CASE REPORT

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Brucellosis with Neutropenia in an Immunocompetent Patient

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ABSTRACT Brucellosis, a prevalent zoonotic disease, can present with a range of hematological abnormalities, including rare neutropenia cases. This report describes a 29-year-old male patient who developed neutropenia due to acute brucellosis. The patient applied to the hospital with complaints of low back pain and sweating and was found to have anemia, neutropenia, elevated liver enzyme levels and hepatosplenomegaly as a result of the examinations. The brucellosis diagnosis was established as a standard tube agglutination test (1/1,280). Hematological parameters improved with antimicrobial treatment and vitamin B_{12} replacement. However, mild leukopenia persisted. The patient was treated with rifampicin 600 mg/day and doxycycline 200 mg/day for 3 months. This case underscores the need to consider brucellosis for the differential diagnosis of neutropenia in endemic regions and highlights the importance of monitoring hematological parameters in patients with this condition.

Keywords: Brucellosis; neutropenia; zoonosis; infectious diseases; hematology

Brucellosis, a common zoonotic disease caused by *Brucella* bacteria, is often transmitted through contact with infected animals or consumption of unpasteurised milk.[1] It can cause various clinical manifestations due to multi-system involvement, including hematological abnormalities. Patients may be presented with hematological manifestations such as anemia, leukopenia and less commonly pancytopenia and thrombocytopenia.[2] However, neutropenia is a rare clinical finding in brucellosis. This report describes a case of brucellosis-associated neutropenia in a previously healthy 29-year-old man.

CASE REPORT

The patient presented with persistent low back pain and night sweats and had a history of consuming cheese made from raw milk. Initial assessments showed normal vital signs. There was pain in the lumbar region, but no motor or neurological deficits were noted. Laboratory findings were as follows: hemoglobin (HGB), 9 g/dl; platelet count, 163x10⁹/L; and white blood count (WBC), 2.5x10⁹/L (neutrophil count 0.93x10⁹/L, 37%). Additionally, bicytopenia was detected. Aspartate aminotransferase (AST), 59 U/L; alanine transaminase (ALT), 78 U/L; lactate dehydrogenase, 387 U/L; C-reactive protein (CRP), 22.7 mg/dl; ferritin, 1,198 ng/ml were found to be elevated. The coagulation and fibrinogen levels were within the normal range. Abdominal ultrasonography revealed mild hepatosplenomegaly, with a liver size of 166 mm and a spleen size of 140 mm. The Rose Bengal test (ADR-Advanced Diagnostics&Research, Türkiye) was positive and the standard tube agglutination test (ADR-Advanced Diagnostics&Research,

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Türkiye) titer was 1/1,280 positive. Based on the current results, bicytopenia due to acute brucellosis was considered and the patient was hospitalized in the infectious disease service for investigation and treatment. Two sets of blood cultures were obtained, and hepatitis and human immunodeficiency virus serology were investigated. A contrast-enhanced lumbar magnetic resonance imaging (MRI) was conducted to exclude the possibility of spondylodiscitis. The treatment regimen comprising rifampicin (600 mg/day), doxycycline (200 mg/day) and gentamicin (5 mg/kg/day) was initiated.

The laboratory findings on the 5th day of treatment were as follows: HGB, 9.2 g/dl; platelets, 154x10^9/L; WBC, 2.19 10^9/L (neutrophil count 0.44x10^9/L, 20%); and neutropenia was detected. AST, 114 U/L; ALT, 170U/L; CRP, 18.9 mg/dl were still elevated. The Epstein-Barr virus and cytomegalovirus serologies, which may cause cytopenia, were compatible with previous infection. The patient, who had no growth in blood culture and no fever since hospitalization, was consulted by an internal medicine physician due to the development of neutropenia. Intravascular coagulation and hemolysis were not detected as causes of anemia and neutropenia. No evidence of malignancy was identified through physical examination, and computed tomography of the neck, thorax, and abdomen revealed no abnormalities. The patient had no history of transfusion, radiotherapy, or chemotherapy. There was no use of illicit drugs or herbal substances. No evidence of autoimmune disease was identified through physical examination or laboratory findings (anti-nuclear antibody negative, anti-dsDNA negative). The peripheral blood smear was compatible with bicytopenia. No atypical cells or blasts were observed, and no additional pathology causing leukopenia was identified, except for low vitamin B_{12} levels (151 pg/mL). Intramuscular 1,000 mcg/day vitamin B_{12} (cyanocobalamin) was started and the hemogram was monitored. The neutropenia persisted on the 6th day of treatment. During this period, no fever was observed.

The laboratory findings on the 9th day of treatment were as follows: HGB, 9.1 g/dl; platelets, 223x10^9/L; and WBC, 2.46x10^9/L (neutrophil count 0.86x10^9/L, 34.9%). The patient who recovered from neutropenia and whose liver function test (LFT) regressed was discharged with rifampicin and doxycycline and weekly vitamin B_{12} replacement. The patient was transferred to the outpatient clinic for further monitoring and treatment.

The laboratory findings on the 1st month of treatment were as follows: LFT was within the normal range, CRP, 5.9 mg/dl; HGB, 11.6 g/dl; platelets, 241x10^9/L; WBC, 2.82x10^9/L (neutrophil count 0.83x10^9/L, 29.7%); and ferritin, 163 ng/ml. With all these results, complicated brucellosis was considered as the patient had bone marrow involvement and treatment was planned to be extended to 3 months.

The administration of doxycycline and rifampicin was terminated in 3 months. However, WBC, 2.60x10^9/L (neutrophil count 0.78x10^9/L, 30%) was detected in the 3rd month and the patient was referred to the hematology department of Van Education and Research Hospital for further investigation into potential underlying pathologies. The results of the laboratory tests indicated that the levels of immunoglobulin (Ig) G, Ig M, Ig A, beta-2 microglobulin, serum free lambda light chain and serum free kappa light chain were within the normal range. Paraprotein was not detected by protein electrophoresis. Immunofixation electrophoresis showed no monoclonal gammopathy. The peripheral blood smear revealed an adequate platelet count, as well as normal lymphocyte and neutrophil structure, count, and maturation. Additionally, the erythrocytes were observed to be normochromic and normocytic. Antinuclear antibody was negative, anti-dsDNA was negative, and the result of the *Helicobacter pylori* stool antigen test was positive. The patient was monitored at the hematology clinic, and a follow-up appointment was scheduled after 3 months. The laboratory findings on the 6th month of treatment were as follows: WBC 3.52x10^9/L (neutrophil count 1.47x10^9/L, 41.9%). Hemogram and neutrophil blood counts between the time of diagnosis and the 6th month of treatment are shown in Figure 1.

Informed consent was obtained from the patient for this case report.

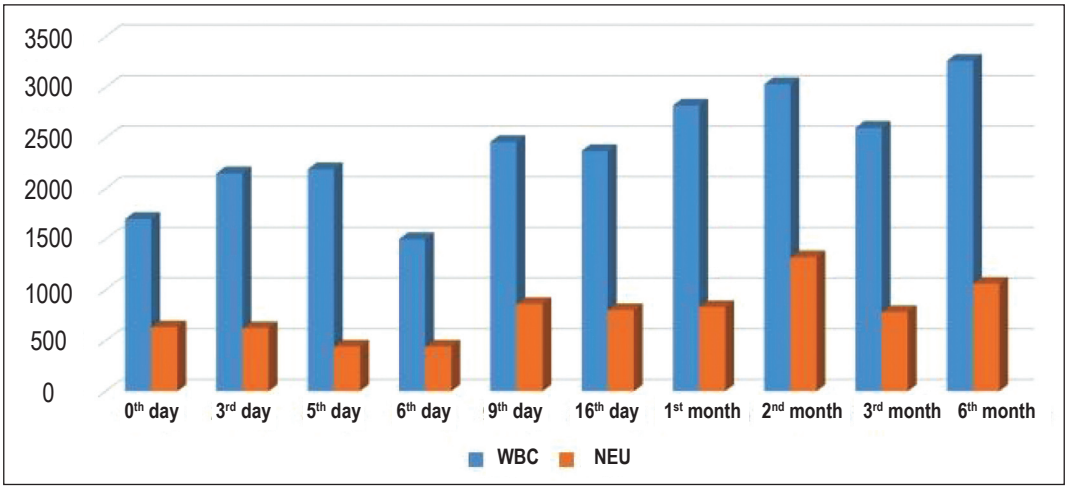

FIGURE 1: Hemogram and neutrophil blood counts at six-month follow-up
WBC: White blood count; NEU: Neutrophil

DISCUSSION

Patients with brucellosis may present with hematological abnormalities such as anemia, leukopenia, thrombocytopenia, and pancytopenia. The main causes include hemophagocytosis, hypersplenism, and bone marrow hypoplasia. A systematic review by Zheng et al. showed anemia in 23.9% of cases, leukopenia in 24.1%, thrombocytopenia in 15.8%, and pancytopenia in 13.2%.[3] A comprehensive study of 622 children in a brucellosis-endemic area in Turkey found hematologic involvement in 46.9% of patients. Anemia (28.6%) was most common, followed by thrombocytopenia (16%) and leukopenia [13.9% (neutropenia 8%)]. Pancytopenia was observed in 7.7%.[4] In a recent study conducted in our country, among 297 patients, the incidence of leukopenia was 18.8%, thrombocytopenia 10.7%, anemia 34.3%, and pancytopenia 4.3%.[5]

Although neutropenia due to brucellosis is rare, several cases have been reported locally.[6-10] Blood counts typically improve with treatment. Our patient had anemia, neutropenia, and prolonged leukopenia, all related to brucellosis. Neutropenia resolved after antimicrobial therapy and B12 supplementation, but leukopenia persisted. A positive H. pylori stool antigen was noted. Wang et al. suggested a possible link between H. pylori and leukopenia, which may explain the persistent leukopenia in our patient.[11]

Humans are commonly infected through raw milk, cheese, or direct animal contact.[1,12] In this case, transmission likely occurred via contaminated dairy products. Brucellosis symptoms often include fever, chills, myalgia, arthralgia, and sweating. However, it can affect multiple systems, leading to diverse clinical manifestations. Osteoarticular involvement may include sacroiliitis, spondylitis, or arthritis.[1,12] Our patient had low back pain, but lumbar MRI excluded spondylitis. Pain was successfully treated, and symptoms resolved.

In endemic regions, hematologic involvement such as leukopenia, anemia, or neutropenia should raise suspicion for brucellosis. It is essential to include brucellosis in the differential diagnosis of neutropenia. A thorough history, epidemiological context, and appropriate testing are critical for accurate diagnosis.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the

potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Çağlar Irmak, Cevdet Furkan Köşker, Tahir Alper Cinli, Hikmet Akar, Bartu Ediz;* ***Design:*** *Çağlar Irmak, Cevdet Furkan Köşker, Tahir Alper Cinli;* ***Control/Supervision:*** *Çağlar Irmak;* ***Data Collection and/or Processing:*** *Çağlar Irmak, Cevdet Furkan Köşker, Tahir Alper Cinli, Hikmet Akar, Bartu Ediz;* ***Analysis and/or Interpretation:*** *Çağlar Irmak, Cevdet Furkan Köşker, Tahir Alper Cinli;* ***Literature Review:*** *Çağlar Irmak, Cevdet Furkan Köşker, Tahir Alper Cinli;* ***Writing the Article:*** *Çağlar Irmak, Cevdet Furkan Köşker, Tahir Alper Cinli;* ***Critical Review:*** *Çağlar Irmak, Cevdet Furkan Köşker, Tahir Alper Cinli, Hikmet Akar, Bartu Ediz;* ***References and Fundings:*** *Çağlar Irmak, Tahir Alper Cinli;* ***Materials:*** *Çağlar Irmak, Tahir Alper Cinli.*

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