

Brucella Melitensis Infection Leading to Septicemia in a Pediatric Patient: A Case Study and Literature Review

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Objective: To enhance the clinical awareness of *Brucella melitensis* by retrospectively analyzing a case of septicemia caused by this bacterial infection in a pediatric patient.

Methods: The clinical data from a case of *Brucella melitensis*-induced septicemia in a child treated at Baoding Hospital, Beijing Children's Hospital, Capital Medical University, in June 2024 were retrospectively reviewed. The patient's condition and biochemical test results were analyzed and summarized.

Results: Three weeks before the onset of illness, the patient had a history of raw beef exposure. The primary clinical manifestation was undulant fever. Hematological tests revealed elevated C-reactive protein and erythrocyte sedimentation rate, accompanied by tenderness in the right hip joint and a positive "4 Sign" on the right side. The hip joint ultrasound was unremarkable. Blood culture identified *Brucella melitensis* after 72 hours of incubation, and serum agglutination test showed positive *Brucella* antibodies with a titer of 1:400. The patient was treated with ceftriaxone for antibacterial therapy, supplemented with doxycycline. Supportive therapy included bicyclol, glutathione, and L-ornithine L-aspartate for hepatoprotection. After 7 days of treatment, the patient's body temperature normalized, joint pain subsided, and liver function significantly improved, with AST decreasing from 215 U/L to 47 U/L and ALT from 213 U/L to 53 U/L. The treatment lasted six weeks. The patient's condition remained stable after discharge, with follow-up blood tests, liver function tests, and blood cultures showing no abnormalities.

Conclusion: For patients with suspected infections, it is crucial to actively identify the causative pathogen and administer appropriate antimicrobial therapy based on laboratory results. Clinicians should emphasize etiological testing, using various staining techniques to improve diagnostic accuracy when identifying bacterial colonies on culture plates.

Keywords: *Brucella*, *Brucella melitensis*, septicemia, infection

Introduction

Brucella melitensis is a Gram-negative coccobacillus belonging to the genus *Brucella*. It is one of the causative agents of brucellosis, also known as undulant fever, Mediterranean remittent fever, or Malta fever.^{1,2} This bacterium primarily infects humans and animals, particularly livestock such as cattle, sheep, and pigs. Transmission to humans occurs through contact with infected animals or consumption of undercooked meat, unpasteurized dairy products, or other contaminated food.³ *B. melitensis* is more prevalent in northern pastoral regions of China, such as Inner Mongolia, Jilin, Heilongjiang, and Xinjiang, but is relatively rare in southern, especially coastal, areas where detection poses greater challenges.⁴ Historically, this pathogen caused significant health issues among British troops stationed in Malta, leading to numerous cases and fatalities.⁵ The clinical manifestations of brucellosis are diverse, with common symptoms including periodic fever, fatigue, excessive sweating, joint pain, and hepatosplenomegaly. In severe cases, it can result in multi-organ

damage and lifelong disability.⁶ The incubation period typically ranges from 1 to 4 weeks. Due to its complex symptomatology and its tendency to mimic other diseases, brucellosis presents considerable challenges in diagnosis and treatment.^{7,8}

According to the World Health Organization, brucellosis remains one of the most common zoonotic diseases globally, with more than 500,000 new cases reported annually, though the actual incidence is estimated to be 10–25 times higher due to underreporting.⁹ The Mediterranean basin, Middle East, Central Asia, sub-Saharan Africa, and parts of Latin America represent the primary endemic regions, with varying prevalence rates. Recent epidemiological studies have documented increasing incidence in several regions, particularly in resource-limited settings, with substantial economic impact on both healthcare systems and livestock production.

Recent advances in brucellosis research have focused on improved diagnostic methods, treatment strategies, and vaccine development. Studies have highlighted the emergence of antimicrobial resistance in *Brucella* strains, complicating treatment protocols worldwide.¹⁰ Diagnostic innovations include the development of molecular techniques with higher sensitivity and specificity. Research has demonstrated the utility of multiplex PCR assays for rapid identification of *Brucella* species, reducing the time to diagnosis from days to hours compared to conventional culture methods.¹¹ Additionally, recent investigations have characterized novel virulence factors in *B. melitensis* that contribute to its intracellular survival and pathogenicity, providing potential targets for vaccine development.¹² While *B. melitensis* infection is well documented, pediatric septicemia cases remain relatively uncommon in non-endemic urban areas. This article retrospectively analyzes the clinical data of a pediatric case of septicemia caused by *B. melitensis*, aiming to enhance clinical awareness and understanding of infections caused by this bacterium.

Clinical Data

Case Presentation

The patient, a 13-year-old girl, was admitted with a chief complaint of intermittent fever for over one month. Approximately one month prior, she experienced fever without obvious precipitating factors, with a maximum body temperature of 39.1°C. The fever was not accompanied by chills or convulsions and resolved to normal with antipyretic medication but recurred, with peak fever episodes occurring 1–2 times per day. The patient occasionally exhibited single bouts of coughing without sputum production, wheezing, vomiting, diarrhea, lethargy, irritability, or urinary discomfort (eg, frequency, urgency, dysuria). One month prior to admission, she was evaluated at this hospital and treated with azithromycin for five days, after which her temperature normalized. However, fever recurred one week later, reaching a maximum of 39.4°C. The fever responded to oral antipyretics, with peak episodes occurring once daily. Symptoms were accompanied by occasional single bouts of coughing and, during febrile episodes, right hip joint pain, which subsided when the fever resolved. There were no associated rashes. Three weeks before the onset of symptoms, the patient had a history of raw beef exposure. She denied any history of drug allergies, surgeries, or contact with infectious diseases. The patient resided in an urban area with good household hygiene conditions. The specific circumstance of raw beef exposure occurred when the patient was helping prepare dinner at home, directly handling uncooked beef with minor cuts on her hands. The patient and her family had no habit of consuming raw meat or unpasteurized dairy products. There were no livestock kept at home, and the patient had not recently visited rural or pastoral areas. This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of hospital, and written informed consent was obtained from the study participant's parent.

Physical Examination

Upon admission, the patient's vital signs were as follows: body temperature 37.1°C, pulse rate 114 beats/min, respiratory rate 26 breaths/min, and blood pressure 113/71 mmHg. She weighed 51 kg. The patient had normal physical development, moderate nutrition, and was alert with stable respiration. There were no rashes on her body, and superficial lymph nodes were not palpable. Examination revealed pharyngeal congestion and grade II bilateral tonsillar hypertrophy without exudate. Cardiopulmonary, abdominal, and neurological examinations showed no abnormalities. Tenderness

was noted in the right hip joint, and the “4 Sign” on the right side was positive. The hip joint ultrasound was unremarkable.

Laboratory Tests

Before admission, the patient's laboratory results were as follows: White blood cell count (WBC) $5.43 \times 10^9/L$, red blood cell count (RBC) $4.57 \times 10^{12}/L$, hemoglobin (HGB) 133 g/L, platelet count (PLT) $155 \times 10^9/L$, neutrophil percentage (N%) 63.2%, lymphocyte percentage (L%) 28.9%, and C-reactive protein (CRP) 4.11 mg/L. The patient received oral azithromycin (10 mg/kg/day) for three days, after which follow-up laboratory results showed: WBC $4.05 \times 10^9/L$, RBC $4.95 \times 10^{12}/L$, HGB 139 g/L, PLT $143 \times 10^9/L$, N% 61.5%, L% 32%, CRP 13.89 mg/L, and serum amyloid A (SAA) 292.37 mg/L. Her liver function test results showed elevated levels of aspartate aminotransferase (AST, 215 U/L) and alanine aminotransferase (ALT, 48.3 U/L), while other related parameters were within normal range (Table 1).

After admission, her laboratory results were WBC $3.92 \times 10^9/L$, RBC $3.97 \times 10^{12}/L$, HGB 113 g/L, PLT $118 \times 10^9/L$, N% 45.3%, L% 49.5%, reticulocyte count 1.41% (normal), CRP 5.11 mg/L, and an increased erythrocyte sedimentation rate (ESR). Her liver function test results were AST 116 U/L (elevated), ALT 213 U/L (elevated), γ -glutamyl transferase (γ -GT) 36 U/L (normal), and lactate dehydrogenase (LDH) 365 U/L (normal). Additional tests showed an elevated SAA level of 116.51 mg/L, a normal procalcitonin level of 0.08 ng/mL, and a ferritin level of 211.9 ng/mL. Routine urinalysis and stool examination were unremarkable. The thyroid function panel showed no abnormalities. Immunoglobulin levels were within normal ranges. Autoimmune tests, including antinuclear antibody spectrum, cytoplasmic anti-neutrophil cytoplasmic antibodies, and perinuclear anti-neutrophil cytoplasmic antibodies, were all negative.

Bacterial Culture, Identification, and Brucella Antibody Testing

A sterile venous blood specimen (4 mL) was collected immediately upon admission, prior to antimicrobial therapy initiation, and serum was separated for the *Brucella* agglutination test, which revealed a positive result for *Brucella* antibodies with a titer of 1:400. No bacterial growth was observed after incubation for 48 h. At 72 h, two distinct colony morphologies appeared on blood agar plates, including white, mucoid colonies and smaller, glossy white colonies (Figure 1A). The Gram stain examination showed that both colony types were Gram-negative and polymorphic, including short and long rods. After 5 days, both colony types developed into white, smooth, granular colonies on blood agar (Figure 1B). Gram stain microscopy revealed Gram-negative coccobacilli (Figure 1C). Preliminary biochemical reactions were positive for oxidase, catalase, and urease (5-minute test). Using the VITEK 2 Compact GN card system, the bacteria were identified as *B. melitensis*.

Table 1 Patient's Laboratory Findings at Different Stages

Parameter	Before Admission	On Admission	Day 7	Day 10	Reference Range
WBC ($\times 10^9/L$)	5.43	3.92	4.78	5.12	4.0–10.0
RBC ($\times 10^{12}/L$)	4.57	3.97	4.23	4.35	3.5–5.5
HGB (g/L)	133	113	119	125	110–160
PLT ($\times 10^9/L$)	155	118	137	149	100–300
N%	63.2	45.3	58.1	60.2	40–75
L%	28.9	49.5	36.4	34.2	20–50
CRP (mg/L)	4.11	5.11	2.35	1.87	0–10
ESR (mm/h)	–	38	22	15	0–20
AST (U/L)	215	116	61	47	0–40
ALT (U/L)	48.3	213	91	53	0–40
γ -GT (U/L)	–	36	37	31	0–50
LDH (U/L)	–	365	305	287	120–250
SAA (mg/L)	292.37	116.51	48.62	22.16	0–10

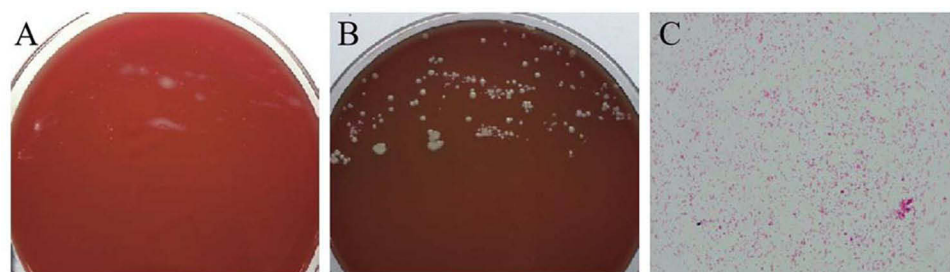


Figure 1 Colony morphology on blood agar plates.

Notes: (A) Colony morphology on blood agar after 3 days of incubation. (B) Colony morphology on blood agar after 5 days of incubation. (C) A direct smear of cultured colonies, Gram-stained, showing bacterial morphology under an oil immersion lens.

Diagnosis and Treatment

Based on microbiological identification, serological agglutination test results, and the patient's clinical presentation, the patient was diagnosed with *B. melitensis*-induced septicemia. Initially, intravenous ceftriaxone and doxycycline were administered for antimicrobial therapy, accompanied by bicyclol, glutathione, and L-ornithine L-aspartate for hepatoprotection.

On day 7 of her stay, the patient's body temperature normalized, and joint pain subsided. Follow-up liver function tests showed AST 61 U/L, ALT 91 U/L, γ -GT 37 U/L, and LDH 305 U/L. The treatment continued until another follow-up on day 10, which showed further improvement in her liver function: AST 47 U/L, ALT 53 U/L, and a slightly increased γ -GT level of 31 U/L. Ceftriaxone and glutathione were discontinued, and oral rifampin, doxycycline, and bicyclol were prescribed before discharge. The patient was discharged with stable condition. Follow-up evaluations were performed at 2 weeks, 4 weeks, and 3 months after discharge. Complete blood count, liver function tests, and blood cultures performed at these intervals were all unremarkable. The total treatment course lasted six weeks, with no recurrence reported.

Discussion

Brucellosis is a zoonotic infectious disease caused by *Brucella* species, which can manifest as either an acute or chronic condition. There are six recognized species within the *Brucella* genus, among which *B. melitensis* is the most prevalent and virulent *Brucella* species, causing the most severe form of human brucellosis, followed by *B. abortus*.¹³ Human infection primarily arises from contact with infected animals or consumption of contaminated animal products. In China, sheep and goats are the principal reservoir for *B. melitensis*, followed by cattle and pigs. Endemic regions in China include Northeast, North, and Northwest China, where livestock farming, meat processing, and dairy production are prominent industries.¹⁴ Infection typically occurs through direct contact with infected animals, handling their tissues or organs, or consuming unpasteurized dairy products. A major outbreak, the "Brucellosis Incident" in Lanzhou, Gansu Province, highlighted the public health impact of this disease. By September 14, 2020, a total of 3245 individuals tested positive for brucellosis.¹⁵ This study retrospectively analyzed a case of *B. melitensis*-induced septicemia in a pediatric patient to enhance the clinical awareness of this pathogen.

Comparing this case with other brucellosis cases reported in the literature, we found that pediatric brucellosis has certain specificities compared to adult cases. Research has shown that while fever and joint pain are common symptoms in both age groups, children often present with more varied hematological and hepatic manifestations. Studies have documented that children with brucellosis frequently present with hepatomegaly and elevated liver enzymes,¹⁶ which aligns with our case presentation. This research also noted that children with brucellosis typically present with non-specific symptoms that can mimic other infectious diseases, highlighting the diagnostic challenges.

Regarding regional distribution, epidemiological analysis of human brucellosis in China has reported that the disease predominantly affects rural areas, though there has been a notable increase in urban cases in recent years.¹⁷ Research has demonstrated changing epidemiological patterns, with food-borne transmission becoming increasingly important in non-traditional endemic areas. This is consistent with our case where the patient was from an urban area and infection likely

occurred through food exposure rather than direct animal contact. Additionally, our patient exhibited more significant liver damage with relatively milder osteoarticular symptoms compared to typical presentations, highlighting the diverse clinical manifestations of brucellosis and emphasizing the importance of maintaining clinical suspicion even in non-endemic regions.

This patient had not recently traveled to endemic regions nor had direct contact with infected animals. The apparent primary cause of infection was most likely exposure to raw beef three weeks prior to symptom onset. The patient primarily presented with undulant fever, elevated CRP and ESR levels, and right hip joint tenderness. The “4 Sign” was positive on the right side, although no abnormalities were detected on hip ultrasound. *B. melitensis* infection most commonly involves the musculoskeletal system, urinary system, and central nervous system. While *B. melitensis*-induced septicemia has been documented in the medical literature, particularly from endemic regions, cases in pediatric patients from non-endemic urban areas remain relatively uncommon, making this case clinically significant for raising awareness among clinicians practicing in similar settings.¹⁸ The development of septicemia in this patient can be attributed to the following factors: (1) Pathogen invasion and proliferation: *B. melitensis* can invade the human body via skin abrasions, mucosal contact, or ingestion of contaminated food. Upon entering the body, the bacteria primarily reside in the mononuclear phagocyte system, where they multiply within macrophages, leading to localized infections.¹⁹ When bacterial load exceeds a certain threshold, the pathogens breach the lymph node barriers and enter the bloodstream, resulting in bacteremia or septicemia. (2) Bacterial immune evasion mechanisms and host immune response: The human immune system mounts a response to *B. melitensis* through neutrophil phagocytosis and antibody production. However, *B. melitensis* exhibits strong antiphagocytic capabilities, making it resistant to neutrophil-mediated killing. The pathogen can also trigger delayed hypersensitivity, which exacerbates tissue damage and inflammation.²⁰ (3) Host factors: The host's immune status significantly influences the progression to septicemia. In this case, the patient had concurrent liver dysfunction, which is a critical factor. The liver plays a pivotal role in combating infections. When liver function is impaired, its ability to clear bacteria diminishes, increasing the likelihood of bacteria breaching the intestinal barrier and entering systemic circulation, ultimately leading to septicemia.²¹ (4) Pathological mechanism: After establishing localized foci of infection, *B. melitensis* can intermittently enter the bloodstream, resulting in recurrent fever and undulant fever. This recurrent infection and inflammatory response can eventually lead to multiple organ dysfunction and septicemia.^{22,23}

An important consideration in this case is the potential impact on reproductive health, given the patient's pubertal age. Studies have documented that brucellosis can affect the female reproductive system. Although our patient showed no reproductive symptoms, long-term monitoring is warranted as research suggests potential sequelae affecting reproductive health even after successful treatment of the acute infection.²⁴ In adolescent females, brucellosis may potentially impact ovarian function, hormonal balance, and future fertility. Therefore, we recommend extended follow-up for this patient, with particular attention to reproductive development and function during puberty.

This case underscores the importance of thorough patient history collection and comprehensive physical examination. Clinicians should consider infectious diseases when patients present with undulant fever, elevated CRP and ESR, joint pain, and a clinical progression that cannot be fully explained by a single diagnosis. To improve diagnostic accuracy, emphasis should be placed on etiological investigations, such as repeated sampling of suspected specimens, concurrent use of serum agglutination tests, and combining different staining techniques with colony growth on culture plates for microbial identification.

This case report is subject to several limitations that warrant acknowledgment. First, the retrospective nature of the study inherently constrains the comprehensiveness and generalizability of the findings, as data collection was limited to existing clinical records. Second, the absence of molecular typing data for the *Brucella melitensis* isolate impedes a comprehensive understanding of strain-specific characteristics, including virulence factors and antimicrobial susceptibility profiles, which could have provided additional insights into the epidemiological context. Third, the relatively brief follow-up period of three months may not fully capture the long-term clinical trajectory or potential latent complications associated with *Brucella melitensis* infection, particularly in pediatric populations. Future research should address these limitations by employing prospective study designs, incorporating advanced molecular techniques, and extending follow-up periods to evaluate long-term outcomes. Such approaches would enhance our understanding of the pathophysiology

and optimal management strategies for *Brucella melitensis* septicemia in pediatric patients from non-endemic urban settings.

Conclusion

This case of *B. melitensis*-induced septicemia in a 13-year-old female patient demonstrates that brucellosis should be considered in the differential diagnosis of patients with undulant fever, even in non-endemic regions. Comprehensive microbiological investigations, including extended blood cultures and serological testing, are essential for accurate diagnosis. Combination antimicrobial therapy proved effective despite hepatic involvement. Preventive measures specific to this type of exposure include proper handling of raw meat, using protective gloves when handling raw animal products, and immediate cleansing of any cuts or abrasions that contact raw meat. Limitations of this case report include its retrospective nature, lack of molecular typing of the *B. melitensis* isolate, and relatively short follow-up period of three months. Further research is needed to better understand *B. melitensis* septicemia pathophysiology in pediatric patients, particularly those from non-endemic regions with atypical exposure histories.

Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Baoding Hospital of Beijing Children's Hospital, Capital Medical University.

Written informed consent was obtained from the study participant's parent.

Consent to Publish

The study participants parent/guardian gave consent to publish.

Funding

This study did not receive any funding in any form.

Disclosure

All of the authors had no any personal, financial, commercial, or academic conflicts of interest separately.

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