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Original Article

Characteristics and outcome of septic arthritis in children

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Background and Purpose: To assess the etiologic agents, presentation, laboratory findings, treatment, clinical outcome and prognostic factors of pyogenic arthritis in pediatric patients.
Methods: We reviewed the medical records of patients under 18 years of age with a diagnosis of septic arthritis from January 1971 to July 2004. Information collected included clinical characteristics, laboratory data, response to therapy and outcome. An unsatisfactory clinical outcome was defined as the development of sequelae including ambulatory disability, limb-length discrepancy, chronic osteomyelitis, and abnormalities of bone growth.
Results: A total of 60 children who met the criteria for diagnosis of septic arthritis were included. The etiologic agent was identified in 71.7% of the patients. *Staphylococcus aureus* was the most common etiologic agent in all age groups (59.0%). The erythrocyte sedimentation rate was higher than 20 mm/h in 89% of patients and soft tissue swelling was the most common radiographic finding (16.7%). Lower extremity involvement was found in 90.8% of patients and the knee joint was most commonly involved. The clinical outcome was unsatisfactory in 28.3% of patients. The duration of symptoms before the initiation of treatment was significantly longer in patients with sequelae (4.2 vs 13.1 days, $p<0.01$), and the neutrophil percentage in peripheral blood was also significantly higher in this group (81.5% vs 65.7%, $p=0.027$).
Conclusions: Delayed treatment and increased neutrophil ratio in peripheral blood were significantly associated with an increased risk of sequelae.

Key words: Adolescent, child, infectious arthritis, *Staphylococcus aureus*

Introduction

Septic arthritis occurs most commonly during childhood, and is an important disease because delayed or inadequate treatment carries a risk of permanent disability. The frequency of septic arthritis is greater in infants and young children because the epiphysis and metaphysis are connected via blood vessels [1,2]. The organisms most commonly enter the joint space through hematogenous seeding during a transient or persistent bacteremia.

Infection of joints can also follow penetrating injuries or contiguous infection [3,4]. The large joints are most frequently affected, especially those of the lower extremity [5-7]. Because children are in a dynamic state of growth, damage of the bone growth plate may lead to long-term morbidity. A variety of factors have been reported to be associated with adverse outcome of septic arthritis, including: neonates and infants, impaired host defense mechanism, pre-existing joint disease, joint prosthesis, infection of the hip or shoulder joint, polyarticular infection, delayed treatment, infection due to methicillin-resistant *Staphylococcus aureus*, presence of associated osteomyelitis, and adequacy of treatment [4,6,8,9]. This retrospective study was conducted to identify the prognostic factors based on an analysis of the correlation between clinical and laboratory parameters and the outcome of septic arthritis.

Methods

The medical records of patients under 18 years of age with a diagnosis of septic arthritis who were admitted to the orthopedic or pediatric department from January

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1971 to July 2004 were reviewed. Patients with chronic arthritis were excluded. Septic arthritis was defined by the presence of typical clinical manifestations (redness, swelling, localized tenderness and pain, and reduced mobility of the joint) together with 1 or more of the following: pus aspirated from joints; isolation of bacterial pathogen from joint fluid or blood; radiological abnormalities (soft tissue swelling, widening of the joint, destruction of cartilage); and radionuclide scan abnormality.

Data were collected on demographic characteristics, presentation, and laboratory parameters (including initial complete blood cell count and differential count erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, joint fluid white blood cell (WBC) count and differential count, red blood cell count, protein, glucose level, and results of cultures from blood or joint fluid). Possible predisposing factors were also recorded, including comorbid conditions, duration of symptoms before the initiation of medical and surgical treatment, findings of radiography and other imaging study, response to treatment (including post-treatment duration of clinical symptoms, fever, leukocytosis, abnormal ESR, or abnormal CRP level) and complications.

Antibiotics were prescribed after admission and adjusted according to the results of antibiotic sensitivity testing of isolates. Patients with septic arthritis were classified according to whether they had an unsatisfactory outcome (defined as development of sequelae) or satisfactory outcome. Identified sequelae included ambulatory disability, limb-length discrepancy, chronic osteomyelitis, and abnormalities of bone growth. If a patient did not survive to discharge, the cause of death was recorded.

Statistical analysis was performed using chi-squared test for parametric data, and Mann-Whitney *U* test for non-parametric data. A p value of less than 0.05 was considered significant.

Results

A total of 60 patients who met the study criteria were identified from review of records, including 36 males and 24 females. There were 10 infants (16.7%), 11 children (18.3%) between the ages of 1 and 5 years, 11 children (18.3%) between 5 and 10 years, and 28 children (46.7%) older than 10 years of age. Single joint involvement occurred in 53 (88.3%), and the knee joint was most commonly involved (30 patients, 46.2%). None of the patients had a prosthetic joint. Joint pain was noted by 56 patients (93.3%) and was the most common clinical manifestation (Table 1).

Table 1. Distribution of affected joints and clinical manifestations in children with septic arthritis (n = 60)

	No. of cases (%)
Joint	
Knee	30 (46.2)
Hip	22 (33.8)
Ankle	7 (10.8)
Shoulder	4 (6.2)
Elbow	2 (3.1)
Clinical manifestation	
Pain	56 (93.3)
Fever	54 (90.0)
Edema	51 (85.0)
Warmth	48 (80.0)
Limitation of motion	46 (76.7)
Erythema	34 (56.7)

Bacterial isolates were found in 43 patients (71.7%), and the rate of pathogen isolation from joint fluid was highest in patients under 12 months of age (88.9%). Among the children with positive cultures from joint fluid, *S. aureus* was the most common species isolated in 23 (59.0%), and was the leading causative pathogen identified in all age groups. The causative pathogens isolated from patients in each age group are shown in Table 2. *Haemophilus influenzae* type b was isolated in only 1 patient (a 10-month-old female with concomitant meningitis). No isolates of *Streptococcus pneumoniae* or *Neisseria gonorrhoeae* were found in this study. Gram-negative pathogens were found in 26.3% of patients with positive joint aspirate culture. A history of trauma to the affected extremity was found in 19 patients (31.7%), and was the most common predisposing factor, followed by upper airway infection in 8, cellulitis in 7, and puncture in 1. Ten patients had underlying diseases as summarized in Table 3.

The average WBC count was 15,154/mm^3 with 66% neutrophils. The mean ESR level was 44 mm/h, and 89% of patients had an ESR higher than 20. CRP level was above 10 mg/dL in 25 patients (58.1%). The appearance of joint fluid varied from a clear, normal looking synovial fluid to pus. Joint fluid WBC count averaged 98,700/mm^3 (range, 6080 to 492,360 cells/mm^3) with predominant neutrophils (more than 85% in all cases).

Initial radiographic examination revealed abnormalities in 19 patients (31.7%), including soft tissue swelling (10), joint widening (7), and osteolytic change (2). Radionuclide scan was performed in 17 patients, with positive findings in 14 (82.4%). Cellulitis

Table 2. Microorganisms isolated from joint aspirates in patients with acute septic arthritis (n = 60)

Microorganisms	Total No. (%)	No. of cases (%)		
		<1 year (n = 9)	1-5 years (n = 12)	>5 years (n = 39)
Staphylococcus aureus	23 (38.3)	4 (44.4)	2 (16.7)	17 (43.6)
Salmonella spp.	4 (16.7)	1 (11.1)	1 (8.3)	2 (5.1)
CoNS	3 (5.0)	0 (0.0)	1 (8.3)	2 (5.1)
Pseudomonas aeruginosa	2 (3.3)	0 (0.0)	0 (0.0)	2 (5.1)
Enterobacter cloacae	2 (3.3)	1 (11.1)	0 (0.0)	1 (2.6)
Group A Streptococcus	1 (1.7)	0 (0.0)	0 (0.0)	1 (2.6)
Klebsiella pneumoniae	1 (1.7)	0 (0.0)	0 (0.0)	1 (2.6)
Haemophilus influenzae type b	1 (1.7)	1 (11.1)	0 (0.0)	0 (0.0)
Yeast	1 (1.7)	1 (11.1)	0 (0.0)	0 (0.0)
Unknown	22 (36.7)	1 (11.1)	8 (66.7)	13 (33.3)

Abbreviation: CoNS = coagulase-negative staphylococcus

was found in 7 patients, and *Staphylococcus* species was isolated in 6 of them (the other patient had Gram-positive cocci in the smear). Puncture wound was found in 1 patient infected by *Klebsiella pneumoniae*.

Drainage of the infected joint was performed in 22 patients (36.7%). Debridement was performed in 12 patients (20%), arthrostomy in 10 (16.7%), and arthrocentesis in 4 (6.7%). Treatment was given within 7 days of symptom onset in 38 patients (63.3%). The duration of follow-up ranged from 3 months to 7 years. At last follow-up evaluation, 34 patients (56.7%) had satisfactory outcome, 17 (28.3%) had unsatisfactory outcome, and 6 were lost to follow-up. Another 3 patients died of illnesses other than septic arthritis, including the following: fungemia, acute renal failure, upper gastrointestinal bleeding, pulmonary edema, and multiple organ failure.

Risk factors related to unsatisfactory outcome are summarized in Table 4. The duration of symptoms before the initiation of treatment was significantly longer in patients with sequelae (4.2 vs 13.1 days, $p<0.01$). The percentage of neutrophils in peripheral blood was also significantly higher in this group (81.5% vs 65.7%, $p=0.027$).

Most patients with multiple joint involvement had unsatisfactory clinical outcome and lower serum WBC count, but this difference was not significant ($p>0.05$). Patients with *S. aureus* isolated from joint fluid had significantly higher peripheral WBC count, higher platelet count, and lower hemoglobin level (20,825 vs 13,042/mm^3, 464,000 vs 233,014/mm^3 and 9.8 vs 11.6 g/dL, respectively; $p=0.017$, 0.027 and 0.029, respectively). Patients with positive blood culture had significantly higher WBC count, higher neutrophil percentage, and lower lymphocyte percentage (17,625 vs 13,373/mm^3, 73.5% vs 54%, and 16.4% vs 27.6%, respectively; $p=0.047$, 0.006 and 0.011, respectively).

Gender, age, surgical intervention, and the presence of associated osteomyelitis were not significantly associated with clinical outcome. However, the mean duration from onset of symptoms to surgical intervention was significantly longer in the unsatisfactory outcome group (18.5 vs 7.1 days, $p<0.05$). Chronic osteomyelitis was the most common complication in this study,

Table 3. Isolated pathogens in the 10 children with septic arthritis and underlying diseases

Underlying disease	No. of cases	Pathogen
Epidermolysis bullosa	1	MRSA
Pontine glioma under chemotherapy	1	Gram-positive cocci
ESRD after transplantation with rejection	2	*Salmonella* sp., *Enterobacter cloacae*
Prematurity	3	MRSA (2), *Enterobacter cloacae*
SLE with CNS involvement	1	*Salmonella* sp.
Severe aplastic anemia	1	*Salmonella* sp.
Hemophilia A with AIDS	1	MSSA

Abbreviations: ESRD = end-stage renal disease; SLE = systemic lupus erythematosus; CNS = central nervous system; AIDS = acquired immunodeficiency syndrome; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *Staphylococcus aureus*

Table 4. Factors associated with adverse clinical outcome

Risk factors	Satisfactory	Unsatisfactory	*p*
Duration of symptoms before initiation of treatment (days)	4.2	13.1	<0.01
Presence of osteomyelitis (%)	20.0	14.3	NS
Surgical intervention (%)	51.4	70.6	NS
Duration of symptoms before surgical intervention (days)	7.1	18.5	0.035
Neutrophil (%)[a]	65.7	81.5	0.027

Abbreviation: NS = not significant

[a]Peripheral blood.

followed by dislocation, ankylosis, leg length discrepancy, and developmental dysplasia of the hip (Table 5).

Discussion

In this study, septic arthritis occurred before 5 years of age in 35% of patients, and over one-half of the patients were younger than 10 years old. *S. aureus* was the etiologic agent in the majority of patients with positive joint aspirate culture (59%), confirming the findings of several previous studies [10-13]. Unlike previous studies [5,14], *N. gonorrhoeae* was not isolated in this series, even though nearly half of the patients were older than 10 years. In the prevaccination era, *H. influenzae* type b was the most common causative agent of septic arthritis [15]. In this study, infection with *H. influenzae* type b was found in only 1 patient, similar to findings of recent studies of pediatric septic arthritis from Taiwan [6,7]. The incidence of invasive *H. influenzae* infection is much lower in Taiwan than in western countries [16,17].

Findings in this study support the established association between immunocompromised status and a higher frequency of Gram-negative bacterial infections [18,19]. All 3 patients with *Salmonella* infection had underlying medical problems and preceding bacteremia, including systemic lupus erythematosus (SLE) with central nervous system (CNS) involvement, end-stage renal disease (ESRD) after transplantation with rejection, and severe aplastic anemia. Of the 2 patients with *Enterobacter cloacae* infection, 1 had ESRD after transplantation with rejection, and the other was a premature neonate.

Septic arthritis was monoarticular in 53 patients (88.3%), a rate similar to that in previous studies [6,15, 18]. Multifocal disease was thought to occur almost exclusively in the neonatal period and to involve a few specific pathogens [15]. In this study, however, none of the patients with multiple joint involvement was a neonate, and similar to the findings of Dubost et al [8], *S. aureus* was the most common pathogen (4 cases, 57%). Three patients with Gram-negative bacteria infections (2 *Salmonella* and 1 *E. cloacae*) had underlying disease and impaired host defense mechanism, including a patient with SLE with CNS involvement receiving long-term systemic corticosteroid therapy, pontine glioma receiving chemotherapy, and a patient with ESRD status post-renal transplantation receiving immunosuppressive therapy.

The vast majority of infections (90.8%) occurred in the lower extremities (knee, hip and ankle), a finding similar to previous reports. In contrast to the findings of Welkon et al [15] and Bennett and Namnyak [20], infection involving the hip and shoulder joints (with or without osteomyelitis) was not associated with poor outcome in this study.

A causative agent was isolated in 43 patients (71.7%) and joint aspirate culture had the highest positive rate (38 patients, 63.3%). Pathogens were identified by blood culture in an additional 5 patients. The age, gender, clinical features, and laboratory abnormalities of patients with pyogenic arthritis were not significantly different from patients without any isolated pathogen. This suggests that the majority of such patients have bacterial arthritis of unknown etiology rather than a disease of non-infectious etiology.

Table 5. Sequelae of pyogenic arthritis (n = 60)

Sequelae	No. of cases (%)
Chronic osteomyelitis	9 (15.0)
Dislocation	4 (6.7)
Ankylosis	4 (6.7)
Leg-length discrepancy	3 (5.0)
Developmental dysplasia of hip	2 (3.3)
Deformity	2 (3.3)
Limited motion	1 (1.7)
Joint instability	1 (1.7)
Weakness	1 (1.7)
Total hip replacement	1 (1.7)
Total	17 (28.3)

Laboratory tests that reflect the degree of inflammatory response are variable in patients with septic arthritis. Diagnosis of septic arthritis was based on clinical history, physical examination, joint fluid examination, and joint fluid and blood culture.

Other laboratory and imaging tests served only as supporting evidence. Peripheral WBC counts in patients with positive joint aspirate culture were less than 15,000/mm^3 in one-half of patients, one-third had ESR less than 20 mm/h, and one-half had CRP less than 10 mg/dL. These findings are similar to those of Klein et al [21], who found that ESR is the most sensitive indicator of septic arthritis, and suggest that normal laboratory tests cannot exclude the diagnosis of septic arthritis.

Plain radiographs from patients with septic arthritis may be normal or may demonstrate widening of joint or soft tissue edema at the time of symptom onset [22, 23]. Bone destruction often takes weeks to manifest radiologically. Osteolytic change, however, was found in 2 of the patients diagnosed soon after the onset of symptoms. All of the patients were treated with antibiotics, and 80% underwent decompression and drainage of the affected joints. Sequelae were found in more than one-fourth of the patients in this study, a rate similar to previous reports [4,9,10]. Delayed treatment was correlated significantly with unsatisfactory clinical outcome in this study and in previous studies [2,4,13, 15]. In this study, we found that response to treatment could be used as an indicator of clinical severity and adequacy of treatment, as reported by Herndon et al [25]. Some discrepancies between this study and previous studies may be ascribed to the small patient number and retrospective data collection.

In conclusion, acute septic arthritis is a potential medical emergency. This study showed that increased neutrophil ratio in peripheral blood and delayed treatment were significantly associated with prolonged morbidity. Analysis of the response to treatment is necessary to select patients who require more aggressive therapy.

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