Original Article

Leukocyte Count in the Synovial Fluid of Children with Culture-Proven Brucellar Arthritis

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Abstract: Brucellosis is an important cause of paediatric septic arthritis in endemic areas. Because the Gram stain is frequently negative and culture results are unavailable at the time of the patient’s admission, the diagnosis of brucellar arthritis is usually entertained on the bases of epidemiological considerations and cytological examination of the synovial fluid aspirate. The aim of this study was to assess the sensitivity of a synovial fluid leukocyte count >50 000 WBC/mm$^3$ for detecting culture-proven brucellar arthritis in children. The medical records of all children with brucellar arthritis diagnosed since 1994 in a hospital serving an endemic area for brucellosis in southern Israel were reviewed. Nine patients (six males and three females), aged 3–14 years, were identified. A single joint was affected in all patients. The median leukocyte count in the synovial fluid was 9500 WBC/mm$^3$ (range 300–61 500 WBC/mm$^3$), and in eight of the nine patients it was less than 50 000 WBC/mm$^3$. *Brucella melitensis* was recovered from the synovial fluid culture in all patients. The diagnosis of brucellar septic arthritis cannot be excluded on the basis of a low leukocyte count in the joint aspirate. A high index of suspicion and use of modern culture techniques are recommended to improve the diagnosis of brucellar arthritis.

Keywords: Arthritis; Brucellosis; Children; Synovial fluid

Introduction

Septic arthritis is an important clinical condition in children which, if neglected, may result in permanent disability [1–4]. Gram-positive organisms such as *Staphylococcus aureus* and *Streptococcus pyogenes* are the most common aetiologic agents worldwide, and a variety of Gram-negative bacteria, including members of the Enterobacteriaceae and Neisseriaceae families, are important causes of septic arthritis in children younger than 2 years of age [1–6]. In areas endemic for brucellosis, such as South America, the Middle East and the Indian subcontinent, joint infections caused by *Brucella* species are also common [6–9].

The diagnosis of septic arthritis is not always easy, especially in young children, in whom the clinical presentation of joint infections is frequently benign and may be confused with other conditions of non-infectious origin [2,4,10]. In addition, Gram-stain examination of the synovial fluid is frequently negative, and culture results are usually delayed for 24 h or more and, therefore, are not available at the time of the patient’s admission [2]. Because of the serious consequences of missing the diagnosis of septic arthritis and the lack of timely bacteriological information, patients with suspected articular infections are usually given empiric antimicrobial therapy based on cytological and biochemical analyses of the joint fluid aspirate [4,11,12]. The presence of >50 000 WBC/mm$^3$ in synovial fluid has been recommended to distinguish septic arthritis from other causes of joint effusion, but the reliability of this criterion is limited [13–16]. It is believed that low leukocyte counts are common in patients with brucellar arthritis, but supporting data are scarce [9,17]. A study was conducted to assess the reliability of this cytological criterion for the diagnosis of brucellar septic arthritis in...
Materials and Methods

Children with clinical arthritis who were treated at the Soroka University Medical Center in southern Israel, underwent a diagnostic joint tap. Joint fluid was aspirated from the affected joint following a strict sterile technique. Because usually only small amounts of fluid were obtained, the synovial fluid specimens were only sent for cytological and bacteriological examination. Cultures of the aspirate were routinely performed on solid media as well as using the lysis centrifugation and broth methods as described elsewhere [18,19]. Presumptive identification of *Brucella* species was performed on the basis of a typical microscopic picture showing small Gram-negative cocobacilli, positive oxidase, catalase and urease tests and negative fermentation of sugars, and confirmed by a positive agglutination with specific antiserum [20].

Screening for *Brucella* antibodies was performed with the Rose Bengal test. Positive sera were then tested by the serum agglutination test (SAT) up to a minimal dilution of 1:2048, and by the 2-mercaptoethanol test (2-ME). A SAT titre $\geq 1:160$ and/or a 2-ME titre of $\geq 1:20$ was considered positive.

The medical records of all patients in whom the diagnosis of acute brucellar arthritis was made between 1 January 1994 and 30 June 2000 were reviewed. Paediatric patients with a synovial fluid culture positive for brucellae and from whom results of the cytological examination of the synovial fluid aspirate were available were identified, and relevant demographic, clinical and laboratory data were extracted from their medical records.

Results

A total of nine children met the criteria for inclusion in the study, six of whom were males. Demographic, clinical and laboratory features of these patients are summarised in Table 1. A single joint was affected in eight children and two joints in one child: the knee was involved in four, the shoulder or the hip in two patients each, and the elbow and wrist in one patient each. In three patients a body temperature of $<38^\circ$C was recorded on admission. No clinical findings other than joint involvement were detected. Leukopenia (4350 WBC/mm$^3$) was diagnosed in one child. Of note is that in eight of the nine patients the leukocyte concentration in the synovial fluid aspirate was $<50\,000$ WBC/mm$^3$. *Brucella melitensis* was recovered from the synovial fluid culture in all cases. In addition, the organism was isolated from blood cultures in five patients and in five children serological tests were positive for *Brucella* antibodies. Patients were treated with a combination of intravenous gentamicin for 1 week and oral doxycycline or trimethoprim-sulfamethoxazole for 4–6 weeks, and all recovered with no orthopaedic sequela.

Discussion

*Brucella* infections continue to affect rural populations living in endemic areas [21]. Arthritis and/or osteomyelitis are frequently observed in the course of the disease, especially among patients with *B. melitensis* infections, in whom the prevalence of skeletal symptoms is over 50% [7,8]. The clinical features noted in our patients, consisting of low-grade fever and monoarticular disease affecting especially the large weight-bearing joints, have been commonly reported in children and adults with brucellosis [7,21]. However, these symptoms are not pathognomonic for the disease and may be caused by other infectious and non-infectious conditions, such as rheumatic disorders, transient synovitis or trauma [21]. In addition, bacteriological confirmation of brucellosis is frequently hampered by the slow-growing characteristics of the genus [20]. Therefore, presumptive diagnosis of the disease and decisions concerning patient management are usually based on epidemiological considerations and non-specific laboratory tests. Information on the cellular composition of the synovial fluid of patients with brucellar arthritis is, however, limited. In 1986, Andonopoulos et al. reported leukocyte counts between 4460 and 8800 WBC/mm$^3$ in five patients with *B. melitensis* arthritis [9]. Ten years later, Colmenero et al. reported peripheral arthritis with clinically demonstrable effusion in only three of 530 adult patients with *B. melitensis* infection [22]. Although the cell count of the synovial fluid in these patients was low, ranging from 5690 to 23 200 WBC/mm$^3$, cultures of the aspirate were negative, suggesting that the arthritis was reactive in nature and not truly septic.

The results of the present study confirm that the cytological findings of the synovial fluid of children with brucellar septic arthritis are not impressive, and the vast majority of patients show leukocyte counts of less than 50 000 WBC/mm$^3$. This finding contrasts with the high leukocyte counts seen in most cases of staphylococcal or streptococcal pyogenic arthritis, and resembles the moderate cellular response observed in children’s