Acta Paediatrica Hungarica, 24 (3), pp 263–267 (1983)

Elevated risk of osteoarticular complications in children with acute Brucella melitensis infection

ELI SHAHAR,[1] ZOHAR BARZILAY,[1] ISAAC SHOHET,[1] GIDEON ALTMAN,[2] BERNARD E COHEN[1]

[1] Department of Paediatrics B, and [2] Microbiology Laboratory, Chaim Sheba Medical Center, Tel-Hashomer, Sackler School of Medicine, Tel-Aviv University, Israel

Infection with brucella microorganisms is considered uncommon in the paediatric age group. We report nine paediatric patients between the ages of 8 to 17 years with acute *Brucella melitensis* infection, who presented with spiking fever, night sweats, anorexia and malaise for 5 to 60 days prior to diagnosis. Four patients developed various osteoarticular complications: migratory arthralgia, hydroarthrosis of the knees, arthritis and osteomyelitis. Therapy with tetracyclines alone or in combination with streptomycin resulted in complete recovery in eight children. This combination failed in one patient who developed severe osteoarticular disease successfully responding to rifampicin. Since infection of bone and joints leads to irreversible damage, early recognition and immediate management are crucial for recovery. Rifampicin might be of benefit in children with severe osteoarticular complications when the traditional anti-brucella regimen fails.

The genus brucella is usually an intra-cellular Gram-negative bacillus infecting the reticuloendothelial system. It causes disease in animals which may be transmitted to humans through direct contact or by ingestion of contaminated by-products. The common symptoms of acute brucellosis include spiking fever, night sweats, anorexia and malaise. Multisystem organ involvement mainly including the cardiovascular, nervous, osteoarticular, and genito-urinary systems is an often described phenomenon in adult patients. However, brucellosis does not always have a common clinical pattern and various manifestations may resemble other infectious diseases.

Brucellosis occurs infrequently during childhood and few reports deal with it in the paediatric age group [1–3]. To date the frequency and clinical significance of osteoarticular complications in children with acute brucella infection is still debated. We report herein nine children with acute *Brucella melitensis* infection of which four had osteoarticular complications. The anti-brucella regimen in such patients will be discussed.

CLINICAL DATA

The diagnosis of brucellosis was based on accepted clinical, biochemical, and serological criteria [6], in nine children admitted during the last 20 years. They were

TABLE I

Clinical and laboratory data of paediatric patients with brucellosis

Case	Age years	Sex	Duration of illness	Blood cultures	Agglutination antibodies	Management	Outcome
1	8	F	14 days	*Br melitensis* ×1	1 : 10 240	Tetr; 24 days	Cured
2	17	F	not recorded	Negative	1 : 640	Tetr; Strep; 21 days	Cured
3	12	M	5 days	*Br melitensis* ×1	1 : 1280	Tetr; 10 days	Cured
4	14	M	14 days	*Br melitensis* ×3	Tetr; Strep; 1 : 10 210	10 days	Cured
5	8	M	21 days	*Br melitensis*	1 : 10 240	Tetr; 14 days	Cured
6	10	F	1 month	*Br melitensis* ×2	1 : 1280	Tetr; 21 days	Cured
7	14	M	2 months	*Br melitensis* ×3	1 : 640	Tetr + Strep; 2 months	Cured
8	11	F	1 month	No data	1 : 10 240	Tetr + Strep; 14 days	Cured
9	14	F	14 days	Negative	1 : 1280	Tetr + Strep	Relapse after 8 days; Recovered following rifampicin therapy

Abbreviations: Tetr — tetracyclines, Strep — streptomycin

admitted following an acute illness with high-grade fever, headaches, night sweats, anorexia and weight loss for five to 60 days before admission to the hospital and the accurate diagnosis. Two patients had spiking fever of the undulant type. A diffuse macular rash was noted in one child (Table I).

Laboratory data. Leukopenia was a common symptom ranging from 3300 to 5700 leukocytes per ml with lymphocyte predominance in five patients (44–94%). Three children had a normal differential count. The erythrocyte sedimentation rate was elevated in four children.

Diagnosis. Specific blood cultures for brucella were obtained in eight of nine patients. In six patients the culture taken immediately after admission was positive. All patients had elevated agglutination titres of 1 : 320 to 1 : 10,240 which increased within one week after admission. (A titre higher than 1 : 180 is indicative of active disease.) The source of infection could be attributed to unpasteurized sheep and goat milk or by-products in 5 patients.

Osteoarticular manifestations and management. Patient No. 5 had migratory arthralgia on admission. Patient No. 2 developed mild arthritis of the right sacro-iliac joint. Patient No. 7 who had migratory arthralgias during the prodromal period subsequently developed arthritis of the right knee and hydroarthrosis of both knees. On the traditional anti-brucella regimen using tetracyclines at a dose of 25 mg/kg/day with I. M. streptomycin at a dose of 20 mg/kg/day, these manifestations gradually subsided in these three children and they became completely asyptomatic. Patient No. 9, a 14-year-old girl, had evidence of infection of the right hip and sacro-iliac joints as well as of the lumbar vertebrae on hospitalization. Al-

TABLE II

Osteoarticular manifestations in children with brucellosis

Case No.	Clinical Data
2	Arthritis — Rt sacro-iliac joint
5	Arthralgia — migratory
7	Arthralgia
	Arthritis — Rt knee
	Hydroarthrosis — both knees
9	Arthritis — Rt hip joint
	Rt sacro-iliac joint
	Rt shoulder joint
	Infection of lumbar vertebrae
	Osteomyelitis — Rt humeral head

though she initially responded to tetracyclines and streptomycin, she developed arthritis of the right shoulder and osteomyelitis of the humerus eight days after initiation of the regimen. Complete recovery was achieved in this patient following additional therapy with oral rifampicin at a dose of 900 mg/day (20 mg/kg/day) for 21 days. On follow-up examination two years later she was found completely asymptomatic (Table II).

Outcome of patients without osteoarticular disease. The children made a complete recovery following the administration of oral tetracyclines for 10–24 days with additional intramuscular streptomycin in two of these patients. No relapse was detected in any patient in the present series.

DISCUSSION

Brucellosis has been considered uncommon during childhood in western countries. Bothwell et al. reported only 17 paediatric patients during the years 1940–1957 [1]. Out of 160 cases of brucellosis in the United States during 1978 only 16 were children [4]. Street et al. [3] reported nine children during the spring of 1973 and stressed the rarity of the disease. A survey of brucellosis in Israel [5], however, detected 42 (24%) of 287 cases under the age of 14 years, indicating that brucellosis was common in children living in the Middle East which is an endemic area.

The question why brucellosis is infrequent in children remains unclarified since the common use of milk and its by-products by children make them more likely to be infected by brucella species. The scarcity of childhood brucellosis has been attributed to a low rate of suspicion while other diseases during childhood may resemble the clinical features of brucella infection [2]. It was also speculated that in contrast to adults the disease in children may have a self-limited course [6], although many

sub-clinical and mild illnesses occur in adults. In Israel infections with *Brucelta melitensis* occur; this is the most virulent strain among brucella organisms and has been associated with acute infection. Those infected with *Brucella abortus* strains, which is common in western countries, may be mildly ill or even asymptomatic [6].

Osteoarticular involvement has been extensively reviewed in adult patients with acute brucella infection [7, 8]. McCullough [9] considered osteoarticular manifestations to be common in childhood brucellosis. Other authors, however, have not verified this observation, reporting a very low rate of joint and bone complications [1, 3]. Four children in this series experienced almost all bone and joint complications of *Brucella melitensis* infection: migratory arthralgia, hydroarthrosis of knees, arthritis of right hip and sacro-iliac joints, and osteomyelitis of the lumbar vertebrae. The course was complicated in one patient with right shoulder arthritis and osteomyelitis of the humerus. The frequent occurrence of osteoarticular complications presented in this series raises the need of its rapid diagnosis and aggressive treatment since brucellosis in bone and joints may cause irreversible damage.

The recommended antimicrobial regimen for patients with acute brucellosis is a combination of oral tetracyclines given for three weeks or longer with intramuscular injections of streptomycin for 7–14 days [10, 11]. Such a regimen resulted in a very low rate of relapses such as 0.9% in a series of 157 patients [10]. In a series of eight children given tetracyclines for 21 days and streptomycin for 14 days, no relapses were recorded [3]. Eight of nine children in the present series rapidly responded to tetracyclines alone or in combination with streptomycin after 10 to 24 days of treatment. Brucella organisms are sometimes protected from these antimicrobial agents due to their intracellular location [12]. This was demonstrated in one of our patients who developed severe bone and joint disease while receiving doxycycline and streptomycin. Additional therapy with rifampicin at a dose of 20 mg/kg daily for 21 days resulted in complete recovery. Since rifampicin acts as an intracellular bactericidal agent [13], it may be of benefit in severe brucella infections especially those with bone and joint disease when the traditional regimen fails. A recent report using rifampicin in children with acute brucellosis has supported this view [14].

References

1. Bothwell PW: Brucellosis in children. Arch Dis Child 37:628, 1962
2. Wallis PE: Brucellosis in children. Br Med J 1:617, 1957
3. Strett L, Grant WW, Alva JD: Brucellosis in childhood. Pediatrics 55:416, 1975
4. Center for disease control: Brucellosis surveillance: Annual summary 1978, Public Health Service, Atlanta 1978
5. Brucellosis in Israel: 1962–1974. Center for brucella surveillance, Biological Institue, Nes-Ziona, Israel
6. Spink WW: Nature of Brucellosis. University of Minnesota Press, Minneapolis 1956

7. Rotes-Querol J: Osteoarticular sites of brucellosis. Ann Rheumat Dis 16:63, 1957
8. Kelly PJ, Martin WJ, Schirger A, Weed LA: Brucellosis of bones and joints. JAMA 174:347, 1960
9. McCullough NB: Symposium of unusual infections in childhood. Pediatr Clin North Am 2:73, 1955
10. Buchanan TM, Faber LC, Feldman RA: Brucellosis in the United States 1962–1972. Medicine 53:403, 1974
11. Pfischner WCE, Ishak KG, Neptune EN, Fox SM, Farid Z, Nor el Din G: Brucellosis in Egypt: A review of experiences with 228 cases. Am J Med 22:915, 1957
12. Spink WW, Bradely GN: Persistent parasitism in experimental brucellosis: Attempts to eliminate brucella with long-term tetracycline therapy. J Lab Clin Med 55:535, 1960
13. Philippon AM, Plommet MG, Kazmierzack A, Marly JL, Nevot PA: Rifampin in the treatment of experimental brucellosis in mice and guinea pigs. J Infect Dis 136:482, 1977
14. Llorens-Terol J, Busquetes RM: Brucellosis treatment with rifampicin. Arch Dis Child 55:486, 1980

Received 15 February 1983

E Shahar MD
Department of Pediatrics B
Chaim Sheba Medical Center
Tel-Hashomer 62621, Israel