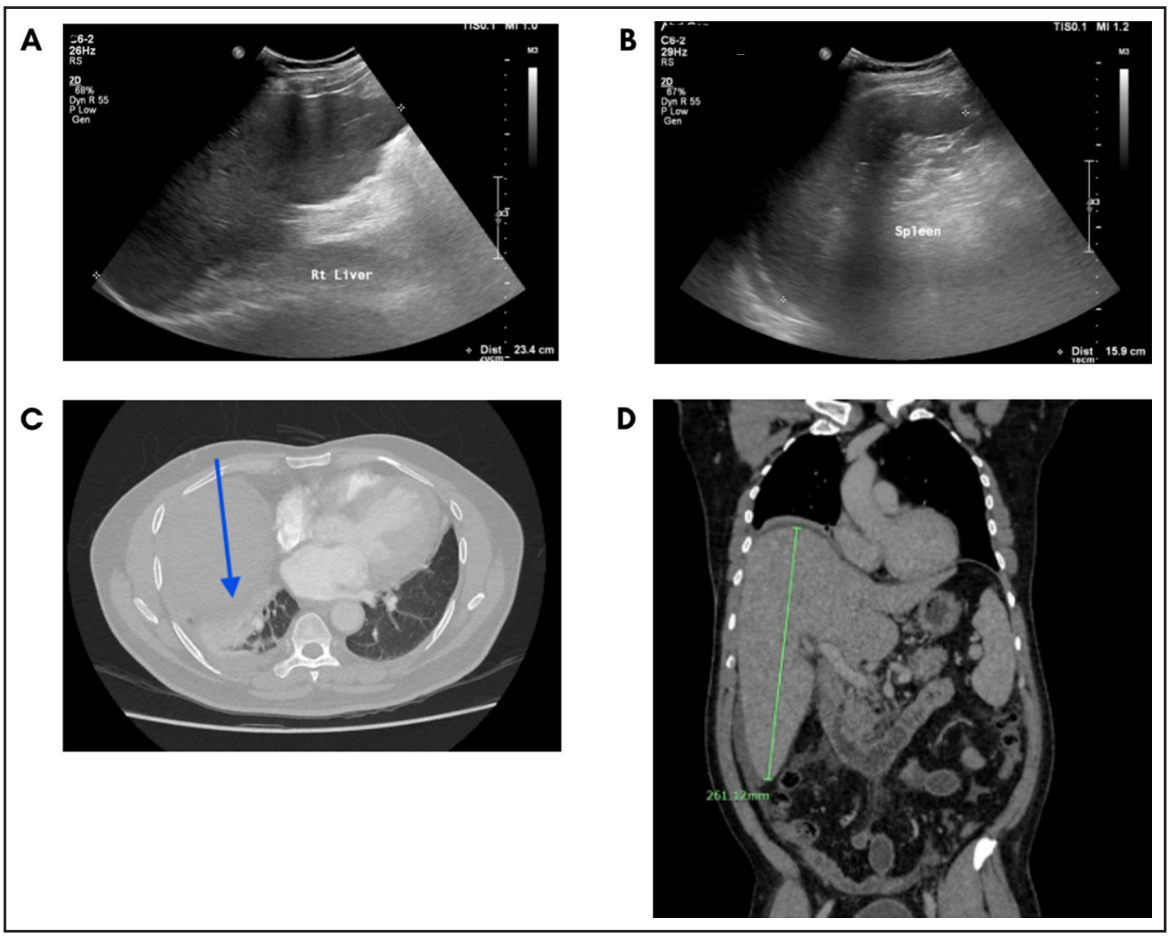

Figure 1. Serial imaging findings. (A) Abdominal ultrasound showing a grossly enlarged liver (23.4 cm in midclavicular length) with no focal lesions or ductal dilatation. Minimal ascites noted at the liver tip, (B) Splenic ultrasound revealing splenomegaly (15.9 cm) with no focal lesions. Splenic parenchyma appears normal, homogenous, and maintains preserved echotexture. No microabscesses detected on high-frequency transducer imaging, (C) Axial CT scan (lung window) demonstrating adjacent collapse consolidation in the right subdiaphragmatic recess (blue arrow) with minimal pleural effusion, (D) Contrast-enhanced coronal CT scan showing massive hepatomegaly (26.1 cm in length) with minimal ascites at the liver tip. Right pleural effusion and collapse consolidation in the right lower lobe are also noted.

murmur at the left lower sternal edge, and abdominal examination demonstrated gross hepatosplenomegaly without tenderness. His laboratory tests showed leukocytosis with a white cell count of 13.4 × 10^9/L (neutrophils 73.1%, eosinophils 6.3%), a hemoglobin level of 11.3 g/dL, and a platelet count of 180 × 10^9/L. Biochemical studies revealed an albumin level of 41 g/L, ALT of 41 U/L, AST of 4 U/L, ALP of 296 U/L, and GGT of 537 U/L. His serum creatinine was 98.1 µmol/L. Inflammatory markers were elevated, with an ESR of 48 mm/hr and a CRP of 89.9 mg/L.

Imaging further delineated the extent of his illness. An abdominal ultrasound demonstrated massive hepatomegaly with minimal ascites (Figure 1A) and splenomegaly measuring 15.9 cm with preserved echotexture (Figure 1B). A contrast-enhanced CT scan confirmed hepatomegaly extending to 26.1 cm, with right-sided pleural effusion and collapse consolidation in the right lower lobe (Figure 1C-D). Transthoracic echocardiography showed thickened aortic and mitral valves with mild mitral regurgitation and trivial tricuspid regurgitation.

A crucial epidemiological clue emerged when his daughter disclosed his history of close contact with approximately 15 unvaccinated cats at his sister's home. This raised the suspicion of zoonotic infection and prompted the treating team to request *B. henselae* PCR as part of the extended workup.

Subsequently, both a liver biopsy and bone marrow examination were performed. Most liver biopsy samples were unremarkable, but one section, serendipitously stained with Warthin-Starry, revealed pleomorphic rod-shaped organisms (Figure 2).

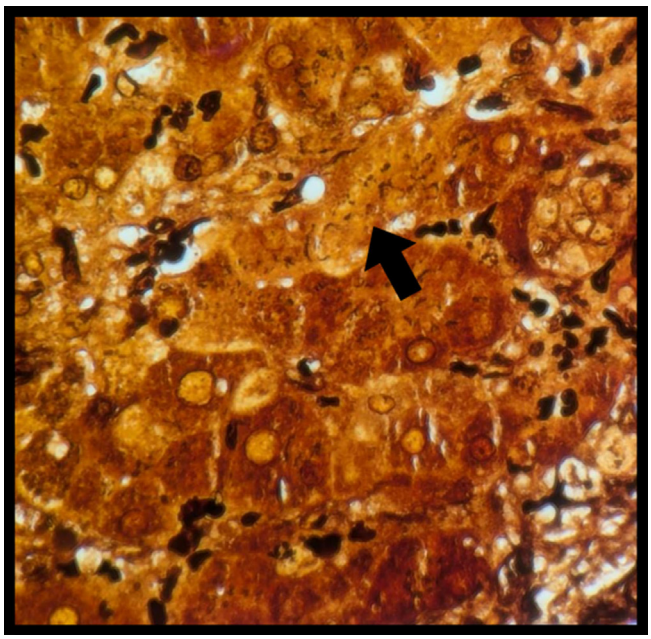

Figure 2. Liver biopsy. Warthin-Starry stain demonstrating scattered, darkly stained, pleomorphic, short rod-shaped organisms, averaging 5 µm in length, against a yellowish background of hepatocytes.

Bone marrow aspirate and trephine biopsy specimens were obtained under aseptic conditions. A portion of the specimen was subjected to molecular testing for detection of *Bartonella* species. Genomic DNA was extracted using the QIAamp DNA Mini Kit (Qiagen, Germany) according to the manufacturer's protocol and stored at –40°C until analysis.

Detection of *Bartonella* DNA was performed using both a commercial real-time polymerase chain reaction (qPCR) assay targeting the β-subunit of RNA polymerase (*rpoB*) gene and an in-house conventional PCR (cPCR) assay targeting the citrate synthase (*gltA*) gene. The qPCR was carried out according to the manufacturer's instructions (BioPerfectus, China) on a QuantStudio 6 Flex Real-Time PCR System (Thermo Fisher Scientific, USA). The in-house cPCR was performed based on the method described by Billeter *et al*. with slight modifications (Billeter *et al*., 2011). Briefly, a 25 µL reaction mixture was prepared containing 10 µL master mix (PCR Biosystems, USA), 1 µL of each primer, 5 µL of template DNA, and 8 µL of water. Amplification was carried out on a Mastercycler Nexus X2 (Eppendorf, Netherlands) under the following cycling conditions: initial denaturation at 95°C for 2 minutes, followed by 45 cycles of denaturation at 95°C for 15 seconds, annealing at 60°C, and extension at 72°C for 1 minute, with a final extension at 72°C for 10 minutes.

PCR products were analysed on a 1.5% agarose gel and visualised using the Bio-Rad ChemiDoc Touch Imaging System (Bio-Rad, USA). The presence of a 790 bp band was considered indicative of *Bartonella* spp. Positive PCR products were subsequently confirmed by Sanger sequencing (Apical Scientific, Malaysia), and the obtained sequences were deposited in GenBank (accession number PZ379614). Both assays identified *B. henselae*, corroborating the diagnosis of disseminated bartonellosis. Interestingly, concurrent serological testing for *Bartonella* IgM and IgG antibodies returned negative, underscoring the limitation of serology in disseminated disease.

In light of these findings, he commenced a treatment regimen of doxycycline and rifampicin. He completed six months of therapy, during which his fever resolved and inflammatory markers normalised.

DISCUSSION

B. henselae is a fastidious, facultative intracellular Gram-negative bacillus transmitted primarily through scratches or bites from cats and occasionally via cat fleas (*Ctenocephalides felis*) (Okaro *et al*., 2021). Beyond classical cat scratch disease, *B. henselae* can cause disseminated infection involving the liver, spleen, bone marrow, and endocardium in both immunocompromised and immunocompetent individuals (Bullard *et al*., 2024). Disseminated disease in otherwise healthy hosts, such as in this case, is increasingly recognised but remains diagnostically challenging due to its nonspecific clinical and laboratory features (Cardoso *et al*., 2025).

The patient's presentation with prolonged pyrexia of unknown origin, hepatosplenomegaly, and raised inflammatory markers necessitated systematic exclusion of several conditions before a diagnosis of disseminated bartonellosis could be established. Tuberculosis was an early consideration given its endemicity in Malaysia, but the absence of pulmonary infiltrates or caseating granulomas on liver histology, combined with the overall clinical trajectory, favoured an alternative diagnosis. Lymphoma was similarly entertained in view of the massive organomegaly and weight loss; however, the lack of peripheral lymphadenopathy and the absence of malignant infiltration on bone marrow histology argued against this. Brucellosis, while a recognised cause of prolonged fever and hepatosplenomegaly, was considered unlikely given the absence of occupational livestock exposure or consumption of unpasteurised dairy products in this patient. Autoimmune conditions, including systemic lupus erythematosus and adult-onset Still's disease, were excluded on the basis of absent supportive clinical and serological features. The identification of pleomorphic rod-shaped organisms on Warthin-Starry staining of the liver biopsy, in the context of significant cat exposure, ultimately directed the diagnostic workup toward bartonellosis, which was confirmed molecularly.

Bacillary peliosis, the vasculoproliferative lesion classically linked to *Bartonella*, is not confined to the liver. It can also affect the spleen, lymph nodes, and bone marrow due to the organism's predilection for endothelial and erythrocytic progenitor cells (Muttineni *et al*., 2025). Histologically, these lesions exhibit sinusoidal dilation and blood-filled cystic spaces. Pathogenesis is mediated by endothelial proliferation driven by vascular endothelial growth factor (VEGF) and hypoxia-inducible factor-1 (HIF-1) activation (Harms & Dehio, 2012). In our patient, hepatosplenomegaly without abscesses or cholestasis suggested an infiltrative, vasculoproliferative process rather than necrotizing infection.

Routine cultures have low sensitivity because *Bartonella* requires prolonged incubation and specific media (Lins *et al*., 2024). Serological assays, while convenient, show variable sensitivity and may yield false-negative results in disseminated or endovascular disease due to low antibody titres or immune complex formation (Cardoso *et al*., 2025). In this case, both *B. henselae* IgM and IgG serology were negative. Histopathological examination provided the first clue: pleomorphic bacilli visible on Warthin-Starry staining of the liver biopsy, though nonspecific, directed further molecular testing.

Molecular assays have become the gold standard for confirmation. PCR amplification of the citrate synthase (*gltA*) gene by conventional PCR and real-time PCR targeting the *rpoB* gene enable rapid, sensitive detection from tissue or bone marrow samples, even in seronegative cases (Bai *et al*., 2023). In our patient, both qPCR targeting *rpoB* and in-house cPCR targeting *gltA* from bone marrow aspirate confirmed *B. henselae* infection, with results corroborated by Sanger sequencing, establishing the diagnosis of disseminated bartonellosis involving the hepatosplenic system and marrow.

Treatment requires agents with good intracellular penetration. The combination of doxycycline and rifampicin remains the preferred regimen for severe or disseminated *Bartonella* infections, including hepatosplenic disease and endocarditis. Our patient completed six months of therapy with this combination, resulting in complete resolution of fever, regression of hepatosplenomegaly, and normalisation of inflammatory markers.

This case underscores the importance of considering *B. henselae* in the differential diagnosis of PUO with hepatosplenomegaly, especially in the presence of cat exposure. The integration of exposure history, histopathology, and molecular diagnostics was pivotal in achieving a definitive diagnosis in this otherwise seronegative case. Clinicians should remain aware that bacillary peliosis can extend beyond the liver to involve the spleen and bone marrow, representing the systemic nature of disseminated bartonellosis.

CONCLUSION

Disseminated *B. henselae* infection should be considered in the differential diagnosis of patients presenting with pyrexia of unknown origin and hepatosplenomegaly, especially in the presence of cat exposure. Conventional diagnostic methods are often inconclusive, and diagnosis may rely on a combination of histological clues and molecular confirmation. Early recognition and appropriate antibiotic therapy can result in complete recovery, highlighting the need for clinician awareness of this uncommon but treatable infection.

ACKNOWLEDGMENT

We thank the Microbiology and Infectious Diseases teams at Hospital Canselor Tuanku Muhriz for their support in managing these cases. Our appreciation also goes to the Bacteriology Unit, Institute for Medical Research (IMR), for performing the molecular tests for *Bartonella* species. We are grateful to all colleagues involved in patient care and to the patients and their families for their cooperation and consent.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

REFERENCES

Bai, Y., Osikowicz, L.M., Hojgaard, A. & Eisen, R.J. (2023). Development of a quadruplex PCR amplicon next generation sequencing assay for detection and differentiation of *Bartonella* spp. *Frontiers in Microbiology* **14**: 1243471. https://doi.org/10.3389/FMICB.2023.1243471

Billeter, S.A., Gundi, V.A.K.B., Rood, M.P. & Kosoy, M.Y. (2011). Molecular detection and identification of *Bartonella* species in *Xenopsylla cheopis* fleas (Siphonaptera: Pulicidae) collected from *Rattus norvegicus* rats in Los Angeles, California. *Applied and Environmental Microbiology* **77**: 7850-7852. https://doi.org/10.1128/AEM.06012-11

Bullard, R.L., Cheslock, M., Goud Gadila, S.K., Maggi, R.G., Breitschwerdt, E.B., Saied, A.A. & Embers, M.E. (2024). A comparison of *Bartonella henselae* infection in immunocompetent and immunocompromised mice. *PLOS ONE* **19**: e0297280. https://doi.org/10.1371/JOURNAL.PONE.0297280

Cardoso, T.L., Gonçalves, J.M. & Hartwig, D.D. (2025). *Bartonella henselae*: a challenging diagnosis with a bright future. *Journal of Microbiological Methods* **239**: 107296. https://doi.org/10.1016/J.MIMET.2025.107296

Harms, A. & Dehio, C. (2012). Intruders below the radar: molecular pathogenesis of *Bartonella* spp. *Clinical Microbiology Reviews* **25**: 42-78. https://doi.org/10.1128/CMR.05009-11

Li, M., Yan, K., Jia, P., Wei, E. & Wang, H. (2022). Metagenomic next-generation sequencing may assist diagnosis of cat-scratch disease. *Frontiers in Cellular and Infection Microbiology* **12**: 946849. https://doi.org/10.3389/FCIMB.2022.946849

Lins, K.A., Piveta, C.S.C., Levy, C.E., Drummond, M.R., Dos Santos, L.S., Sussulini, A. & Velho, P.E.N.F. (2024). The influence of growth time on the identification of *Bartonella henselae* strains by MALDI-TOF mass spectrometry. *Revista do Instituto de Medicina Tropical de São Paulo* **66**: e9. https://doi.org/10.1590/S1678-9946202466009

Muttineni, S., Dronavalli, S., Thanendrarajan, S., Rhee, F.V., Crescencio, J.C.R. & Verma, N. (2025). Disseminated *Bartonella henselae* infection in a patient with relapsed/refractory multiple myeloma following autologous stem cell transplantation. *Cureus* **17**: e95516. https://doi.org/10.7759/CUREUS.95516

Okaro, U., George, S. & Anderson, B. (2021). What is in a cat scratch? Growth of *Bartonella henselae* in a biofilm. *Microorganisms* **9**: 835. https://doi.org/10.3390/MICROORGANISMS9040835

Peng, J., Fan, Z., Zheng, H., Lu, J. & Zhan, Y. (2020). Combined application of immunohistochemistry and Warthin-Starry silver stain on the pathologic diagnosis of cat scratch disease. *Applied Immunohistochemistry and Molecular Morphology* **28**: 781-785. https://doi.org/10.1097/PAI.0000000000000829

Steed, D., Collins, J., Farris, A.B., Guarner, J., Yarar, D., Friedman-Moraco, R., Doane, T., Pouch, S., Marshall Lyon, G. & Woodworth, M.H. (2022). Haemophagocytic lymphohistiocytosis associated with bartonella peliosis hepatis following kidney transplantation in a patient with HIV. *The Lancet Infectious Diseases* **22**: e303-e309. https://doi.org/10.1016/S1473-3099(22)00276-6

Zabari, N., Abdul Hadi, F.S., Seman, Z., Tay, B.Y., Zahidi, J. & Ramli, S.R. (2025). Seropositivity of *Bartonella henselae* among suspected cat scratch disease patients in Malaysia: a 5-year retrospective study (2015–2019). *Tropical Biomedicine* **42**: 162-168. https://doi.org/10.47665/TB.42.2.009