Brucellar arthritis in children and its successful treatment with trimethoprim-sulphamethoxazole (co-trimoxazole)

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SUMMARY The clinical characteristics and the response to treatment with high doses of co-trimoxazole in 12 children with brucellar arthritis were analysed retrospectively. The children lived in an urban area and all but two had a history of unprocessed milk or cheese ingestion. Fever and oligoarthritis of the lower extremities were the most common clinical findings. Control of the disease was achieved by three months of treatment. Compliance with the medication was excellent, and no significant side effects occurred.

Key phrases: chronic infection of the joints, treatment of joint infection, co-trimoxazole therapy.

Human brucellosis is still found in European countries where pasteurisation of milk is commonplace but illegally marketed dairy products are also available. Between 9 and 20% of cases occur in children, and about one third of them develop arthritis.¹ Treatment includes the long term use of tetracycline and streptomycin. In children this form of therapy is limited by side effects and toxicity. Recently, successful control of the disease in adults with co-trimoxazole has been reported.^{2,3} Over a four year period we have seen 12 children with brucellar arthritis and have treated them with high doses of co-trimoxazole. In this report we describe our experiences with this group of patients.

Patients and methods

We reviewed the records of 12 children with brucellar arthritis attending our Paediatric Rheumatology Unit between January 1979 and December 1982. Particular attention was paid to a previous history of ingestion of unprocessed dairy products or contact with cattle, presenting features, musculoskeletal symptoms and signs, and the response to therapy. Laboratory tests reviewed included full

blood counts, urinalysis, SMAC (Thecnicon), and serological tests and blood cultures for brucella.

Results

The mean age of the children was 9.5 years (range 3-14), with an equal sex distribution (male/female 5/7). All but one lived in an urban area. Of the 12, eight had previously ingested unprocessed milk or cottage cheese (one also had contact with cattle). Two did not have clear exposure to contaminated food or animals, and no relevant information was available about the remaining two.

The interval between onset of symptoms and diagnosis ranged from five days to two years. Patients with hip involvement had the longest delay (> five months). Systemic signs and symptoms were absent except for fever (> 38.5°C) in seven patients. All had arthritis and six had arthralgias related to non-inflamed joints (Table 1). The arthritis was characterised mostly by soft tissue swelling without obvious effusions. A total of 21 joints were inflamed (Table 1). Hips, elbows, and knees were often involved, while small joints of the hands, feet, and spine were never affected.

Routine laboratory investigations were unremarkable. Eleven patients had normal blood counts and one eosinophilia. The erythrocyte sedimentation rate was raised (> 20 mm/1st h) in six patients.

Accepted for publication 13 August 1985.
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Table 1 Joints involved in 12 children with brucellar arthritis

Joint	Arthritis* n=21 (%)		Arthralgia* n=13 (%)	
	Unilateral	Bilateral	Unilateral	Bilateral
Hip	2 (9.5)	4 (38.1)	2 (15.4)	—
Elbow	4 (19.0)	—	1 (7.7)	—
Knee	3 (14.3)	—	2 (15.4)	3 (46.2)
Ankle	1 (4.8)	1 (9.5)	—	—
Sacroiliac	1 (4.8)	—	—	—
Shoulder	—	—	—	1 (15.4)

*See text for description.

Biochemical parameters were normal in all but two, who had moderate increases of serum transaminases. *Brucella melitensis* was isolated from the blood of four of the 12 patients. Serological tests were always positive (Table 2).

Radiographic studies showed narrowing of the joint space in two hips and one sacroiliac joint, juxta-articular osteopenia in one elbow, and soft tissue swelling in the remaining joints.

All patients were treated orally for 12 weeks with co-trimoxazole (Table 3). Eleven were followed up for a minimum of two years and one was lost to follow up after six months. The therapeutic response was good, the arthritis subsiding within two to three months in all. Two patients with hip involvement, however, still have functional limitation of the joint. Relapses of the disease were not seen. Compliance with the medication was excellent, and no side effects were seen or reported.

Table 2 Serology and blood culture results in 12 children with brucellar arthritis

Patient No	Blood culture	ATT*	CMT†
1	Positive	320	1280
2	Positive	2560	2560
3	Positive	160	ND‡
4	Positive	320	ND
5	Negative	80	1260
6	Negative	160	320
7	Negative	320	640
8	Negative	40	320
9	Negative	160	640
10	Negative	640	1280
11	Negative	160	1280
12	Negative	640	1280

*ATT=agglutination test tube (dilution⁻¹).

†CMT=Coombs' microtitre test (dilution⁻¹).

‡ND=not done.

Table 3 Co-trimoxazole dosage* used for the treatment of brucellar arthritis in children

Dose (mg/kg body wt/24 h)	Week
90–100	1
50–60	2–4
25–30	5–12

*Dosage refers to sulphamethoxazole because it was used in the standard fixed combination form.

Discussion

Brucellosis should be included in the differential diagnosis of children with oligoarthritis and fever in localities where this infection still occurs.⁴ Several features of the disease merit consideration. First, in our own and in previous experience¹ the absence of recognised exposure to potentially contaminated food or animals does not exclude the diagnosis. Secondly, neither clinical nor routine laboratory abnormalities are distinctive. Awareness is thus important because diagnosis depends on cultural or serological evidence, or both. Thirdly, in contrast with adults,¹ children seldom have axial skeleton involvement.

The efficacy and safety of high doses of co-trimoxazole for treatment of brucellosis in children has not previously been studied. In this regard it might be argued that despite a full course of treatment two of our patients have residual functional hip limitation. However, this can occur in other hip infections despite effective chemotherapy.⁵ Could spontaneous remissions and relapses of the disease¹ have accounted for some of the response? If this were the case we should have seen relapses during the two years of observation. Finally, it should be noted that our patients do not represent the whole spectrum of this disease. Children were referred to our Unit because of arthritis, which is present in only one third of infected patients. Toxicity could limit the treatment with certain drugs. The dose of co-trimoxazole used was higher than that recommended for urinary tract infections, otitis media, and shigellosis,⁶ though similar to the one used in the treatment of *Pneumocystis carinii* infections.⁷ Despite this high dose and the length of treatment we did not encounter significant side effects.

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