Iranian Journal of Pathology (2009)4 (3), 133 - 136

Case Report

Acute Brucellosis with Pancytopenia and Maculopapular Rash

Abasali Omidi[1],Amir Hossein Jafarian[1], Minoo Erfanian[1], Mohammad Javad Yazdanpanah[2]; Masoud Sharifian[3]

1. Dept. of Pathology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Dept. of Dermatology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
3,. Dept. of Internal Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

ABSTRACT

Human brucellosis is common in developing countries and is a multi-system disease with a broad spectrum of clinical manifestations. Cutaneous lesions associated with brucellosis have been rarely reported in the literature. Here we present a case of a 32-year-old man with history of consumption of cheese made from raw milk seen with occurrence of pancytopenia and diffuse maculopapular rash during the course of *Brucella* infection. Physical examination showed fever, splenomegaly, mild hepatomegaly and pruritic maculopapular exanthema over the trunk, arms and legs. Laboratory tests revealed pancytopenia. Parasitic examinations and serologic tests for syphilis, salmonellosis, rickettsiasis, toxoplasmosis, Epstein-Barr virus, human immunodeficiency virus, and hepatitis B and C viruses were negative. There was no history of drug consumption.The *Brucella* agglutination test titer was 1/1280 and histological examination of skin biopsy showed lymphohistiocytic perivascular infiltrates in the upper dermis.Lesions were interpreted as *Brucella*r dermatitis , The patient was subsequently treated with oral doxycycline and rifampin and was discharged in good health. If there is suspicion of exposure to infected food products, brucellosis should be included in the differential diagnosis of pancytopenia in *Brucella*-endemic areas; there may be skin lesions other than purpura that can accompany thrombocytopenia.

Key Words: Brucellosis, Pancytopenias, Skin rash, Iran

Introduction

Brucellosis is a worldwide zoonosis caused by microorganisms of the genus *Brucella* (1). Primarily, it is a disease of animals, such as cattle, sheep, swine, and dogs, and the major sites of infection include the genital organs, mammary glands, and placenta. Humans acquire the disease by the ingestion of raw milk or dairy products made from unpasteurized milk, by direct contact through the broken skin or conjunctiva, or by inhalation of contaminated dust. The clinical manifestations of brucellosis are diverse (1, 2). Cutaneous manifestations are not specific and affect 1-14% of patients with brucellosis.Incidence of pancytopenia is 3-21% among patients affected by brucellosis(3,4). Here we report a case of brucellosis with both pancytopenia and a skin rash that does not

Received: 21 July 2008
Accepted: 20 January 2009
Addredresss communicationions to: Dr Abasali Omidi, Department of pathology, Mashhad University of Medical Sciences, Mashhad, Iran
Email: aomidia@yahoo.com

appear to be related to thrombocytopenia.

Case Report

A 32-year-old farmer from Shirkhan, one of the Sabzevar villages in north –east of Iran, was seen for complaints of extensive pruritic maculopapular skin rash on the trunk and extremities, generalized myalgia and fever over the previous one month. These symptoms were preceded by sweating, fatigue and anorexia, one week before appearance of skin lesions. He reported no preceding episode of any kind of infection or use of any medication. He had been admitted to a rural hospital for these complaints; he was started on an antihistaminic drug for skin lesions, and was recommended to apply to a general hospital for advanced investigation of fever and pancytopenia.On physical examination he was febrile (39 c); blood pressure was normal. The spleen was palpable 2 cm below the costal margin. The skin rash was characterized as a maculopapular nonhemorrhagic exanthema and covered the trunk, arms and legs (Fig. 1). The intensity of the rash was greater over the trunk than the extremities and the lesions were pruritic.Laboratory analysis yielded a hemoglobin level of 10 g/dL, hematocrit of 30%, platelet count of 60 x109/L, leukocyte count of 2x109/L(neutrophils 45.7%,lymphocytes 38.5% and monocytes13.1%,eosinophil 2.7%). The erythrocyte sedimentation rate was 8 mm/1 h; C-Reactive Protein was 3+, Rheumatoid factor was 1+; Urea was 41 mg/dL (10 to 50); creatinine was 0.7 mg/dL (0.5 to 1.2); alanineaminotransferase (ALT) was 56 IU/L (1 to 31); and aspartateaminotransferase (AST) was 33 IU/L (1 to 32).There was no laboratory evidence of hemolysis.Anti-nuclear antibody was negative. Urinalysis and chest X-ray was normal. Abdominal ultrasonography showed abnormal-sized liver and splenomegaly. Bone marrow biopsy was performed and it was hypercellular.Bone marrow culture did not perform. Echocardiography showed minimal nonsignificant pericardial effusion.

Parasitic examinations and serologic tests for syphilis, salmonellosis, rickettsiasis, toxoplasmosis, Epstein—Barr virus, human immunodeficiency virus, and hepatitis B and C viruses were negative. A *Brucella* agglutination test was performed and it was positive, with a titer of 1/1280. Neither *Brucella* species nor other microorganisms were isolated from his blood cultures. On detailed questioning it was learned that he ate cheese made from raw milk 30 days before the appearance of the symptoms. The skin rash did not look like a purpuric eruption associated with the thrombocytopenia so a consultation was made to a dermatologist. According to the consultation, the rash was thought to be *Brucellar* dermatitis. The skin biopsy showed a perivascular lymphohistiocytic reaction (Fig. 2,3). Doxycycline (200 mg/day) and rifampin (600 mg/day) were started. The rash began to disappear within two days and pancytopenia began to resolve within three days of therapy. The patient was discharged from the hospital 7 days later in good health. At the 3-week follow-up, the patient came to control and had made a full clinical recovery; the skin rash was completely resolved and the platelet count had increased from 60x109/L to 150x109/L, Hg from 10 to12 g/dl and leukocyte count from 2x109to3/5x109/l. Antibiotic therapy has been planned to continue until completion of 6 weeks of treatment

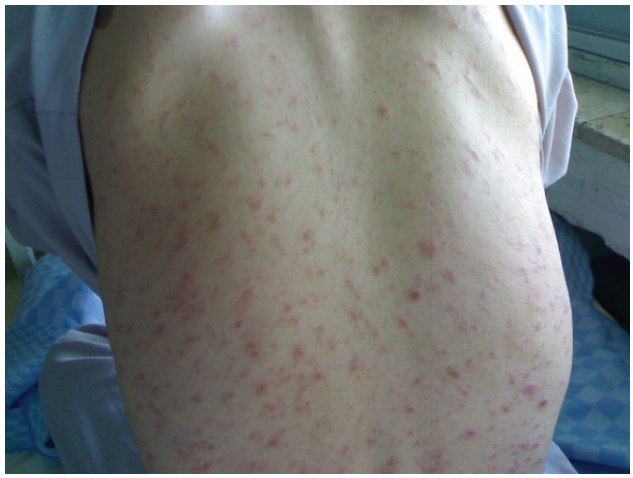

Fig.1: Maculopapular erythroviolaceous rash affecting, trunk, upper and lower extremities

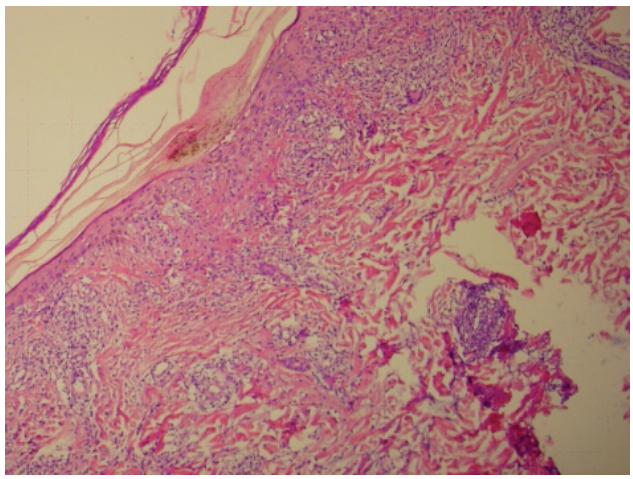

Fig.2: Skin biopsy.Perivascular lymphoh-istiocytic reaction (H&E staining x100)

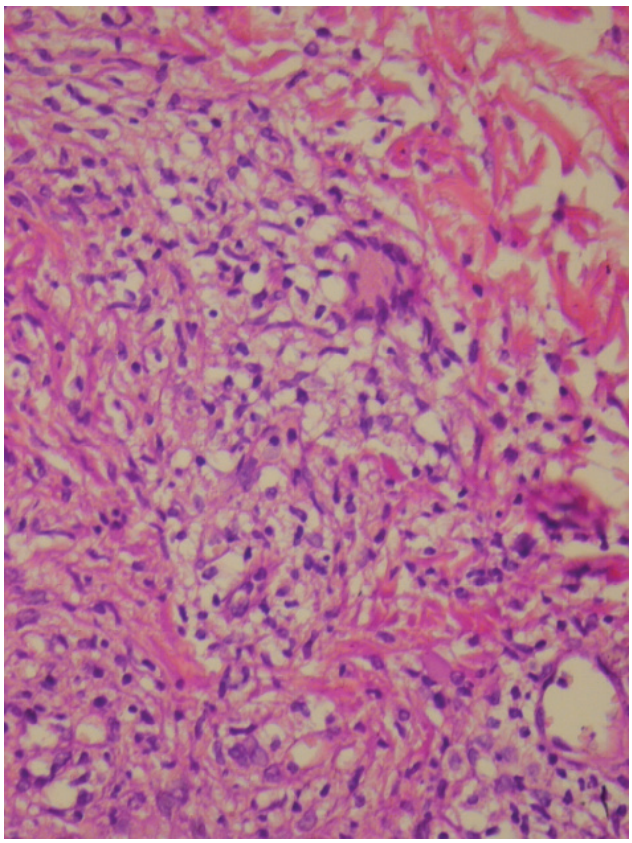

Fig.3: Perivascular lymphohistiocytic reaction with one giant cell(H&E staining x400)

Discussion

Brucellosis is a disease that exists worldwide, especially in developing countries (1, 5). The disease can involve many organs and tissues so it has a broad spectrum of non-specific clinical manifestations that generally occur within two weeks (but sometimes up to three months) after infection (6, 7). In this case, the patient was from an endemic area for brucellosis and reported consuming cheese made from raw milk. He had some signs and symptoms of human brucellosis included fever, myalgia, anorexia, fatigue, sweats and other clinical manifestations such as hepatosplenomegaly.

Hematologic manifestations are variable in brucellosis and usually mild abnormalities such as anemia and leukopenia can be seen (7,8). Pancytopenia seldom complicates the course of acute brucellosis mimicking a primary hematological disease (8-10).

Cutaneous lesions in brucellosis are fairly uncommon and occur in 5 to15 percent of cases (11-13). There are various underlying pathogenic mechanisms of cutaneous lesions such as direct inoculation of the bacteria, hypersensitivity phenomena, indirect skin involvement caused by circulating immune complexes, and direct hematogenous invasion of the skin (12-14).There are no specific lesions caused by brucellosis, and skin involvement occurs in different forms (13). Many lesions, including erythema nodosum, papules, maculopapular lesions, petechiae, purpura, impetiginous and psoriasiform lesions have been described (12-15). Eruption and urticaria-like papules were the most frequent skin findings. Diffuse maculopapular eruption was reported in three patients (13).If there is concomitant thrombocytopenia petechial lesions must be excluded (13) as in our case was done due to pruritus and skin biopsy findings. Usually most of the skin lesions of brucellosis are not pruritic, but rarely pruritic cutaneous lesions were reported (13). On the other hand, concomitant cutaneous diseases such as contact urticaria that did not appear to be related to brucellosis were reported (16). In our case , in regard to rule out this lesions ,there was neither a history of tick-bite nor typical eschar lesion (tache noir) and the skin lesions dose not regress through administration of antihistaminic drugs. Therefore, we speculated that it might be *B. dermatitis* as reported by Berger *et al*. (17). Skin biopsy can be helpful for distinguish the etiology of skin rashes in the patients such as this case, for rule out of other differential diagnosis.

The diagnosis of brucellosis is usually made following positive culture of blood or bone marrow for *Brucella* species. It was reported that in the absence of bacteriologic confirmation, serologic tests can be used (1,2). In endemic countries for brucellosis culture results recovering *Brucella* species from blood or bone marrow is a gold standard, but the rate of isolation from blood varies from 15 to 70 percent depending on the methods used (1). Bacteremia was detected in 38% of all hospitalized brucellosis cases (2) .In this case, the diagnosis was made based on the history of ingestion of raw milk, clinical signs and symptoms supported by serology and resolution of clinical findings after antibiotic treatment for brucellosis.

It is important to emphasize that Cutaneous lesions and pancytopenia are not a usual manifestations of brucellosis (18-20) and it is reported here to remind physicians of the many rare complications of some bacterial diseases, especially brucellosis. We also wish to emphasize the importance of obtaining a detailed history, including ingestion of high-risk foods. Accordingly, *Brucella* infection should also be ruled out in patients with pancytopenia and skin rash with or without fever, especially in endemic regions such as our country Iran (21).

References

1. Koo HL, Ajami NJ, Jiang ZD, Dupont HL, Atmar RL, Lewis D, *et al*. A nosocomial outbreak of norovirus infection masquerading as clostridium difficile infection. Clin Infect Dis 2009 1;48(7):e75-e77.

2. Memish Z, Mah MW, Al MS, Al SM, Khan MY. Brucella bacteraemia: clinical and laboratory observations in 160 patients. J Infect 2000;40(1):59-63.

3. Uyar Y, Carhan A, Ozkaya E, Ertek M. Evaluation of laboratory diagnosis of the first norovirus outbreak in Turkey in 2008. Mikrobiyol Bul 2008;42(4):607-15.

4. Sari I, Altuntas F, Hacioglu S, Kocyigit I, Sevinc A, Sacar S, *et al*. A multicenter retrospective study defining the clinical and hematological manifestations of brucellosis and pancytopenia in a large series: Hematological malignancies, the unusual cause of pancytopenia in patients with brucellosis. Am J Hematol 2008;83(4):334-9.

5. Akova M, Uzun O, Akalin HE, Hayran M, Unal S, Gur D. Quinolones in treatment of human brucellosis: comparative trial of ofloxacin-rifampin versus doxycycline-rifampin. Antimicrob Agents Chemother 1993;37(9):1831-4.

6. Sevinc A, Buyukberber N, Camci C, Buyukberber S, Karsligil T. Thrombocytopenia in brucellosis: case report and literature review. J Natl Med Assoc 2005;97(2):290-3.

7. Gur A, Geyik MF, Dikici B, Nas K, Cevik R, Sarac J, *et al*. Complications of brucellosis in different age groups: a study of 283 cases in southeastern Anatolia of Turkey. Yonsei Med J 2003;44(1):33-44.

8. Akdeniz H, Irmak H, Seckinli T, Buzgan T, Demiroz AP. Hematological manifestations in brucellosis cases in Turkey. Acta Med Okayama 1998;52(1):63-5.

9. Todd KH, Lyde PD. Brucellosis and thrombocytopenic purpura: case report and review. Tex Med 1989;85(3):37-8.

10. Tsirka A, Markesinis I, Getsi V, Chaloulou S. Severe thrombocytopenic purpura due to brucellosis. Scand J Infect Dis 2002;34(7):535-6.

11. Kadanali A, Ozkurt Z, Albayrak A, Ertek M, Parlak M. An unusual presentation of acute brucellosis with fever, jaundice and maculopapular rash. Int J Infect Dis 2006;10(5):409-10.

12.Metin A, Akdeniz H, Buzgan T, Delice I. Cutaneous findings encountered in brucellosis and review of the literature. Int J Dermatol 2001;40(7):434-8.

13. Ariza J, Servitje O, Pallares R, Fernandez VP, Rufi G, Peyri J, *et al*. Characteristic cutaneous lesions in patients with brucellosis. Arch Dermatol 1989;125(3):380-3.

14. Nagore E, Sanchez-Motilla JM, Navarro V, Febrer MI, Aliaga A. Leukocytoclastic vasculitis as a cutaneous manifestation of systemic infection caused by Brucella melitensis. Cutis 1999;63(1):25-7.

15. Ural O, Findik D. Clinical microbiological case: a 22-year-old-man with fever and maculopapular rash. Clin Microbiol Infect 2002;8(4):245, 252.

16. Trunnell TN, Waisman M, Trunnell TL. Contact dermatitis caused by Brucella. Cutis 1985;35(4):379-81.

17. Berger TG, Guill MA, Goette DK. Cutaneous lesions in brucellosis. Arch Dermatol 1981;117(1):40-2.

18. Yalaz M, Arslan MT, Kurugol Z. Thrombocytopenic purpura as only manifestation of brucellosis in a child. Turk J Pediatr 2004;46(3):265-7.

19. Yinnon AM, Morali GA, Goren A, Rudensky B, Isacsohn M, Michel J, *et al*. Effect of age and duration of disease on the clinical manifestations of brucellosis. A study of 73 consecutive patients in Israel. Isr J Med Sci 1993;29(1):11-6.

20. Pappas G, Kitsanou M, Christou L, Tsianos E. Immune thrombocytopenia attributed to brucellosis and other mechanisms of Brucella-induced thrombocytopenia. Am J Hematol 2004;75(3):139-41.

21. Refai M. Incidence and control of brucellosis in the Near East region. Vet Microbiol 2002;90(1-4):81-110.