



Is it Brucellosis or Multiple Myeloma? Or can it be both?

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Abstract

Brucellosis is a zoonotic infection caused by the bacterial genus *Brucella*, which are gram-negative coccobacilli. Multiple myeloma is the clonal malignant neoplasm of plasma cells. Patients with brucellosis may present with hematological findings. It may even cause pancytopenia and mimic acute leukemia. However, coexistence of brucellosis with hematological malignancies, especially multiple myeloma, is rarely encountered and there are only a few cases reported in the literature. Both diseases may cause similar symptoms and laboratory findings, making the differential diagnosis challenging. A 72-year-old male patient presented with malaise, fever and diffuse joint pain. Serological testing for brucellosis turned out positive and he was started on antibacterial therapy. Although his fever had subsided, the laboratory parameters showed no improvement. The patient, who had progressive anemia and persistent high erythrocyte sedimentation rate, was referred to our hematology clinic for further evaluation and was diagnosed with multiple myeloma. He has received chemotherapy along with antibacterial therapy for brucellosis and is still under follow-up. In conclusion, brucellosis can mimic various diseases including hematologic malignancies and can lead to missing the diagnosis of a malignancy when seen concomitantly.

Keywords: Brucellosis; Multiple myeloma; Anemia; Erythrocyte sedimentation rate

Introduction

Brucellosis is a zoonotic bacterial infection that is seen worldwide. The prevalence of brucellosis varies in America and Europe, but it is more common in Asia and developing countries [1]. Brucellosis is caused by infection with *Brucella* species, which are gram-negative coccobacilli. *Brucella melitensis* causes the most invasive and severe cases of brucellosis. *Brucella melitensis* infections are commonly observed in Turkey. The main reasons behind are the consumption of unpasteurized milk and dairy products and direct contact with infected animals or their secretions. It is particularly more frequent in people living in rural areas and dealing with livestock [2,3].

Brucellosis has a wide clinical spectrum which can make it challenging to diagnose and can cause serious hematological findings including pancytopenia. Bone marrow and splenic involvement can also be observed. Patients may present with anemia, leucopenia and high erythrocyte sedimentation rate. Anemia and leucopenia are more frequent in the acute phase, while pancytopenia and thrombocytopenia are less commonly observed [4-6].

Multiple myeloma is the clonal malignant neoplasm of plasma cells and accounts for almost 10% of all hematologic malignancies. The median age at diagnosis for multiple myeloma is the 6th decade and only 2% of the cases occur in people younger than 40 years of age [7-9]. The most common symptoms at presentation are weakness and bone pain. 75% of the patients are observed to have anemia, which causes the weakness. Osteolytic lesions are seen in up to 80% of the cases. Less common findings are hypercalcemia and increased serum creatinine levels. High erythrocyte sedimentation rates usually accompany anemia. Immunoelectrophoresis studies have a higher sensitivity for diagnosis than serum protein electrophoresis. The most common subtype of M protein is IgG with 50%, followed by IgA with 20%, light chain with 20%, IgD with 2% and IgM with 0.5%. Non-secretory multiple myeloma is observed in 2-3% of the cases [10,11].

In this report, we present a case that presented to infectious diseases clinic with weakness, diffuse joint pain and fever, was found to have anemia, high erythrocyte sedimentation rate along with positive serological tests for brucellosis and was referred to our hematology clinic for persistent symptoms despite treatment for brucellosis and diagnosed with multiple myeloma.

Case Presentation

A 72-year-old male patient presented to infectious diseases clinic with weakness, diffuse joint

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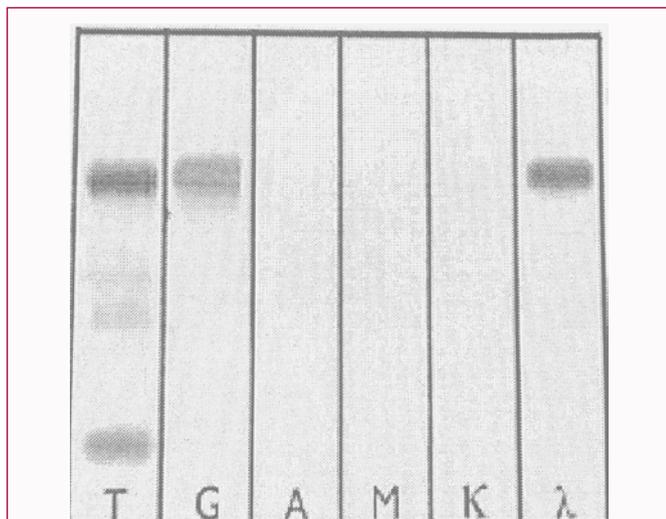


Figure 1: Serum immunoelectrophoresis (Monoclonal gammopathy IgG lambda light chain).

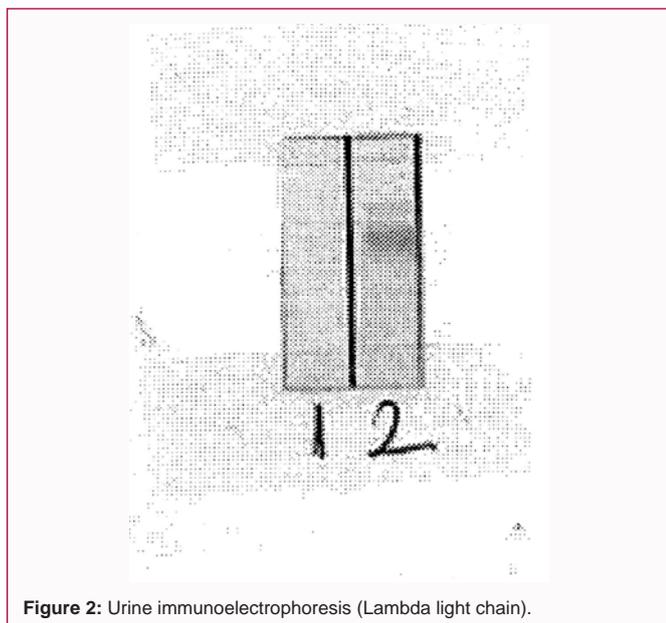


Figure 2: Urine immunoelectrophoresis (Lambda light chain).

pain and fever. First-line laboratory tests revealed anemia and high erythrocyte sedimentation rate (WBC: $8610 \times 10^9/L$, Hgb: 9.6 gr/dL, PLT: $256 \times 10^9/L$, ESR: 95 mm/hr). When specific tests were performed, Rose-Bengal plate test for brucellosis was positive along with 1/320 positivity in standard tube agglutination test. The patient was therefore started on tetracycline and rifampicin for brucellosis. His fever had subsided with treatment, but anemia progressed and erythrocyte sedimentation rate elevation persisted and therefore the patient was consulted with our hematology clinic. Laboratory tests performed showed that serum total protein levels were increased while the albumin/globulin ratio was reversed (total protein: 10.6 g/dL, albumin 2.1 gr/dL, and globulin: 8.5 gr/dL). Also, serum IgG level was 7097 mg/dL, IgA was 46 mg/dL, IgM 46 mg/dL, serum free kappa light chain 9.4 gr/dL, serum free lambda light chain 163 gr/dL and kappa/lambda ratio was 0.05. A serum immunoelectrophoresis (Figure 1) performed afterwards revealed IgG/lambda monoclonal band while urine immunoelectrophoresis (Figure 2) showed lambda free chain. In the light of these findings, bone marrow aspiration and biopsy were performed. Aspiration revealed plasma cell infiltration

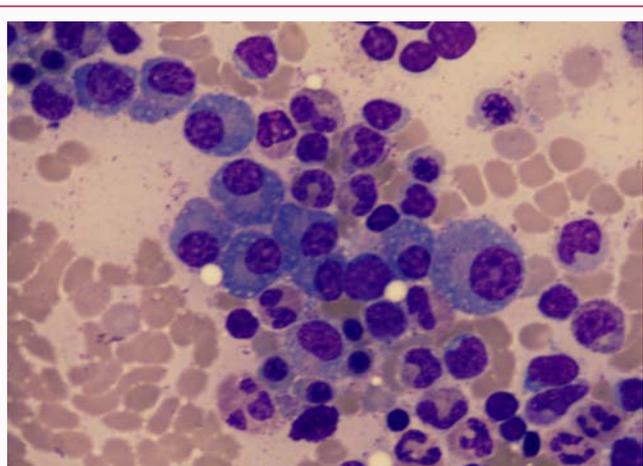


Figure 3: Diffuse plasma cell infiltration in bone marrow (H&E, x100).

(Figures 3). There was no deletion or translocation in cytogenetic analysis of the bone marrow like t(11;14), t(4;14), 17p deletion or 13q deletion. Magnetic resonance imaging showed no lytic bone lesions. The patient was diagnosed with multiple myeloma and started on chemotherapy with a regimen containing bortezomib, cyclophosphamide and dexamethasone. The antibiotherapy for brucellosis continued while the patient received chemotherapy. During follow-up, serologic testing for brucellosis turned negative and antibiotics were discontinued. The patient is still under treatment for multiple myeloma and is tested for brucellosis every 3 months.

Discussion

Patients with brucellosis may present with fever of unknown origin, joint pain and weight loss, while some present with hematological findings [12-14]. In certain cases, brucellosis can cause pancytopenia and mimic acute leukemia. Pancytopenia is reported to be between 3-21% in brucellosis series. Hemophagocytosis, hypersplenism, bone marrow granuloma and immune-mediated mechanisms are among the suggested pathways although the exact pathogenesis is not yet clear. In this patient group, hematological findings return to normal after treatment with antibiotics [15,16].

Brucellosis may unusually co-exist with hematologic diseases, solid organ malignancies or hematologic malignancies [17,18]. Although very rare, there are cases reported in the literature. Acute leukemia, Hodgkin's lymphoma, non-Hodgkin lymphoma and hairy cell leukemia are among the hematologic malignancies that brucellosis is reported to co-exist with [6,17,19]. In the case of a concomitant malignancy, brucellosis patients may have severe anemia and higher sedimentation rate along with serious thrombocytopenia. There are no human studies evaluating the role of *Brucella* infections in leukemia pathogenesis while animal studies on the related subject are available [20]. However, in the light of current literature, it is almost impossible to deduct whether brucellosis triggers hematologic malignancies or the coexistence is purely incidental.

In conclusion, the coexistence of brucellosis and multiple myeloma is quite rare and previous reports in the literature are limited. In our case report, we want to emphasize that, common symptoms and findings of brucellosis can mimic various diseases including hematologic malignancies and can even lead to missing the diagnosis of a malignancy when concomitantly observed.

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