

Acute hematogenous osteomyelitis and septic arthritis in children

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This retrospective study analyzed the clinical, bacteriological, and radiological features of pediatric patients with acute hematogenous osteomyelitis and septic arthritis. Eighty-four patients with septic arthritis and 39 with acute hematogenous osteomyelitis were enrolled. Their age ranged from 13 days to 17 years. In patients with septic arthritis, the hip joint was the most often infected site. The tibia was the most often involved site in acute hematogenous osteomyelitis. A bacteriological diagnosis was established in 78 (63%) patients. Overall, methicillin-susceptible *Staphylococcus aureus* (36 cases) was the most common causative organism identified, followed by methicillin-resistant *S. aureus* (10 cases). The median duration of antibiotic therapy was 33 days. Serum bactericidal titers were obtained for 19 (15%) of the 123 patients. The median duration of hospitalization and antibiotic treatment was not significantly different between patients with and without serum bactericidal titer testing. More patients without serum bactericidal titer testing had symptom relapse which required re-admission for further treatment. In conclusion, the incidence of methicillin-resistant *S. aureus* as a cause of bone and joint infections has been increasing. Serum bactericidal titer is valuable for the management of patients receiving sequential therapy for acute hematogenous osteomyelitis and septic arthritis.

Key words: Osteomyelitis, septic arthritis, serum bactericidal titer

Acute hematogenous osteomyelitis (AHO) and septic arthritis present similar problems in diagnosis and treatment. Both are generally secondary to a bacteremia, and at times they may occur simultaneously in the same patient, or the osteomyelitis may decompress into its adjacent joint and result in septic arthritis [1,2]. Successful treatment of septic arthritis and osteomyelitis in infancy and childhood depends on early recognition and prompt institution of therapy. Initial diagnosis of septic arthritis and osteomyelitis relies on clinical suspicion, bone or joint fluid analysis, blood testing, and radiographic findings. Standard treatment consists of a short course (5-10 days) of intravenous antibiotics followed by a longer course of oral antibiotics [3]. Oral therapy reduces hospital costs, patient discomfort, and nosocomial infections. This study analyzed the clinical, bacteriological, and radiological aspects of bone and joint infection in children during an 11-year period. The value of the use of the serum bactericidal titer (SBT) to assess the

adequacy of oral antibiotic therapy in children was also assessed.

Materials and Methods

The medical records of 231 pediatric patients with a discharge diagnosis of AHO, septic arthritis, or both, who were treated at Chang Gung Children's Hospital during an 11-year period (from January 1990 to December 2000) were included. The age of the patients ranged from 13 days to 18 years. Acute hematogenous osteomyelitis and septic arthritis were defined by clinical criteria (localized tenderness, redness, swelling, or reduced mobility) together with one or more of the following: pus aspirated from bones or joints; positive bacterial culture from specimens of blood, joint fluid, pus obtained directly during surgery or needle aspiration of the involved bone; radiological abnormality (deep tissue swelling, widening of the joint, bone destruction, periosteal new bone formation); and radionucleotide scan abnormality. Patients with signs of both AHO and septic arthritis were primarily assigned to the former diagnosis.

A total of 123 pediatric patients remained in the study group after the exclusion of patients with traumatic wounds or insufficient evidence to confirm

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the diagnosis of AHO or septic arthritis.

Clinical charts, radiographs, and results of radionuclide bone scans and radionuclide gallium scans were reviewed retrospectively. Laboratory data assessed included white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), SBT, and cultures from blood and joint fluids and pus of the lesion site. The various isolates were identified based on the recognition of bacterial colony characteristics on agar plates, morphological characteristics examined after Gram stain and biochemical reactions. Selection of initial antibiotic therapy was based either on results of Gram stain of a smear of material from joint fluids or pus at the lesion site or, if no organisms were seen, on the probable etiology of the disease in the patient's age group. The route of antibiotic therapy was changed from intravenous to oral in patients after a definite decrease in clinical signs of inflammation was noted. After oral antibiotic therapy was started and 2 or more doses had been given, the peak (1 h after the oral dose) and trough (6 h after the oral dose) SBTs were measured. Doses were given between or before meals. The standard method proposed by the National Committee for Clinical Laboratory Standards (NCCLS) was used in serum bactericidal tests. A case was considered community-acquired according to the Center for Disease Control and Prevention criteria [4]. The statistical tests used were the Student's *t* test, Fisher's exact test and chi-square test. A *p* value of <0.05 was considered statistically significant.

Results

A total of 123 pediatric patients with bone and joint infections met the criteria for the study. Six patients with signs of both AHO and septic arthritis were assigned to the AHO group. Eighty-four cases were categorized as septic arthritis and 39 as AHO. The ages of patients ranged from 13 days to 17 years. The median age of patients with septic arthritis was 66 months and that of patients with AHO was 75 months ($p < 0.0005$). Fifty-four percent of the patients with septic arthritis and 59% of those with AHO were males. The sites of infection are shown in Table 1 and 2. In septic arthritis, the hip joint was the most commonly involved site, followed by the knee. In AHO, the tibia was the most commonly involved site, followed by the femur.

A bacteriological diagnosis was established in 78 (63%) of the 123 cases (Table 3). They included 53 (63%) of the 84 cases with septic arthritis and 25 (68%) of the 38 cases with AHO. In one patient with AHO, neither blood nor lesion site pus culture was performed.

Table 1. Location of infection in 94 affected joints in 84 patients with septic arthritis

Location	No. of cases (%)
Hip	45 (48)
Knee	29 (31)
Ankle	7 (7)
Shoulder	6 (6)
Sacroiliac	5 (5)
Elbow	2 (3)

The etiologic agents identified for AHO and septic arthritis are listed in Table 4. Methicillin-susceptible *Staphylococcus aureus* (MSSA) was the most common organism identified, followed by methicillin-resistant *S. aureus* (MRSA). *Haemophilus influenzae* type b infection occurred exclusively in patients younger than 2 years. In infants younger than 1 month, Group B *Streptococcus*, *Escherichia coli*, MRSA and MSSA were the most common causative organisms. Among the 123 patients, community-acquired infection was found in 118 cases and hospital-acquired infection in 5. Among the 5 cases of hospital-acquired infection, the responsible pathogen was MSSA in one patient, *E. coli* in one, and MRSA infection was found in the remaining 3. All hospital-acquired infections were in high-risk neonates requiring intensive support including endotracheal intubation, positive pressure ventilation and percutaneous insertion of long intravenous catheters.

Fifty (91%) of the 123 patients had an elevated ESR, and 94 (88%) had an elevated CRP. Erythrocyte sedimentation rate was not tested in 14 patients with septic arthritis and 3 with AHO. On admission, patients with septic arthritis had significantly higher ESR than those with AHO, with median values of 75 mm/h (range, 3-125 mm/h) and 35 mm/h (range, 2-85 mm/h), respectively ($p < 0.0005$). There was no significant

Table 2. Location of infection in 43 infected bones in 39 patients with acute hematogenous osteomyelitis

Location	No. of cases (%)
Tibia	16 (36)
Femur	10 (22)
Calcaneus	4 (16)
Metatarsal	4 (16)
Radius	2 (3)
Humerus	1 (1)
Ulna	1 (1)
Tarsal	1 (1)
Sacrum	1 (1)
Parietal bone	1 (1)
Spine	1 (1)
Pubic	1 (1)

Table 3. Bacteriological diagnosis of pediatric patients with bone and joint infections (n=123)

Analysis	No. of cases (%)
No etiologic agent identified	45 (37)
Bacteriological diagnosis established	78 (63)
Positive joint fluid or pus of the lesion site and blood culture	18 (23)
Positive joint fluid culture or pus of the lesion site only	37 (47)
Positive blood culture only	23 (30)

difference in the CRP values between septic arthritis and AHO patients ($p=0.27$). The value of CRP in the 70 patients with septic arthritis ranged from 5 to 363.3 mg/L (median, 87.6 mg/L) and in the 36 patients with AHO ranged from 2 to 391.5 mg/L (median, 98.7 mg/L).

In patients with septic arthritis or AHO, the peripheral WBC count was often increased, with left shift. The average WBC count in patients with AHO was $1.41 \times 10^4/\mu\text{L}$ with 54% neutrophils, and $1.67 \times 10^4/\mu\text{L}$ with 61.5% neutrophils in patients with septic arthritis. The difference in the WBC count between the 2 groups of patients was not significant ($p=0.37$).

Fifty-seven (67%) patients with septic arthritis had no osseous radiographic manifestations at the time of diagnosis and they all received radionuclide scan. Typical osseous changes (widening of the joint, destruction of cartilage, displacement of the ossific nucleus within cartilage) developed within 10 to 14 days of diagnosis in 7 (12%) patients. Of the 57 patients without initial X-ray evidence of osseous change, 41 (70%) had an abnormal radionuclide scan. Twenty-one (53%) of the patients with AHO had no osseous radiographic manifestations of osteomyelitis at the time

of diagnosis and they all received radionuclide scan. In 6 (16%) of these patients, typical osseous changes (periosteal new bone formation, bone destruction, osteoporosis, sequestrum formation) developed within 10 to 14 days of diagnosis. Of the 21 patients without initial X-ray changes, 13 (61%) had an abnormal radionuclide scan.

Combined antibiotic and surgical treatment was given in 93 (76%) of the 123 patients. Eighty-five percent of patients with septic arthritis received surgical treatment, as did 56% of the patients with AHO. Seven patients with AHO were readmitted due to recurrence of symptoms after discharge on oral therapy, while only one patient with septic arthritis had a relapse after discharge. There was no mortality in these patients.

Overall the median durations of antibiotic therapy was 33 days. In the AHO group, the median duration of intravenous and oral antibiotic therapy was 17 days and 16 days, respectively, while in the septic arthritis group these durations were 20 days and 13 days, respectively.

Serum bactericidal titers were obtained in 19 (15%) of the 123 patients. Fifteen of the 19 values were determined at the time oral antibiotic therapy was

Table 4. Causative organisms for bone and joint infections by age group in 78 pediatric patients

Organism	No. of cases					
	Total	<1 mo	1 mo-2 yr	3-5 yr	6-10 yr	11-18 yr
MSSA	36	4	8	4	7	13
MRSA	20	3	3	0	4	0
CoNS	4	1	1	0	2	0
<i>Escherichia coli</i>	4	1	3	0	0	0
<i>Streptococcus pneumoniae</i>						
Penicillin-susceptible	2	0	2	0	0	0
Penicillin-resistant	6	0	5	1	0	0
<i>Haemophilus influenzae</i> type b	2	0	2	0	0	0
<i>Pseudomonas aeruginosa</i>	2	0	1	0	0	1
<i>Salmonella</i> spp.						
Group D	3	0	1	1	0	1
Group B	1	0	0	0	0	1
<i>S. typhi</i>	1	0	1	0	0	0
<i>Mycobacterium tuberculosis</i>	2	0	1	1	0	0
Group A <i>Streptococcus</i>	2	0	0	0	1	1
Group B <i>Streptococcus</i>	3	2	1	0	0	0
<i>Propionibacterium</i> sp.	1	0	1	0	0	0

Abbreviations: CoNS = coagulase-negative *Staphylococcus*; MSSA = methicillin-susceptible *S. aureus*; MRSA = methicillin-resistant *S. aureus*

started. There were 4 SBT measurements made in patients receiving intravenous antibiotic therapy. A peak SBT of >1:8 was found in 6 (40%) of the 15 patients on oral antibiotic therapy. Among the other 9 patients, 5 had a peak SBT of 1:4 and 4 of 1:2. Trough SBT >1:2 was demonstrated in 9 (60%) of the 15 patients.

In the 19 patients who received SBT test, the median duration of hospitalization and antibiotic treatment was 23 days and 43 days, respectively, whereas in those without SBT test the median duration was 22 days and 36 days, respectively ($p=0.49$). Seven patients who had not received SBT test were readmitted due to recurrence of symptoms after discharge with oral therapy. Only one patient who had an SBT test was readmitted, but this patient's SBT was determined at the second admission ($p<0.05$).

One patient was lost to follow-up. The vast majority of patients had an unremarkable recovery with resolution of their infection and a return to full motion and function of the involved bones and joints. One patient with septic hip had the sequela of limb length discrepancy.

Discussion

Septic arthritis and AHO occurring during infancy or early childhood present similar problems in diagnosis and treatment. They may occur simultaneously in the same patient [2]. Septic arthritis characteristically involves weight-bearing joints [5], with the knee or hip joint most commonly involved [6]. In a previous study, monosteal lesions of the femur, tibia and humerus accounted for over half of the cases of AHO [6]. Similar results were found in this study.

In previous studies, the leukocyte count was elevated with shift to the left of myeloid cells in about two-thirds of the AHO and septic arthritis patients [7, 8]. Erythrocyte sedimentation rate and CRP is a more sensitive test for septic arthritis and AHO but both are nonspecific indices of inflammation. In a previous study, ESR was elevated in the 50 to 90 mm/h range in over 90% of septic arthritis cases [7]. Patients with AHO may have a normal ESR on the first day of illness, but initial elevation in the 50 to 100 mm/h range is also common [9]. The results of this study were similar to these previous findings. Although the median ESR in this study was significantly ($p<0.005$) different between the 2 groups of patients, substantial overlap in the intermediate ranges made it a poor discriminator for differential diagnosis.

Diagnostic roentgenographic studies of the septic arthritis and AHO may show widening of joints, destruction of cartilage, periosteal new bone formation,

bone destruction, and osteoporosis. However, these findings may not appear in the early stage of the disease. In our series, only 48 (39%) of 123 patients with plain X-ray taken on admission showed these findings. Six (16%) of our patients with AHO showed these findings within 10 to 14 days. This result is in agreement with a previous study, which reported that radiographic changes in AHO might be detected as early as 10 to 14 days after the onset of clinical illness in approximately 20% of the patients [7]. In recent years, bone scan has become a useful diagnostic tool for differentiating septic arthritis from AHO, cellulitis or trauma. Bone scan can confirm the diagnosis as early as 24 to 48 h after the onset of illness [10] and has been reported to have 90% to 95% accuracy [11]. This study also demonstrated the diagnostic value of this technique. Gallium scan had been suggested to be more accurate than bone scan in detecting bone and joint infections in children [10,11]. We used gallium scan as a diagnostic aid in this study when bone scan data were negative.

In previous studies, no bacterial pathogen was identified in one-third of the cases with septic arthritis or AHO [2,12]. In this study, 37% of cases had no etiologic agent identified. In previous studies, the reported positive synovial fluid culture rates in patients with septic arthritis varied from 52% to 82% [12-15]. In a previous study pus obtained from the bone and joint fluid yielded the responsible pathogen in 70% of patients with AHO [6]. In this study, we found a similar positive rate (56% with septic arthritis, 72% with AHO). In previous studies, blood cultures were positive in about 40% to 50% of patients with septic arthritis and AHO [8,12,16]. The blood culture is often the only method that can identify the responsible pathogen [12]. In this series, blood cultures were positive in 33% of cases (41 in 123 cases) compared with 36% to 56% in previous series from Taiwan [17-19]. Due to this low rate and the diversity of organisms causing AHO and septic arthritis, bone or joint aspiration should be invariably performed along with blood cultures for every pediatric patient with suspected bone or joint infection.

S. aureus is the most common causative organism identified in children with septic arthritis. For infants under 2 years of age, *H. influenzae* type b are frequently the next most common pathogen [12]. In children with AHO, *S. aureus* is the predominant pathogen and accounts for 70% to 75% of cases [20]. Other likely pathogens in young children include *H. influenzae* type b and *Streptococcus pneumoniae*. In this study, *S. aureus* was the most common causative agent (59%), which is also in accord with previous studies (31%-78%) from

Taiwan [17-19]. Among these *S. aureus*, 36 (78%) isolates were MSSA and 10 (22%) were MRSA. Methicillin-resistant *S. aureus* have become an increasingly frequent cause of bone and joint infections [10,21]. In Taiwan, several cases of community-acquired MRSA infection have been reported since December 1999 [22]. Seven patients with community-acquired MRSA infection in this study had no identifiable risk factors. This finding is consistent with the study of Wu *et al* from Taiwan [23]. A study performed in an Australian tertiary care unit for neonates showed that all the cases of AHO and/or septic arthritis due to MRSA involved sick premature infants [24]. Nar *et al* found that 3 premature neonates with septic arthritis and/or AHO were infected by MRSA [25]. In this study, 3 hospital-acquired MRSA infected patients were high-risk neonates in the neonatal intensive care unit and only one patient was a premature neonate. There were only 2 cases, one septic arthritis and one AHO, caused by *H. influenzae* type b in this study. In the prevaccination era, *H. influenzae* type b was the most common causative agent for septic arthritis and AHO in children under 2 years of age in western countries [12,26,27]. Since the introduction of the *H. influenzae* type b vaccine in early 1990, there has been a dramatic decline in the incidence of infection with this bacterium [28,29]. In this series, we identified 8 patients with *S. pneumoniae* infection, 6 of whom were infected with penicillin-resistant strains. Penicillin resistance in *S. pneumoniae* has become a common problem worldwide. In a study that analyzed *S. pneumoniae* isolates from throughout Taiwan from 1996 to 1997, and 56.4% were found to be non-susceptible to penicillin [30]. The recent emergence of penicillin resistance in *S. pneumoniae* has made it difficult to choose the most effective antibiotics for treating bone and joint infections caused by this organism.

Previous studies showed that antibiotics should be given parenterally for a minimum of 2 to 3 weeks in septic arthritis and for at least 3 weeks in AHO [6,31]. Recent studies have demonstrated the efficacy of sequential parenteral-oral antibiotic therapy for the management of acute skeletal infections [6]. A serum specimen should be collected 1 h after an oral dose for determination of the bactericidal activity against the isolated pathogen. A peak SBT of 1:8 or greater is generally associated with successful treatment [32]. Some authors have claimed a trough SBT of 1:2 or greater more accurately predicts successful treatment than peak SBT [33]. In this series, a trough SBT of <1:2 was noted in 40% of the 15 patients who received oral antibiotic therapy. The antibiotic dosage was thus

raised in each of these cases and no recurrence was noted. In contrast, recurrent infections were noted in 7 of the patients who did not receive SBT tests, resulting in a recurrence rate of 6%. The importance of SBT test as a useful tool to monitor whether the dosage is adequate for a successful treatment of pediatric bone and joint infections should be emphasized.

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