

Brucellosis-induced Leukocytoclastic Vasculitis

Yousuf Mohammed Al Washahi¹, Zamzam Said Al-Qutaiti^{2*}, Kalpana Garuda Prakash³, Verna Menon⁴, Ahmed Said Al Salami⁴, Maimouna Said Al Farsi⁵ and Mayar Ali Al Bahrani⁶

¹Dermatology Department, Sohar Hospital, Sohar, Oman

²Dermatology Residency Training Program, Oman Medical Specialty Board, Muscat, Oman

³Dermatology Department, Sohar Extended Health Center, Sohar, Oman

⁴Pathology Department, Sohar Hospital, Sohar, Oman

⁵Dermatology Department, Al Nahdha Hospital, Muscat, Oman

⁶Almultaqa Health Center, Directorate General of Health Services North Batinah, Sohar, Oman

Received: 29 September 2023

Accepted: 30 November 2023

*Corresponding author: r2112@resident.omsb.org

DOI 10.5001/omj.2026.09

Abstract

Brucellosis is a zoonotic bacterial infectious disease caused by *Brucella* spp., which is transmitted to humans through contact with animal products and body fluids. The resulting disease is multisystemic, with the skin rarely involved at presentation or during the disease course. We present a case of a 36-year-old female who presented with a history of intermittent fever, polyarthralgia, and painful non-pruritic round erythematous scaly plaques with raised borders on her extremities of one-month duration. Laboratory findings showed positive serology for brucellosis, and a skin biopsy showed leukocytoclastic vasculitis. She was successfully treated with a combination therapy of prednisolone and antibiotics (doxycycline and rifampicin) with complete resolution of all symptoms.

Keywords: Brucellosis; Vasculitis; Leukocytoclastic vasculitis; Small vessel vasculitis.

Introduction

Brucellosis is one of the most common zoonotic infectious diseases worldwide. It is caused by intracellular Gram-negative coccoid or rod-like aerobic bacteria from the genus *Brucella*. The disease is transmitted to humans via direct or indirect contact with infected animals or through the consumption of infected animal products like raw meat or dairy products.^{1,2} It is mostly encountered in the Middle East, Central Asia, China, India, sub-Saharan Africa, and parts of Mexico and Central and South America.¹ So far, four *Brucella* species have been identified to cause human disease. *B. melitensis* (found in goats, sheep, and camels) is the most common cause of brucellosis in humans. Others include *B. abortus* (isolated from cattle), *B. suis* (isolated from swine), and *B. canis* (isolated from dogs).¹ Brucellosis is a multisystemic infection. It can affect different organ systems like osteoarticular, genitourinary, central nervous system, cardiovascular system, respiratory system, and ocular system.³ It can present with a wide spectrum of clinical manifestations that are non-specific and can therefore lead to misdiagnosis and a delay in proper treatment.² Patients may present with intermittent fever, weight loss, depression, hepatomegaly, splenomegaly, and joint pain.³ Fever (87%), tiredness (63%), arthralgia (62%), and muscular discomfort (56%) are the primary clinical characteristics of this disease.^{4,5} Skin involvement is less common and is observed in less than 10% of cases.¹

Leukocytoclastic vasculitis is one of the rarest cutaneous manifestations of brucella infection, and it is seldom reported in the literature. Here we present a novel case of a young female who had systemic manifestations, underwent

a comprehensive workup by a multidisciplinary team, and was finally diagnosed with Brucella-induced leukocytoclastic vasculitis.

Case Report

A 36-year-old previously healthy female, presented with a one-month history of painful erythematous scaly plaques over both upper and lower limbs. It initially started in the dorsum of the right hand and then spread to both forearms and the left lower limb anteriorly. The eruption was non-itchy and associated with a burning sensation. This rash was preceded and accompanied by recurrent episodic fever occurring three-to-four times a month, polyarthralgia, muscular pain, and recurrent episodes of vertigo. The vertigo initially started two years prior, remained for two months, and was accompanied by episodes of sudden vision loss for minutes, followed by blurred vision, which remained for days then disappeared. She had a brain MRI after the first episode of vertigo and impaired vision, which showed normal brain parenchyma with a small 3.6 mm pituitary lesion suggestive of a calcified small hemorrhagic focus within the gland. A second follow-up MRI done two months later showed a normal study.

There was no history of similar episodes of rashes in the past. The patient had no history of taking raw cow or camel milk, no history of contact with animals or pets, and no family history of connective tissue diseases.

On examination, there were multiple tender and well-demarcated annular erythematous and scaly plaques with raised borders on both upper limbs and left lower limb, mainly on extensor aspects. Some of these plaques were eroded and semi-ulcerated [Figure 1]. In addition, there was one small erythematous plaque on the tip of her nose. There was no petechial or purpuric rash, no mucosal or genital involvement, and no malar rash. Hair, nails, and systemic examinations were unremarkable.

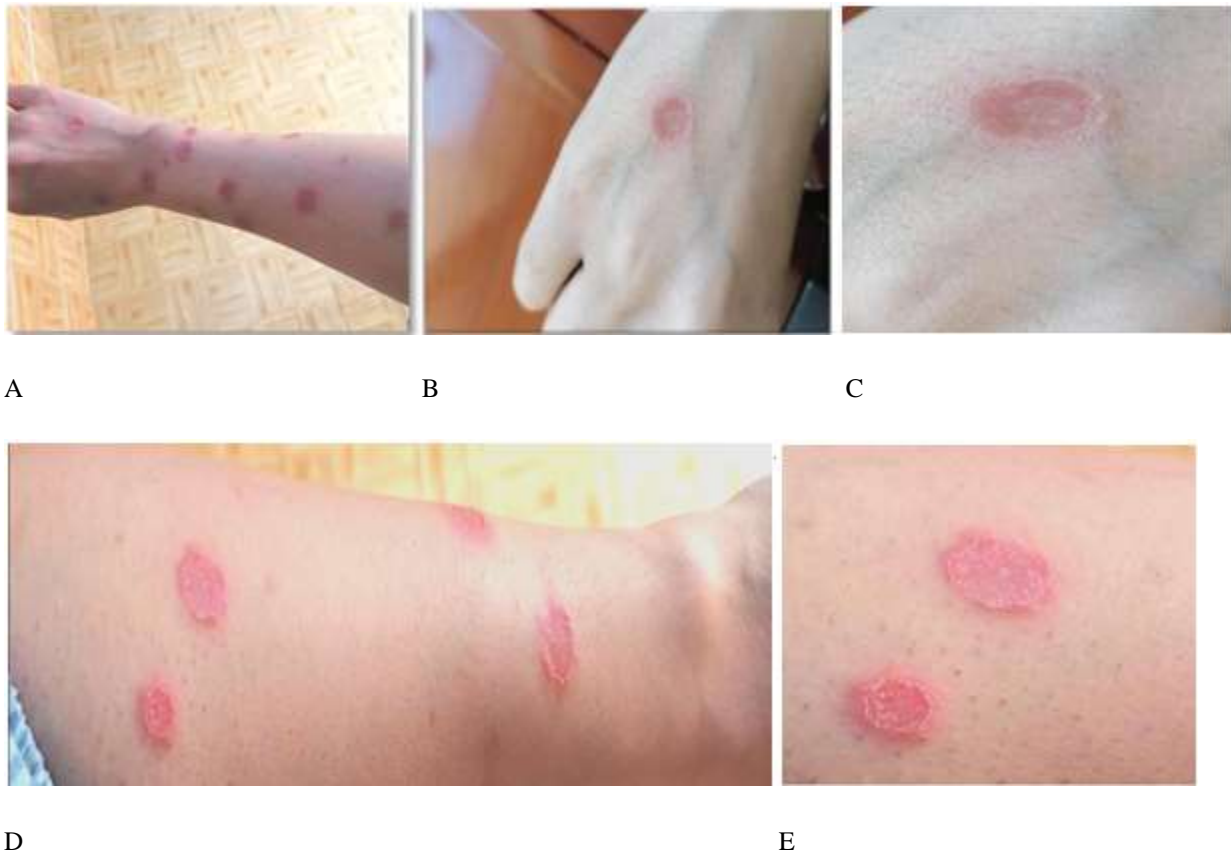


Figure 1: (a) Scattered annular erythematous and scaly plaques over the right upper limb. (b) Erythematous plaque with central erosion on the dorsum of the patient's right hand. (c) On high magnification for the skin lesion in figure 1B, it showed eroded and some ulceration ring like plaque on dorsum of right hand. (d) Multiple well-demarcated

erythematous and scaly plaques with raised borders on the patient's left upper limb. (e) On high magnification, annular erythematous plaques.

A differential diagnosis list was formulated, including superficial and deep fungal infections, nummular dermatitis, vasculitis, sporotrichosis spread like rashes, Behçet disease, Sweet syndrome, and disseminated granuloma annulare. Wood's lamp showed no fluorescence. The burning sensation along with the tenderness were against fungal infections so fungal scraping was not done and we preferred to go directly to skin biopsy which will also show the fungal elements and the other possible pathologies. Routine blood investigations were grossly normal except for mild neutrophilia ($5.48 \times 10^3/\mu\text{L}$ [1–4.8]). Skin punch biopsy was taken from right upper limb lesion showed irregular acanthosis, epidermis covered with thick parakeratotic crust showing aggregates of neutrophils and plasma cells. There was intraepidermal neutrophilic bullae and subepidermal blister formation with neutrophil infiltrate. The dermis showed marked edema, fibrin, red blood cell extravasation, and infiltrate composed of neutrophils, mononuclear cells, and histiocytes. There were focal crushing artifacts, and a few preserved vessels showed swelling of endothelial cells, smudged walls, and fibrin deposits around and within vessel walls. A small amount of nuclear dust was also present. Special PAS stain showed dermatophyte spores within hair follicles [Figure 2]. Gram stain was negative, and features were in favor of pustular dermatoses with leukocytoclastic vasculitis and dermatophyte spores with no hyphae seen.

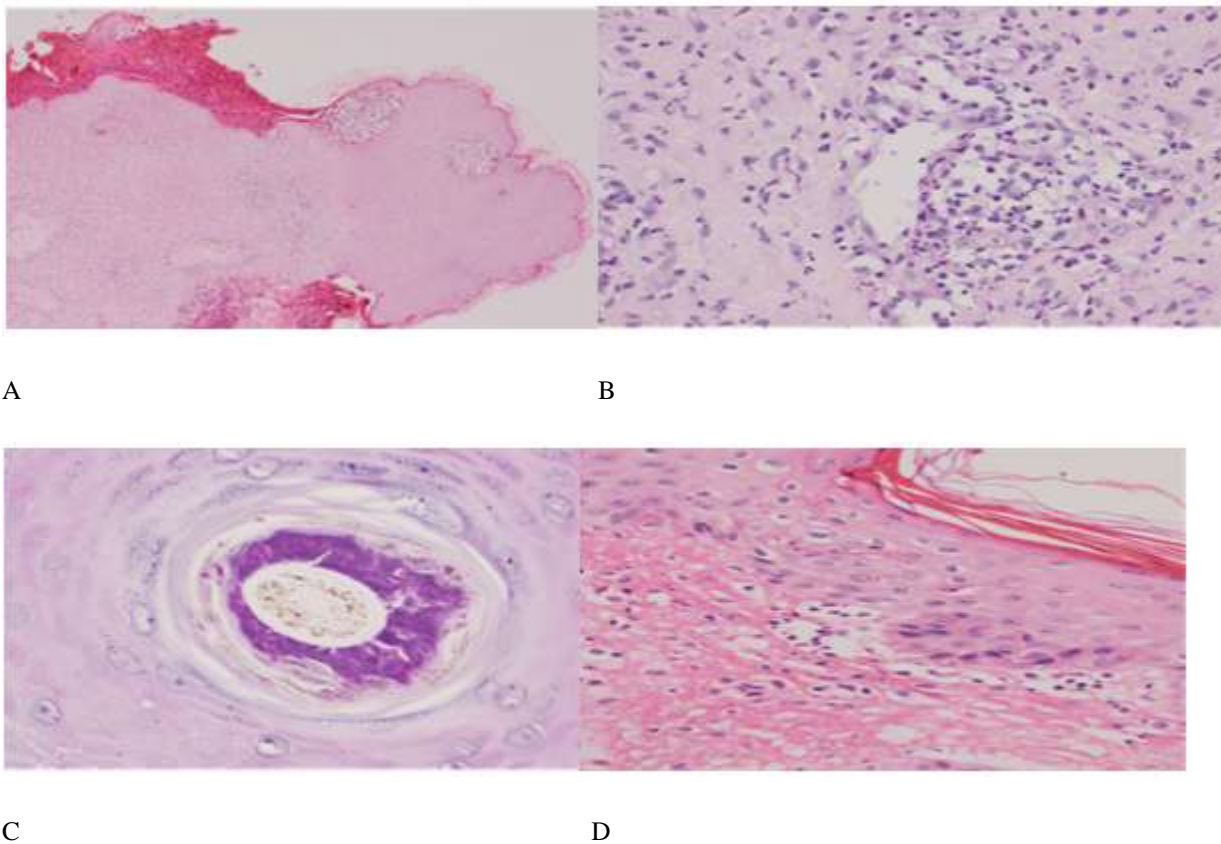


Figure 2: (a) H&E stain, magnification $10 \times$. A canthotic epidermis, covered with thick parakeratotic crust, containing aggregates of neutrophils and plasma cells. Intraepidermal neutrophilic vesicles are also seen. (b) H&E stain, magnification $40 \times$. Blood vessel showing prominent endothelial cells, smudged walls, neutrophils within and around vessel wall. (c) PAS stain, magnification $40 \times$. Dermatophytes spores and hypha within hair follicle. (d) H&E stain, magnification $20 \times$. Subepidermal blood vessel dilation with prominent fibrin and neutrophilic infiltrate.

With the above biopsy result of leukocytoclastic vasculitis along with her chronic recurrent fever, she was labeled as a case of pyrexia of unknown origin and underwent a comprehensive workup. The following tests were done, including ANA, cytoplasmic antineutrophil cytoplasmic autoantibody (C-ANCA), creatinine kinase (CK), ESR, CRP, complements C3 and C4, antistreptolysin (ASO) titer, HIV, hepatitis profiles, RA factor, brucella antibodies and interferon-Gamma release assays (IGRA). Imaging studies were also performed, including chest X-ray and abdominal ultrasound. All were normal except *B. melitensis* and *B. abortus* antibodies titer was reported to be positive with results

of 1:20 and 1:160, respectively. Incidentally, she was also found to be a hepatitis B carrier. Direct immunofluorescence was not done as we found no clues toward bullous disorders or SLE from history and investigations.

From the above history, clinical examination, and investigation results, a most likely rare diagnosis of leukocytoclastic vasculitis due to brucellosis was suggested. Although there were dermatophytes spores were present, the rash distribution, and the clinical (presence of tenderness rather than itching) and histopathological pictures were not suggestive of pathogenic fungal elements at all. The fungal spores were considered a coincidental finding. Additionally, the presence of leukocytoclastic vasculitis in skin biopsy is not related to tinea and is extremely rare.

The patient was cautiously treated with oral prednisolone 20 mg OD tapered every three days until reaching 5 mg. The last dose continued for 14 days, along with Rifampicin 600 mg once daily and Doxycycline 100 mg twice daily, both for six weeks. No topical antifungal was given for the explained reasons. Following treatment, she experienced a full and complete recovery from the previous skin eruption, as well as fever and other symptoms, within three weeks after starting the treatment. In subsequent follow-ups months later, the patient reported no new lesions or symptoms suggestive of brucellosis and no vasculitis rashes, only post-inflammatory hyperpigmentation over the previous skin lesions, which were fading gradually with time.

Discussion

Brucellosis is a multisystemic bacterial infection of zoonotic origin. Cutaneous manifestations observed in brucellosis are rare and nonspecific with only 1–14% of the patients affected with it.⁶ It was first described in 1940.^{7,8} The organism induces skin rashes by direct invasion of the skin, deposition of immune complexes, direct inoculation, or via the hematogenous route of spread.⁶ This probably explains the diversity of rashes reported. Ariza et al. reported 6% of 436 patients with brucellosis had cutaneous manifestations with the mostly observed ones being disseminated violet erythematous papulonodular eruption, and erythema nodosum-like lesions.³ Other rashes described were erythema, papules, petechiae, urticaria, impetigo-like, eczematous, chronic ulceration, and subcutaneous abscess [Table 1 and 2].^{1,3,9}

Table 1: Cutaneous rashes associated with brucellosis in general.^{6,8}

Most frequent skin lesions associated with brucellosis.

Papulonodular lesions

Erythema nodosum-like lesions

Maculopapular eruptions

Petechiae, purpura

Contact urticaria

Rare skin lesions associated with brucellosis

Vasculitis lesions

Subcutaneous abscesses

Chronic ulcerations

Liquefactive panniculitis

Recurrent epidermal cyst

Livedo reticularis

Table 2: The commonest rashes reported with brucellosis.⁸

Cutaneous lesion	Percentage (%)
Maculopapular eruptions	25
Erythema nodosum-like lesion	25
Psoriasiform lesion	12.5
Palmar erythema	12.5
Malar eruption	12.5

Our case had erythematous tender scaly red plaques with raised margins. Brucellosis-related vascular involvement was less often described in the literature. Leukocytoclastic vasculitis (LCV), also called hypersensitivity vasculitis, is a type of necrotizing, immune complex-mediated vasculitis that affects small vessels, mainly dermal capillaries, and venules. The etiology of it is unknown in nearly half of the cases, but it can be triggered by viral, bacterial infections, autoimmune rheumatological conditions, medications, and even malignancies [Table 3].^{3,10}

Table 3: Causes of small vessels vasculitis.^{10,11}

Association	Incidence	Causes of small vessels vasculitis		
		Common	Uncommon	Rare
Idiopathic	50%	Agent/Disease		
		Bacterial		
		Beta-hemolytic streptococci, especially group A <i>Mycobacterium leprae</i>	<i>Neisseria meningococcus</i> (in chronic meningococemia) <i>Mycobacterium tuberculosis</i> , atypical mycobacteria	<i>Mycoplasma pneumoniae</i> , <i>Chlamydia pneumoniae</i> , <i>Chlamydia trachomatis</i> , Brucella <i>Bartonella henselae</i> , <i>Salmonella</i> , <i>Campylobacter jejuni</i> , <i>enterocolitica</i> , <i>Treponema pallidum</i>
		Septic vasculitis*		
Infection	15–20%	Infective endocarditis	<i>Neisseria meningitidis</i> (acute), <i>Neisseria gonorrhoea</i> , <i>Staphylococcus aureus</i> <i>Rickettsia</i> , Gram-negative rods, <i>Escherichia coli</i> , <i>Klebsiella</i> , <i>Pseudomonas</i> , disseminated fungal infections (immunocompromised hosts) <i>Candida</i> , <i>Aspergillus</i> , <i>Fusarium</i> , <i>Mucor</i> .	<i>Francisella tularensis</i>
		Viral		
		Upper respiratory tract infection Hepatitis C, B, and A viruses including vaccines	HIV Parvovirus B19	Cytomegalovirus, Varicella zoster virus, influenza virus including vaccine
Inflammatory disorders	15–20%	Autoimmune connective tissue diseases – Rheumatoid arthritis – SLE – Sjögren syndrome	Inflammatory bowel disease, Behçet disease, hypergammaglobulinemic purpura of Waldenström, Seronegative spondyloarthropathies	Sarcoidosis, cystic fibrosis, primary biliary cirrhosis, bowel-associated dermatosis–arthritis syndrome, gluten enteropathy
Drug exposure†	10–15%	Antibiotics, esp. β-lactams penicillin, cephalosporin, sulfonamides, minocycline, quinolones, macrolides Cardiovascular Thiazides, hydralazine, quinidine Other Allopurinol, bortezomib, penicillamine, G-CSF, NSAIDs, Propylthiouracil, Streptokinase	Antimicrobials Quinine, Vancomycin Cardiovascular ACE inhibitors, beta-blockers, furosemide, other cocaine, adulterated with levamisole, COX-2 inhibitors, interferons, leukotriene inhibitors, methotrexate, oral contraceptives, phenytoin, retinoids, sulfonyleureas, TNF-α inhibitors, warfarin	Antimicrobials Mefloquine, Cardiovascular Amiodarone, Neuropsychiatric Atypical antipsychotics, gabapentin, phenothiazine SSRIs, Other Insulin, metformin, methamphetamine, rituximab, Miscellaneous Radiographic contrast media, Food/drug additives, vitamins

Neoplasms	2–5%	Plasma cell dyscrasias	Solid organ carcinomas (IgA vasculitis in adults >> other forms of CSVV)
		Monoclonal gammopathies	
Genetic disorders	Rare	Multiple myeloma	Immunodeficiency syndromes Familial Mediterranean fever and other periodic fever syndromes
		Myelodysplasia	
		Myeloproliferative disorders	
		Lymphoproliferative disorders	
		Hairy cell leukemia	
		Alpha-1 antitrypsin deficiency	

The pathogenesis of the vasculitis in brucellosis is not fully understood.^{12,13} However, the presumed hypersensitivity reaction in small blood vessels due to disease antigens is probably the cause.¹²

Fortunately, this disease-induced vasculitis can usually respond to antibiotic treatment.⁶ Nagore et al. and Karaali et al. reported quick regression of the rashes within 48 hours after proper disease-oriented antibiotic treatment.¹³ The same authors also reported spontaneous resolution.¹³ In our case, a complete clinical response was achieved in three weeks. The delay in response to treatment could probably be explained by the severity of the condition at presentation, the vasculitic nature of the rash, and the use of systemic steroid in an infectious process.

Conclusion

Brucellosis has a non-specific wide spectrum of clinical manifestations. Early diagnosis and intervention can prevent serious complications associated with this multisystemic dangerous disease. Brucellosis induced leukocytoclastic vasculitis is rare, but it needs to be considered in the endemic areas like the Middle East, especially when there is suggestive history, suspicious contact, and suggestive specific or nonspecific symptoms and signs.

Disclosure

The authors declared no conflicts of interest. Written consent was obtained from the patient.

References

1. Ekinci Ö, Ebiñç S, Doğan A, Aslan M, Demir CF. Acute brucellosis presenting as leukocytoclastic vasculitis. *Hematology, Transfusion and Cell Therapy* 2020;42(S1):60.
2. Zheng R, Xie S, Lu X, Sun L, Zhou Y, Zhang Y, et al. A systematic review and meta-analysis of epidemiology and clinical manifestations of human brucellosis in China. *Biomed Res Int* 2018 Apr;2018:5712920.
3. 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.
4. Cheikh M, Kabli A, Sendi E, Almoallim H. P-ANCA systemic vasculitis induced by brucellosis in an elderly male patient. *Case Rep Rheumatol* 2021 Nov;2021:6117671.
5. Bouomrani S, Mrad H, Teber SB. Cutaneous leukocytoclastic vasculitis revealing acute brucellosis: a case report. *American Journal of Medical Case Reports* 2021;9(6):335-338.
6. Karaali Z, Baysal B, Poturoglu S, Kendir M. Cutaneous manifestations in brucellosis. *Indian J Dermatol* 2011 May;56(3):339-340.
7. Milionis H, Christou L, Elisaf M. Cutaneous manifestations in brucellosis: case report and review of the literature. *Infection* 2000;28(2):124-126.
8. Korkmaz P, Kartal ED. Skin manifestations associated with brucellosis. *EMJ Dermatol* 2016;4(1):119-125.
9. Metin A, Akdeniz H, Buzgan T, Delice I. Cutaneous findings encountered in brucellosis and review of the literature. *Int J Dermatol* 2001 Jul;40(7):434-438.

10. Al-Busafi SA, Al-Suleimani A, Al-Hamadani A, Rasool W. Tenofovir-induced Leukocytoclastic Vasculitis. *Oman Med J* 2017 Sep;32(5):429-431.
11. Bologna JL, Schaffer JV, Cerroni L. *Dermatology: 2-volume set*. 4th ed. Elsevier Health Sciences; 2017. p. 415-416.
12. Catakli T, Arikan FI, Acar B, Dallar Y. Cutaneous vasculitis in a patient with acute brucellosis. *Clin Exp Dermatol* 2009 Oct;34(7):e387-e388.
13. Uçmak F, Uçmak D, Bestas R, Azizog Lu Anli R, Adanir H. Acute brucellosis associated with leukocytoclastic vasculitis and splenic infarct. *Infez Med* 2014 Dec 1;22(4):326-330.