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Septic arthritis in children: relationship of causative pathogens, complications, and outcome

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This retrospective study investigated the causative pathogens, complications, and outcome of 58 children who were hospitalized for septic arthritis at a tertiary care hospital in southern Taiwan from July 1988 to December 2000. The mean age was 3 years (range, 12 days-16 years). The males/females ratio was 1.2:1. Ninety percent of the cases involved lower extremities (knee, hip, and ankle) with the hip being the most common site of infection (54%). Joint pain (81%) was the most common clinical presentation, followed by fever (74%), local warmness and swelling (72%), and limitation of motion (64%). Erythrocyte sedimentation rate was elevated (≥20 mm/h) initially in 89% of the cases. The predominant causative organism was *Staphylococcus aureus* (43%, 25/58), 6 isolates of which were methicillin-resistant, followed by coagulase-negative *Streptococcus* (6), *Streptococcus pneumoniae* (3), *Salmonella* spp. (3), *Haemophilus influenzae* type b (2), and group B *Streptococcus* (2). The concomitant complications of septic arthritis were sepsis (9%, 5/58) and meningitis (2%, 1/58). Ten patients had sequelae, including limitation of motion (6), limping gait (2), limb-length discrepancy (1), and abnormalities of bone growth (1). This study found that *S. aureus* was the most common infecting microorganism in septic arthritis in children. Septic arthritis with concomitant osteomyelitis and infection due to methicillin-resistant *S. aureus* was associated with a significantly increased risk of sequelae (relative risk, 46.4, 95% CI, 2.9-748.8; relative risk, 16. 2, 95% CI, 1.3-204.9, respectively).

Key words: Children, osteomyelitis, septic arthritis, *Staphylococcus aureus*

Septic arthritis remains an important and serious disease of childhood because of its potential to cause permanent sequelae. The incidence of septic arthritis in children is approximately 5.5 to 12 cases per 100 000 individuals [1]. Acute septic arthritis is an inflammation of the joint space caused by invasive hematogenous bacterial inoculation of joint. Symptoms of septic arthritis may include fever, joint pain, erythema, swelling, tenderness, and limitation of motion of the joint. The hip and knee are the most commonly involved joints, with the condition predominantly occurring in infants and young children [2,3]. The initial diagnosis and treatment of the septic arthritis is based on clinical manifestations, laboratory data, and/or radiographic findings. Optimal treatment always consists of medical and surgical therapies [2]. Sequelae are often due to delayed diagnosis, inadequate treatment, and concomitant complications. The aims of this hospital-based study were to investigate the clinical spectrum, laboratory findings, complications, and sequelae of septic arthritis during the past decade at a tertiary care hospital.

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Patients and Methods

We retrospectively reviewed medical records of all patients less than 18 years old with a diagnosis of septic arthritis at the National Cheng Kung University Hospital from July 1988 to December 2000. The demographic data, clinical features, concomitant complications, and outcome were analyzed. Laboratory data including peripheral blood cell counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), synovial fluid analysis, and culture results were collected.

Septic arthritis was defined as the aspiration of purulent material from the joint space and/or the isolation of bacterial pathogen from joint fluid. Osteomyelitis was confirmed by positive culture from aspiration specimen of the involved bone or positive radiographs and/or bone scan. Patients with septic arthritis were divided into 2 groups: septic arthritis with sequelae and those without. Sequelae included ambulatory disability, limb-length discrepancy, and

abnormalities of bone growth. The study was divided into 2 periods: the first from July 1, 1988 to December 31, 1994, and the second from January 1, 1995 to December 31, 2000. The causative agents were compared between the 2 periods.

Differences in age, causative pathogens, laboratory data, and complications were compared between the 2 groups by chi-square test or Fisher's exact test. Relative risk (RR) and 95% CI were also estimated. Logistic regression modeling was used for multivariate analysis of factors potentially associated with the sequelae in univariate analysis. SPSS 9.0 for Windows (SPSS Inc., Chigaco, IL, US) was employed to analyze the data and differences with values of $p<0.05$ were considered significant.

Results

A total of 58 patients (32 boys and 26 girls), with a median age of 3 years (range, 12 days-16 years), were included. The male/female ratio was 1.2 :1. More than half (36/58, 62%) of the patients were younger than 5 years and 33% (19/58) were infants less than 1 year of age. *Staphylococcus aureus* was the most common infecting organism in all age groups. *Salmonella* and group B *Streptococcus* predominated in children younger than 1 year. In contrast, 83% of coagulase-negative staphylococci (CoNS) was isolated from patients older than 2 years. Fifty-six (97%) children were healthy prior to the onset of septic arthritis. Two patients had underlying diseases: one had chromosome anomaly and the other received total colectomy and ileocecal valve resection due to necrotizing enterocolitis in the newborn period. Joint pain (47/58, 81%) was the most common clinical presentation, followed by fever (43/58, 74%), local warmness and swelling (42/58, 72%), and limitation of motion (37/58, 64%). Infections of the lower extremities (knee, hip, and ankle) accounted for about 92% (56/61) of the total number of cases, with the hip being the most common site of infection (33/61, 54%). Ninety-five percent of children had a single joint involved. Table 1 shows the locations of affected joints.

Table 1. Localization of affected joints in children with septic arthritis (n = 58)

Joint	No. of cases (%)
Hip	33 (54)
Knee	17 (28)
Ankle	6 (10)
Shoulder	5 (8)
Total	61 (100)[a]

[a]Three patients had involvement of 2 joints.

Table 2. Initial laboratory findings in 58 pediatric patients with septic arthritis

Laboratory finding	No. of cases (%)
Elevated ESR (≥20 mm/h) (n = 56)	50 (89)
Tc-99m bone scan (n = 37)[a]	33 (89)
Synovial fluid culture (n = 57)[b]	36 (63)
X-ray findings (n = 43)[c]	22 (51)
WBC >15 000 /mm^3 (n = 58)	23 (40)
Positive blood culture (n = 52)	14 (27)[a]

Abbreviations: ESR = erythrocyte sedimentation rate; WBC = white blood cell

[a]33 cases had septic arthritis; 19 had concomitant osteomyelitis.

[b]A total of 43 cases had etiologic agents identified.

[c]X-ray findings on admission: joint space widening and soft tissue swelling.

Forty percent of the patients had an increased peripheral white blood cell count above 15 000 cells / mm^3. C-reactive protein ranged from 1 to 340 mg/L, with a mean of 59 mg/L. The mean ESR at admission was 65 mm/h. Erythrocyte sedimentation rate was elevated (≥20 mm/h) initially in 89% of the cases. Twenty-seven percent of the patients (14/52) had bacteremia. Culture of the synovial aspirates yielded etiologic organisms in only 63% of cases (36/57). Initial laboratory findings in the 58 pediatric patients with septic arthritis are listed in Table 2. The predominant organisms were *S. aureus* (25), 6 of which were methicillin-resistant *S. aureus* (MRSA), followed by CoNS (6), *Streptococcus pneumoniae* (3), *Salmonella* spp. (3), *Haemophilus influenzae* type b (Hib) (2), and group B *Streptococcus* (2). Table 3 summarizes the microorganisms isolated from 58 patients with acute septic arthritis in 2 different time periods. An increase in the number of cases of *S. aureus* joint infection was noted in the second part of the study period ($p=0.185$). *Salmonella* spp. and Hib joint infection were found only in the first period.

Forty-three patients received combined antibiotic treatment and surgical drainage, and 15 patients received antibiotics alone. The concomitant complications of septic arthritis were sepsis (9%, 5/58) and meningitis (2%, 1/58). Concomitant osteomyelitis was found in 19 (33%) of the patients. Therapy-related problems (drug fever and drug rash) occurred in 12% of the patients. Pathogens in patients with osteomyelitis were *S. aureus* (53%, 10/19), *Salmonella* spp. (11%, 2/19), CoNS (5%, 1/19), and unidentified (32%, 6/19). Localization of bone involvement was in the femur (9 patients), tibia (4), pubic (2), humerus (2), radius (1), scapula (1), calcaneus (1), talus (1), and acetabulum (1).

The duration of follow-up period ranged from

Table 3. Microorganisms isolated from 58 patients with acute septic arthritis at different study periods

Microorganism	No. of cases (%)		
	1988-1994	1995-2000	Total
Staphylococcus aureus[a]	10 (35)[b]	15 (52)[c]	25 (43)
Coagulase(-) *Staphylococcus*	3 (10)	3 (10)	6 (10)
Streptococcus pneumoniae	1 (3)	2 (7)	3 (5)
Salmonella spp.	3 (10)	0	3 (5)
Haemophilus influenzae b	2 (7)	0	2 (3)
Group B *Streptococcus*	1 (3)	1 (3)	2 (3)
Other[d]	1 (3)	1 (3)	2 (3)
Unknown	8 (28)	7 (24)	15 (26)
Total	29 (100)	29 (100)	58 (100)

[a] p=0.185.
[b] Three isolates were methicillin-resistant *S. aureus*.
[c] Three isolate were methicillin-resistant *S. aureus*.
[d] Other pathogens included *Escherichia coli* (1 case) and *Enterobacter cloacae* (1 case).

6 months to 5 years (median, 13 months after hospitalization). No patient had relapse of infection. Follow-up of these patients showed that 10 patients had developed sequelae, including limitation of motion (6), limping gait (2), limb-length discrepancy (1), and abnormalities of bone growth (1). The 10 patients with sequelae had the following characteristics: 80% were under 1 year old at the time of diagnosis; 9 patients had concomitant osteomyelitis; 4 had joint symptoms for 4 days or more before diagnosis; and 7 had *Staphylococcus* as the causative organism and 2 had *Salmonella* spp. The clinical features of the 10 patients with sequelae following septic arthritis are summarized in Table 4. Risk factors for the occurrence of sequelae following septic arthritis are shown in Table 5. High risk was associated with infections at age below 1 year, shoulder arthritis, white blood cell count over 15 000 / mm^3, concomitant osteomyelitis, and infection due to MRSA (p<0.05). Infants with *Salmonella* arthritis and concomitant osteomyelitis were apt to have sequelae (RR, 1.3, 95% CI, 0.9-1.7). Risk factors identified by multiple logistic regression were concomitant osteomyelitis and infection due to MRSA (RR, 46.4, 95% CI, 2.9-748.8; RR 16.2, 95% CI, 1.3-204.9, respectively).

Discussion

Most children with septic arthritis were previously healthy. In this series, 97% of the cases were healthy before onset of septic arthritis. Pyogenic arthritis is a disease that occurs in children, most commonly in infants and toddlers. In this study, 62% of children with septic arthritis were younger than 5 years.

The hip was the most common site of infection. Previous studies reported that septic shoulder occurred with 3% to 5% incidence in children with septic arthritis [4-6]. Septic shoulder is a primarily disease of infancy [7,8]. Four of the 5 patients with septic shoulder in this

Table 4. Clinical characteristics of 10 patients with chronic sequelae following septic arthritis

Case no.	Age/sex	Joint involved	Pathogen	Delayed treatment (day)	Osteomyelitis	Sequelae[a]
1	21 d/M	Knee	MSSA	0	Femur	Limping gait
2	8 mo/F	Shoulder	MRSA	4	–	Shoulder stiffness
3	13 d/M	Knee	Unknown	0	Femur	Abnormalities of bone growth
4	19 d/F	Shoulder	MSSA	3	Humerus	Shoulder stiffness
5	5 yr/M	Ankle	MRSA	0	Tibia	Abnormalities of bone growth
6	10 mo/M	Shoulder	*Salmonella enteritidis*	30	Humerus	Limitation of ROM
7	4 yr/M	Knee	MRSA	3	Femur	Limitation of ROM
8	43 d/F	Knee, ankle	MRSA	6	Femur, tibia	Limitation of ROM
9	7 mo/M	Hip	CoNS	3	Femur	Limping gait
10	11 mo/F	Knee	*Salmonella choleraesuis*	14	Shoulder, femur, tibia	Limb length discrepancy

Abbreviations: MSSA = methicillin-susceptible *Staphylococcus aureus*; MRSA = methicillin-resistant *Staphylococcus aureus*; CoNS = coagulase-negative staphylococci; ROM = range of motion
[a] Follow-up: 1 month to 5 years (median, 2 months).

Table 5. Potential risk factors for sequelae in 58 patients with septic arthritis

Risk factor	SA with sequelae (n = 10)	SA without sequelae (n = 48)	Univariate analysis RR (95% CI)	Multivariable analysis RR (95% CI)
Age <1 year	8	11	13.5 (2.5-72.9)[a]	
Hip	1	31	0.6 (0.1-0.5)[a]	
Knee	5	12	3.0 (0.7-12.2)	
Shoulder	3	2	9.9 (1.4-69.9)[b]	
MRSA	4	2	15.3 (2.3-102.4)[a]	16.2 (1.28-204.9)[b]
MSSA	2	17	0.5 (0.1-2.4)	
Salmonella	2	1	11.8 (0.9-145.3)	
Delayed treatment ≥4 days	4	23	0.7 (0.2-2.9)	
Osteomyelitis	9	10	34.2 (3.9-302.6)[a]	46.4 (2.9-748.8)[a]
Sepsis	2	3	3.8 (0.5-26.1)	
WBC >15 000 /mm^3	9	14	21.9 (2.5-189.1)[a]	
CRP > 50 mg/L	5	16	2.2 (0.5-10.5)	
ESR >50 mm/h	8	27	2.8 (0.5-14.8)	
Osteomyelitis + age <1 year	7	0	3.3 (1.3-8.6)[a]	
Osteomylitis + *Salmonella*	2	0	1.3 (0.9-1.7)[b]	

Abbreviations: SA = septic arthritis; RR = relative risk; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *Staphylococcus aureus*; WBC = white blood cell; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate

[a] $p<0.01$.

[b] $p<0.05$.

study were under 1 year of age. A high occurrence (60%) of sequelae was associated with shoulder involvement. None of the 5 patients with septic shoulder had a history of antecedent trauma or infected intravenous catheter site.

An etiologic agent was found in 74% of patients through either synovial fluid culture and/or blood culture. Negative cultures may be ascribed to prior antibiotic therapy and/or to the inhibitory effect of pus on bacteria. This study found that *S. aureus* was the most common infecting microorganism in septic arthritis in children. *S. aureus* arthritis is a rapidly destructive disease of the joint in childhood. *S. aureus* septic arthritis can occur as a complication of septicemia or local trauma [9]. Staphylococcal pathogenicity depends upon the host immune system in dealing with a wide variety of bacterial surface factors including the cell wall, capsular polysaccharide, collagen receptors, and fibronectin-binding protein [10]. The tropism of *S. aureus* to septic joints is related to collagen receptors on the surface of pathogenic strains of *S. aureus* [11]. In this study, 24% of *S. aureus* isolates were MRSA. The rate of *S. aureus* septic arthritis increased from 35% from 1988 to 1994 to 52% from 1995 to 2000. There was no significant increase in the rate of isolating MRSA between the 2 study periods (3/10 vs 3/15). Methicillin-resistant *S. aureus* infection in children is more likely to be hospital-acquired than community-acquired [12]. Gorak *et al* [13,14] reported community-acquired MRSA infections in previously healthy children without identified predisposing factors. All 6 cases of MRSA septic arthritis in this study were community-acquired infection and diagnosed in otherwise healthy patients.

The invasive diseases caused by Hib in Taiwan include meningitis, pneumonia, septicemia, cellulitis, and septic arthritis [15-17]. In the United States, septic arthritis accounted for almost 7.6% of all systemic diseases caused by Hib in children [18], while it accounted for about 3% of all invasive Hib diseases in Taiwan children [17]. Before vaccination, Hib accounted for 34% to 41% of septic arthritis in children less than 2 years of age in western countries [19,20]. In this study, only 2 (3%) patients had Hib septic arthritis. *H. influenzae* type b is no longer the predominant isolate in young children with septic arthritis after implementation of Hib immunization [2,21]. In previous studies, Hib septic arthritis often preceded or was accompanied by upper respiratory infection and/or otitis media (43%) [2,22]. Preceding respiratory illness was uncommon in patients of this study because Hib is not a common cause of septic arthritis. Septic arthritis caused by Hib was concurrent with meningitis (30%) and osteomyelitis (22%) [22]. In this study, neither of the 2 cases of Hib septic arthritis was complicated with meningitis or osteomyelitis.

In 1986, Welkon *et al* [2] reviewed 95 cases of septic arthritis and found that approximately 1% was caused by *Salmonella* species . In this study, *Salmonella* species was associated with 5% of pediatric cases of septic arthritis. The reported incidence of bacteremia among children with non-typhoidal *Salmonella*

gastroenteritis varies between 6.5% and 24.3% in Taiwan [23,24]. *Salmonella* septic arthritis may develop during the course of *Salmonella* bacteremia in infants. In Taiwan, a previous study indicated a higher incidence of extraintestinal complications of *Salmonella* serogroup D1 infection [24,25]. *Salmonella* C1 was the most common cause of septic arthritis in adults [26, 27]. *Salmonella choleraesuis* had a high predilection for bone and joint infection [27]. One isolate of *Salmonella* belonging to group D1 (*Salmonella enteritidis*) and one belonging to C1 (*S. choleraesuis*) were isolated in this study. One patient had concurrent gastroenteritis and the other had prolonged fever without a focus. Factors contributed to the development of *Salmonella* septic arthritis included hemoglobinopathy, systemic lupus erythematosus, and previous trauma [28]. In this study, *Salmonella* septic arthritis occurred in 2 previously healthy infants. The virulence of bacteria and the immaturity of immune system increased the risk of occurrence of septic arthritis in the infants [29].

Previous reports showed that the development of sequelae in septic arthritis was significantly associated with the following conditions: 1) delay of treatment; 2) involvement of the hip or shoulder; 3) inadequate treatment; 4) concomitant osteomyelitis; and 5) *S. aureus* as the causative organism [2,5,30-33]. In this study, chronic sequelae were associated with infection at age less than 1 year, shoulder arthritis, white blood cell count over 15 000 /mm^3, concomitant osteomyelitis, and infection due to MRSA ($p<0.05$). Neonates in particular are at high risk for the development of sequelae because of immaturity of immune function and concomitant osteomyelitis. Delayed diagnosis (≥4 days) and treatment (47%) was common in this study and was not associated with development of sequelae. Initial empirical antibiotic therapy for septic arthritis in the study included a penicillinase-resistant penicillin (such as oxacillin) and an agent against gram-negative bacteria (such as gentamicin). Oxacillin will cover the most common infectious organisms and may be used as initial antibiotic therapy. Septic arthritis of the hips and shoulders should be treated immediately with surgical drainage. In this study, inadequate treatment was not a likely risk factor because of correct initial antibiotic therapy and no delay in appropriate surgical drainage of the joint.

In summary, an increase in the number of cases of *S. aureus* joint infection was found during the study period. Methicillin-resistant *S. aureus* posed a major challenge in treatment. *Salmonella* septic arthritis may develop following *Salmonella* gastroenteritis and bacteremia in infants. It appears, however, that children with septic arthritis are particularly vulnerable to sequelae if the illness occurs within the first year of life. A high incidence of concomitant osteomyelitis (33%) was noted in this series. In infancy, septic arthritis with concomitant osteomyelitis and infection due to MRSA was associated with an increased risk of sequelae.

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