Unusual manifestations of brucellosis

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Abstract

Brucellosis is an important public health problem in the Mediterranean countries, including our country. Furthermore, because of different symptoms and clinical findings, the disease could be confused with several other diseases. In this article, three unusual findings of brucellosis are presented: pancytopenia, endocarditis and meningitis.

Key words: brucellosis, endocarditis, meningitis, pancytopenia.

Introduction

Brucellosis remains the commonest zoonotic disease worldwide with more than 500,000 new cases annually [1]. The symptoms of brucellosis are non-specific; therefore, it may be difficult to diagnose [2]. The disease may be overlooked and misdiagnosed because of atypical clinical manifestations. The purpose of this paper is to emphasize atypical presentations of brucellosis.

Case 1

A 26-year-old female presented with fever, night sweats, headache and malaise for one week. The patient had been initially presented to a general practitioner with the same symptoms five days before admission and given antibiotic treatment (second-generation cephalosporin) and paracetamol. On admission her vital signs were as follows: body temperature: 38.5°C, arterial blood pressure: 70/30 mmHg, heart rate: 118/min and respiration rate: 14/min. Physical examination revealed hepatosplenomegaly. Laboratory tests showed haemoglobin: 10.2 g/dl, white blood cells: 2700/mm^3 with polymorphs 35%, lymphocytes 52%, monocytes 10% and eosinophils 3%. The platelet count was 37 × 10^9/l. Erythrocyte sedimentation rate (ESR) was 32 mm in the first hour. C-reactive protein (CRP) was 98 mg/dl. Brucella standard tube agglutination (STA) test was negative (or 1/80 titre). Grubel-Widal and monospot tests were negative. Blood and urine cultures were negative; three blood cultures for Brucella were also negative after 14 days of incubation. On day 6., *Brucella* spp. were isolated from bone marrow culture. Clinical and haematological findings improved with the treatment of brucellosis with streptomycin (1 g/d *i.m.*) and doxycycline (2 × 100 mg/d *p.o.*).

Case 2

A 50-year-old male presented with malaise, fever, cough, night sweats for ten days. On admission his vital signs were as follows: body

temperature: 38.0°C, arterial blood pressure: 110/70 mmHg, heart rate: 86/min, respiration rate 20/min. Physical examination revealed cardiac murmur and hepatosplenomegaly. Laboratory tests showed haemoglobin: 11.1 g/dl, white blood cells: 15600/mm^3, platelets: 406 × 10^9/mm^3, CRP: 85 mg/dl, ESR: 44 mm/h, AST: 75 U/L (N: 0-31), ALT: 21 U/L (N: 0-34), rheumatoid factor: 148 (N: 0-15) IU/ml. Echocardiogram showed vegetation of 15 × 13 mm on posterior mitral leaflet. STA was positive at a titre of 1/640. On day 4., *Brucella* spp. were isolated from blood culture. The patient was put on treatment with doxycycline (200 mg/d *p.o.*), rifampicin (1 × 600 mg/d *p.o.*) and ceftriaxone (2 × 1 g/d *i.v.*). The surgery was planned for endocarditis.

Case 3

A 41-year-old male presented with fever and confusion. On admission his vital signs were as follows: body temperature: 38.5°C, arterial blood pressure: 130/70 mmHg, heart rate: 87/min and respiration rate: 18/min. On physical examination, he had neck stiffness and confusion. Kernig's and Brudzenski's signs were negative and focal neurological signs were not detected. Blood parameters revealed the following values: haemoglobin: 14 g/dl, white blood cells: 10600/mm^3 (polymorphs 55%, lymphocytes 24%, monocytes 18%, eosinophils 3%); platelets: 223 × 10^9/mm^3. Serum electrolytes, creatinine levels and liver parameters were within normal limits. A lumbar puncture performed on admission showed 450 leucocytes/mm^3. The Gram staining of cerebrospinal fluid (CSF) was negative. Glucorrhachia/glycaemia was 11/85 mg/dl and the protein concentration was 271 mg/dl. The STA titre in CSF was 1/10. A presumptive diagnosis of bacterial meningitis was established. Therapy with intravenous ceftriaxone (2 × 2 g/d) was initiated. On day 8., *Brucella* spp. were isolated from CSF culture. Doxycycline (200 mg/d) and rifampicin (1 × 600 mg/d) were added to the treatment. Symptoms regressed with the treatment.

Discussion

Brucellosis is a common zoonotic disease in endemic areas such as Turkey. It is a disseminated

Table I. Characteristics of the patients

	Case 1	Case 2	Case 3
Age/Sex	26/F	50/M	41/M
Symptoms	Fever, night sweats, headache, malaise	Fever, cough, night sweats, malaise	Fever, confusion
Pathological findings	Fever, hypotension, hepatosplenomegaly	Fever, cardiac murmur, hepatosplenomegaly	Fever, neck stiffness, confusion
Laboratory findings			
Haemoglobin [g/dl]	10.2	11.1	14
White blood cells	2700/mm^3	15600/mm^3	10600/mm^3
Platelet	37 × 10^9/mm^3	406 × 10^9/mm^3	223 × 10^9/mm^3
CRP [mg/dl]	98	85	3.2
ESR [mm/h]	32	44	
RF [IU/ml]		148	
STA	1/80	1/640	1/10 (in CSF)
CSF			450 leucocytes/mm^3 Glucorrhachia/glycaemia: 11/85 mg/dl Protein: 271 mg/dl
Echocardiogram		Vegetation of 15 × 13 mm on posterior mitral leaflet	
Culture	*Brucella* spp. were isolated from bone marrow culture	*Brucella* spp. were isolated from blood culture	*Brucella* spp. were isolated from CSF culture
Treatment	Doxycycline + streptomycin	Doxycycline + rifampicin + ceftriaxone	Doxycycline + rifampicin + ceftriaxone

F – female, M – male, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, STA – standard tube agglutination, RF – rheumatoid factor, CSF – cerebrospinal fluid

infection that may present with a broad spectrum of clinical manifestations; therefore, it may be difficult to diagnose [2].

The haematological abnormalities (leucopenia, anemia, thrombocytopenia) are common in brucellosis but pancytopenia is rare. The pathogenesis of pancytopenia in brucellosis has not been clearly understood, but it seems to be multifactorial. Several possible mechanisms have been suggested for pancytopenia caused by brucellosis, such as hemophagocytosis, hypersplenism, bone marrow granulomas, bone marrow hypoplasia, and immune destruction [3]. In presented case 1, pancytopenia may be caused by hypersplenism. On the other hand, blood culture is the gold standard in the diagnosis of brucellosis. The sensitivity of blood culture depends on several factors such as previous use of antibiotics and phase of the disease. Bone marrow cultures may provide higher sensitivity, yield faster culture times, and may be superior to blood cultures when evaluating patients with previous antibiotic use [4, 5]. In our case, blood cultures were negative probably due to the used antibiotic.

Endocarditis occurs in less than 2% of cases, but it accounts for the majority of brucellosis-related deaths [2, 6]. Brucella endocarditis may develop on valves, previously damaged by rheumatic fever or congenitally malformed, but may also occur on previously normal valves. The clinical features are distinguishable from those of endocarditis caused by other organisms. The aortic valve is the most commonly affected cardiac valve [2, 6]. In our case 2, the mitral valve was affected. The diagnosis of endocarditis was made in accordance with Duke's criteria. Brucellosis may lead to complications that affect different organs and systems; among them endocarditis is a rare but serious complication.

Neurologic manifestations of brucellosis occur in 5% of patients [4]. Among the clinical manifestations, meningitis has been the most frequent presentation in clinical series and usually presents in an acute or chronic form. However, it has been noted that < 40% of the patients with brucellar meningitis exhibit meningeal signs. In our case, we observed neck stiffness. The diagnosis of brucellar meningitis depends on the demonstration of meningeal inflammation, abnormal CSF findings, and direct or indirect evidence of Brucella in the CSF [2, 7]. Cerebrospinal fluid analysis reveals a lymphocytic pleocytosis, elevated protein content, and low to normal glucose levels. Gram stains are usually negative and cultures are positive in less than one quarter of the cases; however, the diagnosis is based on the presence of specific antibodies in the cerebrospinal fluid [2, 4]. In our case, the diagnosis was made by microorganism isolation at the CSF and the antibodies detection in the CSF.

In conclusion, brucellosis is an important health problem especially in endemic areas. It may mimic many diseases (infectious or non-infectious). In patients living in endemic regions, considering brucellosis in differential diagnosis may lead to early diagnosis and treatment, and may decrease the complications.

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