CASE REPORT AND LITERATURE REVIEW

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ACUTE BRUCELLOSIS-ASSOCIATED DEEP VEIN THROMBOSIS: A CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract

Deep vein thrombosis (DVT) is a potentially serious vascular condition with multiple well-established risk factors, including immobility, surgery, trauma, malignancy, and inherited or acquired thrombophilias. Infectious causes of DVT are rare but have been increasingly recognized, with brucellosis being one such unusual infectious etiology. Brucellosis is a zoonotic infection caused by *Brucella* species, endemic in many regions, including the Middle East, Mediterranean countries, and parts of Latin America. While musculoskeletal manifestations such as arthritis, spondylitis, and sacroiliitis are commonly reported, vascular complications like DVT are seldom described. Highlighting these rare presentations is important for early recognition and appropriate management. We report the case of a 22-year-old woman with no prior chronic illnesses who presented with a 10-day history of bilateral leg pain, swelling, and redness. She was initially referred to the rheumatology clinic with a provisional diagnosis of arthritis. On physical examination, both ankles were erythematous, warm, and edematous; Homan's sign was positive in the left leg. Doppler ultrasonography confirmed DVT in the affected limbs. Laboratory tests revealed elevated acute-phase reactants, including erythrocyte sedimentation rate and C-reactive protein. Blood cultures grew Gram-negative *coccobacilli*, and serological tests, including rose bengal and serum tube agglutination, were positive for *Brucella*. Following infectious diseases consultation, a diagnosis of acute brucellosis was made, and combination therapy with rifampicin and doxycycline was initiated. Concurrently, anticoagulation therapy with warfarin was initiated under the guidance of the cardiovascular surgery team. The patient's clinical symptoms gradually improved with combined antimicrobial and anticoagulant therapy. Brucellosis, though rare, should be considered in the differential diagnosis of DVT, especially in endemic regions. Early recognition allows timely antimicrobial and anticoagulant therapy. Clinicians should suspect infectious causes of DVT in patients with limb swelling, pain, or systemic symptoms, even without classical risk factors.

Keywords: Brucellosis, deep vein thrombosis, arthritis, infectious DVT, case report

INTRODUCTION

Brucellosis is a zoonotic infection caused by *Brucella* species and remains a significant public health concern, particularly in developing countries (1). Despite ongoing control efforts, the disease continues to affect thousands of people annually, primarily through occupational exposure among veterinarians, farmers, and slaughterhouse workers (2). Human infection most commonly occurs via direct contact with infected animal

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tissues, such as skin cuts or abrasions, or through consumption of unpasteurized milk and dairy products. Less commonly, inhalation of contaminated aerosols or laboratory exposure may lead to infection (1,3).

The clinical presentation of brucellosis is highly variable, ranging from mild, self-limiting flu-like symptoms to severe, multi-organ involvement (2). This variability often complicates early diagnosis, particularly in endemic regions with limited healthcare resources. Brucellosis predominantly affects young and middle-aged adults, whereas the incidence among infants and the elderly remains relatively low (1). The disease may manifest acutely or progress to a chronic course, potentially leading to persistent symptoms, recurrent fevers, fatigue, and organ-specific complications (3).

Musculoskeletal involvement is among the most frequent and clinically significant manifestations of brucellosis. Rheumatologic complications—including arthritis, spondylitis, sacroiliitis, osteomyelitis, and tenosynovitis—occur in 20-85% of patients (2,4). These manifestations are clinically important because they can cause functional impairment, chronic pain, and long-term disability. The pattern and severity of musculoskeletal involvement depend on several factors, including patient age, disease duration, and the infecting *Brucella* species. For instance, *Brucella* melitensis infections are often associated with more severe joint involvement than *Brucella* abortus (4). Early recognition of these complications is essential to prevent chronic morbidity.

Beyond musculoskeletal manifestations, brucellosis can affect multiple organ systems, including the liver, spleen, genitourinary tract, and central nervous system (2,3). Hematologic abnormalities such as anemia, leukopenia, and thrombocytopenia are also common. The systemic inflammatory response in brucellosis may predispose patients to vascular complications, including thrombotic events, which are rare and not fully understood (5).

Deep vein thrombosis (DVT) is a potentially life-threatening condition characterized by the formation of thrombi in the deep venous system, most commonly in the lower extremities (5). Prompt diagnosis and management are critical to preventing serious complications, including pulmonary embolism, post-thrombotic syndrome, and thrombus propagation. DVT risk is influenced by both transient factors—such as surgery, immobilization, and acute illness—and chronic or persistent conditions, including advanced age, malignancy, and inherited or acquired thrombophilia (5).

The pathogenesis of venous thrombosis has traditionally been described by Virchow's triad: venous stasis, endothelial injury or dysfunction, and hypercoagulability (5). While mechanical and hemodynamic factors remain important, increasing evidence suggests that systemic inflammation and infection can also promote thrombus formation. Inflammatory mediators released during infection can alter endothelial function, activate coagulation pathways, and enhance platelet aggregation, creating a prothrombotic state (3,5). Several infections—including bacterial, viral, and parasitic diseases—have been associated with thrombotic events, emphasizing the role of infection-induced inflammation in thrombogenesis (5).

Although thrombosis associated with brucellosis is rare, case reports indicate that the infection may trigger venous and, less commonly, arterial thrombotic events (4,5). Proposed mechanisms include endothelial dysfunction mediated by systemic inflammation, direct vascular invasion by *Brucella* species, and activation of the coagulation system (4). Awareness of this potential complication is particularly important in endemic regions, where failure to recognize an infectious cause of DVT may delay appropriate antimicrobial therapy and adversely affect outcomes (5).

Given the wide spectrum of brucellosis manifestations—including musculoskeletal involvement, systemic inflammation, and rare thrombotic events—clinicians in endemic areas should maintain a high index of suspicion when evaluating patients with unexplained joint symptoms or thrombotic complications (1,2). Understanding the interplay between infection, inflammation, and thrombosis is essential for accurate diagnosis, timely intervention, and optimal patient management. Although vascular complications are uncommon, recognition may improve patient outcomes and prevent serious sequelae (5).

CASE REPORT

A 22-year-old woman with no prior chronic illnesses was referred to the rheumatology clinic with a 10-day history of pain and swelling in both legs, accompanied by elevated acute-phase reactants. On admission, her general condition was good; she was alert and cooperative. Vital signs were as follows: temperature 36.4 °C, blood pressure 120/70 mmHg, and heart rate 89 bpm. Abdominal examination revealed hepatosplenomegaly. Extremity examination showed marked pitting edema over the bilateral pretibial and ankle regions, tenderness to palpation, and positive Homan's and Moses signs .

Color Doppler ultrasonography of the lower extremities demonstrated an echogenic thrombus within the dilated left popliteal vein. Abdominal ultrasonography confirmed hepatosplenomegaly. Laboratory findings were as follows: white blood cell count: 5,600/mL; C-reactive protein (CRP): 97.36 mg/L; erythrocyte sedimentation rate (ESR): 40 mm/h; AST: 25 U/L; ALT:

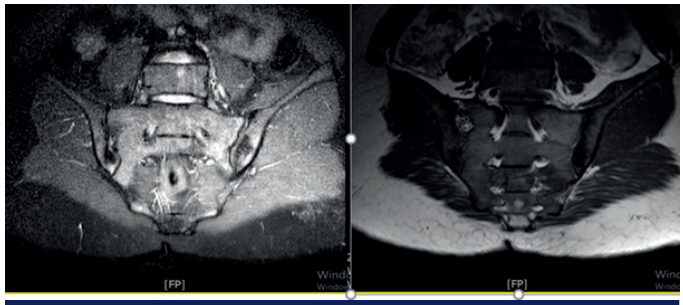

Figure 1. The patient's sacroiliac magnetic resonance images weighted respectively by T2 and T1

32 U/L; BUN: 16 mg/dL; creatinine: 0.54 mg/dL; and D-dimer: 5.5 µg/mL.

Screening for DVT etiology revealed normal protein C, protein S, and antithrombin III levels, with no evidence of activated protein C resistance or antiphospholipid antibodies. Autoimmune markers—including antinuclear antibody, extractable nuclear antigen panel, anti-neutrophil cytoplasmic antibody, rheumatoid factor, and anti-cyclic citrullinated peptide—were all negative.

Because the patient reported inflammatory back pain and had suspicious sacroiliitis on X-ray, sacroiliac magnetic resonance imaging (MRI) was performed. Imaging revealed periarticular sclerosis without active bone marrow edema (Figure 1). Hepatitis markers were negative. Blood cultures grew Gram-negative *coccobacilli*, whereas urine cultures were sterile.

Based on these findings, the infectious diseases department was consulted. Both the rose bengal test and the standard tube agglutination test were positive at a titer of 1:640, confirming the diagnosis of acute brucellosis. Treatment was initiated with rifampicin (600 mg/day) and doxycycline (200 mg/day). For management of DVT, the patient was treated with enoxaparin (0.6 mL/day) and non-steroidal anti-inflammatory drugs. On day 4, warfarin (5 mg/day) was added, and enoxaparin was discontinued on day 8.

The patient's symptoms and laboratory parameters gradually improved, and she was discharged with prescriptions for rifampicin, doxycycline, and warfarin. At 1-month follow-up, Doppler ultrasonography showed significant regression of thrombotic lesions. A 6-week course of rifampicin and doxycycline, and a 6-month course of warfarin were planned.

A written informed consent was obtained.

DISCUSSION

Venous thrombosis is an uncommon but increasingly recognized complication of brucellosis. Evidence from case reports and small series suggests that *Brucella* infection may trigger thrombotic events even in the absence of classical risk factors. In the present case, DVT developed in a young woman without a history of immobilization, malignancy, or inherited thrombophilia, indicating that *Brucella* infection itself may act as a direct precipitant (6). This observation aligns with reports describing venous thrombosis in patients with active or subacute brucellosis, underscoring the need to consider infectious etiologies in unexplained thrombotic events.

Brucellosis is endemic in the Mediterranean region, the Middle East, and parts of Latin America and Asia (6). While vascular complications are more frequently arterial—manifesting as aneurysms, endarteritis, or mycotic emboli—venous thrombosis has been sporadically reported in cerebral venous sinuses, portal veins, central retinal veins, and the deep veins of the lower extremities (7). Most cases involve young or middle-aged adults without underlying coagulopathies, suggesting that the prothrombotic effects of *Brucella* may be underrecognized in endemic regions. Venous thromboembolism should therefore be considered in atypical thrombotic presentations.

Clinically, brucellosis-associated DVT often presents with nonspecific systemic symptoms such as fever, malaise, fatigue, arthralgia, myalgia, and hepatosplenomegaly. Local signs—including limb swelling, pain, warmth, and tenderness—may mimic rheumatologic or orthopedic conditions (7). In our patient, bilateral leg pain and edema, together with elevated inflammatory markers, prompted evaluation for both infectious and rheumatologic causes.

The mechanisms underlying *Brucella*-induced thrombosis are likely multifactorial. *Brucella* species are facultative intracellular pathogens capable of surviving within macrophages and endothelial cells, allowing chronic immune activation, granulomatous inflammation, and localized endophlebitis. These processes may directly damage vascular endothelium, favoring thrombus formation (8). Systemic inflammation further contributes because infection triggers the release of proinflammatory cytokines such as tumor necrosis factor-alpha, interleukin-6, and interferon-gamma. These mediators promote tissue factor expression, inhibit natural anticoagulant pathways, and activate platelets, creating a hypercoagulable state (8).

Granulomatous inflammation of vessel walls may also induce localized endothelial dysfunction, amplifying thrombotic risk. Histopathological studies in reported cases document perivascular infiltration, endothelial swelling, and immune complex deposition, supporting the hypothesis of immune-mediated vascular injury in *Brucella*-associated thrombosis (9). Laboratory evaluation often shows elevated acute-phase reactants, such as CRP and the ESR, whereas classical

thrombophilia markers—including protein C, protein S, antithrombin III, and antiphospholipid antibodies—are typically normal, distinguishing these events from primary hypercoagulable states (9).

Imaging is essential for diagnosis. Doppler ultrasonography is the first-line modality for detecting lower extremity DVT, providing details on thrombus location, extent, and venous flow. Additional findings, including hepatosplenomegaly or localized inflammation, may be identified in brucellosis cases. MRI can assess musculoskeletal involvement in patients with arthralgia or back pain (6).

Management requires a dual approach that addresses infection and thrombosis. Standard antimicrobial therapy consists of doxycycline and rifampicin for at least 6 weeks, with streptomycin or gentamicin added in severe cases. Prompt treatment not only eradicates infection but also mitigates inflammation that may predispose to thrombosis. Concurrent anticoagulation, usually starting with low-molecular-weight heparin followed by oral anticoagulants, such as warfarin or direct oral anticoagulants, for 3-6 months, prevents thrombus progression and embolic complications (10). Serial imaging guides the duration and effectiveness of anticoagulation therapy.

Recognizing *Brucella* as a potential cause of DVT has important diagnostic and therapeutic implications. In endemic regions, clinicians should maintain a high index of suspicion when evaluating young, otherwise healthy patients with unexplained thrombotic events, especially when systemic symptoms or risk factors for infection are present. Comprehensive assessment—including history, serologic testing, and microbiologic cultures—is crucial for timely and accurate diagnosis (6,10).

Although rare, venous thrombotic complications of brucellosis represent a clinically significant phenomenon. The interplay between systemic inflammation, immune-mediated endothelial injury, granulomatous endophlebitis, and hypercoagulability likely drives pathogenesis. Early identification, thorough evaluation, and prompt combined antimicrobial and anticoagulant therapy are key to optimizing outcomes. Larger case series and mechanistic studies are needed to clarify the precise pathways linking *Brucella* infection to venous thrombosis and to establish evidence-based management strategies (6-10).

CONCLUSION

This case highlights that venous thrombosis, although rare, can be a significant complication of brucellosis. Immune-mediated endothelial dysfunction, systemic inflammation, and coagulation disturbances are likely contributors to thrombus formation. Clinicians should consider *Brucella* infection in patients with unexplained venous thrombosis, particularly in endemic regions and in the absence of traditional risk factors. Early diagnosis and timely initiation of combined antimicrobial and anticoagulant therapy are essential to prevent complications and improve patient outcomes. Awareness of this association may facilitate prompt recognition and comprehensive management of both the thrombotic event and the underlying infection.

Ethics

Informed Consent: A written informed consent was obtained.

Footnotes

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REFERENCES

1. Qureshi KA, Parvez A, Fahmy NA, et al. Brucellosis: epidemiology, pathogenesis, diagnosis and treatment-a comprehensive review. Ann Med. 2023;55:2295398.
2. Njeru J, Wareth G, Melzer F, et al. Systematic review of brucellosis in Kenya: disease frequency in humans and animals and risk factors for human infection. BMC Public Health. 2016;16:853.
3. Moreno E. Retrospective and prospective perspectives on zoonotic brucellosis. Front Microbiol. 2014;5:213.
4. Sanaei Dashti A, Karimi A. Skeletal involvement of *Brucella* melitensis in children: a systematic review. Iran J Med Sci. 2013;38:286-92.
5. Jin M, Fan Z, Gao R, Li X, Gao Z, Wang Z. Research progress on complications of brucellosis. Front Cell Infect Microbiol. 2023;13:1136674.
6. Tolaj I, Mehmeti M, Ramadani H, Tolaj J, Dedushi K, Fejza H. Brucellosis associated with deep vein thrombosis. Infect Dis Rep. 2014;6:5441.
7. Li X, Li X, Cheng Z. Brucellosis involving the aorta and iliac arteries: a systematic review of 130 cases. Front Bioeng Biotechnol. 2023;11:1326246.
8. Ferrero MC, Bregante J, Delpino MV, et al. Proinflammatory response of human endothelial cells to *Brucella* infection. Microbes Infect. 2011;13:852-61.
9. Korkmaz P, Kıdır M, Namdar ND, Özmen A, Uyar C, Değer AN. A case of brucellosis with recurrent attacks of vasculitis. Case Rep Infect Dis. 2016;2016:5740589.
10. Koubaa M, Frigui M, Cherif Y, et al. Deep vein thrombosis associated with acute brucellosis: a case report and review of the literature. Korean J Intern Med. 2013;28:628-30.