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Acute osteomyelitis and septic arthritis in children

A referral hospital-based study in Iran

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Summary Information concerning the epidemiology of acute osteomyelitis (OM), septic arthritis (SA) and concurrent OM and SA in children is limited. The aim of this study was to describe the epidemiology of OM, SA and concurrent OM and SA in children. During the 4 years of the study, 63,999 patients were admitted to the Children's Hospital, Tehran, Iran. We identified 111 patients with OM and/or SA during the 4-year period. There were 72 cases of OM (11 cases per 10,000 children) and 90 cases of SA (11 cases per 10,000 children). Concurrent OM and SA accounted for 0.17% of all cases (n = 51). The erythrocyte sedimentation rate and C-reactive protein were elevated in the majority of both infections. *Staphylococcus aureus* was the most frequent pathogen responsible for both OM and SA in any age group. The lower limb was the most frequently affected (femur: 33/72, 46%; tibia or fibula: 22/72, 31%; foot: 5/72, 7%). The most frequent involved joints were hips (n = 31, 34%) and knees (n = 31, 34%). The present study showed high frequency of patients with concurrent SA and OM. Therefore, prompt recognition and proper diagnosis of pediatric OM and SA is highly recommended.

Keywords Inflammatory diseases · Iran · Osteomyelitis · Septic arthritis · Children

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Introduction

Acute osteomyelitis (OM) and septic arthritis (SA) are two inflammatory diseases that affect bone and synovial joints, and both are primarily caused by bacterial infection [1–3]. They can occur alone or in combination. The incidence of these diseases is about eight cases per 100,000 children annually and high prevalence of them is found in children aged less than 5 years; however, recently, an increase in their incidence has been observed and is thought to be more common in low-income countries [2, 4].

Early diagnosis and initiation of proper treatment of OM and SA are essential to obtain a better outcome and avoid devastating sequelae. These diseases cannot be treated correctly because they could be associated with sepsis and with complications such as joint destruction, growth failure, and death of the patient if they are not correctly treated [3].

The pathogens responsible for OM and SA infections in children have changed with alterations in immunization practices and emergence of resistant bacteria [5].

Unfortunately, in several cases, the culture is negative and the other invasive procedures are not performed in the first years of life [3].

Staphylococcus aureus is definitely the most frequent pathogen responsible for OM and SA in any age group, and it is responsible for up to 70–90% of confirmed cases [6].

In children less than 2 months of age, *Streptococcus agalactiae* and other Gram-negative organisms are re-

ported as other potential pathogens. However, in children between 2 and 5 years of age, *Streptococcus pyogenes* and *Streptococcus pneumoniae* should be considered [7]. *Haemophilus influenzae* type b was considered a common cause of acute osteoarticular infections in children [8]. However, after the introduction of large-scale vaccination programs, the number of cases of OM and SA due to *H. influenzae* type b has significantly decreased [3].

Information concerning the epidemiology of OM, SA and concurrent OM and SA in children is limited because of several factors. They are uncommon diseases and few reports of series containing more than 50 cases have been published [7]; therefore, the aim of this study was to describe the frequency of OM, SA and concurrent OM and SA in children.

Material and methods

Patient population

After approval by our institutional review board, we performed a retrospective study of children up to 16 years old who were admitted at our hospital for OM and/or SA between April 2010 and March 2014. All patients underwent appendicular musculoskeletal MRI examinations for any suspected musculoskeletal infection, including suspected OM, SA, or both. In addition, clinical records were reviewed to confirm the diagnosis on the basis of a combined review of MRI findings; microbiology, pathology, and operative reports; orthopedic consultation; infectious disease service notes; and discharge summaries. Diagnosis was made by blood or synovial fluid, histology, imaging, and/or clinical presentation. Surgery was indicated when the largest dimension of fluid collection was >1 cm, and ranged from percutaneous drainage to wound debridement and wash out.

Laboratory studies including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and culture results were reviewed.

Data were collected by a trained data abstractor. The data extracted from the medical records were the patient's age, sex, bone(s) involved, results of bone aspirate culture and blood culture.

Definitions

Acute osteomyelitis

Acute osteomyelitis was defined as a clinical episode in which a patient had at least one or more of the following: fever higher than 37.5 °C, leukocytosis (White Cell Count [WCC] >13,000/ml), raised ESR (> 20 mm) or a positive blood culture plus one of more of the following: positive technetium bone scan, bony point tenderness and/or swelling and redness or findings consistent with osteomyelitis on plain X-ray, CT scan or MRI or a positive microbiological culture from a bone biopsy or bone aspirate [9].

Septic arthritis

Septic arthritis was defined as a clinical episode in which a patient had at least one or more of the following: fever higher than 37.5 °C, leukocytosis (WCC >13,000/ml), raised ESR (>20 mm) or a positive blood culture plus one of more of the following: technetium bone scan consistent with septic arthritis, joint pain and tenderness and restricted range of movement, joint effusion detected clinically or with ultrasound or a positive culture from aspirated joint fluid or pus cells and/or bacteria detected on microscopy of joint fluid and a negative culture (if patients had received prior antibiotic therapy; [9]).

Statistical analysis

Descriptive statistics were used to summarize all demographic and laboratory characteristics of the patients. All statistical analyses were done using the statistical package SPSS 16.0 (SPSS Inc. Chicago, IL, USA).

Results

Number of episodes

During the 4 years of the study, 63,999 patients were admitted to the Children's Hospital, Tehran, Iran. There were 72 cases of OM (11 cases per 10,000 children) and 90 cases of SA (11 cases per 10,000 children) during the study period. Concurrent OM and SA accounted for 0.17% of all cases. We identified 111 patients with OM and/or SA during the 4-year period. Twenty-one subjects had only OM, 39 cases had only SA and 51 cases had concurrent OM and SA. In all groups (OM, SA and concurrent OM and SA), the majority of cases were boys (Table 1).

Patient demographics

The demographic characteristics of all cases are described in Table 1. In the OM group, there were 48 males and 24 females (male:female ratio 2:1). The age range was from 2 weeks to 16 years. In the SA group, there were 61 males and 29 females (male:female ratio 2.1:1) and the age range was from 5 days to 16 years.

The majority of cases with OM and/or SA was less than 5 years (66% of cased with OM, 72% of cases with SA and 62% of cases with concurrent OM and SA) (Table 1).

The mean duration of hospital stay in cases with OM, SA and concurrent OM and SA were 18, 19.2 and 20.2 days, respectively.

The underlying conditions identified for the majority of patients was trauma (n = 36, 40% in cases with OM and n = 26, 36% in cases with SA, respectively). Immunodeficiency was found in 6% of cases with SA and 11% of cases with OM.

Table 1 Clinical characteristics of cases with septic arthritis (*SA*), acute osteomyelitis (*OM*) and concurrent SA and OM

		SA	OM	Concurrent SA and OM
		N (%)	*N* (%)	*N* (%)
Sex	Male	61 (68)	48 (67)	35 (69)
	Female	29 (32)	24 (33)	16 (31)
Age	≤1 month	10 (11)	7 (10)	7 (14)
	1 month to 1 year	24 (27)	21 (29)	17 (33)
	1–5 years	25 (28)	24 (33)	13 (25)
	5–10 years	22 (24)	13 (18)	9 (18)
	≥10 years	9 (10)	7 (10)	5 (10)
Culture	*S. aureus*	17 (19)	11 (15)	11 (22)
	Pseudomonas aeruginosa	1 (1)	1 (1)	1 (2)
	Gram-negative cocci	1 (1)	0 (0)	0 (0)
	Streptococcus spp	4 (4)	2 (3)	2 (4)
	Coagulase-negative Staphylococci	5 (6)	2 (3)	2 (4)
	Mycobacterium tuberculosis[a]	1 (1)	1 (1)	1 (2)
	Klebsiella pneumoniae	1 (1)	2 (3)	1 (2)
	Aspergillus spp	1 (1)	1 (1)	1 (2)
	Escherichia coli	1 (1)	1 (1)	1 (2)
	Enterobacter spp	1 (1)	0 (0)	0 (0)
	Negative	41 (46)	29 (40)	20 (39)
	Not performed	16 (19)	22 (31)	11 (22)
Surgery	Open	44 (49)	30 (42)	27 (53)
	Close	22 (24)	10 (14)	10 (20)

[a]Detected using PCR method

Table 2 Laboratory characteristics of cases with septic arthritis (*SA*), acute osteomyelitis (*OM*) and concurrent SA and OM

	SA	OM	Concurrent SA and OM
WBC (Mean ± SD)[a]	13,361 ± 5509	12,980 ± 55.4	13,282 ± 5994
WBC (Mean ± SD)[b]	9235 ± 2794	9566 ± 3022	9662 ± 2865
PMN (Mean ± SD)[a]	53.7 ± 19.2	49.9 ± 18.9	51.7 ± 19.3
PMN (Mean ± SD)[b]	40.7 ± 16.8	38.5 ± 15.7	38.6 ± 14.7
ESR (Mean ± SD)[a]	59.9 ± 34.2	54.4 ± 32.7	59.7 ± 35.3
ESR (Mean ± SD)[b]	36.1 ± 23.5	32 ± 21	34 ± 22.7
CRP (Median ± IQ)[a]	48 ±20	30 ± 8.9	40 ± 12
CRP (Median ± IQ)[b]	6 ± 0.8	3.3 ± 0.8	2.6 ± 0.6

[a]At admission
[b]At discharge
WBC White Cell Count, *PMN* Polymorphonuclear leukocytes, *ESR* Erythrocyte sedimentation rate, *CRP* C-reactive protein, *SD* Standard deviation, *IQ* Interquartile range

Laboratory findings

Erythrocyte sedimentation rate (ESR) and CRP were elevated in the majority of both infections, with no significant difference in the proportion of patients with an elevated ESR in SA compared with OM. More than half of the cases with SA (n = 50) had leukocytosis of more than 13,000/mm^3. The ESR ≥40 mm/h and CRP ≥30 mg/l were found in 72% (n = 65) and 63% of cases (n = 57) with septic arthritis.

In the OM group, an elevation of the white blood cell count over 13,000/ml was seen in 35%. Eighty-six of the 102 children had an ESR performed on admission and this investigation was elevated (20 mm or greater) in 70% the patients.

Laboratory results on admission and discharge are shown in Table 2.

S. aureus was the most frequent pathogen responsible for both OM and SA in any age group, and it is responsible in 52% of confirmed cases (17/33 in SA group and 11/21 in OM group, Table 1).

Thirty-three subjects with SA had positive culture (3 have positive blood culture and the rest of them had positive synovial fluid). The most frequent isolated bacteria was *S. aureus* (n = 19, 52%) followed by coagulase-negative staphylococci (n = 5, 15%) and *Streptococcus* spp. (n = 4, 12%) (Table 1). *Streptococcus* spp. was isolated from 75% of cases less than 1 month (n = 3) and one case was 10 months old.

The lower limb was the most frequently affected (femur: 33/72, 46%; tibia or fibula: 22/72, 31% and

foot: 5/72, 7%) followed by the upper limb (humerus: 6/72, 8%; radius or ulna: 2/72, 3.0%), vertebrae (1/72, 1%) and other sites (3/72, 4%). The most frequent involved joints were hips (n = 31, 34%) and knees (n = 31, 34%).

Discussion

The cause and epidemiology of SA and OM have changed over recent years. The present study shows a high number of patients with concurrent SA and OM in comparison to the literature. According to previous reports, OM can occur concurrently with SA at a rate of 3–33% [10, 11], while in our study it was seen in 46% of cases (n = 51). There are concerns about the increased rate of these infections in children in our study. Delay in diagnosis of patients with OM might be one of the probable reasons for the high concurrent rate with SA. Delays in treatment of OM may not only lead to complications such as concurrent septic arthritis, but can also lead to subperiosteal abscess, pyomyositis, deep vein thrombosis, permanent impairment, septicemia, multiorgan failure, and even death [11]. Therefore, a high index of suspicion is highly required as early treatment of OM. On the other hand, lower socioeconomic status such as overcrowding, poor hygiene, and sanitation have been proposed as causes of increased infection rates [4].

Similar to previous reports, there was a higher incidence of these diseases in males, most likely because they are more physically active, which predisposes them to repeated microtrauma [2, 12–14].

In our study, no causative pathogen was identified in 46% of SA and 40% of OM cases. Recent studies have reported that a causative pathogen is not identified (negative cultures) in 38–55% of osteoarticular infections [4, 5].

In the Calvo et al. study, among 641 children, 299 cases (46%) were OM and 232 (36%) were SA and isolation of bacteria was significantly higher in patients with SA than cases with SA (55% SA vs 33% OM) [15], while in our study the frequency of isolated bacteria in the two groups was not significantly different (33/80, 41% in SA vs 21/72, 29% in OM, $P \geq 0.05$).

In another study, among 79 patients, 57 (72%) had concurrent OM and SA and 22 (28%) had septic arthritis alone [4]. Brischetto et al. reported that ethnic discrepancy has a role in 10-fold higher rate of bone and joint infections in indigenous populations [4].

S. aureus was the confirmed pathogen in 52% of cases which was similar to other reports [4, 12] and lower than reported by the studies Brischetto et al. in Northern Australia, Russell et al. in Edinburgh and Calvo et al. in Spain [4, 13, 15].

Lower-limb osteomyelitis and knee arthritis predominantly occurred in children [16]. The lower limbs mainly involved were tibia and femur that was consistent with previous reports [4]. Hips, knees, and ankles are the most frequently involved joints [4–6] and in this study the most frequent involved joints were hips (n = 31, 34%) and knees (n = 31, 34%).

The most common site for microbiological yield was in sampling of the affected joint in (91%) of patients, whereas the remaining (9%) had positive blood cultures. In the Brischetto et al. study, 23% had positive blood culture and the rest of them had positive culture of the affected joint [4]. In the Russell et al. study, culture of articular fluid was positive in 45.7% (21/46) of cases and 33.3% of children (13/39) had positive blood culture [13].

Proper diagnosis of OM and SA are certainly important. In our study, treatment was based on antimicrobial susceptibility test results in cases with positive isolated cultures. Patients with negative bacterial cultures were treated with first generation cephalosporin and cloxacillin. When improvement was not obtained, clindamycin was administered and the majority of these patients were treated.

In conclusion, efficient and safe management of pediatric OM and SA mandates prompt recognition and proper diagnosis. Since 39–46% of our cases with acute osteomyelitis, septic arthritis as well as concurrent osteomyelitis and septic arthritis had negative bacterial culture, improvement of facilities for detection of pathogens including polymerase chain reaction testing are highly recommended [17].

Conflict of interest S. Mahmoudi, B. Pourakbari, K. Borhani, M. Khodabandeh, S.K. Valian, A. Aziz-Ahari, and S. Mamishi declare that they have no competing interests.

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