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Pancytopenia as a rare complication of acute Brucellosis: A case report

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Case Report

Abstract

Human Brucellosis still challenges many physicians, especially in developing countries where it is still a very common, but sometimes ignored disease. Its reemergence in developed countries and its status as a class B bioterrorist agent has recently attracted much interest. Having over 500,000 new cases annually, Brucellosis is known as one of the most common zoonotic infections in the world and "the great imitator" because of many clinical and hematological manifestations. Brucellosis is still endemic in many developing countries and remains under-diagnosed and sometimes missed reported. Although this province (Kurdistan, Iran) is a Brucella endemic area with a very high prevalence and incidence rate, except for very few and negligible case reports, we did not find any reports or epidemiological study regarding this zoonotic infection. This is the first reported case of Brucellosis with pancytopenia from this western province of Iran which has been neglected. Our case was a 16-year-old girl referred with protracted fever during the last month and undetermined diagnosis. She also suffered from generalized pain, pale skin, sweating, anorexia, and weight loss. After clinical surveying, taking history, and physical examination, Brucella infection was suspected. Diagnosis confirmed by standard tube agglutination test (STA), 1/640. The patient was successfully treated with doxycycline, rifampicin, and ceftriaxone.

KEYWORDS: Brucellosis, Pancytopenia, Zoonotic Infection, Kurdistan, Iran

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Introduction

Brucellosis or Malta fever is the most common zoonotic infection in the globe caused by a gram-negative, non-motile, facultative intracellular bacterium that belongs to the genus of Brucella.[1] It affects animals like sheep, goats, cattle, and pigs as the primary host and humans as the secondary.[2] It is still a common health problem in some Middle Eastern and Mediterranean countries including Iran.[3] Over the last ten years, the infection has re-emerged especially in Eastern Europe, the Balkans, and Eurasia. Brucellosis, although almost eradicated in many parts of the world, still remains widespread and endemic in developing countries.[4] It is very contagious for humans and the disease, unless diagnosed and treated both promptly and effectively, can become chronic, affecting multiple body systems.[5] The World Health Organization (WHO) has designated Brucellosis as a historically "neglected" zoonosis.[1]

In desirable situations and strong health systems less than 1 out of 8 Brucellosis case is diagnosed in opportune and reported.[1] While basic science and epidemiology of human Brucellosis is known, it is often under-detected

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and overlooked, therefore highlighting its status in endemic area and reporting rare cases may attract global attention.[6]

Kurdistan province of Iran is an endemic region of Malta fever with a very high prevalence and incidence rate.[3] Unfortunately no comprehensive and reliable epidemiological report from this area is available. So, in addition to case report, an estimation of this neglected important zoonotic infection in this province is presented.

Case Report

A 16-year-old girl referred to our university hospital from a rural clinic presented with prolonged fever and undetermined diagnosis. She suffered from generalized pain, pale skin, sweating, anorexia and weight loss over the previous one month. Physical examination showed fever (39° C), splenomegaly without hepatomegaly and lymphadenopathy.

In laboratory test results, hemoglobin (Hb), hematocrit (Hct), leukocytes and platelets count were decreased significantly. Laboratory analysis on the admission day showed leukopenia (white blood cell count = 3000/mm^3), thrombocytopenia (Plt = 35,000), and anemia (Hb = 7.72 g/dl, Hct = 26.02%). Evaluation of the peripheral blood smear (PBS) revealed neutrophils = 61%, lymphocytes = 27%, and eosinophils = 2%. The blood smear was also positive for anisocytosis, poikilocytosis, and hypochromia. Both urine and blood cultures were negative for pathogenic bacterial infections. The erythrocyte sedimentation rate and C-reactive protein (CRP) were 12 mm/1 h and 3+, respectively. The biochemical tests revealed an increase in the alanine aminotransferase (ALT) 149 U/l (normal range is 5-40), and aspartate aminotransferase (AST) 174 U/l (normal range is 5-40). The other laboratory results were within normal ranges.

Because of pancytopenia and weight loss, hematological malignancies were suspected. Normal erythroid and myeloid maturation in bone marrow aspiration ruled out an underlying malignancy. On the other hand, because of abnormal AST and ALT liver involvement was obvious. Although both urine and blood cultures were negative and white blood cells (WBC) count was decreased, protracted bacterial fever or viral infections were under discussion. At last, Malta fever and Typhoid fever were under suspicion. Antibodies against typhoid fever were only positive for O and H antigens at titer 1/80. However, standard tube agglutination (STA) for Brucella species was positive at a titer of 1/640.

Therefore, according to the clinical and laboratory findings treatment for Brucellosis was started and patient was administered doxycycline 100 mg orally twice daily, rifampicin 450 mg orally once daily, and ceftriaxone 4 g/day intravenously (all for eight weeks).[7] By the fifth day of the treatment, her fever subsided and hematological findings improved (Hb = 9.1 g/dl, Ht = 28.4%, Plt = 78000/mm^3, WBC = 2300/mm^3, neutrophils = 40%, lymphocytes = 59%, eosinophils 1%). PBS was still positive for anisocytosis, poikilocytosis and hypochromia.

The patient discharged from the hospital with the recommendation of ceftriaxone and rifampicin. After 8 weeks of treatment, all hematological parameters were within normal ranges and on later follow up samples showed no evidence of Brucella seropositivity.

Discussion

Malta fever is a systemic infection caused by Brucella species. These bacteria transmit from animals to humans and colonize in different body tissues, dominantly in lymphoreticular system.[8] Main reason for reporting this case is to advise physicians to consider Brucella infection in febrile patient who present with pancytopenia in the endemic areas, knowing that health education especially to villagers about routs of transmission, prevention methods, food supply, and delivery supervision could decrease the prevalence of the disease. The disease has a high morbidity and a broad spectrum of clinical manifestations ranging from asymptomatic disease to severe and/or fatal

illness.[2] As it is one of the leading infections causing fever of unknown origin, it can mimic those of other febrile illnesses.[9] The incubation period is usually one to four weeks.[8]

Hematological abnormalities include anemia, leukopenia, thrombocytopenia, pancytopenia, bleeding diathesis, and coagulation disorders, such as disseminated intravascular coagulation (DIC). Up to 87.5% of patients with pancytopenia induced by Brucella infection have positive blood cultures and almost all of them had positive Brucella antibody.[8]

Brucellosis is notorious for relapsing even after adequate treatment.[10] Relapse usually occurs within the first six months following completion of treatment. Causes of relapse include inadequate choice of antibiotics, shortened treatment duration, lack of adherence, or localized foci of infection. Relapse due to antibiotic resistance is rare;[10] hence, significant of its prompt and proper management.

Due to evading immune system and tendency to relapse, its eradication is very difficult.[2] Physicians in endemic areas always say "everything can be Malta fever until proven different".[1] Non-specific complications may initially lead clinicians to a differential diagnosis other than Brucella.[9] Hematologic complications during the course of Brucellosis, with numerous patterns of cytopenia or lymphocytosis has been reported.[11] However, one should always take into account the postscript to the above-mentioned rule, which says that "in endemic areas everything can be Brucellosis, but Brucellosis is not the only possible diagnosis." This has been demonstrated in some studies where hematologic complications that might have been attributed to concurrent. Brucellosis was actually due to underlying undiagnosed hematologic malignancies.[8,12]

In our case, in spite of living in a rural endemic area of Brucellosis and having a positive history of consumption of un-pasteurized dairy products, unfortunately there was no early diagnostic suspicion of Brucellosis and the patient suffered from a prolonged fever. Her family also tended as a shepherd. Although anemia in Brucellosis is expected due to bone marrow involvement, numerous other pathogenic mechanisms can be implicated.[10]

Brucellosis is a notifiable disease, yet its cases remain often unrecognized and underestimation; reflecting inadequacy of diagnostic laboratory services in most of the endemic area, especially un-developed countries.[13] The geographical pattern of this zoonotic infection is constantly changing.[14] The causes of its re-emergence and recent increase in the incidence of Brucellosis including socioeconomic changes, wars and political turbulence in some countries, inadequate control programs in un-developed countries, ease of human international travel recently, uncontrolled animal transportation across open borders, and at last Brucellosis is a complex disease that has different cycles of expansion and regression.[13,15]

Brucella bacteremia may be complicated by: infective endocarditis, fatal endotoxic shock that may be associated with DIC, multiorgan failure, microangiopathic hemolytic anemia (MAHA) with bleeding tendency and pancytopenia and death.[2] Despite the severity of these complications, the early use of appropriate antimicrobial therapy usually leads not only to clinical improvement but also to normalization of the hematological parameters and the coagulation profile.[9]

On a few occasions, Brucellosis has been encountered in patients with acute leukemia and solid tumors.[1,2] As reported cases of Brucellosis developed in patients with malignant disorders living in countries that are endemic for this infection, the dominant presenting features of Brucellosis were febrile neutropenia and pancytopenia.[2]

Kurdistan province of Iran with a population of 1.5 million people is an endemic region of Malta fever with a very high prevalence and incidence rate.[3] According to the statistics of Iranian Ministry of Health, in 2012 the incidence rate was 50/100000 (unpublished data). But upon over 15 years' experience of Brucella

treatment in this endemic area, it is obvious that its real burden is much higher, maybe over 10 times, i.e. 500/100000 new cases annually. Miss diagnosis, overlook, and finally and failure in reporting are the main reasons for mismanagement of the disease.

In conclusion, physicians should have a high index of suspicion regarding Malta fever when evaluating patients presenting with prolonged pyrexia, pancytopenia, and a history risk of consumption of non-pasteurized dairy products.

Conflict of Interests

Authors have no conflict of interests.

References

1. Madkour MM. Madkour's Brucellosis. 2nd ed. New York, NY: Springer; 2001.
2. Pappas G, Akritidis N, Bosilkovski M, Tsianos E. Brucellosis. N Engl J Med 2005; 352(22): 2325-36.
3. Moradi GH, Esmaiel Nasab N, Ghaderi E, Sofi Majidpour M, Salimzadeh H. Brucellosis in Kurdistan Province from 1997 to 2003. Annals of Alquds Medicine 2006; 2(1): 32-7.
4. Godfroid J, Al DS, Pappas G, Roth F, Matope G, Muma J, et al. A "One Health" surveillance and control of brucellosis in developing countries: moving away from improvisation. Comp Immunol Microbiol Infect Dis 2013; 36(3): 241-8.
5. Pappas G. Treatment of brucellosis. BMJ 2008; 336: 678.
6. Akhvlediani T, Clark DV, Chubabria G, Zenaishvili O, Hepburn MJ. The changing pattern of human brucellosis: clinical manifestations, epidemiology, and treatment outcomes over three decades in Georgia. BMC Infectious Diseases 2010; 10: 346.
7. Ariza J, Bosilkovski M, Cascio A, Colmenero JD, Corbel MJ, Falagas ME, et al. Perspectives for the treatment of brucellosis in the 21st century: the Ioannina recommendations. PLoS Med 2007; 4(12): e317.
8. Al-Anazi KA, Al-Jasser AM. Brucella bacteremia in patients with acute leukemia: a case series. J Med Case Rep 2007; 1: 144.
9. Davis CHE, Troy SB. Brucellosis. N Engl J Med 2005; 353: 1071-2.
10. Aysha MH, Shayib MA. Pancytopenia and other haematological findings in brucellosis. Scand J Haematol 1986; 36(4): 335-8.
11. Crosby E, Llosa L, Miro QM, Carrillo C, Gotuzzo E. Hematologic changes in brucellosis. J Infect Dis 1984; 150(3): 419-24.
12. Eser B, Altuntas F, Soyuer I, Er O, Canoz O, Coskun HS, et al. Acute lymphoblastic leukemia associated with brucellosis in two patients with fever and pancytopenia. Yonsei Med J 2006; 47(5): 741-4.
13. Doganay M. Editorial (Hot Topic: Human Brucellosis: Update of Bacteriological, Clinical, Diagnostic and Therepeutical Features). Recent Patents on Anti-Infective Drug Discovery 2013; 8(1): 2-3.
14. Tonna I, Tonna A. Brucellosis. New England Journal of Medicine 2005; 353(10): 1071-2.
15. Fanni F, Shahbaznejad L, Pourakbari B, Mahmoudi S, Mamishi S. Clinical manifestations, laboratory findings, and therapeutic regimen in hospitalized children with brucellosis in an Iranian Referral Children Medical Centre. J Health Popul Nutr 2013; 31(2): 218-22.