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Brucellosis in Children

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ABSTRACT

Background: Brucellosis, a multisystem infection that may imitate other conditions, shows a low incidence during childhood and may be misdiagnosed. Brucellosis has become a major medical problem in a number of the provinces in Iran.
Objectives: To study the epidemiology, clinical and laboratory features, and management of brucellosis.
Patients and Methods: We reviewed the charts of all patients who were diagnosed with brucellosis and showed an agglutination titer of 1:160 or more for Brucella at the Department of Pediatric Infectious Diseases, Qods Hospital from March 1995 to March 2004. We collected information on the age, gender, history of unpasteurized milk or milk-product ingestion, presenting symptoms, and physical signs of the patients. We also collected results of routine laboratory tests, treatment, and treatment outcome.
Results: Patients younger than 12 years of age constituted all cases of brucellosis admissions. One hundred seventy-five patients (107 male and 68 female, 1.6:1 ratio) were diagnosed with brucellosis and had a Brucella titer of 1:160 with an odds ratio (OR) of 1:160. Eighty-seven patients (50%) were 1-6 years of age, 86 patients (49%) were 7-12 years of age, and only 2 patients were < 1 year of age. One hundred (57%) patients were from rural areas, and 75 (43%) were from cities. The most frequent seasons of disease occurrence were summer (76, 43%) and spring (52, 30%); there were fewer cases in winter (24, 14%) and autumn (23, 13%). One hundred fourteen cases (65%) had a history of consuming unpasteurized milk or milk products. The most frequent symptoms were arthralgia (79%) and fever (78%). The most common physical findings were fever (51%) and arthritis (26%). Of the cases, 157 (89.5%) were acute, and 17 (9%) were chronic. A normal white blood cell count was found in 123 cases (71%); anemia, in 33 (19%); increased erythrocyte sedimentation rate (ESR), in 92 (53%); positive C-reactive protein (CRP), in 85 (48%), and positive radiologic changes, in 20 (11%). The most common antibiotics used were cotrimoxazole plus gentamycin in 83 cases (47.5%) and cotrimoxazole plus rifampin in 72 cases (41%).
Conclusions: Brucellosis presents in various ways and should be differentiated from arthritis in countries where Brucella is endemic. Symptoms, signs, and first-line laboratory findings are not distinguishing; accordingly, agglutination tests and, if possible, blood culture should be performed in any child with prolonged fever. Treatment is effective, but disease prevention by education of high-risk families is indicated.

▸ *Implication for health policy/practice/research/medical education:*
This article would be beneficial for health practice and medical education.

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1. Background

Brucellosis is a zoonotic disease primarily transmitted to humans through the consumption of unpasteurized milk and milk products. Additional modes of transmission in endemic areas are less common (1). Although human brucellosis is endemic in several areas of the world (500,000 cases/year), the number of reported cases has markedly dropped in some countries as a result of obligatory milk pasteurization, slaughter of infected animals, and aggressive vaccination (2). The clinical presentation of brucellosis is non-specific, and the infection varies in its course and severity; in humans, it presents as a multisystem disease involving many organs and tissues (3).

Brucella organisms can live and even multiply within mononuclear phagocytic cells; this explains the extended and relapsing clinical course of the disease and the difficulty in its management (1, 4). The absolute diagnosis of brucellosis requires isolation of the bacteria from blood or tissue samples. The sensitivity of the blood culture varies depending on individual laboratory practices and how actively cultures are obtained. The percentage of cases with positive cultures ranges from 15% to 70% (4, 5).

Bone marrow cultures are considered the gold standard for the diagnosis of brucellosis, because the relatively high concentration of *Brucella* in the reticuloendothelial system makes it easier to detect the organism. Bacterial elimination from the bone marrow is equivalent to microbial eradication (4). However, harvesting bone marrow for culture remains an invasive, painful technique. Still, the results have been universally reproducible (4).

There are 2 broad categories of serologic methods for diagnosing brucellosis: those based on antibody production against lipopolysaccharide and those based on antibody production against other bacterial antigens. Developed by Bruce, the serum agglutination test remains the most popular diagnostic tool for brucellosis. Titers greater than 1:160 are considered diagnostic in conjunction with a characteristic clinical presentation (4). In addition, a new dipstick test offers a rapid and reliable substitute for diagnosing acute brucellosis (6).

2. Objectives

The present study was performed to evaluate the clinical and laboratory findings, management modalities, complications, and outcomes of brucellosis in children in Qazvin, Iran. This is of particular interest, because there are similar reports from other parts of the country with demographic and epidemiologic characteristics different from those of Qazvin; this study will allow a comparison of the findings from these different areas (7-9). While pasteurization of milk and milk products are developing in Iran, childhood brucellosis continues to be common in Iran, and knowledge about the disease and changes in its clinical course, complications, and outcome remain important.

3. Patients and Methods

This discriptive study investigated 175 children ≤ 12 years of age with brucellosis who were treated in the Department of Pediatric Infectious Diseases, Qazvin Medical University from March 1995 to March 2004. In this study all patient with definit diagnosis of brucellosis were enrolled. Signs, symptoms, laboratory findings, treatment modalities, complications, and outcomes were retrospectively analyzed. Laboratory diagnosis of brucellosis was made using results of standard tube agglutination methods. Titers of 1:160 or greater, using continuous serum dilutions, were considered a positive result (10). From medical records, we collected information on age, gender, urban or rural location, season of admission, history of unpasteurized milk or milk-product ingestion, family history of brucellosis, and history of animal exposure. Information on clinical symptoms (arthralgia, fever, anorexia, weakness, sweating, nausea and vomiting, gastroenteritis, cough, and weight loss) was also collected. In addition, information on clinical signs (fever, arthritis, splenomegaly, hepatomegaly, lymphadenopathy, and limitation of motion) was collected from the medical records. Data on laboratory findings (hemoglobin [Hb], erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], tube agglutination test, and 2-mercaptoethanol [2-ME]), radiologic findings, and other information was collected. The data was analyzed with statistical method using SPSS software.

3.1. Definitions and Abbreviations

3.1.1. 2-ME

2-ME, a foul-smelling sulfhydryl compound that acts as a reducing agent, was used to differentiate between IgG and IgM in a mixture by disrupting the disulfide bonds of IgM so that only IgG is measurable.

3.1.2. Acute Brucellosis

Acute infection presents with high fever, malaise, headache, sweats, and arthralgia (duration < one month).

3.1.3. Chronic Brucellosis

Chronic brucellosis occurs after 1 year of illness and usually requires bone marrow biopsy for diagnosis.

4. Results

From March 1995 to March 2004, 175 patients (age ≤ 12 years) were diagnosed with brucellosis at our hospital. All were non-bacteremic cases (reports on *Brucella* bacteremia are scarce) (11) and were diagnosed on the basis of symptoms suggestive of brucellosis and a serological titer of 1:160 or greater. Analysis of the seasonal distribution of hospitalization revealed that 76 patients (43%)

were admitted during summer, while 52 (30%) were admitted during spring. Only 24 patients (14%) were admitted in winter, and 23 patients (13%) were admitted in autumn.

Among the 175 patients with brucellosis, 61% were male and 39% were female. Among the 175 patients in whom the symptom duration prior to hospitalization was obtained, 144 (82%) had a duration of less than or equal to one month, and 31 (18%) had a duration of greater than one month. One hundred fourteen (65%) had a history of consuming unpasteurized milk or milk products, and 58 (33%) had contact with infected cattle. Forty-four patients (25%) had a family history of brucellosis. The disease was acute in 89.5%, and the remaining patients had a history of brucellosis. The symptoms and signs presented by the patients are shown in *Tables 1* and *2*.

The most frequent symptom was arthralgia (79%) (*Table 1*). The most common physical finding was fever (51%) (*Table 2*). The most frequent joint involvements were of the knee (31%), multiple joints (22.5%), and hip (18%). Of the 175 patients, the initial Wright seroagglutination titer was equal to 1:640 in 53 patients (30%), 1:1,280 in 29 patients (16.5%), 1:320 in 29 patients (16.5%), and 1:2,560 in 18 patients (10%).

The hemoglobin values were within the normal range in 142 patients (81%), and the remaining patients had anemia (19%). The white blood cell (WBC) counts were within the normal range in 123 patients (71%), and 29 patients (16.5) had leukocytosis. The ESR was within the normal range in 92 patients (53%), and 80 patients (45%) had moderate to severe ESR elevation. Eighty-five patients (48%) had mild to severe CRP elevation; 38 patients (22%) had normal CRP, and there was no record of CRP in the remaining patients. The initial agglutinating antibody titer was 1:640 in 53 patients (30%), 1:1,280 in 29 patients (16.5%), and 1:320 in 29 patients (16.5%). The highest initial agglutinating titer was 1:2,560 in 18 patients (10%). The 2-ME titer was 1:320, 1:80, 1:160, 1:640, and 1:1,280 in 26 (15%), 24 (14%), 21 (12%), 15 (8.5%), and 15 (8.5) patients, respectively. Osteoarticular investigations revealed radiologic changes in 20 patients (11%). Management regimens in the 175 patients consisted of combinations of 2 agents: co-trimoxazole plus gentamycin (47.5%), co-trimoxazole plus rifampin (41%), and other combinations (11.5%).

Table 1. Frequency of Presenting Symptoms

Symptom	No. (%)
Arthralgia/Arthritis	138 (79)
Fever	137 (78)
Excessive sweating	77 (44)
Weakness	71 (40)
Anorexia	50 (28)
Chills	41 (23)
Abdominal pain	36 (20)
Headache	34 (19)
Nausea and vomiting	28 (16)
Cough	27 (15)
Weight loss	25 (14)

Table 2. Frequency of Signs

Sign	No. (%)
Fever	90 (51)
Arthritis	46 (26)
Splenomegaly	35 (20)
Hepatomegaly	25 (16)
Lymphadenopathy	21 (12)

5. Discussion

Childhood brucellosis remains a significant community health problem in Iran, despite a trend toward an overall decrease in the disease (7, 9). The yearly incidence of brucellosis in our hospital has declined over time, but there remain reports of childhood brucellosis in provinces of Iran (7, 9). Therefore, the evaluation of the clinical features and laboratory findings of brucellosis in children is of great importance.

In this study, there was a clear preponderance of males with brucellosis, consistent with other studies in Iran and other countries (11-14). Few subjects were younger than 1 year of age (2 cases in the present study), consistent with previous studies (15, 16). This may be explained by the fact that milk is less contagious than dairy solids or that breast milk may have anti-*Brucella* activities and prevent exposure to infected milk (1, 17). Brucellosis may also present as an asymptomatic/nonspecific, milder, self-limited course in this age group (1, 18). Brucellosis occurred mainly in school-aged children (50%) and was highest in summer (43%), which is consistent with other studies (9, 19).

Similar to other studies, the majority of patients (65%) had a history of consuming unpasteurized milk or milk products (9, 12, 13, 19). Over 58% of the patients had a history of close animal contact, as previously reported (12). Family members of 44% of the patients had a history of brucellosis. However, previous reports on brucellosis among family members are scarce.

The period of illness prior to diagnosis was less than 1 month in 82% of the patients, consistent with other studies (12, 20). The clinical manifestations in our study are similar to those reported by others in Iran as well as in other countries (3, 7, 9, 13, 20, 21). A combination of fever and arthralgia or arthritis was very common and particularly valuable for diagnosis. In agreement with other studies (3, 5, 12, 21, 22), arthritis or arthralgia most commonly involve the knee and hip joints. None of the children showed involvement of the sacroiliac joint, as was found in a previous study (1, 23). However, unlike another study (22), patients were treated with combinations of 2 agents: cotrimoxazole plus gentamycin (47.5%), cotrimoxazole plus rifampin (41%), and other combinations

(11.5%).

We emphasize that the eradication of brucellosis, a worldwide disease, can be achieved only by aggressive preventive measurements, including elimination of the vector, elimination of infected animals, vaccination of newborn animals, education, and enforcement of control measures.

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Authors' Contribution

Nothing to declare.

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