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Case Report

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False-Positive Rose-Bengal Test in A Patient with Systemic Sarcoidosis - A Case Report

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Abstract

Background: *Brucellosis is a zoonotic infection endemic in regions such as Israel, where it remains prevalent among specific subpopulations. Diagnosis relies heavily on serologic testing, with the Rose Bengal test (RBT) commonly used as a rapid and sensitive screening tool. However, its specificity is variable, and false-positive results have been reported in other infectious and inflammatory conditions.*

Case Summary: *We describe a patient who presented with fever of unknown origin and systemic inflammatory findings, initially raising suspicion for brucellosis based on a positive RBT. Subsequent investigations, however, revealed histopathologic evidence of sarcoidosis and excluded brucellosis.*

Conclusion: *To our knowledge, this is the first reported case of a false-positive RBT in a patient with systemic sarcoidosis. This case underscores the diagnostic challenges in endemic areas where overlapping clinical features may lead to misinterpretation of serologic screening results. Clinicians should interpret positive RBT findings cautiously and confirm the diagnosis with specific testing to prevent unnecessary antimicrobial therapy and delays in appropriate management.*

Introduction

Brucellosis is a zoonotic infection caused by the bacteria of the Brucella spp.(1) It is endemic in certain regions, including Israel, where it is particularly prevalent among the Arab population.(2,3) Brucella infection may present with a wide spectrum of clinical manifestations, ranging from non-specific constitutional symptoms to focal organ involvement. One of its more elusive presentations is fever of unknown origin (FUO) (4,5).

Due to the non-specific nature of the clinical features, laboratory confirmation is essential for establishing a diagnosis of brucellosis and initiating treatment. Among the various diagnostic tools available, the Rose Bengal test (RBT) is widely used as a rapid, inexpensive, and highly sensitive screening tool (6,7). However, despite its sensitivity, the specificity of the RBT is variable, and false-positive results have been documented in patients with other infectious or inflammatory conditions (8).

Sarcoidosis is a systemic granulomatous disorder of unknown etiology, characterized by non-caseating granulomas in affected organs (9). It can involve nearly any organ system and often presents with systemic symptoms such as fever, rash, arthralgia, and occasionally as FUO (10,11).

Given the inflammatory nature and potential for polyclonal antibody activation, sarcoidosis may theoretically cause false-positive serologic test results. The association between sarcoidosis and false-positive RBT is not established in the literature and was even excluded in some studies (12). To the best of our knowledge, this is the first reported case of its kind.

Here we report a case of a patient who initially presented with FUO and was ultimately diagnosed with systemic sarcoidosis. During the diagnostic workup, the patient had a positive RBT, which initially raised concern for brucellosis. However, confirmatory testing was negative for brucellosis, and the clinical picture, along with radiologic and histologic findings, established the diagnosis of sarcoidosis. This case highlights the diagnostic challenges posed by overlapping clinical presentations and the limitations of screening tests in endemic settings.

Case presentation

A 60-year-old woman of Arab origin was admitted to the Internal Medicine Department with fever and polyarthralgia. Her medical history was noted for hypothyroidism, iron-deficiency anemia, and obesity. One week before admission, the patient developed polyarthralgia involving the wrists, elbows, knees, and ankles. Two days before admission fever up to 38.8°C was documented, accompanied by bilateral wrist

swelling and a non-pruritic macular rash involving the palms (Figure 1) and upper abdomen (Figure 2).

On physical examination upon admission, the patient was afebrile and hemodynamically stable. Tenderness was noted in multiple joints without signs of synovitis/arthritis. Pulmonary and cardiac auscultation were unremarkable. A maculopapular rash was observed over the upper abdomen and palms (Figure 1 + 2).

Figure 1- Macular rash involving the palm

Figure 2- Macular rash involving the upper abdomen

Initial laboratory evaluation revealed leukopenia (3.69 × 10⁹/L; normal range: 4.5-11.0 × 10⁹/L), hemoglobin 9.4 g/dL (normal range: 13.5-17.5 g/dL), and a normal platelet count (216 × 10⁹/L). C-reactive protein was elevated at 10.4 mg/dL (normal range: 0-0.5 mg/dL). Serum electrolytes, creatinine clearance, and liver enzymes were within normal limits. Ferritin was 107 µg/L (normal range: 13-150 µg/L), albumin 3.5 g/dL (normal range: 3.5-4.5 g/dL), and angiotensin-converting enzyme (ACE) levels were within normal limits (61.9 U/L; normal range: 16-85 U/L). Urinalysis showed leukocyturia (75 leukocytes/µL) without hematuria or proteinuria. Antinuclear antibody (ANA) was negative, and complement levels (C3 and C4) were within normal limits.

Chest X-ray revealed bilateral hilar lymphadenopathy that was not observed in previous X-rays (Figure 3). A Rose-Bengal test for Brucella returned positive, serologic tests for Coxiella burnetii (Q Fever), and Rickettsia spp returned negative. Blood cultures were found to be sterile. Given the clinical findings of fever, rash, lymphadenopathy, and elevated inflammatory markers, without any focal signs of infection, treatment was initiated with doxycycline, under the presumed diagnosis of Brucellosis.

Figure 3- Chest X-ray demonstrating hilar lymphadenopathy

With a lack of clinical improvement, a computed tomography (CT) scan of the chest-abdomen and pelvis was performed, which demonstrated multiple enlarged mediastinal and hilar lymph nodes (up to 3 cm in diameter) and splenomegaly. Lymph nodes in other sites were not enlarged, and no pathological findings were found in the liver (Figure 4).

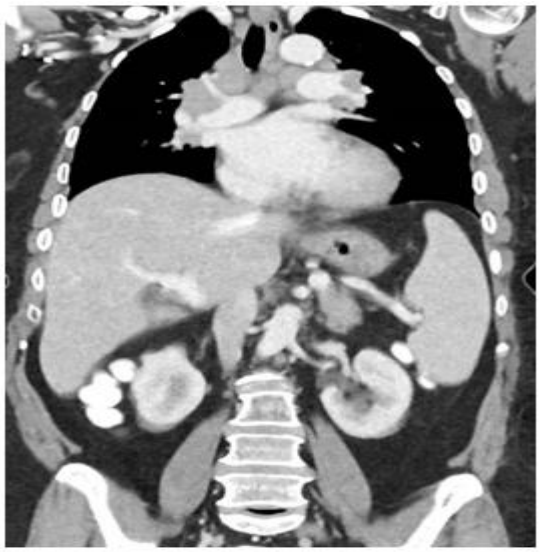

Figure 4- Contrast-enhanced chest CT shows the mediastinal and bilateral symmetric hilar lymphadenopathy with mild spleen enlargement

A mediastinal lymph node biopsy, as well as skin biopsy from the palmar rash were performed and revealed non-caseating granulomatous inflammation consistent with sarcoidosis (Figure 5).

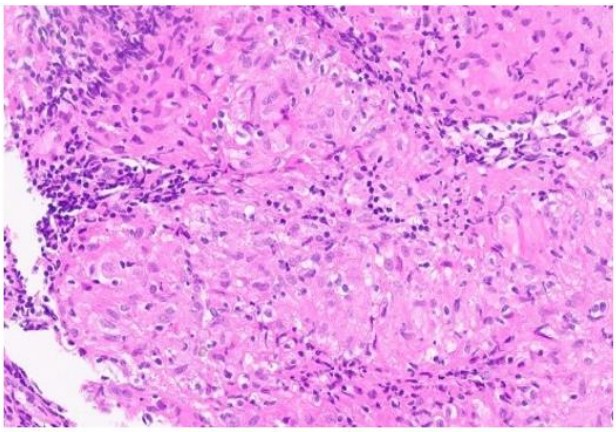

Figure 5- H&E pathology slide from mediastinal lymph node biopsy demonstrating epithelioid granuloma without necrosis in lymphoid tissue.

At this point, the antibiotic therapy was stopped, and treatment was initiated with corticosteroids. Within a few days, a significant clinical improvement was observed in the rash and joint symptoms. Confirmatory serologic tests for Brucella were negative. Given the lack of microbiologic evidence for infection, along with histologic confirmation and clinical response to immunosuppression, the RBT was interpreted as false-positive in the setting of systemic sarcoidosis.

Discussion

The RBT is a rapid, inexpensive screening tool for brucellosis, with high sensitivity but variable specificity. False-positive RBT results have been documented in patients with other infectious, inflammatory, and autoimmune diseases. In endemic regions such as Israel, where brucellosis remains prevalent, particularly among certain subpopulations, RBT is often utilized early in the evaluation of patients presenting with FUO. In such settings, a positive result may significantly influence diagnostic and therapeutic decisions. Our patient, who resides in an endemic area and presented with FUO and systemic symptoms, was therefore at risk of being misdiagnosed with brucellosis based on RBT alone.

Sarcoidosis is a systemic granulomatous disease that may mimic brucellosis. Symptoms such as prolonged fever, arthralgia, and rash can be found in both diseases. In this case, the patient's initial presentation suggested an atypical infection, prompting empiric antibiotic therapy.

The negative confirmatory test for Brucella, together with the clinical, radiographic, and histopathologic findings, shifted the diagnosis toward systemic sarcoidosis. Clinical improvement with corticosteroid therapy further reinforced the inflammatory rather than infectious etiology of the patient's illness.

To our knowledge, this is the first description of a false-positive RBT in a patient with an initial presentation of systemic sarcoidosis.

This case illustrates the complexity of diagnosis posed by overlapping syndromes and highlights the limitations of relying solely on serologic screening tests without confirmatory evidence. One should remain cautious in interpreting positive RBT results in patients with known or suspected systemic inflammatory diseases such as sarcoidosis. Clinical correlation and confirmatory testing are essential to avoid misdiagnosis, unnecessary antimicrobial treatment, and delays in appropriate treatment.

Conclusion

This case emphasizes the need for caution when interpreting screening tests, particularly in regions where certain diseases are endemic. While the Rose Bengal test remains a useful initial tool for detecting Brucella infection, its limited specificity may lead to false-positive results in patients with alternative inflammatory or granulomatous conditions. Clinicians should avoid overreliance on a single test result and ensure that test findings are consistent with the overall clinical and epidemiologic context. Confirmatory testing and consideration of alternative diagnoses are essential to prevent misdiagnosis, unnecessary antimicrobial therapy, and delays in appropriate treatment.

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