HAEMATOLOGICAL MANIFESTATIONS OF BRUCELLOSIS

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Abstract- Brucellosis is a major health problem in many parts of the world, particularly in the Mediterranean and Middle East. Very few data on the frequency and diversity of haematological abnormalities occurring in brucellosis have been reported. In the present study 85 patients with brucellosis in Imam Khomeini Hospital during 1997-2002 were investigated retrospectively to determine the haematological changes during the active course of this infection. Inclusion criteria included a compatible clinical picture with either a positive blood culture or bone marrow culture for brucella organism or a brucella antibody titre of 1/80 (Wright agglutination test), and 2ME (2-mercaptoethanol) of 1/40 or coomb's Wright with any titre. Anemia was detected in 43.5% patients, leukopenia in 13.6%, thrombocytopenia in 12.5% and pancytopenia in 2.4% of patients. Unusual complications were detected in two patients, one with mouth bleedings, the other with purpuric skin lesions of the lower extremities, both patients had endocarditis. As brucellosis is common in our region it may be considered in patients whose blood picture reveals haemolytic anemia, leukopenia, thrombocytopenia or pancytopenia, particularly when the disease is epidemiologically suspected.

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Key words: Brucellosis, haematological manifestation, leukopenia, thrombocytopenia, pancytopenia.

INTRODUCTION

Brucellosis is a bacterial zoonosis transmitted directly or indirectly to humans from infected animals (1). It constitutes a major health problem in many parts of the world, particularly in the Mediterranean and Middle East. Routs of transmission from animals to humans include direct contact with infected animals or their secretions through cuts or abrasions in the skin, by way of infectious aerosols inhaled or inoculate in the conjunctiva, or by ingestion of unpasteurized dairy products (2).

Although brucellosis has been controlled or eradicated in many developed countries, it still remains a health problem in developing hyperendemic countries, as in Iran. In Iran, efforts to eradicate *brucella melitensis* infection from sheep and goat population have been much less successful; in addition, consumption of unpasteurized dairy products especially cheeses and milk and ice-cream in many area of Iran make eradication very difficult.

Brucellosis is a multisystem disease with a broad spectrum of clinical manifestations. As no characteristic constellation of symptoms and signs exists, the diagnosis may be readily missed (1). Haematological abnormalities including anemia, leukopenia and thrombocytopenia can be encountered during the course of the disease, which can be misdiagnosed as a hematologic malignancy (3).

In this study, the most common haematological manifestation of brucellosis in hospitalized patients at Imam Khomeini Hospital during 1997-2002 were investigated, which could help in rapid diagnosis of this disease.

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MATERIALS AND METHODS

Records of the preceding 5 years (from 1997-2002) of 85 patients with brucellosis from Imam Khomeine Hospital were studied retrospectively.

Inclusion criteria included a compatible clinical picture with either a positive blood culture or bone marrow culture for brucella organism or a brucella antibody titre of 1/80 (Wright agglutination test), and 2ME (2-mercaptoethanol) of 1/40 or coomb's Wright with any titre. Cases not fulfilling the above mentioned criteria were excluded.

On the basis of questionnaire, demographic records of patients and results of laboratory (serology and blood culture and hematologic records) selected and studied.

RESULTS

Records of 85 patients were reviewed, consisting of 56 (65.98%) males and 29 (34.10%) females. Most of the patients were in age range of 15-35 years and median age was 38 years.

Most of female patients were housewives and male were farmers or shepherds. Ingestion of unpasteurized dairy products asked from 70 patients which was positive in 45 (64.3%) patients. The most common complain was fever (52.9%). Low back pain was detected in 29.41% and arthralgia in 23.52%. Positive family history of brucellosis was found in 16 patients (18.8%). Duration of hospitalization was from 7 to 14 days. Table 1 shows frequency of brucella complications or manifestations. Lymphadenopathy, splenomegaly and hepatomegaly were detected in 5 (5.9%), 8 (9.41%) and 10 patients (11.9%), respectively.

Table 1. Frequency of clinical presentation of brucellosis

Features	F	*P*
Constitutive symptoms (*eg*, malaise, arthralgia)	60	70.58
Epididymoorchitis	7	8.23
Arthritis	7	8.23
Spondylitis	4	4.7
Neurobrucellosis	4	4.7
Endocarditis	3	3.52
Total	85	100

Abbreviations: F, frequency; P, percent.

Haematological findings included leukopenia in 11 (13.6%), anaemia in 30 (43.5%), thrombocytopenia in 8 (12.5%) and pancytopenia in 2 (2.4%) patients (Table 2). The results of serology of brucellosis are shown in Table 2. Erythrocyte sedimentation rate (ESR) was above 20 in 56 patients (65.9%), and 55 (64.7%) patients had CRP above 2-positive. Blood culture was positive in 13 (15.3%) patients; bone marrow culture was performed only in 5 patients, which was positive in one patient. Two patients had negative serology, but diagnosis was confirmed with positive blood culture.

Two patients died during treatment of brucellosis; one was a 65 years old male with past history of hypertension and renal-carcinoma and had brucella endocarditis. The other patients was an 80 years old female without underlying illness with brucella spondylitis. Two patients presented with bleeding tendency (mouth bleeding and purpuric skin lesions), both had positive blood culture and brucella endocarditis.

Table 2. Frequency of haematological and serological findings

Haematological and serology findings	F	P
WBC count (mm^3)		
Normal (4300-10.800)	59	72.83
Leukopenia (< 4.300)	11	13.85
Leukocytosis (> 10.800)	11	13.85
Total	81	100
HB		
Normal (male: 13-18, female: 12-16)	39	56.5
Anemia: (male: <13, female: <12)	30	43.5
Total	69	100
Platelet count		
Normal: (130.000-400.000)	48	75
Thrombocytopenia (< 130.000)	8	12.5
Thrombocytosis (> 400.000)	8	12.5
Total	64	100
Serology/Blood culture		
Positive Wright test and 2 ME	76	89.4
Positive Wright and blood culture	5	5.9
Negative Wright with positive Coombs' test	2	2.4
Negative serology positive BC	2	2.4
Total	85	100

Abbreviations: F, frequency; P, percent; WBC, white blood cells; HB, haemoglobin; BC, blood culture.

DISCUSSION

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 (1).

In our study, brucellosis was much more common in males. This could be due to occupational exposure, as in farmers, shepherds or veterinarians. In Torres-Padilla, Geyik and Bikas *et al.* studies, occupational exposure was a risk factor for this disease too (4-6). Concerning the age of patients, the most common age was from 15 to 45 in our study, a finding similar to Almuneef *et al.* study (7).

Fever was the most common presenting symptom, followed by weakness and sweating, as in other studies (8). Osteoarticular complains, the most common complication of brucellosis, was observed in 22.8% of our patients as in study by Barroso *et al.* (9). Because of reticuloendothelial involvement, hepatosplenomegaly can be observed in brucellosis. This was found in 8 (9.41%) of our patients, much less than Namiduru and Barroso studies in which hepatosplenomegaly was present in 56.6% and 37.5% of patients, respectively (8, 9).

Blood culture was positive in 13 (15.3%) of our patients, and it was interesting that 2 patients had negative serology test, who had brucella endocarditis. In a study conducted in Jordan, positive blood culture was found in 23.4% of patients (10), and in study of Dimitrov it was found in up to 74.1% (11).

Haematological disturbances in brucellosis are common and have been reported in the literature (15) in particular leukopenia, and relative lymphocytosis, along with mild anaemia and thrombocytosis (12). The frequencies of haematological findings in study of Akzdeniz *et al*. in Turkey on 233 patients showed leukopenia in 21%, anaemia in 44%, thrombocytopenia in 26% and pancytopenia in 8% (3). Another study of haematological changes during active course of brucellosis showed that leukopenia occurs in 45%, anaemia in 74%, thrombocytopenia in 39.5%, and pancytopenia in 21% (13). Our results showed leukopenia in 13.6%, anaemia in 43.5%, thrombocytopenia in 12.5% and pancytopenia in 2.4%. So the most common haematological abnormalities in this study were anaemia and leukopenia.

Hypersplenism, haemophagocytosis and granulomatous lesions of the bone marrow appear to play a fundamental role in producing these abnormalities of the peripheral blood. Pancytopenia in brucellosis is multifactorial and is attributed to hypersplenism and bone marrow involvement. Rarely, marked pancytopenia or isolated deficits can be attributed to diffuse intravascular coagulation, hemophagocytosis, or immunologically mediated cellular destruction (14). In a study conducted in Saudi Arabia, changes compatible with hypercellularity, increase eosinophile, plasma cell, histiocyte and heamophagocytosis were found in 87.5% of patients with pancytopenia (15). Unfortunately, we were unable to study these changes in our patients.

Tsirka *et al.*, from Greece, reported one case of brucellosis with haemolytic anemia and severe thrombocytopenia (16). Another report from Turkey presents two patients with severe epistaxis and isolated thrombocytopenia which was initially diagnosed as idiopathic thrombocytopenia purpura, but which was finally attributed to brucellosis (17). In our study we had two patients with bleeding tendency, one with mouth bleeding and another with purpuric rash of lower extremities; both had brucella endocarditis with positive blood cultures.

In sum, practically every organ and system of the human body can be affected in brucellosis, so the haematological consequences of brucellosis should always be kept in mind in the differential diagnosis of anaemia, leukopenia, thrombocytopenia and pancytopenia especially in our areas where brucellosis is an endemic disease.

Conflict of interests

The authors declare that they have no competing interests.

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