Brucellosis: Presentation, Diagnosis and Treatment: Case Report

Authors
Zain Fathalddien MD, M. Khader Alzawahreh, MD, Atallah Al Issa, MD

Abstract
Introduction: Brucellosis is one of the commonest zoonotic infections worldwide. the disease is endemic in Saudi Arabia, the Middle East, and the Mediterranean area, and whether in an endemic region or not, it remains a diagnostic puzzle due to occasional misleading unusual presentations and non-specific symptoms. Presented here is our experience acute brucellosis at family and community medicine department FCM, Sharurah Armed Forces Hospital, Medical Services Department, Ministry of Defense and aviation, Kingdom of Saudi Arabia.

Case Presentation: A 65-year-old man presented to F&CM department complains of chronic low grade fever, joint pain and general weakness and malaise this was followed by Non-blanch able maculopapular eruptions on anterior part of tibia. He was evaluated, investigated, and managed in outpatient clinic many times without proper diagnosis. Work up for the cause of fever was inconclusive. He was diagnosed with thrombocytopenia so the patient was referred to internist, managed and discharged as a case of Idiopathic thrombocytopenia with unspecific fever. Patient came again to F&CM department with the same chronic symptoms. In absence of alternate diagnosis and clinical setting, therapy resulted in no improvement in patient's condition. Finally, the patient was evaluated by our CDC at F&CM department, requested a serological lab tests where he was diagnosed with brucellosis and treated successfully. Patients were treated with 6 week course of Doxycycline and Rifampicinc with a six-month follow-up.

Conclusion: Brucellosis is an infection with multiple presentations, and whether in an endemic region or not, a thorough history of exposure and clinical suspicion are required since the misdiagnosis may lead to withholding of adequate treatment and more complications.

Introduction
Brucellosis is a systemic infection with a broad clinical spectrum, ranging from asymptomatic disease to severe and/or fatal illness. Clinical and laboratory features vary widely. The main presentations are acute febrile illness, with or without signs of localization, and chronic infection as well. It caused by gram-negative bacilli, the genus Brucella. Almost every organ is involved in different degrees. Brucellosis, constituting a major health problem in many parts of the world--particularly in the Mediterranean and the Middle East-Human brucellosis is an important zoonotic disease and is especially concerning in the Kingdom of Saudi Arabia (KSA), where livestock importation is. As no specific characteristic of symptoms and signs exists, the diagnosis may be readily missed. Hematological abnormalities ranging from a fulminant state of disseminated intravascular coagulopathy to subtle hemostatic alterations have
been reported in Brucella infection. Immune mediated thrombocytopenia is also a clinically important mechanism that can be encountered during brucellosis. Brucella infection may cause severe thrombocytopenia, mimicking a primary hematological disease that is reversible after appropriate antimicrobial therapy. In cases of brucellosis-induced immune thrombocytopenic purpura, a short-term standard dose of corticosteroid treatment might be an alternative and additional treatment as an urgent approach for thrombocytopenia while initiating anti-brucellosis treatment.

Case Presentation
A 65-year-old man presented to F&CM department complains of chronic low grade fever, joint pain and general weakness and malaise this was followed by maculopapular eruptions on anterior part of tibia. He was evaluated, investigated, and managed in outpatient clinic many times without proper diagnosis. Work up for the cause of fever was inconclusive. He was diagnosed with thrombocytopenia so the patient was referred to internist, managed and discharged as a case of Idiopathic thrombocytopenia with unspecific fever. Patient came again to FMC by the same chronic symptoms. In absence of alternate diagnosis and clinical setting, therapy resulted in no improvement in patient's condition. Finally, the patient was evaluated by our CDC at F&CM department, patient c/o low grade fever, joint pain, there was no other clue on history to localize the cause of fever. There was no history of travel or contact with ill patients. There was no history of hypertension, diabetes, stroke, bleeding disorders or tuberculosis in the past. No previous history of confirmed autoimmune disease. He took empirical antibiotics with symptomatic treatments which resulted minor relief in his symptoms. On examination, the patient was alert and conscious looks well and active with no pallor, cyanosis or jaundice. Hehadlow grade fever with oral temperature of 37.9 celsius, blood pressure was 123/75 mm of Hg. There was a Non-blanch able maculopapular eruptions on the anterior parts of tibias. There was no other skin rash elsewhere. There was no peripheral lymph node enlargement. Examination of respiratory and cardiovascular system was normal. Abdomen examination revealed splenomegaly. Motor, sensory and cranial nerves examination was normal. Meningeal signs were negative. Patient was referred for serological tests where he was diagnosed as brucellosis and treated successfully. Patient was treated with 6 weeks course of Doxycycline and Rifampicin with a six-month follow-up. Other Investigations revealed normal hemoglobin (14.4 gm/dl), total leukocyte counts (11500/mm$^3$) and differential leukocyte counts (neutrophils 62.7%, lymphocytes 25.7%, monocytes 10.8% and basophils 1%) and mild thrombocytopenia (78.4 × 10$^3$/mm$^3$). Blood biochemistry showed normal fasting sugar (104 mg/dl), urea (20 mg/dl), creatinine (0.9 mg/dl), calcium (8.1 mg/dl), sodium (140 mg/dl) and potassium (4.0 mg/dl). Liver function tests revealed mildly raised ALT (57.8 U/L) with normal AST (31.5 U/L), Erythrocyte sedimentation rate was 40 mm/hr. Chest radiograph did not show any abnormality. However, investigations revealed serology positive for Brucella with positive B. Abortus and agglutination test of 1:320. The patient was managed as outpatient with rifampicin and doxycycline therapy and follow up, later he became in good health. The follow-up of the patient revealed normal hematological findings together with a progressive reduction in the titer of the agglutination test for Brucella. When last seen almost six month of completion of therapy was asymptomatic.

Discussion
Brucellosis is a zoonotic infection transmitted to humans by contact with fluids from infected animals (sheep, cattle, goats, pigs, or other animals) or derived food products such as unpasteurized milk and cheese. It is one of the most widespread zoonosis worldwide. Brucellosis
has high morbidity both for humans and animals; it is an important cause of economic loss and public health problems in many developing countries. The prevalence of brucellosis has been increasing due to growing international tourism and migration.

Brucella are small, nonmotile, facultative intracellular aerobic rods it cause a systemic infection with a broad clinical spectrum, ranging from asymptomatic disease to severe and/or fatal illness. Clinical and laboratory features vary widely. The main presentations are acute febrile illness, with or without signs of localization, and chronic infection.

Clinical manifestations of brucellosis include fever, night sweats, malaise, anorexia, arthralgia, fatigue, weight loss, and depression. Patients may have a multitude of complaints with fever in the absence of other objective findings. The onset of symptoms may be abrupt or insidious, developing over several days to weeks. The musculoskeletal (osteomyelitis, arthritis or abscess) and genitourinary systems (epididymo-orchitis), are the most common sites of involvement. Pulmonary, Gastrointestinal, Ocular involvement can present as well. Neurobrucellosis, endocarditis occur in 1 to 2 percent of cases which is relatively rare.

Hematological and dermatological abnormalities of brucellosis have been reported in the literature. The incidence of thrombocytopenia was reported in the range of 2%-30%. And Dermatologic manifestations occur in up to 10 percent of patients.

Although brucellosis has been controlled or eradicated in many developed countries, it still remains a health problem in developing countries. As no characteristic constellation of symptoms and signs exists, the diagnosis may be readily missed. The nonspecific antibiotic usage also lowered the rate of positive blood cultures and led to difficulties in the diagnostic work-up.

Human brucellosis is an important zoonotic disease and is especially concerning in the Kingdom of Saudi Arabia (KSA), where livestock importation is significant. Humans can acquire brucellosis by direct inoculation through cuts and skin abrasions, especially from handling animal tissues or secretions, via the conjunctiva, inhalation of infected aerosols and ingestion of contaminated food such as raw milk, cheeses made from unpasteurized milk, or raw meat.

The diagnosis of brucellosis should be considered in an individual with otherwise unexplained fever and nonspecific complaints who has a possible source of exposure. Laboratory tools for diagnosis of brucellosis include culture and serology. Ideally, the diagnosis is made by culture of the organism from blood or other sites, such as bone marrow or liver biopsy specimens. Serologic tests include tube agglutination and enzyme-linked immunosorbent assay.

Treatment of brucellosis includes combination of drugs which include tetracycline, streptomycin, co-trimoxazole (TMP-SMX) and rifampicin. The aim the treatment is to treat current infection and prevention of relapse. Various regimens described are Streptomycin plus doxycycline, rifampicin plus doxycycline, or TMP-SMX with Streptomycin or rifampicin. Usual duration of treatment is 6-weeks.

Brucellosis may be prevented via vaccination, which is effective for cattle, sheep, and goats, but requires a sustained vaccination program over several years. Other measures include the quarantine of herds and the slaughter of infected animals (with protective measures in slaughterhouses). Pasteurization of milk is also very important for the prevention of transmission to humans.

Conclusion
Brucellosis remains a challenging problem in endemic areas and it is an infection with multiple presentations, and whether in an endemic region or not, a thorough history of exposure and clinical suspicion are required since the misdiagnosis may lead to withholding of adequate treatment and more complications. Brucellosis is a frequently missed cause of pyrexia of unknown origin.
However, if suspected, diagnosis is easy and treatment is usually satisfactory.

Consent
Written informed consent was obtained from the patient for publication of this case report.

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