Received: 26 December 2023 | Revised: 14 January 2024 | Accepted: 27 January 2024

DOI: 10.1002/ccr3.8496

CASE REPORT

Clinical Case Reports Open Access WILEY

Perforation of the terminal ileum caused by brucellosis: A case report

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Key Clinical Message

Brucellosis, caused by gram-negative coccobacilli of the genus *Brucella*, is a zoonotic disease with bone and joint complications being common. However, acute abdomen with intestinal perforation is rare. We present a case of a 69-year-old man diagnosed with acute diffuse peritonitis and intestinal perforation due to *Brucella* infection. Surgical intervention revealed ileocecal perforation with wheel spoke-like necrosis. The patient underwent partial resection, ileum closure, and ileostomy. Positive blood culture and *Brucella* agglutination confirmed the diagnosis. Targeted tetracycline and aminoglycoside treatment led to recovery.

KEYWORDS

acute abdomen, bowel perforation, brucellosis, inflammatory bowel disease

1 | INTRODUCTION

Brucellosis, also known as undulant fever, is the most common zoonosis in the world and an important public health concern in many developing countries. The epidemic areas include the Middle East, Central Asia, China, the Indian subcontinent, and Africa.[1] In China, the majority of cases occur in the northeastern and northwestern pastoral areas, with *Brucella melitensis* being the most common pathogen, followed by *Brucella abortus* and *Brucella suis*, which can be transmitted to humans through direct contact with infected animals, ingestion of unprocessed dairy products, and consumption of infected meat.[2] A study found that marine species can also cause human infections.[3] The transmission route is complicated. It is mainly transmitted through direct contact with skin and mucosa, and can also be transmitted through the digestive tract by drinking unpasteurized dairy products, through inhaling aerosol contaminated by *Brucella* into the respiratory tract, and in rare cases through human-to-human transmission by sexual transmission or mother-to-child transmission.[4,5]

Brucellosis has acute, subacute, and chronic forms. Localized infections, complications, and relapses may also occur. Its clinical manifestations include fever, profuse sweating, fatigue, anorexia, weight loss, muscle and joint pain, liver and spleen enlargement, and lymph node enlargement. It can affect multiple organs and systems, and bone and joint involvement is its most common complication.[6,7] However, cases of abdominal infection caused by *Brucella* are extremely rare. According to literature review, only one case of pancreatitis[8] and one case of ileal perforation[9] caused by *Brucella* infection have been reported.

Brucellosis has a complex pathogenesis, with toxins, bacteria, and immune reactions involved in its development and progression, and bacteremia, sepsis, and toxemia may occur during the course of the infection.[10] The lipopolysaccharides in *Brucella* and the bacterium itself can cause trigger immune reactions involving multiple tissues, organs and systems, and can also cause autoimmune

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reactions.[11] However, the mechanism of intestinal perforation caused by *Brucella* infection remains unclear. Here we report a case of intestinal perforation in a man with brucellosis.

2 | CASE PRESENTATION

A 69-year-old male was admitted to the hospital with a 2-day history of abdominal pain and fever. He denied experiencing chest, waist, bone, or joint pain, as well as nausea, vomiting, or diarrhea. Significantly, 3 months earlier, he had participated in lamb delivery, resulting in stillbirth. Subsequently, he developed fever and abdominal pain, with symptom improvement after a 3-day course of oral antibiotics (norfloxacin). The patient had no known history of hepatitis or tuberculosis infection. Further investigation into the patient's medical history revealed that he maintains a considerable number of sheep at home, with no other livestock present, and no known contact with other animals. This additional information enhances our understanding of the patient's potential exposure to *Brucella*.

It is crucial to highlight that the incubation period for brucellosis ranges from 1 week to 3 months, with an average of 2–4 weeks. This timeframe aligns with the reported onset of symptoms by the patient, providing valuable context to the potential source of infection and assisting in the diagnostic evaluation.

3 | PHYSICAL EXAMINATION FINDINGS

The patient's vital signs were documented as follows: body temperature was 37.8°C, heart rate was 80 beats/min, respiratory rate was 23 breaths/min, and blood pressure was 110/75 mmHg. On physical examination, ulceration and crusting of the epidermal mucosa of the lower lip were observed (Figure 1A). The patient demonstrated generalized abdominal tenderness, marked rebound tenderness of the lower abdomen, and weak bowel sounds. Furthermore, there was no evidence of hepatomegaly, splenomegaly, or lymphadenopathy. However, the patient reported multiple migratory myalgias and arthralgias throughout the body, without persistent lower back pain, localized tenderness, percussion tenderness, or associated muscle spasms, and restricted spinal mobility. Despite findings on the abdominal CT scan (Figure 2) indicating features such as fatty liver, small intestinal dilatation, thickening of the small intestine near the ileocecum, effusion in the intestine with bubble shadows, a small pelvic effusion, and free air under the diaphragm, splenomegaly was notably absent.

4 | DIAGNOSIS AND TREATMENT

The patient was diagnosed with diffuse peritonitis and intestinal perforation, undergoing emergency exploratory laparoscopy. The procedure revealed a small intestine adhesion, dilation, thickening, separation, and adhesion of the ileum. At a distance of about 20 cm proximal

FIGURE 2 Abdominal computed tomography showing fatty liver, dilatation of the small intestine, thickening of the intestine adjacent to the ileocecum, effusion in the intestinal lumen with bubble shadows, a small pelvic effusion, and free air under the diaphragm. There is no splenomegaly.

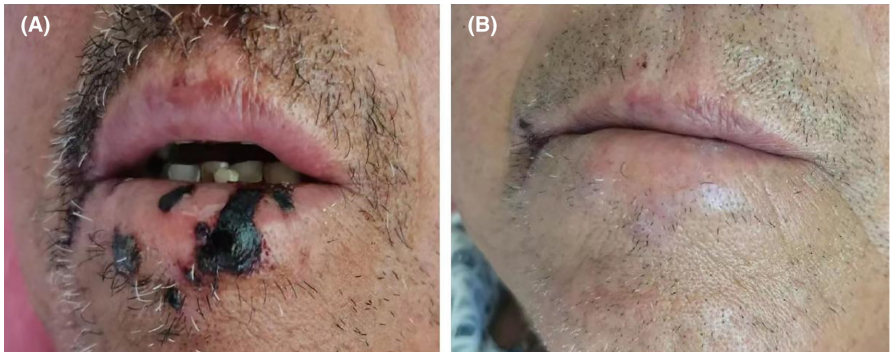

FIGURE 1 (A) Photograph of the lesion on the patient's lower lip showing scabbing. (B) Photograph of the patient's lip after healing of the lesion.

to the ileocecum, a perforation of about 0.5 × 0.5 cm with leakages of intestinal secretions into the abdomen was observed (Figure 3A). The tissue in the 20 cm area surrounding the intestinal perforation displayed wheel spoke-like necrosis (Figure 3B). Despite efforts to improve perfusion, the 20 cm severely necrotic segment of small intestine was resected, and a segment was retained to create a fistula at McBurney's point. The patient received postoperative treatment with ceftazidime 2 g intravenously twice daily.

Postoperatively, blood culture revealed strongly positive serum agglutination for *Brucella* 3 days after the surgery. Tests at the local Center for Disease Control confirmed the diagnosis with a positive Rose Bengal plate agglutination test and a standard tube agglutination test titer of 1:800. Antibiotics were switched to oral doxycycline 0.1 g daily and rifampicin 150 mg daily for 3 days, resulting in the normalization of the patient's body temperature and healing of oral ulcers (Figure 1B). Colonoscopy 10 days after the surgery showed no abnormality in the mucosa of the retained necrotic intestine. The histopathological report noted ileal perforation, with massive neutrophil and lymphocyte infiltration in the full thickness of the adjacent intestinal wall, consistent with the pathological changes of intestinal necrosis (Figure 4). The patient recovered and was discharged with instructions to continue oral antibiotics for 4 weeks.

4.1 | Conclusion

Acute abdomen with intestinal perforation caused by *Brucella* infection is extremely rare. This case emphasizes the importance of considering brucellosis in regions with high endemicity, particularly when presented with atypical manifestations. Early diagnosis and intervention are crucial for favorable outcomes.

5 | DISCUSSION

Brucella is a gram-negative coccobacillus with unique capabilities for invading both phagocytic and non-phagocytic cells, evading the immune system within the intracellular milieu. This characteristic renders brucellosis a systemic disease, potentially involving nearly all organs and systems.

Due to the nonspecific signs and symptoms associated with *Brucella* infection, clinical diagnosis becomes intricate, necessitating a high index of suspicion to ensure accurate identification. Relevant literature underscores the pivotal role of comprehensive medical history collection, encompassing recent exposure to common host animal species, notably cattle, sheep, goats, pigs, camels, buffalo,

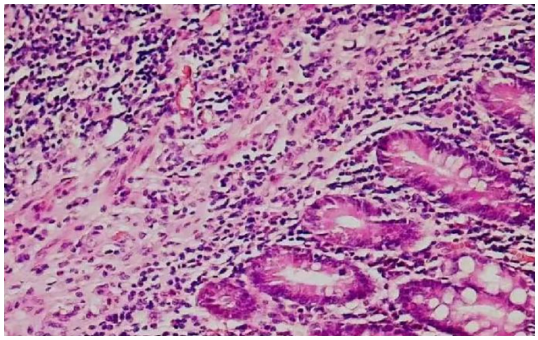

FIGURE 4 Histopathology of the resected ileal segment adjacent to the perforation showing massive neutrophil and lymphocyte infiltration throughout the full thickness of the intestinal wall, consistent with the pathological changes of intestinal necrosis (HE stain; magnification ×40).

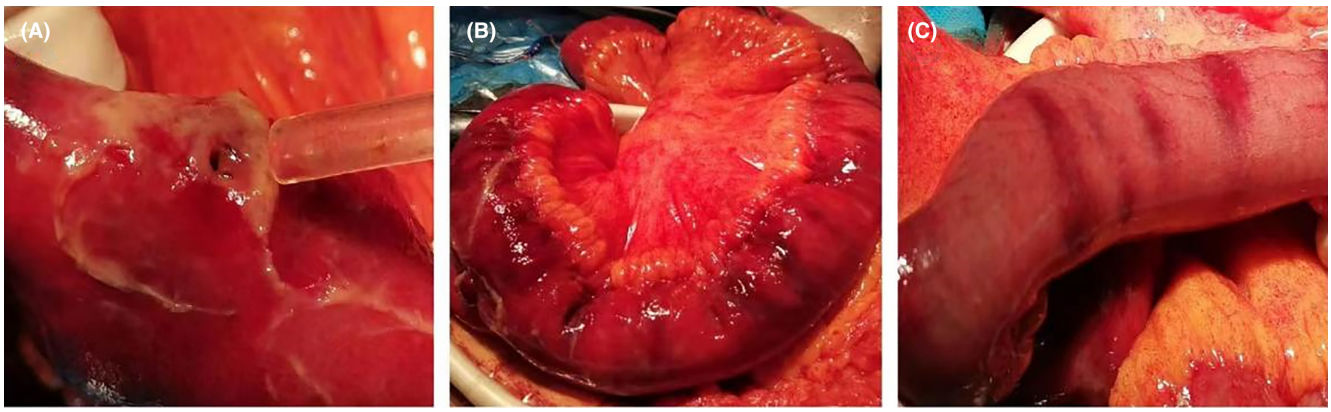

FIGURE 3 Photographs of the intestine taken during surgery (A). Perforation of the small intestine, measuring approximately 0.5 × 0.5 cm, about 20 cm proximal to the ileocecum, with intestinal secretions are flowing into the abdominal cavity. (B) The 20 cm area surrounding the site of the intestinal perforation shows wheel spoke-like necrosis. (C) Part of the necrotic intestine has been retained.

and dogs. Additionally, a history of consuming raw or improperly processed milk and dairy products, as well as the ingestion of meat and organs from host animals, is crucial. Occupational exposure, travel, or residence in endemic areas further heightens the likelihood of diagnosis. The gold standard for diagnosing brucellosis involves culture and bacterial isolation. The post-cure definitive diagnosis can be established by obtaining samples from blood, bone marrow, or other tissues. Generally, hematology tends to normal, as in the case patient, but there may be decreases or increases in white blood cells. Serological testing is the most commonly used method to diagnose brucellosis. The standard agglutination test is considered positive when the titer is 1/160 or higher with evidence of active infection.[12]

In this patient, the distal ileum was perforated and the intestinal necrosis presented a wheel spoke shape. Inflammatory bowel disease was once considered as a possible diagnosis during the surgery, and postoperative antibiotics were administered. Colonoscopy 10 days after the operation showed that there was no abnormality in the mucosa on the part of necrotic intestine retained during the operation, ruling out a diagnosis of inflammatory bowel disease.

In exploring the mechanisms of tissue invasion and survival of *Brucella*, its unique ability to invade cells, particularly within macrophages, becomes evident. In the intestinal milieu, *Brucella* may employ specific proteins, such as U-Omp, to evade host defenses, successfully infiltrating mucosal tissues, and establishing infection.[13] Additionally, the membrane protein PrPC is considered a potential receptor for *Brucella*, and its interaction with the pathogen facilitates infection occurrence.[14]

During the infection process, *Brucella* not only disrupts cellular processes within macrophages but also triggers a complex immune response. The imbalance in this immune response may lead to tissue damage and impairment of the intestinal mucosa, creating conditions conducive to intestinal perforation. The Th1-mediated production of pro-inflammatory cytokines such as IL-1β, IL-6, TNF-α, and IFN-γ has a protective effect against *Brucella*, while the production of IL-17 in the intestinal mucosa is also deemed crucial.[15–19] However, the presence of $CD4^+$ $CD25^+$ Tregs and IL-10 may have a negative impact on the immune response against *Brucella*.[20]

Furthermore, *Brucella* can induce localized tissue damage, particularly at the site of infection. This damage may result in direct cell destruction, potentially leading to perforation and the leakage of intestinal contents into the abdominal cavity. During the inflammatory process, vascular damage may also occur, causing local changes in blood flow and ischemia, thereby affecting tissue integrity.

6 | CONCLUSIONS

The atypical clinical manifestations of brucellosis, coupled with the absence of specific laboratory tests, have posed challenges for clinicians. This case report offers documentation of distal ileum perforation attributed to *Brucella* infection. In routine clinical scenarios, when encountering patients with unexplained fever, it is crucial for clinicians to meticulously inquire about potential *Brucella* exposure in their medical history. Timely auxiliary assessments, such as *Brucella* culture and imaging studies, should be conducted to facilitate early diagnosis of brucellosis and mitigate the risk of misdiagnosis.

AUTHOR CONTRIBUTIONS

Chun Wang: Writing – original draft. **Xiaoran Yang:** Writing – original draft. **Jia Zhou:** Methodology. **Yong Yang:** Conceptualization; investigation. **Xu Liu:** Investigation; visualization. **Xuzhao Li:** Writing – review and editing.

FUNDING INFORMATION

No funding or sponsorship was received for publication of this article.

CONFLICT OF INTEREST STATEMENT

All authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the writing of the report.

ETHICS STATEMENT

Ethics approval was not required because the article is a case report, not a research study. All activities related to the writing of this report were performed in accordance with the Helsinki Declaration of 1964, and its later amendments. The patient provided consent for publication of this report.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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How to cite this article: Wang C, Yang X, Zhou J, Liu X, Yang Y, Li X. Perforation of the terminal ileum caused by brucellosis: A case report. *Clin Case Rep*. 2024;12:e8496. doi:10.1002/ccr3.8496