



The Open Orthopaedics Journal

Content list available at: www.benthamopen.com/TOORTHJ/

DOI: 10.2174/1874325001610010007



Brucellosis Suspicion is the Most Important Criterion for Diagnosis Particularly in Endemic Regions

Baris Yilmaz¹, Guzelali Ozdemir¹, Erdem Aktas², Baran Komur^{3,*}, Serdar Alfidan⁴, Serdar Memisoglu⁵ and Tahir Mutlu Duymuş³

¹ Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey

² Dr. A. Yurtaslan Ankara Onkology Training and Research Hospital, Ankara, Turkey

³ Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey

⁴ Private Sifa Hospital, Isparta, Turkey

⁵ Private Primer Hospital, Gaziantep, Turkey

Abstract:

Introduction:

Brucellosis is a zoonotic infectious disease that remains endemic in developing countries. The purpose of this study is to emphasize the need for considering brucellosis as a diagnosis, since this disease has a high risk of complications among young patients when not treated appropriately.

Methodology:

A total of 88 brucellosis cases with blood cultures that were positive for the pathogen were evaluated retrospectively in this study.

Results:

The patients included 33 males (37.5%) and 55 females (62.5%) with a median age of 8.9 years (range: 5-14 years). A total of 43.1% (n=38) of the cases included occupational exposure to animals as a possible infection source. The consumption of raw milk products, especially cheese, was present in 52.2% (n=46) of the cases. Clinically, 55 of the cases were acute (62.5%), 23 of the cases were subacute (26.2%) and 10 of the cases were chronic (11.3%). The distribution of the joint pain complaints was as follows: 62.5% (n=55) of patients reported hip pain, 22.7% (n=20) of patients reported knee pain, 11.4% (n=10) of patients reported lumbar-back pain and 3.4% (n=3) of patients reported pain in other joints. A total of 59.1% (n=52) of the cases had been examined by another doctor at least once and mistreated.

Conclusion:

Complication rates and the rate of chronic infection increase with delayed diagnosis, and clinical doubt is the most important criterion for diagnosis, particularly in endemic regions.

Keywords: Brucella, brucellosis, brucellosis in children, joint pain.

INTRODUCTION

Brucellosis, which is caused by bacteria of the genus *Brucella*, is one of the most common zoonotic diseases in the world [1]. Today, brucellosis is either eradicated or under control in many developed countries. Brucellosis is considered to be an occupational disease and is seen in farmers, veterinarians, laboratory personnel and animal

* Address correspondence to this author at the Turgut Ozal St. Halkali No. 1, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey; Tel: +90-212-5574000; Fax: +90-212-5714290; E-mail: barankomur@gmail.com

caretakers. In addition, brucellosis is endemic in Mediterranean and Middle Eastern countries, including Turkey [2 - 4].

In Turkey, brucellosis is a very common disease among animals and people, particularly in the Central, Eastern and Southeastern Anatolian regions. Sheep, goats, cows and buffalo are the most important animals in Turkey that play a role in the spread of the disease [5]. The *Brucella* spp. that cause the disease are transmitted from animal reservoirs to humans through direct contact with infected animals or more commonly through the consumption of raw animal products, such as unpasteurized milk. Four out of six *Brucella* species are pathogenic to human beings. *Brucella melitensis* is transmitted by sheep and goats, *Brucella abortus* is transmitted by cows, *Brucella suis* is transmitted by pigs and *Brucella canis* is transmitted by dogs [5]. In most cases of human brucellosis, the causative agent is *Brucella melitensis* [6].

Particularly in young patients and individuals who are not receive adequate treatment, brucellosis is important because it has a high rate of complications, such as unsuccessful treatment, relapse, chronic infection, focal complications and mortality. Orthopedics polyclinic admissions are high, particularly when patients have joint- related complaints.

The purpose of this study is to emphasize that brucellosis should be considered in patients with joint pain, particularly in endemic regions.

METHODOLOGY

We evaluated retrospectively a total of 88 childhood brucellosis cases. We collected the patients' data from hospital fonex data system. The patients reported joint pain at orthopedic and traumatology clinics in Adiyaman Besni State Hospital endemic regions between 2011 and 2013. The blood cultures of all patients were positive for *Brucella* spp. at the end of the examinations.

Patients presented with joint pain, fever, no trauma etiology and etiological risk factors (in the literature, the reported risk factors for brucellosis include the consumption of unpasteurized milk and dairy products, direct contact with livestock, the presence of brucellosis in family members and residence in the countryside) were suspicious with brucellosis disease. If clinical presentation was suspicious, we used serological tests. Wright agglutination test titers of 1/160 and above are used in diagnosis of brucellosis disease. All the diagnoses were verified by pediatricist.

The patients provided a medical history and were evaluated according to gender and age, region of residence, and whether their family members were treated for the same disease. To identify the source of infection, the cases were examined for raw milk and dairy product consumption, particularly the consumption of cheese made from raw milk, and for familial occupation in animal husbandry.

The cases were grouped according to the clinical presentation of the disease during admission, and the patients were questioned to determine whether they had been previously examined by another doctor. If the patients had been evaluated previously, the diagnosis and treatment regimen were recorded.

In another evaluation, the primary joint complaints of the patients that were made during admission were assessed regionally. A patient's complaints of problems other than joint pain were also included in this study.

RESULTS

The patients in this study included 33 males (37.5%) and 55 females (62.5%), for a total of 88 children. The mean age of the sample was 8.9 years (range: 5-14 years). A total of 66 of the cases (75%) lived in the countryside. The presence of another family member who was treated for the same disease was only reported in 8 (9.1%) of the cases.

The source of infection was familial occupation in animal husbandry in 43.1% (n=38) of the cases. Habitual consumption of raw dairy products, especially cheese, was present in 52.2% (n=46) of the cases.

During clinical assessment, 55 (62.5%) of the cases were acute, 23 (26.2%) of the cases were subacute and 10 (11.3%) of the cases were chronic. A total of 7 cases (7.9%) relapsed during the follow-up period.

A total of 59.1% (n=52) of the individuals had been examined by another doctor at least once for complaints of joint pain and were typically treated symptomatically for joint pain rather than for brucellosis.

The distribution of the joint pain complaints was as follows: 62.5% (n=55) of the patients reported hip pain, 22.7% (n=20) of the patients reported knee pain, 11.4% (n=10) of the patients reported lumbar-back pain and 3.4% (n=3) of the patients reported pain in other joints. A total of 16 (18.1%) of our patients reported pain in multiple joints.

Other common complaints in our cases included fever in 87.5% (n=77) of patients, night sweats in 43.1% (n=38) of patients, muscle pain in 45.4% (n=40) of patients, weakness in 42.1% (n=37) of patients and a lack of appetite in 28.4% (n=25) of patients (Table 1).

Table 1. Symptoms of patients with brucellosis.

Symptom	Number of Patients	Case Percentage
Arthralgia	78	88.6%
Fever	77	87.5%
Myalgia	40	45.4%
Sweating	38	43.1%
Weakness	37	42.1%
Lack of Appetite	25	28.4%
Lumbar-Back Pain	10	11.3%
Nausea	7	7.9%
Vomiting	6	6.8%
Headache	4	4.5%
Abdominal Pain	1	1.1%

DISCUSSION

Brucellosis is a zoonotic infectious disease that remains endemic in Turkey [4]. Blood cultures, serology and the polymerase chain reaction are used for laboratory diagnoses. Although culture is the ideal diagnostic method, the slow growth of the agent and difficulties in growing the agent using standard blood cultures reduce the sensitivity of the assay. Therefore, serological tests are commonly used to diagnose brucellosis. Titers of 1/160 and above in the widely used tube agglutination test (Wright) typically support a brucellosis diagnosis in cases with active infection. So we benefited from this method during diagnosis in cases for which the clinical presentation was suspicious.

Table 2. Treatment combinations used for brucellosis cases.

	Number of Patients	Case Percentage
Rifampicin + doxycycline	67	76.1%
Rifampicin + doxycycline + streptomycin	11	12.5%
Ceftriaxone + tetracycline	5	5.6%
Rifampicin + TMP-SMX	3	3.4%
Ceftriaxone + doxycycline + rifampicin	2	2.2%

Approximately 20-33% of brucellosis cases occur in children in endemic regions [4, 7]. Our study involved only the childhood age group. However, despite the fact that childhood brucellosis series in the literature reported that male cases were more common [8 - 10], 62.5% (n=55) of the cases in our series were female.

Patients diagnosed with brucellosis may also have family members with brucellosis. In a prospective study in which other family members were evaluated for brucellosis, 13- 20% seropositivity and 10-12% acute brucellosis were reported [11]. In a study conducted by Almuneef *et al.*, the family members of 55 acute brucellosis cases (n=404) were evaluated serologically; 13% of the family members were seropositive, and 74% of these seropositive cases were symptomatic [12]. Therefore, every family member of patients diagnosed with acute brucellosis must be examined and serological tests must be performed. This approach will likely be very useful for the control of the disease in Turkey, where brucellosis remains endemic.

In the literature, the reported risk factors for brucellosis include the consumption of unpasteurized milk and dairy products, direct contact with livestock, the presence of brucellosis in family members, residence in the countryside, travel to endemic regions, migration from endemic regions and working in a laboratory [13 - 15]. A total of 43.1% (n=38) of our cases had a familial occupation in animal husbandry as a possible source of infection. The consumption of raw dairy products, especially fresh cheese, was present in 52.3% of cases (n=46).

Similar to adult cases, the most common complaints in childhood brucellosis cases are joint pain and fever [10, 16]. Peripheral arthritis is the most common osteoarticular affection described in brucellosis cases [17 - 19]. Peripheral joint pain is most commonly experienced in the large joints that bear burdens, such as the hip and knee, which is consistent with our cases [17, 20 - 22]. A total of 16 (18.1%) of our patients reported pain in multiple joints. Osteomyelitis of the

long bones is a rare complication in brucellosis cases [15], and this complication was not observed in our series.

In the literature, the rate of relapse in childhood brucellosis was reported to be 6.6-14% [9, 17]. The rate of relapse in our study was 7.9% (n=7). It is conspicuous that in a study conducted by Buzgan *et al.* in Turkey including 1,028 cases, the relapse rate was reported to be 4.7%; in the group of cases with osteoarticular affection, this rate was 8.5% [16]. In brucellosis, relapse is not linked to the development of resistance. Relapse is typically related to the inappropriate dose, combination and duration of antibiotic treatment. Single-drug therapy is not preferred due to the high rate of relapse. Relapse rates are considerably reduced with combined and long-term treatments. The American Academy for Pediatrics emphasizes that adding rifampicin to treatment regimens will reduce the rate of relapses in brucellosis patients [4]. In light of this information, we administered proper combined treatments to our patients (Table 2).

Brucellosis has a rich clinical manifestation because it affects nearly every organ of the body. Due to the increased complication rates and the predisposition to chronic disease that are associated with late diagnosis, brucellosis must be considered during differential diagnosis in patients who are admitted to health establishments with complaints such as fever, sweating and joint pain and in patients with a fever of an unknown origin. Suspicion is the most important criterion for diagnosis, particularly in endemic regions. As an important indicator of this fact, 59.1% (n=52) of our cases were examined previously for joint pain by at least one other doctor and given a symptomatic treatment for joint pain rather than treatment for brucellosis. This finding demonstrates the importance of our study. Brucellosis apparently is very common in countries such as Turkey. The risk factors include consumption of unpasteurized milk along with direct contact with either livestock or family members with the disease.

Treatment delayed in 59% of the cases on the basis of these findings. This situation can increase complication rates. Suspicion was important to approach diagnosis on the basis of these clinical findings. Successful treatment was applied through our suspicion.

In conclusion, similar statistical studies of brucellosis, which is a zoonotic disease that remains endemic in Turkey, is important because doctors must be reminded of the disease when comparing case series between regions in Turkey. The case volume is high in orthopedic polyclinics, especially when patient complaints are joint related. Therefore, it is important to consider brucellosis as a diagnosis in patients presenting with joint pain, particularly in endemic regions.

LIST OF ABBREVIATION

Brucella spp. = *Brucella* species

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

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Received: June 16, 2015

Revised: September 3, 2015

Accepted: September 11, 2015

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