Acute brucellosis: a dramatic presentation with septic shock and severe thrombocytopenia

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Abstract

Brucellosis is an endemic zoonosis in Portugal, progressing as a multisystemic disease with a broad spectrum of clinical manifestations, that can be caused by several species of Brucella, the most common being *B. melitensis*. Hematological abnormalities, including anemia, leukopenia and thrombocytopenia, may be found during the course of the disease.

The authors describe the case of a 53 year-old man, native of Cape Verde and residing in Portugal for 25 years, with a condition of prolonged fever and had a dramatic evolution, with septic shock, severe thrombocytopenia and hemorrhagic dyscrasia.

The disease was diagnosed as acute brucellosis, and confirmed through blood cultures. Despite the severity of the clinical situation, the prompt institution of haemodynamic support, blood transfusion, invasive ventilation and appropriate antibiotics led to a satisfactory clinical outcome.

The diagnosis of brucellosis can be delayed, particularly when only less common manifestations are present. With this case it was our purpose to highlight the importance of maintaining a high degree of suspicion in order to correctly diagnose cases with less familiar clinical presentations.

Key words: brucellosis, thrombocytopenia, septic shock.

INTRODUCTION

Brucellosis is an endemic zoonosis in Portugal, whose annual incidence, although underestimated, has decreased from the 70 cases per million inhabitants recorded in 1999 to less than 14 cases per million inhabitants in 2003.[1] It is a chronic, multisystemic granulomatous disease, with a wide spectrum of clinical manifestations, caused by an intracellular bacteria.

Four species of Brucella can cause the disease in Humans: *B. melitensis, B. abortus, B. suis* and *B. canis*, with the majority of cases being caused by *B. melitensis*.

Transmission to Humans occurs through the consumption of unpasteurised dairy products, direct contact with infected animals and their products of conception, or the inhalation of aerosols.[2]

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The diagnosis of Brucellosis may be delayed, particularly if infrequent manifestations are present, and a high level of clinical suspicion is necessary for early diagnosis. The symptoms are non-specific, the most frequent being: fever, night sweating, anorexia, headaches, arthralgia and back pain.[3,4,5]

Various hematological alterations have been reported, ranging from benign alterations to disseminated intravascular coagulation. The most common alterations are anemia and leukopenia. Thrombocytopenia may also occur, in association with anterior alterations, or in rarer cases, in isolation.[6,7]

CLINICAL CASE

Male, aged 53 years, Black, born in Cape Verde, resident in Portugal for 25 years, visited the Emergency Service with vomiting, diarrhea, diffuse abdominal pain and prostration for the previous two days. Patient reported symptoms lasting one month that included fever, accentuated in the evenings, chills, dry cough, migraines and weight loss, though he was unable to say how much weight he had lost.

Besides coming into contact with beef cattle on the farm where he worked, there were no relevant epidemiological data, trips abroad, or risk factors for immunodeficiency.

Patient mentioned smoking, use of alcohol, and latent syphilis. He was not taking any type of medication.

TABLE I

Evolution of the analytical results over the course of hospitalization

	Admittance	6th day	14th day
Erythrocytes (x10^{12}/L)	4,14	3,43	2.88
Hemoglobin (g/dL)	13,6	10,93	9,3
Hematocrit	0,386	31,8	0,266
MCV (fl)	93,2	92,6	92,4
MCH (pg)	32,9	31,8	32,3
Prothrombin Time / control (sec)	15/13,5	15,5/13,5	14,0/13,5
APTT /control (sec)	48,1/28,7	43,8/28,7	31,8/28,7
Fibrinogen (mg/dL)	—	385	336
Leukocytes (x10^{9}/L)	3,5	2,94	5,0
Neutrophils (%)	77	70,4	61
Lymphocytes (%)	22	27,9	33
Platelets (x109/L)	45	18	73
LDH (U/L)	4170	1608	1422
PCR (mg/dL)	25,95	19,3	3,19
Creatinine (mg/dl)	1,40	0,90	0,60
ALT (U/L)	94	89	86
AST (U/L)	282	368	75
Alkaline phosphatase (U/L)	125	207	—
ALT (U/L)	113	213	—

On admittance, he had blood pressure of 127/69mmHg, radial pulse 128 bpm, regular and rhythmic, and axillary temperature of 39.4ºC. He was oriented in space and time, but with confused speech. The mucosa were pale, with signs of dehydration. No petechiae or ecchymoses were detected. There were no peripheral enlarged lymph nodes. Cardio--pulmonary examination showed decreased vesicular murmur in the lower half of the right hemithorax, without heart murmurs or other abnormal sounds. The abdomen was painful on palpitation, without defense, and no hepatosplenomegaly was detected. The rest of the physical examination was normal.

The laboratory results showed that he had leukopenia, thrombocytopenia, high C-reactive protein (CRP), elevated transaminases and high lactate dehydrogenase (LDH) *(Table I)*.

The electrocardiogram did not show any relevant alterations, and the chest radiograph showed slight paracardiac infiltrate on the right. Abdominal CT revealed heterogeneous hepatomegaly, with appearance suggestive of nonspecific periportal edema, and no other relevant alterations.

The patient was admitted with a diagnostic hypothesis of sepsis of undetermined origin. Blood cultures were taken, and empiric antibiotics started immediately, with Meropenem 1gr 8/8h IV.

The clinical symptoms worsened progressively, and on the 6th day of hospitalization, the patient suffered an abrupt alteration in state of consciousness, haemodynamic deterioration and respiratory insufficiency, compatible with septic shock.

He was transferred to the Intensive Care Unit (ICU) where he required haemodynamic support, transfusion (erythrocyte concentrate, platelets and fresh, frozen plasma) and invasive ventilation. The severe thrombocytopenia continued, complicated with abundant epistaxis, without haemoptysis. Chest radiograph showed diffuse, bilateral alveolar and interstitial infiltrate.

On admittance to the ICU, two necrotic cutaneous lesions were detected in the lower limbs. These lesions were interpreted as possible "taches noires", leading to a hypothesis of rickettsiosis. Meropenem was suspended, and Doxycycline, associated with Penicillin, was initiated. The latter antibiotic was suspended after exclusion of endocarditis by transoesophageal echocardiogram.

It is emphasized that there was a significant improvement with the new antibiotic instituted with apyretic on the 2nd day and suspension of vasopressor amines on the 4th day.

On the 15th day of hospitalization, the *Brucella species* was isolated in the blood cultures, therefore Doxycycline 100 mg 12/12 was continued, associated with Rifampicin 600 mg day.

The clinical, analytical and radiological findings

revealed an accentuated and progressive improvement, with resolution of all the abnormal data. No other microorganisms were isolated in the urine or sputum samples, the serological tests for Rickettsia conorii were negative, and Wright's reaction was positive.

The patient was discharged from Hospital on the 37th day after admission, in clinical and analytical remission, and antibiotic therapy was maintained for 6 weeks.

DISCUSSION

Brucellosis is a major medical and public health problem in Portugal. Even in endemic areas like ours, it is rare to find Brucellosis with as dramatic a presentation as this one, with septic shock and severe thrombocytopenia, as in the case described.

The hematological complications arising during acute brucellosis are rare, and usually take the form of mild pancitopenia.[8] The incidence of thrombocytopenia in brucellosis ranges from 2.4 to 33%[7] although severe thrombocytopenia with hemorrhagic dyscrasia is rare. Severe thrombocytopenia with epistaxis, as in the case in discussion, can simulate a primary hematological disease, but it is reversible after appropriate antibiotic therapy, often within 2 to 3 weeks.[9,10]

The etiology of thrombocytopenia remains obscure, and various mechanisms have been proposed: Hypersplenism, bone marrow depression, disseminated intravascular coagulation (DIC), lesion of the platelets by bacteria and mediated by the immune system.[7] Rare cases of severe thrombocytopenia associated with purpura and spontaneous hemorrhage, are more frequently attributed to immune causes.[8]

The definitive diagnosis of brucellosis requires isolation of bacteria from the blood culture, bone marrow or other samples of biological liquids or tissues. The sensitivity of the blood cultures depends on the individual laboratory practices, the amount of bacteria in the blood, and the method used, and ranges from 15 to 70%.[11] Because Brucella is a slow growing bacteria, the results of the blood cultures may not be available for several days or weeks.[11,12]

The diagnosis of acute brucellosis may be delayed, if septic shock or severe thrombocytopenia is present, as these manifestations evoke other nosological entities.

In the case presented, the positive blood cultures were determining factors for the diagnosis and start of appropriate therapy.

Given the possible immune cause for thrombocytopenia, various authors suggest the use of corticoids for its treatment, similar to the treatment for immune thrombocytopenic purpura. Therefore, effective antibiotic therapy should be initiated as quickly as possible, for control of infection. Other authors defend corticotherapy only in patients with a high risk of hemorrhage, as adequate antibiotic therapy reverts the thrombocytopenia in the majority of cases,[7] as occurred in the clinical case presented here.

This rare presentation of brucellosis is an example of the multiple forms of presentations of this disease, given that it can involve practically all the organs and systems, sometimes in dramatic form, hence the importance of including it in the differential diagnosis.

In endemic zones, it is essential to be aware of all the clinical details and give special attention to the epidemiological factors. In non-endemic zones with low prevalence of the disease, in today's scenario of international travel, it is essential to maintain a high level of suspicion for the diagnosis. ■

References

1. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. Lancet Inf disease 2006;6(2):91-99.

2. Pappas G, Akritidis N, Bosilkovski M, Tsianos E. Brucellosis. N Engl J Med 2005; 352:2325-2336.

3. Memish ZA, Balkhy HH. Brucellosis and International Travel. J Travel Med 2004; 11(1):49-55.

4. Troy SB, Rickman LS, Davis CE. Brucellosis in San Diego: epidemiology and species-related differences in acute clinical presentations. Medicine (Baltimore) 2005; 84 (3):174-187.

5. Sauret JM, Vilissova N. Human brucellosis. J Am Board Fam Pract 2002; 15(5):401-406.

6. Crosby E, Llosa L, Miro Quesada M, Carrillo C, Gotuzzo E. Hematologic changes in brucellosis. J Infect Dis 1984; 150 (3):419-424.

7. 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):290-293.

8. 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):139-141.

9. Sevinc A, Kutlu NO, Kuku I, Ozgen U, Aydogdu I, Soylu H. Severe epistaxis in brucellosis-induced thrombocytopenia: a report of two cases. Clin Lab Haematol 2000; 22(6):373-375.

10. Tsirka A, Markesinis I, Getsi V, Chaloulou S. Severe thrombocytopenic purpura due to brucellosis. Scand J Infect Dis 2002; 34 (7) 535-536.

11. Aliskan H. The value of culture and serological methods in the diagnosis of human brucellosis. Mikrobiyol Bul 2008; 42(1):185-195.

12. Mantur BG, Amarnath SK, Shinde RS. Review of clinical and laboratory features of human brucellosis. Indian J Med Microbiol 2007; 25(3):188-202.