American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2026; 27: e954208
DOI: 10.12659/AJCR.954208

Received: 2026.05.21
Accepted: 2026.10.14
Available online: 2026.10.30
Published: 2026.XX.XX

# A 72-Year-Old Male Land Surveyor With Chronic Recurrent Fever, Orchiepididymitis, Nasal Ulcers, and Skin Rash Due to Brucellosis (Undulant Fever)

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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**Financial support:** None declared
**Conflict of interest:** None declared

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**Patient:** Male, 72-year-old
**Final Diagnosis:** Probable chronic-phase brucellosis (undulant fever) with clinically suspected recurrent right epididymo-orchitis
**Symptoms:** Chronic recurrent fever • night sweats • asthenia • weight loss • recurrent right scrotal pain and swelling • right ankle arthralgia • macular skin rash • hemorrhagic nasal crusting of uncertain etiology
**Clinical Procedure:** —
**Specialty:** Infectious Diseases
**Objective:** Unusual clinical course

**Background:** Brucellosis is a globally prevalent zoonosis caused by bacteria of the genus *Brucella*. It poses a persistent clinical challenge due to its propensity for chronicity, high relapse rates, and substantial underreporting. This report describes the case of a 72-year-old male land surveyor with Hashimoto's thyroiditis, a history of acute myocardial infarction, and type 2 diabetes mellitus who presented with chronic recurrent fever, orchiepididymitis, nasal ulcers, and skin rash due to brucellosis (undulant fever).

**Case Report:** A 72-year-old male land surveyor with a decade-long history of recurrent fever, orchiepididymitis, and pulmonary granuloma developed acute fever, sweats, rash, and nasal crusting during hospitalization for myocardial infarction. Standard serological tests, blood cultures, and polymerase chain reaction assays were repeatedly negative during subsequent evaluation. A diagnosis of chronic-phase brucellosis was established based on occupational exposure to infected cattle (*Brucella abortus*), a historical reactive Rose Bengal test (1: 160), compatible clinical features, and systematic exclusion of alternative etiologies (vasculitis, tuberculosis, fungal infections, and endocarditis). Sustained remission was eventually achieved with an individualized 6-month empiric rescue regimen comprising 3 antimicrobial agents (doxycycline, rifampin, and ciprofloxacin). The patient completed 6 months of post-treatment follow-up without recurrence.

**Conclusions:** Establishing a diagnosis of chronic-phase brucellosis remains challenging when contemporaneous microbiological and serological assays are negative. In such contexts, a detailed occupational history, compatible clinical features, and systematic exclusion of alternative etiologies are critical to guide clinical management. Baseline endocrine comorbidities should be considered strictly as hypothesis-generating contextual factors, rather than established causal drivers of bacterial persistence.

**Keywords:** Brucellosis • Diabetes Mellitus, Type 1 • Endocrine System Diseases • Hypothyroidism • Zoonoses
**Full-text PDF:** https://www.amjcaserep.com/abstract/index/idArt/954208

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## Introduction

A recent study estimated the global incidence of brucellosis at approximately 1.6 to 2.1 million new cases annually, substantially higher than previous historical estimates. These cases primarily occur in Africa and Asia, followed by specific regions within the Americas and Europe [1,2]. In Brazil, the disease has a higher prevalence in regions with greater agricultural and livestock activity, such as the South and Midwest, and predominantly affects men [3]. The purchase of untested breeding animals, failures in vaccination programs, and the presence of flooded areas are important risk factors contributing to widespread distribution of the infection [4]. Official data substantially underestimate the true incidence of brucellosis, which may be up to 5 times higher due to underdiagnosis of atypical forms [5].

Brucellosis is a bacterial zoonosis caused by species of the genus *Brucella*; *Brucella melitensis* (sheep and goats), *Brucella abortus* (cattle), *Brucella suis* (swine), and *Brucella canis* (dogs) are the main human pathogens. *Brucella* species are gram-negative, aerobic, facultative intracellular coccobacilli capable of surviving within host macrophages [6,7]. The genus exhibits tropism for the mononuclear phagocytic system and erythritol-rich tissues, such as the testes, uterus, and placenta [6,8]. The pathogenic mechanism depends on smooth lipopolysaccharide, which reduces toxicity to macrophages and favors intracellular survival [5]. High endogenous concentrations of erythritol in the testes and epididymis stimulate bacterial growth, causing necrotizing inflammatory reactions and orchiepididymitis in up to 20% of infected men [5,9]. Extensive evaluations of systemic complications emphasize that focal organ involvement can span musculoskeletal, genitourinary, cardiovascular, and endocrine domains [10].

Transmission occurs through the consumption of unpasteurized dairy products; contact with infected secretions, tissues, or abortion-related fluids; and inhalation of aerosols [3,7,11,12]. Brucellosis is a major occupational hazard for livestock workers, veterinarians, and land surveyors [3,7,11,12]. Clinical manifestations include undulant fever, night sweats, fatigue, arthritis, orchiepididymitis, and osteoarticular complications [10,13,14]. Approximately 13.3% of brucellosis cases progress to chronicity [15]. Underlying conditions such as type 2 diabetes mellitus and thyroid dysfunction may alter host immune responses [16-19]. Previously published clinical studies and case series have described diagnostic delays, protracted clinical courses, and multisystem involvement in patients with occupational risk factors [12].

This report describes the case of a 72-year-old male land surveyor with Hashimoto's thyroiditis, a history of acute myocardial infarction, and type 2 diabetes mellitus who presented with chronic recurrent fever, orchiepididymitis, nasal ulcers, and skin rash due to brucellosis (undulant fever).

## Case Report

A 72-year-old male land surveyor presented with a decade-long history of recurrent fevers, night sweats, asthenia, and intermittent right-sided orchiepididymitis. His medical history was notable for type 2 diabetes mellitus and Hashimoto's thyroiditis. Approximately 10 years before presentation, while working in an agricultural region, he had direct occupational exposure to cattle infected with *B. abortus*, including handling placental tissues and participating in livestock vaccination. Later that year, he developed a pulmonary granuloma accompanied by high fever, profuse sweating, weight loss, right ankle arthralgia, and right-sided orchiepididymitis. Tuberculosis and endemic mycoses were ruled out at that time. He received an initial empiric course of oral doxycycline (100 mg twice daily)

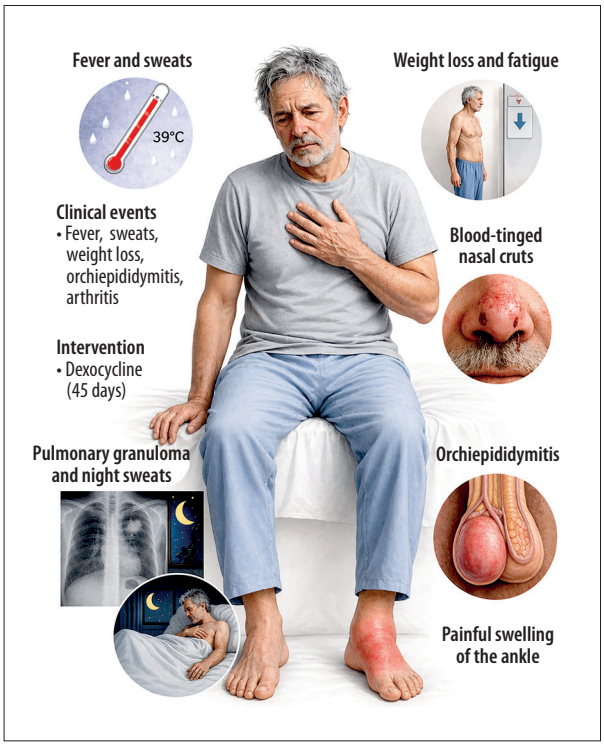



**Figure 1.** Conceptual illustration of multisystem clinical features in an older patient with brucellosis. The diagram illustrates potential manifestations involving multiple organ systems, including fever, profuse night sweats, weight loss, fatigue, hemorrhagic nasal crusting of uncertain etiology, orchiepididymitis, ankle arthralgia, and pulmonary granulomatous disease. This conceptual image was prepared by the authors with the assistance of ChatGPT-5 (OpenAI). Not all depicted manifestations were microbiologically or histopathologically confirmed to be caused by *Brucella*.

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for 45 days, which resulted in partial clinical improvement and resolution of the pulmonary granuloma, although intermittent fevers and urogenital symptoms persisted (**Figure 1**). The patient's clinical course is detailed in **Table 1**.

Approximately 9 years before presentation, a serum Rose Bengal agglutination test was reactive at a titer of 1: 160, providing historical serological evidence of exposure. Automated blood cultures (BACTEC FX system; 8-10 mL per bottle, 2 sets

**Table 1.** Serial laboratory parameters, medication exposures, and clinical course before, during, and after antimicrobial therapy.

| Phase / time frame | Clinical presentation | Key laboratory values (reference ranges) | Concurrent medications and doses | Antimicrobial regimen changes and rationale |
|---|---|---|---|---|
| **Approximately 10 years before presentation (initial exposure)** | Fever, sweats, pulmonary granuloma, right-sided orchiepididymitis, right ankle arthralgia | Tuberculosis and fungal workup: negative | Insulin glargine 18 units once daily; insulin lispro 4 units, 3 times daily; levothyroxine 25 mcg once daily | Oral doxycycline 100 mg twice daily for 45 days (partial response; granuloma resolved) |
| **Approximately 9 years before presentation** | Intermittent fever, scrotal pain | Rose Bengal: reactive (1: 160); blood cultures and IS711 PCR: negative | Unchanged | Observation |
| **Approximately 3 years before presentation** | Recurrent asthenia and fever | TST, T-SPOT.TB, Ziehl-Neelsen staining, perinuclear ANCA, cytoplasmic ANCA, and ANA: negative or nonreactive | Unchanged | Observation |
| **Days 1-10 of index hospitalization** | Acute myocardial infarction, heart failure | LVEF 15%; creatinine 0.90 mg/dL (0.70-1.20); potassium 4.3 mmol/L (3.5-5.0) | Clopidogrel 75 mg once daily; aspirin 100 mg once daily; atorvastatin 40 mg once daily; metoprolol 50 mg once daily; lisinopril 10 mg once daily | None |
| **Days 11-14 (exacerbation)** | Spiking fevers, night sweats, macular skin rash, nasal crusting, right scrotal tenderness | CRP 48 mg/L (< 3.0); ESR 62 mm/h (< 20); TSH 6.04 mIU/L (0.4-4.5); HbA1c 7.7% (< 5.7%); Rose Bengal, STA, ELISA, PCR, and 3 sets of blood cultures: negative | Levothyroxine titrated to 75 mcg once daily; insulin adjusted | Diagnostic workup; evaluation for endocarditis (no vegetations on echocardiography) and vasculitis |
| **Days 15-21** | Nasal crusting resolved (day 3 of treatment); fever decreased | Creatinine 0.92 mg/dL; potassium 4.4 mmol/L; CRP 22 mg/L | Unchanged | Oral doxycycline 100 mg twice daily and oral rifampin 900 mg once daily initiated |
| **Days 22-26** | Clinical improvement | Creatinine increased to 1.80 mg/dL; BUN 38 mg/dL (7-20) | Unchanged | IV gentamicin 5 mg/kg/day added (day 8 of treatment); subsequently discontinued due to nephrotoxicity |
| **Days 27-33** | Recurrent fever, night sweats, active orchiepididymitis | Creatinine 1.40 mg/dL; CRP 35 mg/L | Unchanged | Empiric reduction of rifampin to 600 mg once daily, followed by recurrence of clinical manifestations |

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**Table 1 continued.** Serial laboratory parameters, medication exposures, and clinical course before, during, and after antimicrobial therapy.

| Phase / time frame | Clinical presentation | Key laboratory values (reference ranges) | Concurrent medications and doses | Antimicrobial regimen changes and rationale |
|---|---|---|---|---|
| **Days 34-41** | Persistent scrotal pain and fever | Serum potassium increased to 6.2 mmol/L; creatinine 1.10 mg/dL | Lisinopril temporarily held | Oral trimethoprim-sulfamethoxazole 80/400 mg, 3 tablets twice daily, added; discontinued after 7 days due to hyperkalemia |
| **Days 42-56** | Rapid resolution of fever and scrotal tenderness | Potassium normalized to 4.5 mmol/L; CRP 8.0 mg/L | Lisinopril restarted at 10 mg once daily | Oral ciprofloxacin 500 mg twice daily added; doxycycline 100 mg twice daily continued; rifampin restored to 900 mg once daily |
| **Approximately 6 months after treatment initiation (end of treatment)** | Complete clinical remission, weight gain | CRP < 3.0 mg/L; ESR 12 mm/h; creatinine 0.95 mg/dL; ALT 24 U/L (10-40); AST 22 U/L (10-40) | Cardiovascular and endocrine therapies continued | Completed 6-month triple-antimicrobial regimen |
| **Approximately 6 months after treatment completion** | Sustained remission without relapse | CRP < 3.0 mg/L; ESR 10 mm/h; creatinine 0.94 mg/dL; potassium 4.4 mmol/L | Cardiovascular and endocrine therapies continued | Completed 6 months of post-treatment follow-up (12-month follow-up protocol ongoing) |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ANA, antinuclear antibodies; ANCA, antineutrophil cytoplasmic antibodies; BUN, blood urea nitrogen; CRP, C-reactive protein; ELISA, enzyme-linked immunosorbent assay; ESR, erythrocyte sedimentation rate; HbA1c, hemoglobin A1c; IV, intravenous; LVEF, left ventricular ejection fraction; PCR, polymerase chain reaction; STA, standard tube agglutination; T-SPOT.TB, T-cell spot test for tuberculosis; TSH, thyroid-stimulating hormone; TST, tuberculin skin test.

incubated for 21 days) and serum polymerase chain reaction (PCR) targeting the insertion element IS711 were negative. No intervening animal exposures, occupational contacts, travel, or consumption of unpasteurized dairy products occurred during the subsequent 9 years; the patient had not received antimicrobial therapy in the 2 years preceding the most recent testing.

Over the subsequent 9 years, the patient experienced recurrent episodes of low-grade fever, asthenia, and scrotal pain. Approximately 3 years before presentation, infectious and autoimmune evaluations were repeated. Ziehl-Neelsen staining, Löwenstein-Jensen cultures, and T-cell spot test for tuberculosis (T-SPOT.TB) to detect *Mycobacterium tuberculosis* were negative; serological tests for *Leishmania*, *Treponema pallidum*, human immunodeficiency virus, *Histoplasma*, and *Paracoccidioides* were nonreactive. Antineutrophil cytoplasmic antibodies (perinuclear ANCA and cytoplasmic ANCA) and antinuclear antibodies (ANA) were nonreactive.

During the index hospitalization, the patient was admitted with an acute myocardial infarction complicated by heart failure. Transthoracic echocardiography demonstrated a left ventricular ejection fraction of 15%, without valvular vegetations or regurgitant lesions, making culture-negative endocarditis less likely. During hospitalization, he experienced acute exacerbation of systemic symptoms, including spiking fevers, night sweats, macular eruptions on the hands and feet (**Figure 2**), right scrotal swelling with pronounced tenderness, and morning expulsion of hemorrhagic nasal crusts (**Figure 3**).

Otorhinolaryngological evaluation with flexible nasal endoscopy revealed diffuse mucosal hyperemia and superficial friability of the anterior nasal septum without overt ulceration, bone necrosis, or gross tissue destruction. Nasal swab bacterial cultures, direct potassium hydroxide preparations, and fungal cultures were negative. Nasal mucosal biopsy was deferred due to severe post-acute myocardial infarction hemodynamic instability and a high bleeding risk associated with

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**Figure 2.** Cutaneous macular findings in a 72-year-old man. (**A**) Dorsal view of the foot showing mild diffuse erythema with macular lesions. All toes are anatomically intact; the apparent absence of digits is attributable to plantar flexion and the photographic angle. (**B**) Dorsum of the hand demonstrating sparse erythematous to violaceous macular lesions. These undifferentiated clinical findings resolved during antimicrobial therapy without a specific histopathological diagnosis.

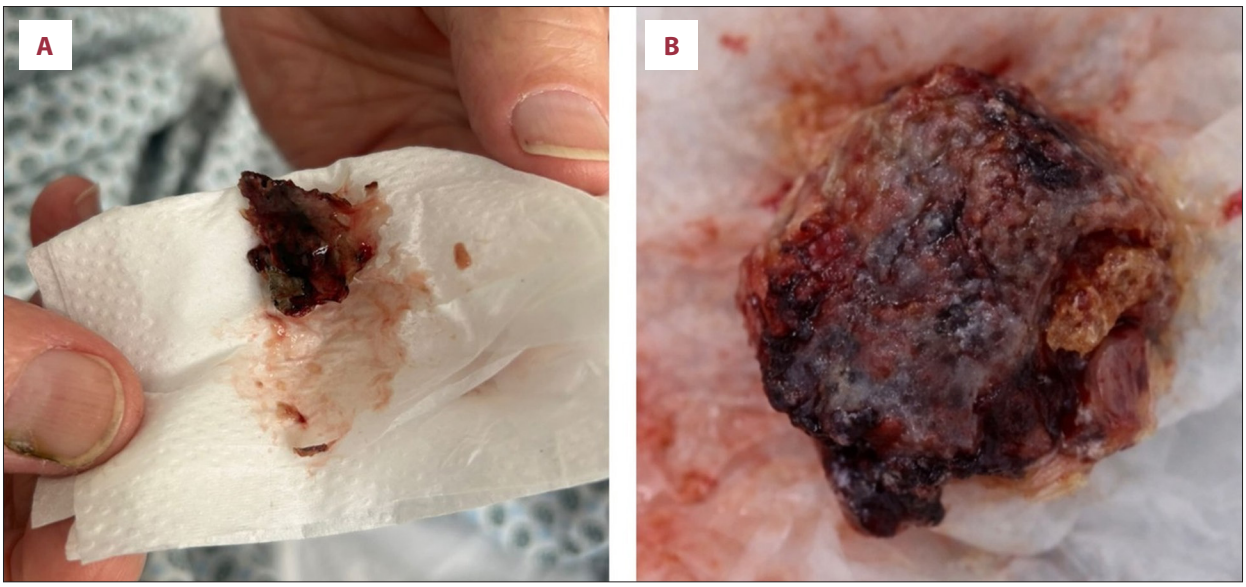



**Figure 3.** Spontaneously expelled hemorrhagic nasal crusts of uncertain etiology in a 72-year-old man. (**A**) Irregular fragment of hemorrhagic material with a friable consistency on absorbent paper, collected during hospitalization. (**B**) Magnified view demonstrating dark hemorrhagic crusting. No histopathological, polymerase chain reaction, or microbiological confirmation was obtained. The findings were interpreted as an undifferentiated clinical manifestation of uncertain etiology.

dual antiplatelet therapy. The nasal crusting was classified as an undifferentiated clinical finding of uncertain etiology that may have been unrelated to brucellosis.

During this admission, serum glucose levels fluctuated. The hemoglobin A1c level was 7.7% (reference range: < 5.7%), indicating glycemic control within the individualized target range of 7.5% to 8.0% appropriate for an older adult with severe ischemic cardiomyopathy. The patient was administered basal-bolus insulin (insulin glargine 18 units daily and insulin lispro 4 units before meals). Thyroid function testing revealed a thyroid-stimulating hormone level of 6.04 mIU/L (reference range: 0.40-4.50

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mIU/L); free thyroxine was not measured due to limited institutional availability. Levothyroxine sodium was titrated to 75 mcg daily, in accordance with standard guidelines for thyroid hormone replacement in older adults with cardiac disease [20].

Contemporaneous microbiological and serological testing during the index hospitalization—including repeat Rose Bengal testing, standard tube agglutination, enzyme-linked immunosorbent assay (IgM/IgG), 3 sets of automated blood cultures incubated for 21 days (BACTEC FX), and serum IS711 PCR—repeatedly yielded negative results. Additional testing to exclude alternative etiologies revealed nonreactive ANCA and ANA, normal complement C3 (112 mg/dL; reference range: 90-180 mg/dL) and complement C4 (24 mg/dL; reference range: 10-40 mg/dL) levels, normal serum protein electrophoresis, and negative deep fungal cultures. Pelvic magnetic resonance imaging demonstrated T2 hyperintensity and enlargement of the right epididymis and testis without abscess formation, fluid collections, or testicular torsion. Doppler ultrasound confirmed preserved vascular perfusion.

Given the strong history of occupational exposure to *B. abortus*, compatible clinical syndrome, historical seropositivity, and systematic exclusion of alternative etiologies, a diagnosis of chronic-phase brucellosis was established, and an individualized empiric rescue regimen was initiated. Oral doxycycline (100 mg twice daily) and oral rifampin (900 mg once daily) were initiated during hospitalization; nasal crusting subsequently resolved. One week later, intravenous gentamicin (5 mg/kg once daily) was added; this was discontinued after 5 days due to acute kidney injury (serum creatinine increased from 0.90 to 1.80 mg/dL). A subsequent empiric reduction in the rifampin dose to 600 mg daily was followed by recurrence of clinical manifestations (fever, night sweats, and scrotal pain).

Oral trimethoprim-sulfamethoxazole (80/400 mg, 3 tablets twice daily) was added approximately 3 weeks after treatment initiation but discontinued 7 days later due to severe hyperkalemia (potassium 6.2 mmol/L; reference range: 3.5-5.0 mmol/L), exacerbated by angiotensin-converting enzyme inhibitor therapy. The regimen was changed to oral ciprofloxacin (500 mg twice daily), oral doxycycline (100 mg twice daily), and full-dose oral rifampin (900 mg once daily). This triple-drug combination resulted in prompt resolution of fever, scrotal pain, and skin lesions, accompanied by normalization of inflammatory markers (C-reactive protein [CRP] decreased from 48 mg/L during early exacerbation to < 3.0 mg/L after 6 months of treatment).

The 6-month antimicrobial course was completed, and the patient subsequently completed 6 months of post-treatment follow-up with sustained clinical remission. Continued long-term monitoring (ongoing 12-month protocol) remains necessary to confirm the durability of the clinical response.

## Discussion

This case illustrates the diagnostic and therapeutic complexities of managing chronic-phase brucellosis in an older patient with pronounced cardiovascular and endocrine comorbidities. In chronic stages, serological tests and PCR assays may yield nonreactive results due to waning antibody titers, low-grade bacteremia, or intracellular sequestration within host macrophages (**Figure 4**) [21,22]. Pathogen persistence relies on sophisticated intracellular survival pathways within *Brucella*-containing vacuoles that resist phagolysosomal killing [21,23], complemented by immune evasion strategies such as upregulation of interleukin-10 production by CD4+ T cells [24] and accumulation of immunosuppressive myeloid-derived suppressor cells [25]. Furthermore, human studies have demonstrated that chronic brucellosis is characterized by impaired cell-mediated immunity and reduced interferon-gamma production [26-28]. The historical Rose Bengal reactivity (1: 160) provides evidence of past infection but cannot establish the persistence of viable bacteria a decade later without contemporary microbiological or molecular confirmation [22]. Therefore, the diagnosis rested on a probable clinical framework incorporating exposure history, clinical features, exclusion of alternative diseases, and clinical response to treatment.

Alternative differential diagnoses were systematically evaluated. Culture-negative endocarditis was assessed by echocardiography, which demonstrated a left ventricular ejection fraction of 15% without valvular vegetations. Systemic vasculitis was considered less likely based on negative ANCA results, normal complement levels, and the absence of necrotizing nasal lesions on endoscopy. Tuberculosis and fungal infections were considered less likely based on negative T-SPOT.TB testing, cultures, and staining. Nevertheless, negative laboratory findings do not definitively exclude these conditions.

The nasal findings were classified as hemorrhagic nasal crusting of uncertain etiology. In the absence of histopathological examination or positive nasal cultures, these crusts cannot be confirmed as manifestations of focal brucellosis and may represent an unrelated mucosal process. Similarly, the cutaneous macular lesions and ankle arthralgia resolved during antimicrobial therapy but remain undifferentiated clinical findings.

Urogenital involvement was clinically diagnosed as recurrent orchiepididymitis. Magnetic resonance imaging confirmed right epididymal and testicular inflammation without abscess formation or torsion. Although urogenital brucellosis is well documented, including rare instances of progression to necrotizing lesions or testicular abscesses [29], the absence of microbiological confirmation means that this finding represents clinically suspected—rather than microbiologically verified—focal brucellosis.

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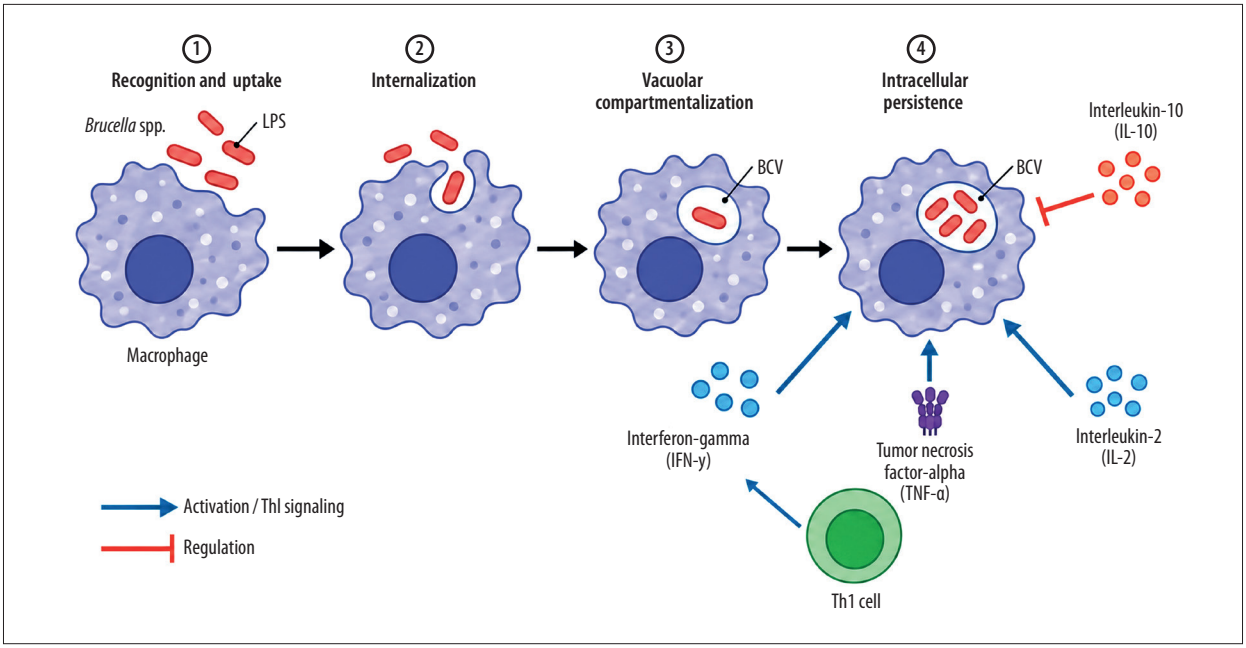



**Figure 4.** Artificial-intelligence-assisted conceptual illustration of *Brucella* uptake and intracellular trafficking within host macrophages. The schematic depicts bacterial recognition and uptake, internalization, compartmentalization within a *Brucella*-containing vacuole, and intracellular persistence. Key cytokines involved in macrophage activation and Th1 immune modulation, including IFN-γ, TNF-α, IL-2, and IL-10, are also represented. Abbreviations: BCV, *Brucella*-containing vacuole; IFN-γ, interferon-gamma; IL, interleukin; LPS, lipopolysaccharide; Th1, T-helper type 1; TNF-α, tumor necrosis factor-alpha. This conceptual image was prepared by the authors with the assistance of ChatGPT-5 (OpenAI).

The 6-month regimen of oral doxycycline, rifampin, and ciprofloxacin should be considered an individualized empiric rescue strategy, rather than a standardized guideline-recommended regimen. Standard first-line regimens include doxycycline plus an aminoglycoside or doxycycline plus rifampin for 6 to 8 weeks [8,30,31]. In our patient, aminoglycoside-induced nephrotoxicity and trimethoprim-sulfamethoxazole-induced hyperkalemia required treatment modifications. Ciprofloxacin was incorporated as an alternative oral agent with intracellular activity [32,33]. Symptom resolution and normalization of CRP and erythrocyte sedimentation rate indicate clinical improvement temporally associated with therapy, not definitive microbiological evidence of bacterial eradication.

Endocrine comorbidities, including type 2 diabetes mellitus and subclinical hypothyroidism, are best viewed as contextual, hypothesis-generating factors. A historical association among brucellosis, diabetes, and impaired metabolic defenses has long been recognized [34]. Modern molecular studies have shown that hyperglycemia and diabetes disrupt the Th1/Th2 cytokine balance and suppress macrophage activation [35-37]. Furthermore, high glucose concentrations stimulate maladaptive inflammatory signaling in vascular smooth muscle cells [38], whereas neuroendocrine stress pathways exacerbate immunosuppression [39]. Thyroiditis has also been reported in connection with brucellosis and vascular involvement [40-42]; poorly controlled diabetes and thyroid dysfunction can impair leukocyte function and cell-mediated immunity in vitro [15,16,43]. Recent literature emphasizes that vascular smooth muscle and endothelial cells serve as key structural components involved in innate immune regulation and systemic responses [17]. Furthermore, comprehensive reviews by Wang et al [18] and Little et al [19] highlight how metabolic disturbances, cardiovascular disease, and insulin resistance interact to alter systemic pathophysiology and host resilience. These concepts provide a theoretical context for understanding complex multisystem presentations in older adults with multimorbidity. However, in the absence of free thyroxine measurements, cytokine profiling, or cellular immunity assays, no direct causal link can be established between these comorbidities and persistent clinical disease in our patient.

## Conclusions

This report describes chronic-phase brucellosis management in an older patient with cardiovascular and endocrine comorbidities. When contemporaneous serological tests, cultures, and PCR assays yield negative results, a probable clinical diagnosis must rely on a detailed exposure history, compatible clinical features, and systematic exclusion of alternative diseases. Resolution of clinical symptoms and normalization

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of inflammatory markers during antimicrobial therapy indicate clinical improvement, rather than microbiological proof of bacterial eradication. Empiric multidrug antimicrobial regimens tailored to mitigate organ toxicity must be interpreted cautiously as individualized rescue strategies. Underlying diabetes and thyroid dysfunction represent contextual clinical factors, not proven causes of chronic infection. This case suggests that clinicians should consider chronic brucellosis in older adults with prior livestock exposure and recurrent febrile orchiepididymitis, even when current microbiological and serological tests are negative.

**Acknowledgments**

This article is part of the final project of Letícia Furtado Alves for the Medical Residency in Internal Medicine at the Faculty of Health Sciences (ESCS)/Foundation for Teaching and Research in Health Sciences (FEPECS)/State Secretariat of Health of the Federal District (SES-DF), Brasília, Brazil. The authors acknowledge that Figures 1 and 4 were prepared with the assistance of ChatGPT-5 (OpenAI) for visual conceptualization. Artificial intelligence (AI)-based software tools (Gemini AI, Google; ChatGPT, OpenAI) were used solely for linguistic refinement, grammar optimization, and technical translation assistance to meet academic English standards.

**Department and Institution Where Work Was Done**

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**Informed Consent Statement**

The research project was approved by the Research Ethics Committee of FEPECS (CEP) under protocol number 92285125.8.0000.5553. The patient freely provided written informed consent for the publication of this case report.

**Declaration of Figures' Authenticity**

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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