RESEARCH ARTICLE

Evaluation of epidemiological data of 541 patients with brucellosis in Siirt, a city in south-eastern Anatolia

Güneydoğu Anadolu Bölgesinde bulunan Siirt ilinde 541 bruselloz olgusunun epidemiyolojik verilerinin irdelenmesi

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ABSTRACT

Objectives: We intended to examine 541 brucellosis cases by offering our experiences regarding this preventable infectious disease that is significant for our country.

Methods: We evaluated 1210 hospitalized patients between the dates of January 2006 and December 2010 in Siirt General Hospital and 541 brucellosis cases were reviewed retrospectively. Patients with Rose Bengal plate test positive and has Wright agglutination test a titer of 1:160 or higher were included in this study.

Results: A 53.6% of brucellosis cases were male and 46.4% were female. The mean age (±SD) of patients was 41.23±2.7 years. Between the ages 31 and 50 is the range brucellosis is most commonly encountered in both men and women. Hematological evidence discovered that for 67% of patient's sedimentation is 20-40 mm/hour, 53% leukocyte count is in normal range, 36% of patients had leukocytosis, 10% had leukopenia, and 8% had thrombocytopenia. Most common three symptoms were joint pain (90%), myalgia (75%) and fatigue (70%). The most involved systems were musculoskeletal (28%), hematological (22%), and gastrointestinal systems (20%). Most commonly encountered systemic findings were sacroiliitis (20%), anemia (14%) and liver dysfunction (12%). Brucella was observed most commonly is May (30%) in Siirt. A 47% of our cases are occupied in agriculture and stockbreeding that are risky occupations regarding brucellosis, supports the conventional data regarding brucellosis epidemiology.

Conclusion: Despite the campaigns, infection rate is still high and it affects both animal industry and human health in our country. Data about brucellosis should be validated by large multicenter studies. *J Clin Exp Invest 2013; 4 (2): 136-140*

Key words: Brucellosis, infectious disease, endemic disease, Rose Bengal, agglutination tests.

ÖZET

Amaç: Ülkemiz açısından önem arz eden ve önlenebilir bir enfeksiyon olan bruselloz ile ilgili deneyimlerimizi sunarak konuyu irdelemek amacıyla 541 bruselloz olgusu değerlendirilmiştir.

Yöntemler: Ocak 2006-Aralık 2010 tarihleri arasında yatırılarak takip ve tedavileri yapılan 1210 hasta geriye dönük olarak incelenmiş, Rose Bengal pozitif ve Wright aglutinasyon testi titresi 1/160 ve üzeri olan 541 bruselloz olgusu çalışmaya dahil edilmiştir.

Bulgular: Çalışmamıza alınan 541olgunun %53,6'sı erkek %46,4'ü kadın olup, yaş ortalamaları 41,23±2,7 idi. Hem erkeklerde hem de kadınlarda brusellozun en sık görüldüğü yaş aralığı 31-50 yaş arası olmuştur. Hematolojik bulgulardan hastaların %67'sinde sedimentasyon 20-40 mm/saat, %53'ünde lökosit sayısı normal aralıkta iken, hastaların %36'sında lökositoz, %10'unda lökopeni, %8'inde trombositopeni bulunmuştur. En sık gözlenen üç semptom eklem ağrısı (%90), kas ağrısı (%75) ve halsizlik (%70) olmuştur. En sık tutulan sistemler sırasıyla kas iskelet (%28), hematolojik (%22) ve gastrointestinal sistemler (%20) olmuştur. Kas iskelet sistemi bulgularından sakroileit (%20), hematolojik bulgulardan anemi (%14) ve gastrointestinal sistemden ise karaciğer fonksiyon bozukluğu (%12) en sık raslanan sistemik bulgular olmuştur. Bu endemik hastalığın en çok (%30) gözlemlendiği ay Mayıs olmuştur. Olgularımızın %47'sinin bruselloz açısından riskli meslek olan tarım ve hayvancılıkla uğraşıyor olması, bruselloz epidemiolojisi hakkındaki klasik bilgileri destekler niteliktedir.

Sonuç: Önleyici programlara rağmen bu enfeksiyonun oranı hala yüksek olup, hem insan sağlığını hem de hayvancılık sektörünü etkiler. Bundan dolayı bu yaygın enfeksiyon hastalığı ile ilgili daha geniş serilerin irdelendiği çalışmalara ihtiyaç duyulmaktadır.

Anahtar kelimeler: Bruselloz, enfeksiyöz hastalıklar, endemik hastalık, rose bengal, aglütinasyon testleri.

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INTRODUCTION

Brucellosis is a worldwide zoonotic infection caused by intracellular bacteria of the genus Brucella, and Brucella melitensis is the most prevalent strain. It affects both humans and animals, and causes economic cost and significant public health problems in many countries. Brucellosis is an endemic disease in Turkey. It is especially common in the middle and southeastern regions of our country [1].

It is generally a disease seen in young people and adults; it is less commonly seen in children and elderly. There are no specific clinical symptoms for brucellosis. It affects especially lymphoreticular system organs (liver, bone marrow, spleen, and lymph nodes) and rarely heart, genitourinary system organs, central nerve system [2,3].

Human brucellosis is a systemic disease and patients with brucellosis have nonspecific symptoms and they have in a high risk of complications. The most frequent clinical symptoms are chill, intermittent fever, night sweating and joint pain. Fever occurs over 40ºC and causes miscarriages in pregnant women. Infertility can occur in result of orchids in men [4,5]. Joint symptoms of brucellosis are arthritis, arthralgia, sacroiliitis and spondylitis due to vertebral stiffness. Gastrointestinal, skeletal, and genitourinary findings are common but neuro-brucellosis, pericarditis, and pancytopenia are rare complications of brucellosis. If the disease is not diagnosis early and not consider the differential diagnosis, the treatment chance will be missed. Sometimes, the disease can result in death because of its serious complications; infective endocarditis and meningoencephalitis [2-4].

Several approaches were used for treatment of brucellosis. Doxycycline and streptomycin combination or rifampicin and trimethoprim-sulfamethoxazole combination can be used in treatment of this disease. Another choice is the combination of rifampicin with ofloxacin [6].

The aim of our study was to emphasize the demographic, epidemiological, clinical, occupational structures and seasonal patterns and laboratory features of 541 brucellosis patients, and their outcomes, during a 2-year period in the endemic region of Siirt in Southeastern Anatolia.

METHODS

We evaluated 1210 hospitalized patients retrospectively between the dates of January 2006-December 2010 in Siirt General Hospital and 541 brucellosis cases were reviewed. Patients with Rose Ben-gal plate test positive and has Wright agglutination test a titer of 1/160 or higher were included in the present study.

Wright tube agglutination test was performed according to the recommendations of the manufacturer (Seromed, Turkey). The sera were tested in dilutions of 1/40, 1/80, 1/160, 1/320, 1/640, 1/1280, and 1/2560; and titers of 1/160 and over were accepted as positive for brucellosis.Rose Bengal test was performed with slide agglutination method. The sera were treated with Sero-Lam Brusella Rose Bengal Plate Test (Seromed, Turkey) as described by the manufacturer and observation of agglutination on the slide were accepted as presence of the brucella antibodies and evaluated as positive for the disease.

The data received from the patient's files in clinic archive. Age, gender, occupation, seasonal specifications of the disease, duration of symptoms at admission, history of drinking of raw milk, eating of milk products, clinical symptoms, results of physical examination and laboratory results were recorded.

"Detection of Rose Bengal test positives and a titer of 1/160 or higher of Wright agglutination test" or "Reproduction of Brucella bacteria in any culture" was used for diagnosis criteria with clinical symptoms such as arthralgia, fever, sweating, chills, headache, and malaise.

Statistical analysis: Data analysis was performed using the SPSS software (ver. 15.0 for Windows; SPSS Inc., Chicago, IL). Data are shown as means ± standard deviations or medians, where appropriate. Descriptive statistics are expressed as numbers and percentages.

RESULTS

A 53.6% of patients were male and 46.4% were female. The mean age of brucellosis cases was 41.23±2.7 years. Brucellosis found most commonly in both men and women between 31 and 50 years of ages.

Hematological evidence discovered that for 67% of patients sedimentation were 20-40 mm/hour, 27% of patients sedimentation were 40-70 mm/hour, 54% leukocyte count of the patients were between normal range (5,000-10,000/mm^3), 36% of patients had leukocytosis, 10% had leukopenia, 8% had thrombocytopenia and 14 % had anemia (Table 1).

Most commonly three symptoms were; joint pain 90%, myalgia 75% and weakness 70% (Table

2). The most involved systems were musculoskeletal 28%, hematological 22%, and gastrointestinal systems 20%. Most commonly systemic findings were sacroiliitis 20% of skeletal system, anemia 14% of hematological symptoms and liver dysfunction 12% of gastrointestinal system (Table 3).

The average hospitalization time of cases is approximately 6.2±1.3 days, which comprises the time for acquiring test results and initial treatment.

Distributions of patients according to their occupation were shown in Table 4. The majority of the cases occupational group was agriculture and stockbreeding 47%. Housewives 33% were ranked second. The month in which majority of the cases (30% of patients) applying to hospital was May (Figure 1).

Bacteria were isolated in only 14 of 70 cultures of patients. Bone marrow culture was not obtained from any of the patients.
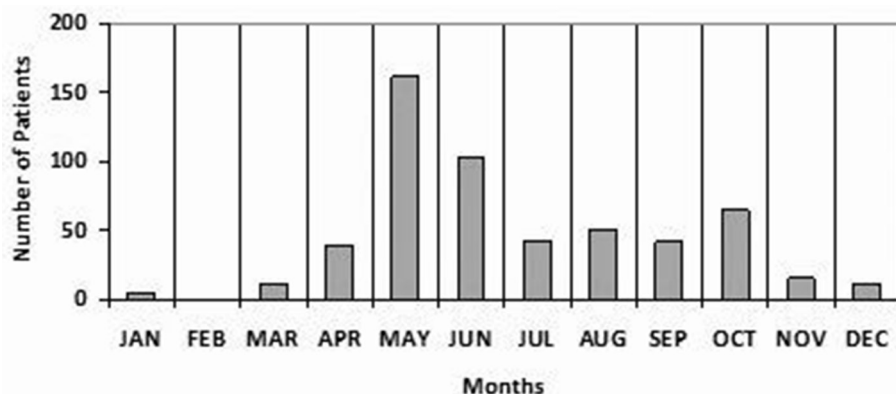

Figure 1. Distribution of cases according to application months

Table 1. Laboratory findings of patients

Laboratory findings	n (%)
Erythrocyte Sedimentation Rate (41-70 mm/h)	148 (27)
Erythrocyte Sedimentation Rate (21-40 mm/h)	364 (67)
Erythrocyte Sedimentation Rate (1-20 mm/h)	29 (5)
The Number of leukocyte (>10,000/mm^3)	198 (37)
The Number of leukocyte (5,000-10,000/mm^3)	287 (53)
The Number of leukocyte (<5,000/mm^3)	56 (10)
Anemia (Hb <12 mg/dL)	78 (14)
Thrombocytopenia (<100,000/mm^3)	44 (8)
ALT (>50 IU/ml)	67 (12)
Rose Bengal positivity	541 (100)
Wright agglutination positivity	541 (100)
Isolation from blood culture	14 (20)

Table 2. Clinical signs and findings of patients

Clinical signs and findings	n (%)
Joint pain	487 (90)
Myalgia	403 (75)
Weakness	380 (70)
Fever (>38°C)	334 (61)
Night sweats	286 (53)
Splenomegaly	60 (11)
Hepatomegaly	56 (10)
Lymphadenopathy	54 (10)
Abdominal pain	23 (4)

Table 3. Systemic involvement of patients

System involvement	n (%)
Musculoskeletal involvement	151 (28)
Sacroiliitis	104 (19)
Peripheral arthritis	42 (8)
Spondylitis	5 (1)
Gastrointestinal involvement	113 (21)
Hepatitis	67 (12)
Vomiting	35 (7)
Diarrhea	11 (2)
Hematological system involvement	122 (23)
Thrombocytopenia (<100,000/mm^3)	44 (8)
Anemia (<12 mg/dL)	78 (15)
Genitourinary system involvement	3 (1)
Epididymo-orchitis	3 (1)
Neurological system involvement	0
Dermatological system involvement	0

Table 4. The distribution of patients according to the occupation

Job	n (%)
Agriculture and animal husbandry	256 (47)
Housewife	182 (34)
Student	62 (12)
Self-employed	14 (2.5)
Officer	14 (2.5)
Pensioner	13 (2)

DISCUSSION

Brucellosis is a zoonotic infection and isolates from commonly in animals such as goat and sheep. It is not eradicated completely from the world. Every year 500 thousand recent brucellosis cases occur on the world, and the occurrence rate in our country was found between 1% and 26.7%, depending on the region [5-6]. Brucellosis is a systemic infection disease and it has very heterogeneous clinical spectrum. Varying in spectrum between light form and lethal forms and symptoms and signs in clinical charts are not always original. Nonspecific symptoms are usually observed such as fever, exhaustion, sweating, and myalgia. The prevalence and pattern of symptoms and clinical findings depend on age of patient, individual immune response and duration of disease [7].

In our country brucellosis is commonly observed in Eastern and Southeastern Anatolia [8,9]. Cheese with added herbs is produced in provinces of Van, Diyarbakır, Bitlis, Siirt, Batman, Kars, and Hakkari. Brucellosis rate increases in these regions because of not boiling the milk enough or not being pasteurized [10,11].

Production of cheese with added herbs and sheep's milk increase on April, May, and June especially. This condition explains why brucellosis cases increase especially during spring months. According to epidemiological data of 2005 by the Republic of Turkey Ministry of Health, morbidity rate of brucellosis was one in 100,000 until the 1980's and it was increased gradually in later years. Then it was 20.3 in 100,000 in year 2005 [12].

In our country primary symptoms were found to be fever 43-83%, night sweating 69%, lumbar pain 22-33%, headache 28-44%, lack of appetite 34-53%, joint pain 20-76%, myalgia 56%, exhaustion 14-81%, gait disorder 11-18%, mental confusion 6% and weight loss 2-36%. Our results were similar to previous studies [13].

In brucellosis musculoskeletal system is generally the most involved system and its involvement rate is 14-49% [14,15]. Musculoskeletal involvement is determined to be 28% in our patients.

Frequent involvement of reticuloendothelial system organs such as liver and spleen in brucellosis can be observed. Insignificant elevated transaminases can be seen depending on hepatosplenomegaly. These elevated transaminases usually do not require treatment. In 12% of our patients, serum transaminases were determined above the normal range, 10% has hepatomegaly, and 9% has splenomegaly. They didn't need any treatment. In some patients with elevated serum transaminases, elevation could be depending on antibiotics and analgesics which used in threatment. Therefore serum transaminase should be followed up regularly to protect hepatotoxic effects of tetracycline and rifampicin under.

Hematological variety is common in brucellosis, however they don't have diagnostic character and usually they don't require therapy. Leukocyte levels are generally normal or decrease in brucellosis. In our study, leukocyte levels are in range of 4,000-10,000/mm^3 in 53% of patients, 36% of patients had leukocytosis, 10% had leukopenia. In other studies about the subject, similar results are obtained [15]. Thrombocytopenia and anemia are seen in brucellosis; however, they don't require therapy: In our study, 8% of the patients had thrombocytopenia ≤100,000/mm^3 and 14% had anemia (Hb <12g/dL).They didn't need any treatment.

Dermatological symptoms and signs are rare complications in brucellosis and they were not seen in our patients. Neurological findings are uncommon but life-threatening complications of brucellosis. Incidence of neurological manifestation are between the ranges of 0-25% in previous studies [15,16]. These different results are due to diagnostic methods and difference between case definitions. No neurobrucellosis case was observed in our study.

Occupation distribution of brucellosis patients were also examined in the present study, the highest rated occupational groups are found to be occupied in agriculture and stockbreeding. Similar result is obtained in previous studies from Turkey that supporting conventional data [17].

Blood cultures were taken from 70 patients; reproduction was observed only fourteen of the cultures. In our country, culture positives are found to be 12-70% [15,18,19], this rate is between 72-84% in international studies. The difference is related to antibiotics therapy before taking blood culture. This

condition decrease culture positives rate [20,21]. One of the reasons of lowered culture positives in our and our country's studies is incompetence of laboratory practices and resources. The other important reason can be frequent empiric antibiotic administration to patients with fever.

Our country is an endemic region for brucellosis, diagnosis and treatment of the disease is very important. Despite the effort programs in our country, infection rate is still high and it affects both animal industry and human health.

We intended to examine this subject by offering our experiences regarding this preventable infectious disease that is significant for our country. Data about this common systemic infectious disease should be supported with large multicenter studies, the personnel in first degree health service should be helped to become aware and the people should be educated about symptoms of the disease and ways of transmission.

REFERENCES

1. Dogbane M, Mesa Alp E. In: Topcu AW, Soyletir G, Doganay M, eds. Infectious Diseases and Microbiology. 3rd ed. Istanbul. Nobel Medical Books, 2008:897-909.

2. Young EJ. Brucella Species. Eds.: Mandell GL, Douglas RG, Bennett JE: Principles and Practice of Infectious Diseases. 6th ed. Philadelphia. Churchill Livingstone, 2005:2670-2673.

3. Black FT. Brucellosis. Eds.: Cohen J, Powderly W: Infectious Diseases. 2nd ed. Edinburgh. Elsevier Limited, 2004:1665-1668.

4. SOA Shamelian. Diagnosis and Treatment of Brucellosis. The Netherlands Journal of Medicine 2000;56:198-199.

5. Ceylan E, Irmak H, Buzgan T. Brucellosis Seroprevalence of Human and Animal Populations in Some Villages of Van. Van Journal of Medicine 2003;10:1-5.

6. Kaleli I, Kocoglu T, Ozen M, Aksit F. The Prevalence of Brucellosis in Denizli. Infeks Journal 1999;13:231-233.

7. Memish Z, Mah MW, Al Mahmoud S, et al. Brucella bacteremia: Clinical and laboratory observations in 160 patients. J Infect 2000;40:59-63.

8. Yüce A, Alp Cavus S. Brucellosis in Turkey: An Overview. Klimik 2006;19:87-97.

9. The Ministry of Health the Republic of Turkey Epidemiology Monthly Report Brucellosis. 2004;3:88-91.

10. Demiroglu YZ, Turunc T, Calıskan H, et al. Brucellosis: retrospective evaluation of the clinical, laboratory and epidemiological features in 151 cases. Mikrobiyol Bul 2007;41:517-527.

11. Demirturk N, Demirdal T, Erben N, et al. Brucellosis: a retrospective evaluation of 99 cases and review of brucellosis treatment. Trop Doct 2008;38:59-62.

12. The Ministry of Health the Republic of Turkey. Statistics/Yearbook of Labour Directorate General of Primary Health Care. Ankara: Ministry of Health 2005.

13. Vardar I, Turker N, Cebelli I, et al. Brucellosis: 120 Adult Patients with Clinical, Laboratory Evaluation, and Treatment Characteristics. Izmir Ataturk Journal of Hospital Medicine 2002;40:67-70.

14. Cesur S, Capar Y, Demir P. A Retrospective Study of 104 Cases Journal of Brucellosis Infection 2004;18:169-173.

15. Gur A, Geyik MF, Dikici B, et al. Complication of brucellosis in different age groups: A study of 283 cases in Southeastern Anatolia of Turkey. Yonsei Medical Journal 2003;44:33-44.

16. Montaud AR, Jimenez FJ, Zancada F, et al. Neurobrucellosis mimicking migraine. Eur Neurol 1991;31:30-32.

17. Tekin R, Karakoç Z, Demirpençe O, et al. Retrospective Analysis of 286 Brucellosis Cases in the Southeast of Turkey. Journal of Clinical and Experimental Investigations 2012;3:335-339.

18. Tasova Y, Saltoglu N, Yilmaz G. Brucellosis: 238 Cases of Clinical, Laboratory Evaluation, and Treatment Characteristics. Infectious Journal 1998;12:307-312.

19. Tansel O, Yavuz M, Kuloglu F, Akata F. Evaluation of Forty Cases of Brucellosis Admitted to the University Hospital of Trakya. Journal of Infectious 2003;17:1-4.

20. Colmenero JD, Reguera JM, Fernandez-Nebro A, et al. Osteorticular complications of brucellosis. Ann Rheum Dis 1991;50:23-26.

21. Ariza J, Gudiol F, Pallares R, et al. Treatment of human brucellosis with doxycycline plus rifampin or doxycycline plus streptomycin. Ann Intern Med 1992;117:25-30.