Iranian J Publ Health, Vol. 36, No.3, 2007, pp.27-32

Original Article

Etiology and Antimicrobial Susceptibility of Bacterial Septic Arthritis and Osteomyelitis

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(Received 2 Dec 2006; accepted 22 Apr 2007)

Abstract

Background: To assess the distribution and resistance of the pathogens responsible for septic arthritis and osteomyelitis over a 10 years period in children admitted to Children's Medical Center Hospital, Tehran, Iran.

Methods: Microbiologic and clinical presentation reports from 145 cases of septic arthritis and osteomyelitis from March 1995 to February 2005 were retrospectively reviewed.

Results: Of 145 cases, 71(49%) had positive culture: 71.8%(51/71) of organisms were isolated from synovial fluid alone, 8.4%(6/71) from blood culture alone and 19.7% (14/71) from both synovial fluids and blood cultures. *Staphylococcus aureus* was the most common pathogen isolated, making up 60.5% of all positive cultures, followed by *Klebsiella* spp. (14%) and coagulase-negative staphylococci (8.4%). Thirty eight percent of *S. aureus* and 84% of coagulase-negative staphylococci isolates were resistant to cloxacillin. All isolates of *S. aureus* were susceptible to clindamycin and also, 89% were susceptible to vancomycin. Among *Klebsiella* spp., amikacin was shown to be very effective, with susceptibility rates of 100%. *Haemophilus influenzae* was identified in only 2% of all patients.

Conclusion: The present study highlights the importance of characterizing the etiology and antibiotic susceptibility of organisms causing septic arthritis or osteomylitis in children.

Key words: *Antimicrobial agents, Osteomyelitis, Aarthritis septic*

Introduction

Septic arthritis (SA) refers to all joint infections caused by pyogenic bacteria. It is not a common condition; the overall estimated incidence in Europe is reported as 2-6 cases per 100 000 population per year (1-2). Osteomyelitis can be described as 'acute or chronic' and 'haematogenous or contiguous', according to the duration and source of infection, respectively (3). Osteomyelitis in pediatric patients is usually haematogenous in origin and mainly occurs in the long bones (4). There is distinct variability in the causative organisms of SA and osteomyelitis in different parts of the world. In most European and North American reports the most common bacterial isolates in septic joints have been *Staphylococci* and *Streptococci* (1-2, 5-8), with *Neisseria gonorrhoeae* particularly prevalent in North America. Iran is a Middle East country with endemic pathogens charcteristic of that region. Despite advances in antiiotic treatment, SA still results in considerable morbidity and mortality in fragile patients. Prognosis worsens when appropriate antibiotic treatment is delayed (9). In the absence of clear indiation of the causative organisms, the initial choice of antibiotics is empirical. However, studies have shown an increasing incidence of gram negative bacilli (2, 10). Other studies have shown an inreasing emergence of methicillin-reistant *Staphyococci* (MRSA) and *Pneumococci* (7, 11).

In many parts of the world, including Iran, information regarding the etiology and antibiotic resistance of bacteria isolated from SA and osteomyelitis are absent. Epidemiological studies have demonstrated that data regarding susceptibility patterns of bacteria from a geographical region are

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essential for controlling the local spread of resistance in geographical regions. Moreover, understandding of bacterial susceptibility is crucial for rational treatment of infections and infection control programs. To illustrate the distribution and sensitivity pattern of pathogens causing SA and osteomyelitis, we report the related data from patients in Children's Medical Center (CMC) Hos-pital in Tehran, Iran.

Materials and Methods

The present retrospective study included 145 cases of SA and osteomyelitis (61 cases with SA, 38 with osteomyelitis and 46 with both SA and osteomyelitis) who were admitted to the CMC hospital from Mar 1995 to Feb 2005. SA and osteomyelitis were defined by clinical criteria (12): i) Microbial pathogen identified in, or isolated from, synovial fluid or joint tissue or bone biopsy, ii) Typical features of SA or osteomyelitis with pathogen isolated from blood iii) Pus obtained from the joint or subperiosteum, but culture was sterile due to previous administration of antibiotics, iv) Pathologic or radiographic evidence of osteomyelitis with clinical features of osteomyelitis. Age, sex, trauma history, fever, previous antibiotic therapy, and underlying diseases such as immunodeficiency, hemophilia, steroid treatment, malignancy and diabetes were recorded. After review of microbiology reports, information about isolates and antimicrobial susceptibility was collected and recorded. The antimicrobial selected for analysis were those commonly included in the treatment of patient with SA and osteomyelitis in Iran. Isolation and identification of organisms were performed by conventional biochemical test in the microbiology laboratory of CMC hospital. Antimicrobial susceptibility testing of isolates was performed by the disk diffusion method as stated earlier (12, 13).

Results

SA and osteomyelitis were more common in males than females (56% for males versus 44% for females). Mean age of our patients was 18 mo with range of 6 d to 15 yr. The most frequent presenting symptom was pain reported by 69.6% of the patients followed by fever in 68% of them. Leukocytosis, defined as leukocyte counts above 11×10^9/L, was recorded in 47.5% of the patients. The most common involved joints in patients with SA were knee and hip by 29.6% and 17.2%, respectively. In 50% of patients, arthritis was diagnosed in a single joint. In addition, femur and tibia with 13.7% and 11%, respectively, were the most common bones that involved by osteomyelitis in our patients. Three patients had immunodeficiency. Two of them had chronic granulumatous disease and one case had X-linked agammaglobulinemia. Forty seven percent of the cases were culture positive; 71.83% of microorganisms recovered from synovial fluid alone, 8.45% from blood cultures alone, and 19.71% from both synovial fluid and blood cultures. Twenty nine percent of culture negative patients had received antibiotics before admission. The diagnosis of culture-negative SA or osteomyelitis was established based on clinical features and response to antibiotic therapy, synovial fluid characteristics, biopsy, and imaging studies. Table 1 shows organisms that isolated from this series of patients. Gram positive bacteria accounted for 78.87% of all isolated bacteria.

Overall, *Staphylococcus aureus* was the most frequent group of recovered organisms, consisting 61% of all isolates followed by *Kelebsiella* spp. comprising 14.2% of all.

The antimicrobial susceptibility patterns of common pathogens isolated from patients with SA and osteomyelitis or both are shown in Table 2. Rates of antibiotic resistance among coagulase negative *Staphylococci* were higher than *S. aureus* strains.

Table 1: The organisms isolated from 71 children with septic arthritis and osteomyelitis.

Organism	no.	%
Staphylococcus aureus	43	61
Klebsiella spp	10	14.2
Coagulase negative *Staphylococci*	7	10
Group B *Streptococci*	5	7.2
Haemophilus influenzae	2	2
Enterobacter spp.	2	2
Streptococcus pneumonia	1	1.5
Campylobacter spp.	1	1.5

Table 2: Susceptibility pattern of bacterial species isolated from children with septic arthritis and osteomyelitis.

Organism	Antimicrobial Susceptibility Percent												
	Amikacin	**Gentamicin**	**Kanamycin**	**Vancomycin**	**Clindamycin**	**TMP-SMZ**	**Cephalothin**	**Chloramphenicol**	**Erythromycin**	**Ceftazidime**	**Cloxacillin**	**Ampicillin**	**Penicillin**
Staphylococcus aureus	88	79	86	89	100	76	78	91	76	71	62	5	0
Klebsiella spp.	100	30	40	NA	NA	50	25	50	NA	NA	NA	0	NA
Coagulase negative *Staphylococci*	33	50	NA	67	75	67	83	83	0	0	16	67	16
Group B *Streptococci*	25	60	NA	100	100	0	80	100	80	50	100	50	60
Haemophilus influenzae	100	100	100	NA	NA	100	NA	100	NA	NA	100	100	100
Enterobacter spp.	100	50	50	NA	NA	50	0	0	NA	0	NA	0	NA
Streptococcus pneumonia	100	100	NA	100	100	100	100	100	0	0	0	100	0
Campylobacter spp.	100	100	NA	100	100	100	100	100	0	0	0	100	0

NA, not assessed

Discussion

To our knowledge, this is the first large-scale study about occurrences, etiology and antimicrobial susceptibility pattern of bacteria that cause SA and osteomyelitis in Iran.

These data seems to be essential because i) information about occurrences and clinical characteristics of patients with SA and osteomyelitis are unknown, ii) data regarding the etiology and antimicrobial susceptibility of bacteria that cause SA and osteomyelitis are scarce and iii) understanding of etiology and antimicrobials susceptibility of major bacteria that cause SA and osteomyelitis in Iranian children provide essential information regarding rational use of antibiotics in these settings.

The male preponderance of SA and osteomyelitis in our series is similar to earlier studies (14, 15). We found that the clinical and laboratory signs of SA and osteomyelitis can be subtle. A normal temperature or white blood cell count is a common finding. This study supports that the most common age of presentation is before 2-yr old (16, 17).

Thirty eight percent of our patients had history of trauma before infection, thus we should ask about trauma when we take the medical history. When a child presents with either SA or osteomyelitis, microbiological cultures should be taken before administration of antibiotics. Our findings lend support to this concept that no bacterial pathogen is identified in one-third of the cases with SA or osteomyelitis (18-20). The main sites of SA are the knee and hip, followed frequently by ankle and elbow (21-25). In the case of osteomyelitis, tibia and femur are the most common involved bones (26-27).

It has been known for years that a specific bacterial etiology was determined in approximately 70% of patients with osteoarthritis, and the etio-

logical agent was influenced by the age of patients. While *S. aureus*, Group B *Streptococci* and gram negative organisms are isolated in newborns, in older infants, *Haemophilus influenzae* becomes a prominent pathogen. However, *S. aureus* is the most common organism n older children (22-24, 27-28).

In our series, staphylococcal isolates were highly resistant to cloxacillin, which raises concern about the use of cloxacillin as an appropriate choice for treating staphylococcal infections in Iran.

MRSA have become a frequent cause of bone and joint infections in the world (29-32). Coagulase negative *Staphylococci* were found in 9% of our staphylococcal osteoarthritis. This finding is less than other reports from the world (1, 2). However, coagulase- negative *Staphylococci* are sometimes though to be present as a result of skin contamination of the sample while obtaining the specimen and a positive growth of this organism may not therefore be reported (2).

Vancomycin has been widely used in Iran for treatment of infections caused by MRSA. Our data showed that, resistance rates to vancomycin among staphylococcal isolates are growing. This mandates the adherence to universal infection control measures to prevent the spread of multi-resistant strains.

Klebsiella was the second organisms that caused SA or osteomyelitis in our patients. As all of the *Klebsiella* spp. isolates were susceptible to amikacin, this antimicrobial is a suitable first choice.

In our study, *Streptococci* were found in 9% of all isolates. Forty percent of Group B *Streptococci* were resistant to penicillin, thus other alternatives such as cloxacillin, vancomycin or clindamycin should be selected as empiric therapy.

Our finding about frequency of *H. influenzae* in Iran is in sharp contrast to reports of western countries and elsewhere. In the pre-vaccination era, *H. influenzae* type b was the most common causative agent for SA and osteomyelitis in children under 2 yr of age in western countries (33). As immunization against *H. influenza* is not a routine practice in Iran, we should have more positive cultures for *H. influenza*. At present the nature of this unpredictability is not clear.

Our findings give a picture of SA and osteomyelitis in Iranian children. *S. aureus* is still the most common cause; however, methicillin-re-sistant strains are now emerging. For currently obscure reasons *H. influenza* is not a common pathogen in SA and osteomyelitis in Iran. The results of this study could be used as a guide for empiric treatment of SA and osteomyelitis in Iranian children

Acknowledgements

Authors would like to thank the staffs of medical archive office of Children's Medical Center for providing the patients' medical records. Authors warrant that there is no conflict of interest in preparing the manuscript.

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