Brusellozis: 127 Olgunun değerlendirmesi

Emel Türk Arıbaş[1] , Abdullah Yılmaz[2], Mehmet Bitirgen[3]

[1]Doç.Dr.S.Ü.Meram Tıp Fakültesi İnfeksiyon Hastalıkları ve KlinikMikrobiyoloji AD,Konya
[2] Uz. Dr.SSK Hastanesi,Bursa
[3]Prof.Dr.S.Ü.Meram Tıp Fakültesi İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD,Konya

Özet

Bu çalışmada, bruselloz tanısı ile izlenen 127 olguda bulaş yolları, klinik, laboratuvar ve tedavi özellikleri değerlendirildi. Yaşları 14-86 (ort:45.79) arasında değişen olguların 72 (%56.69)' ı kadın, 55 (%43.30)' u erkek idi. Olguların 76 (%59.83)' sında bulaş yolu olarak hayvancılıkla uğraşma, çiğ süt ve süt ürünleri tüketimi saptandı. En sık rastlanan yakınmalar; ateş (%50.39), artralji (%46.45), halsizlik (%39.37) ve terleme (%30.70) olarak belirlendi. Fizik muayene bulgusu olarak en sık saptanan anormallikler sırasıyla ateş (%33.07), hepatomegali (%19.6), artrit (%14.17) ve splenomegali (%11.81) idi. Sadece 3 olguda menenjit ve birinde orşit vardı. Olguların tamamında STA testi ≥ 1/160 bulundu ve % 4.72' sinde Brucella spp. izole edildi. Tedavide 93 hastaya doksisiklin + rifampisin ve 30 olguya doksisiklin + streptomisin 6 hafta süreyle uygulandı. Doksisiklin + rifampisin uygulanan hastalarda relaps %5.3 ve doksisiklin + streptomisin uygulananlarda %3 olarak saptandı. Aralarındaki fark istatistiksel olarak anlamlı değildi.

***Anahtar Kelimeler**: Brusellozis,Tanı, Komplikasyon, Tedavi*

Brucellosis : Evaluation Of 127 Cases

Abstract

In this study, 127 patients diagnosed as brucellosis were evaluated about transmission routes, clinical, laboratory and therapeutic features. Ranging between 14-86 (mean:45.79) years, 72 (%56.96) of the patients were female, 55 (%43.30) were male. In 76 (%59.83) of the cases, infection was releated with stock raising and consuming unpasteurised milk and milk products. The most frequently complaints detected were fever (%50.39), arthralgy (%40.45), lack of appetite (%39.37) and sweating (%30.70). As physical examination findings, the most frequently abnormalities were detected as fever (%33.07), hepatomegaly (%19.60), arthritis (%14.17), splenomegaly (%11.81). Only in 3 cases meningitis and in one orchitis had developed as complication of brucellosis. In all cases the standart tube aglutination (STA) test titer was found ≥ 1/160 and in %4.72 of the cases Brucella spp. could be isolated. 93 patients received a combination therapy composed of doxycycline plus rifampin for 6 weeks and 30 cases used doxycycline plus streptomycin for 6 weeks. The patients who received doxycycline plus rifampin had a relaps rate of %5.3, wherease the rate of the other group which received doxycycline plus streptomycin was found as %10. The difference between two groups was not statistically significant (p>0.05).

***Key Words:** Brucellosis,Diagnosis, Complications, Treatment*

Introduction

In developing countries, especially in the mediterranean countries including Turkey, brucellosis is presently an important public health problem. Brucella infection virtually derive directly or indirectly from animal exposure.The most frequently infection sources are unpasteurised milk and milk products (1,2). The infection is usually determined by fever, malodorus sweats, headache, lack of appetite, weight loss and back pain. In addition to this general signs, every patient can show different clinical manifestations. Predominantly somatic complaints can be found, wherease physical examination findings are absent or few in amount. Sometimes there are difficulties in the diagnosis of the disease; the chronic course of the disease and the possibility of a relaps arise as difficulties in the therapy (1,3,4). In this study, patients diagnosed as brucellosis were evaluated about the transmission route of the infection; clinical, laboratory and therapeutic features.

Patients and Methods

In this study, 127 cases diagnosed and hospitalised as brucellosis at the Department of Infectious Diseases were included. The diagnostic criteria was the isolation of the Brucella spp. from blood and/or detecting spesific antibody with a titer ≥1/160 by STA. The diagnosis of neurobrucellosis was made by analysis of the cerebro spinal fluid CSF (leucocyte count and formula, protein and glucose levels) and testing STA, using CSF instead of serum. Hemoculture was made by using diphasic hemoculture medium (DİFCO) and for the STA test, Brucella abortus antigen was used, prepared by the Refik Saydam Hıfzısıhha İnstitute.

The history and physical examination findings were recorded for all the patients. Hemoglobin, leucocyte, erytrocyte, sedimentation rate, alanine aminotransferase (AST) and aspartate aminotransferase (AST) values were determined.

Patients diagnosed as brucellosis received 1) Doxycycline (2x100mg/day,oral) + rifampin (2x300mg/day,oral) for 6 weeks; 2) Doxycycline (2x100mg/day) + streptomycin (1gr/day, i.m.) for 6 weeks. One patient with pregnancy received rifampin (2x300mg/day) + ceftriaxone (2gr/day, i.m.) and 3 patients with neurobrucellosis received streptomycin(1gr/day,)+ rifampin (2x300mg/day) + doxycycline (2x100mg/day) . The patients were followed up at least for 6 months, including the therapy period. The cases responded to the therapy, but showed clinical sign and findings following the therapy during the follow up period, were regarded as relaps cases. Statistically analysis were made by chi-square tests.

Results

The 127 brucellosis cases included in the study consisted of 72 (56.69 %) female and 55 (43.30 %) male, having an avarage age of 45.79 (14-86). The distribution of the patients according to their ages can be seen in Table-1. The possible source of the infection was detected in 76 (59.83) cases, wherease in 51 (40.17 %) cases it remained unknown (Table-2). The clinical sign and findings are in Table-3, the laboratory findings shown in Table-4. For the 3 cases diagnosed as meningitis; a pleositosis with a lymphocyte predominance in the CSF was detected and the glucose levels were low or in normal ranges, but the CSF protein levels were increased.

Among the patients followed up after the therapy for neurobrucellosis and brucellosis with pregnancy, no relaps was detected. However, in the group which received doxycycyline + rifampin, in 5 out of 93 (5.3 %) relaps was detected; wherease 3 of the 30 patients (10 %) had a relaps which used doxycycline + streptomycin as combination therapy. But the difference wasn't significant, statistically ($p>0.05$).

Discussion

Brucellosis is a disease seen worldwide; but in developed countries, it is noted that the prevelance of the disease is decreasing due to eradication of the sick animals and the decreasing consumption of pasteurised milk and milk products. Similarly, the disease is rare in the west regions of our country; wherease in the southern east regions where stock raising is frequently and the consumption of raw milk or milk products (cheese, butter and cream) is even more frequently, the prevelance of the disease is higher. In a wide comprehensive study, it was found that the highest seropositivity in Turkey was as follows: Diyarbakır, Konya and Antalya (5-7).

Human are infected from brucellosis via different ways; especially dealing with stock raising and nourishment with raw milk and milk products are the main ways. In Turkey, the most frequently way of getting the infection is by the consumption of raw milk and milk products (1-3,6). In the region of Konya, in which we performed the study, with a rate of 59.50 %, dealing with stock raising and consuming raw milk and milk products are also the main infecting ways. Thats why, the environs folk should be informed about the disease, transmission route of the infection and a healthy preperation of milk products. Especially, the sufficient inspection of the foodstuffs like this is important in the control of the disease.

Brucellosis is a disease affecting each age, with the same ratio in both sex (4,6,8). In our study, we found that the cases consisted of different age groups and sex, but with similarly ratio.

In brucellosis, the complaints and clinical manifestations are various; the disease emerges in different aspects (1,3,4,6). The most frequently complaints are fever, sweating, headache, lack of appetite, myalgia, joint and back pain, weight loss, sore throat and cough (1,3-6). When Table-3 is inspected, it will be clear that the most detected symptoms are fever, joint pain, sweating, weakness, lack of appetite and headache.

Although somatic complaints are too much in brucellosis, physical abnormalities could also be too many. Some patients can arive with an acute onset of the disease showing hepatosplenomegali, lymphadenopathy, arthritis, epididymorchitis, meningitis and pneumonia (2,3,6). In our cases, we detected fever in 33.07 % of the patients; hepatomegaly in 19.68 %, splenomegaly in 11.81 %, arthritis in 14.17 % and lymphadenopathy in 3.14 % of the patients. In various studies performed in Turkey (1,4,9,10), similar results have been reported. In brucellosis, it is possible to develop a complication belonging to any system (2,3). Among 127 cases, 29 (18 with arthritis, 8 sacroileitis and 3 spondylitis) showed symptoms and signs releated with the osteoarticular system, 3 with the central nervous system and 1 releated with the genitourinary system. Similarly with the results of other studies (1,4,5,11-13), in our cases we found that the most frequently complication observed was releated with the osteoarticular system.

Anemia is a sign frequently seen in brucellosis. The leucocyte count can be normal or low; a relative lymphocytosis and a minimum change in the erytrocyte sedimentation rate (ESR) can be observed. The liver enzymes (transaminases) may be elevated (1-4, 14). By analysing Table-4, we can see that 44.80 % of the cases showed anemia, more than half of the cases (52.75 %) had a normal leucocyte count; but lymphocytosis was observed in about 50 % of the patients. Also in 50 % of the cases, the aminotransferases were elevated abow the normal ranges. Our findings correlated with the results of other studies performed in Turkey (1,4,5).

The definite diagnosis of the disease was made by history, supporting clinical and laboratory signs and especially by the isolation of the microorganism in hemoculture and/or bone marrow culture. The isolation rate from hemoculture ranges between 15-70 % (2,3,12). The culture positivity rate from the studies in our country were as follows: 2.9 %, 12 % and 17.1 % (1,4,5,15). In 6 (4.72 %) of our cases we were able to isolate the

agent from hemoculture. Although this result is between the values of those found in other studies in Turkey, it is relatively low. This may be releated to the use of antibiotics, at time before a definite diagnosis could be made.

The Rose-Bengal Test, STA, Coombs' Test and ELİSA are the main serological methods for the detection of the antibodies in serum (2,3). Especially the Rose-Bengal Test and STA are the most common tests used in indirectly diagnosis of the disease. For the acute disease, the titer is usually ≥ 1/160 (3,4). In this study, for all cases the serum antibody titer was found ≥ 1/160. Evaluating the history, epidemiological features and clinical signs together; it was shown that a high antibody titer found by STA is a save method in the diagnosis of brucellosis.

For the therapy of brucellosis, there are various alternatives. The WHO (World Health Organization) has recommended in 1986, the use of doxycycline (200mg/day) + rifampin (600-900mg/day) combination therapy for 6 weeks. Nevertheless, a combination with doxycycline + streptomycin was found to be as effective as the first combination; and especially in patients with spondylitis it is even more effective (2,6). In this study, among the 93 patients who received doxycycline + rifampin, 5 (5.3 %) showed a relaps; wherease among the 30 patients who used doxycycline + streptomycin, 3 (10 %) had a relaps. But the difference between two groups wasn't significant, statistically ($p>0.05$) and thats why we decided that both of this therapeutic alternatives are efficacious in the therapy of brucellosis.

In conclusion; in the view that brucellosis is a disease presenting with various clinical sign and symptoms and regarding that the disease is endemic in our region; for cases presenting diagnostic difficulties, brucellosis should be kept in mind. The eradication of the disease in our region requires: The animals which make good use of their milk should be kept healthy and the consumption of raw milk and milk products could be avoided by.

Yazışma Adresi:
Dr. Emel TÜRK ARIBAŞ
Selçuk Üniversitesi MeramTıp Fakültesi İnfeksiyon Hastalıkları Anabilim Dalı
42080- Konya

TEL: +90 332 3232600/2033
FAX: +90 332 3232641
e-mail: eturk@selcuk.edu.tr

References

1. Taşova Y, Saltoğlu N, Yılmaz G, İnal S, Aksu HSZ. Brucellosis: An evaluation of clinical, laboratory and treatment features of 238 adult cases. Turk J Infect 1998;12: 307-12.

2. Young EJ. Brucella species. In: Mandell GL, Bennet JE, Dolin R. editors. Principles and practice of infectious diseases. 5th ed. Philadelphia: Churchill-Livingstone: 2000 p. 2386-93

3. Madkour MM. Brucellosis. In: Fauci AS, Braunwald EB, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL. editors. Harrison's principles and practice of internal medicine. 14th ed. New York: Mc Graw Hill: 1998 p. 969-71

4. Ulusoy S, Dirim Ö, Erdem İ, Yüce K, Büke M, Karakartal G et al. Evaluation of 75 cases of acute brucellosis. Clinical, laboratory and therapeutcal aspects.Turk J Infect 1995;9: 263-65

5. Arslan Ş, Öner Af, Çaksen H, Cesur Y, Ceylan T, Ataş B et al.Childhood brucellosis:a retrospective study of 103 cases. Turk J Pediatrics. 1999;42: 479-86

6. Sözen TH. Brucellosis. In: Wilke Topçu A, Söyletir G, Doğanay M.editors. Infectious diseases. İstanbul: Nobel Medicine Bookshops:1996 p. 486-91.(Turkish)

7. Ayaz C,Usta T,Kaya H ,Arıtürk S.Scintigraphic evaluation of lumbosacral pain in brucellosis.Turk J Infect 1997;11:103-105

8. Malik GM. A clinical study of brucellosis in adult in Asiar Region of Southern Saudi Arabia. Am J Trop Med Hyg 1997;56: 375-7

9. Turgay H, Hoşoğlu S, Aydın K, Arıtürk S. Brusellosis: Clinical and laboratory findings in 98 patients. Med J Ege Univ 1991;1:153
10. Hacıbektaşoğlu A, Barut A, İnal A, Özer FT. Serologic and clinical characteristics of brucellosis in young adult and middle aged. In: Tümbay E, Hilmi S, Anğ Ö.editors. Brucella and brucellosis in man and animals. İzmir: Publications of the Turkish Microbiolgical Society. Number:16. Ege University Press: 1991 p.168.
11. Zaks N, Sukenik S, Alkan M, Flusser D, Nevman L, Buskila D. Musculoskeletal manifestations of brucellosis: A study of 90 cases in Israel. Semin Arthritis Rheum 1995;25: 97-102
12. Colmenero JD, Regura JM, Martos F, Sanchez-Demora D, Delgado M, Causse M et al. Complications associated with Brucella melitensis infection: A study of 530 cases. Medicine-Baltimore 1996;75: 195-211
13. Bruchanan TM, Faber LC, Feldman RA. Brucellosis in the United States, 1960-1972: An abattoir-associated diseases. Part1.Clinical features and therapy. Medicine 1974;53: 403-13
14. Aysha MH, Shayib MA. Pancytopenia and other hematological findings in brucellosis. Scand J Hematol 1986;36: 336
15. Aktaş F, Şenol E, Yetkin A, Gürdoğan G, Ulutan F. Relation of clinical and laboratory findings with the duration of illness in brucellosis. J Turk Mıcrobiol Society 1994;24:164-69

Table 1. The distribution of the brucellosis cases according to age.

Age of patients	Number of patients	%
< 20	12	9.44
21-30	16	12.59
31-40	17	13.38
41-50	22	17.32
51-60	28	22.04
>60	32	25.19

Table 2. The possible routes of transmission.

Routes of transmission	Number	%
Dealing with stock raising	36	28.34
Raw or unpasteurised milk and milk products	40	31.49
Unknown origin	51	40.15

Table 3. Distribution of clinical symptom and findings of the cases

Symptoms	Number of cases	%
Fever	64	50.39
Arthralgy	59	46.43
Back pain	45	35.45
Weakness	50	39.37
Sweating	39	30.70
Lack of apetite	26	20.47
Headache	14	11.02
Abdominal pain	12	9.44
Swollen joint	9	7.09
Weight loss	7	5.54
Cough	6	4.72
Vertigo	4	3.14
Pruritus	1	0.78
Clinic findings		
Fever	42	33.07
Hepatomegaly	25	19.68
Arthritis	18	14.17
Splenomegaly	15	11.81
Sacroileitis	8	6.28
Lymphadenopathy	4	3.14
Meningitis	3	2.36
Spondylitis	3	2.36
Orchitis	1	0.78

Table 4. The laboratory results of the cases.

Laboratory results	Number of patient	%
Leucocyte count		
Normal(4000-9000/mm3)	67	52.75
Leukopenia(<4000/mm3)	24	18.89
Leucosytosis(>9000/mm3)	36	28.34
Leucocyte formula		
Normal	60	47.24
Lymphomonocytosis	66	52.75
Anemia	57	44.88
Erytrocyte sedimentation rate (ESR)		
>20mm/hour	85	66.92
<20mm/hour	42	33.07
AST (>40 IÜ)	50	39.37
ALT (>40 IÜ)	50	39.37
STA positivity ≥1/160	127	100.0
STA positivity in CSF	3	2.36
Hemoculture positivity	6	4.72