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Brucellosis Presenting with Pancytopenia and Massive Splenomegaly: A Case Report from an Endemic Region

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ABSTRACT

Brucellosis is a significant zoonotic disease endemic to the Middle East, Central America, and sub-Saharan Africa, caused by the Gram-negative coccus Brucella. It primarily affects livestock such as cattle, pigs, and sheep, with humans contracting the infection via contaminated aerosols, food, or direct contact with infected animals. The clinical presentation of brucellosis varies but typically includes fever (acute, subacute, or chronic), arthralgia, fatigue, and symptoms stemming from splenic involvement such as hepatosplenomegaly and lymphadenopathy. A case study of a 23-year-old female with severe anemia, fatigue, massive splenomegaly, and a positive Brucella IgG ELISA test illustrates the complexity of diagnosis, which often involves ruling out other conditions through comprehensive laboratory assessments. The patient presented with pancytopenia, microcytic hypochromic anemia, and normal liver enzyme levels alongside previous episodes of intermittent fever. This underscores the diagnostic challenges the disease poses due to its nonspecific symptoms and variable clinical course. Brucellosis is often misdiagnosed, mistaken for primary hematological conditions due to the absence of specific markers. However, timely and accurate diagnosis is crucial, as mismanagement can lead to severe complications. The gold standard for diagnosis remains blood culture, albeit time-consuming. Treatment typically involves a combination of antibiotics, including Rifampicin and Doxycycline, for 6 weeks, with relapses being rare but possible. Despite its capacity to affect various organs, brucellosis primarily impacts the reticuloendothelial system. Awareness of its clinical manifestations and hematological abnormalities is essential in endemic regions to facilitate early identification and management of this often overlooked infectious disease.

Keywords: Brucellosis, Reticuloendothelial System, Rifampicin, Doxycycline.

INTRODUCTION

A frequent zoonotic disease that is native to the Middle East, Central America, and sub-Saharan Africa is brucellosis [1]. The cause of brucellosis is a Gram-negative coccus. Cattle, pigs, and sheep are among the vulnerable species. Humans typically contract the disease by inhaling contaminated aerosols, consuming contaminated milk and unsterilized food, or coming into close contact with diseased animals. Personnel working in laboratories are similarly vulnerable to Brucellosis. Human-to-human transmission of brucellosis is not common [2]. Clinically, brucellosis can exhibit broad clinical variability and

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resemble a number of multisystemic disorders. Fever is the most typical brucellosis manifestation. It may show up as chronic, subacute, or acute. Other typical symptoms include arthralgia, sweating, bodily pains, anorexia, weariness, and malaise. The reticuloendothelial system is primarily affected by Brucella, which can lead to hepatosplenomegaly and lymphadenopathy, which are common physical examination findings in these patients. Hematological changes associated with this condition are characterized by leukopenia and anemia; nonetheless, thrombocytopenia or pancytopenia are still extremely infrequent [3].

CASE PRESENTATION

A 23-year-old female presents with moderate left upper quadrant dragging abdominal and central chest pain, and fatigue, admitted to our outpatient clinic. On examination, severe pallor and sternal tenderness are present, along with massive splenomegaly (Figure 1) (Hackett's grade 4). She has no other comorbidities or history of alcohol intake. She eats a balanced, non-vegetarian diet. There is no icterus, clubbing, edema, lymphadenopathy, or neck vein engorgement. Previously, she was admitted 4 years ago for fatigue and abdominal pain, for which she was transfused with 3 units of blood transfusion. On inquiring about her past history, she reported intermittent fever associated with abdominal pain. There is no history of melena, hematemesis, jaundice, paroxysmal nocturnal dyspnea, rash, joint pain, significant weight loss, or intake of herbal medicines. The patient had never used tobacco products or alcohol. The patient had history of close contact with diseased domestic animals.

Laboratory examination revealed significant findings in this 23-year-old female patient. She presented with pancytopenia, characterized by hemoglobin (Hb) level of 6.5 g/dL, total leukocyte count (TC) of 1200 cells/mm^3, and platelet count of 100,000/mm^3. Further hematological indices showed microcytic hypochromic anemia with MCV of 62 fL, MCH of 17 pg, and MCHC of 27 g/dL. The corrected reticulocyte count was 0.85%. Other laboratory results included Procalcitonin of 0.06 ng/mL and an elevated ESR of 30 mm/hr. Thyroid function tests indicated a TSH level of 7 mIU/L and FT4 level of 1.5 ng/dL. Stool examination ruled out ova, parasites, or eggs. Serological tests for hepatitis B surface antigen (HbsAg), anti-hepatitis C virus (HCV), and HIV were negative, as were Coomb's tests. Screening for malaria, typhoid, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) was negative. Hemoglobin typing excluded hemoglobinopathies. Ferritin level was low at 10 ng/mL, while albumin was within normal limits at 3.2 g/dL. Liver enzymes showed elevated AST at 53 U/L, ALT at 22 U/L, and ALP at 217 U/L. Mantoux test was negative. Other metabolic markers including corrected calcium, phosphorus, BUN, urea, creatinine, and uric acid were within normal ranges. Vitamin B12 and folate levels were normal. Liver Fibroscan indicated a stiffness of 12 kPa, with normal portal and hepatic vein Doppler findings. 2D echocardiography revealed normal left ventricular ejection fraction (LVEF) of 70%, normal valvular function, and no evidence of clot, vegetation, or regional wall motion abnormalities (RWMA). Serological testing for Brucella IgG ELISA was positive. Bone marrow study showed a normocellular marrow with mild erythroid hyperplasia (Figure 2) and no evidence of LD bodies. These comprehensive investigations provide a detailed profile to guide further diagnostic and therapeutic considerations for the patient's condition.

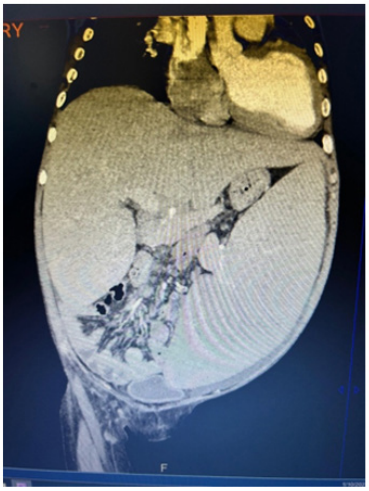

Figure 1. Massive Splenomegaly on USG.

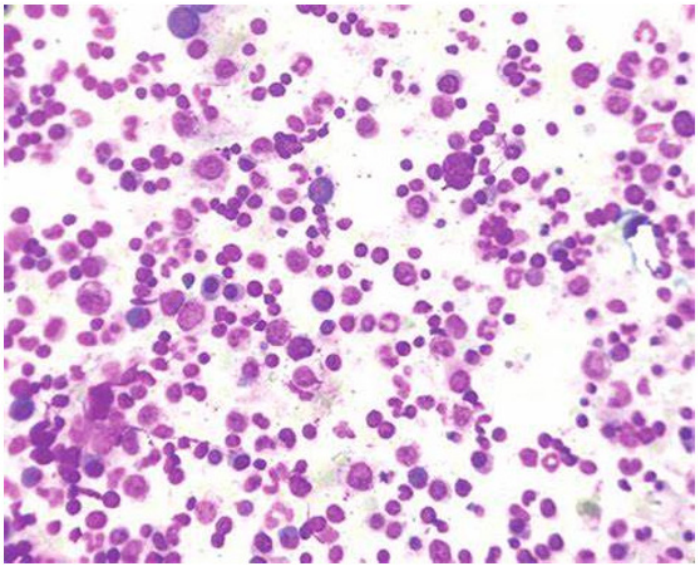

Figure 2. Normocellular Marrow with Erythroid Hyperplasia.

DISCUSSION

With more than 500,000 new instances of human brucellosis reported each year, it is the most prevalent zoonotic disease in the world. One of the several species of the Gram-negative coccobacillus Brucella is its cause. Most wealthy countries have eradicated brucellosis. Nonetheless, it continues to be a major cause of sickness and mortality in the Middle East, India, sub-Saharan Africa, Central America, and South America. When diagnosing brucellosis, a quick history must be taken. Food, employment, and travel history are crucial in determining the best course of action for this disease's inquiry [4].

The most frequent cause of brucellosis in humans is B.melitensis. Sheep, camels, and goats are the main hosts. Additional species that can infect humans with brucellosis include B. abortus (which primarily infects cows), B. suis (which infects pigs), and B.canis (which infects dogs) [5].

Human-to-human transmission of the disease is rare. It occurs mostly in endemic nations when infected meats and unpasteurized dairy products are consumed. In developed countries, infection most typically occurs via occupational exposure, such as inhalation of infectious aerosols in microbiology laboratories. On the other hand, direct skin or mucosal contact with infected livestock might also result in the infection [6].

Because Brucella is a facultative intracellular bacteria, it might take weeks or months for symptoms to appear after the disease is transmitted. Phagocytic cells take up bacteria and use a variety of strategies to avoid intracellular death mechanisms. This allows the bacteria to proliferate inside the host cell and spread hematogenously throughout the body. There is a marked preference for reticuloendothelial system organs [7].

The typical presentation of brucellosis is a slowly developing fever, malaise, arthralgias, and night sweats that are accompanied by a strong, unusual, moldy odor, there are differences in the pattern of fever, it can be mild, prolonged or relapsing, with or without rigors. Weight loss, arthralgia, low back pain, headaches, dizziness, anorexia, dyspepsia, abdominal discomfort, coughing, and depression are possible further symptoms. Physical examination results are inconsistent and nonspecific; lymphadenopathy, splenomegaly, and/or hepatomegaly may be seen [8].

The most prevalent type of localized brucellosis is osteoarticular disease, which includes spondylitis, sacroiliitis, and peripheral arthritis. Focal brucellosis with genitourinary involvement (Epidymitis, Orchitis, Tuboovarian Abscess) is the second most prevalent variant. Up to 10% of cases include neurologic involvement, including meningitis (acute or chronic), encephalitis, brain abscesses, myelitis, and radiculitis. As many as 3% of infections, there is cardiovascular involvement. Endocarditis, myocarditis, pericarditis, and endarteritis are possible diagnoses. Up to 2% of cases had pulmonary involvement (bronchitis, interstitial pneumonitis, pleural effusion, and hilar lymphadenopathy) [9].

Although the exact pathophysiology of pancytopenia in brucellosis is unknown, a number of processes, including hypersplenism, hemophagocytosis, disseminated intravascular coagulation (DIC), medullary hypoplasia, and granulomatosis, can account for these hematologicalabnormalities. The cause of pancytopenia is unknown in roughly 7% of instances. We have observed that, given the outcome of the myelogram, which objectified erythroblastic hyperplasia, hypersplenism is the most likely cause. Furthermore, splenomegaly but not hepatomegaly

occurred per our observation. Anemia affected 21.5% of patients, thrombocytopenia affected 18.8% of patients, and leukopenia affected 14.6% of patients in a Turkish research study involving 484 cases of brucellosis. As many as 2–14% of afflicted patients, pancytopenia may develop. Because there are no illness-specific markers to differentiate cytopenias caused by brucellosis from noninfectiousetiologies, brucellosis is sometimes misdiagnosed as a primary hematologic disease or cancer. Fortunately, treating the underlying brucellosis usually resolves hematologic symptoms [10].

Due to the lengthy incubation period and unpredictable clinical picture, brucellosis is frequently difficult to diagnose in a timely and reliable manner. The gold standard diagnostic test is the isolation of Brucella from blood cultures, however results can take several weeks. Serologic investigations can be obtained in a matter of days which are only marginally sensitive [11].

For six weeks, oral Rifampicin (600/900 mg) plus doxycycline (100 mg twice daily) or streptomycin (IM/IV 1g 2-3 weeks) plus Oral Doxycycline or Oral Doxycycline plus Gentamicin (IM/IV 7-10 days) is the preferred treatment for brucellosis; Alternatively, trimethoprim-sulfamethoxazole, and quinolones can be used. Relapses are uncommon and typically happen in the first year of treatment, usually due to poor adherence to medication. It is not necessary for the antibiogram to succeed. The majority of strains respond well to the medications used for brucellosis [12].

CONCLUSION

Though it can affect any organ in the body, reticuloendothelial system is usually the affected organ by brucellosis. The diagnosis of brucellosis should be brought up in the presence of clinical findings that show an undulating fever and hematological abnormalities, such as pancytopenia is particularly found in our nation where the disease is still endemic.

DISCLOSURES

CONFLICT OF INTEREST DECLARATION

The writers say they have no conflicts of interest.

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