Microbiology of Bone and Joint Infections in Injecting Drug Abusers

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Abstract

Background The literature contains variable reports on the causative organisms of osteomyelitis and septic arthritis in patients with injecting drug abuse and on the rate of oxacillin-resistant *S aureus*. It is important to have a clear notion of the organisms to initiate empiric antimicrobial therapy.

Questions/purposes We therefore determined the spectrum of organisms in bone and joint infections in patients who were injecting drug users.

Methods We retrospectively reviewed the medical records of 215 patients (154 male, 61 female) with a history of injecting drug abuse and concurrent bone and/or joint infection from 1998 to 2005. The mean age was 43 years (range, 23–83 years). Osteomyelitis was present in 127 of the 215 patients (59%), septic arthritis in 53 (25%), and both in 35 (16%). The lower extremity was most commonly involved (141 cases, 66%), with osteomyelitis of the tibia present in 70 patients (33%) and septic knee arthritis in 30 patients (14%).

Results Cultures yielded predominately Gram-positive bacteria: *Staphylococcus aureus* in 52% and coagulase-negative *Staphylococcus* in 20%. The proportion of

oxacillin-resistant *S aureus* among *S aureus* infections increased from 21% in 1998 to 73% in 2005. Gram-negative organisms were present in 19% of infections and anaerobes in 13%. Patients with osteomyelitis had a higher prevalence of polymicrobial infections (46% versus 15%), infections due to Gram-negative organisms (24% versus 9%), and anaerobic infections (19% versus 6%) compared to patients with septic arthritis.

Conclusions These findings suggest broad-spectrum empiric antibiotic therapy, including vancomycin, should be considered for bone and joint infections in patients with injecting drug abuse.

Level of Evidence Level IV, diagnostic study. See Guidelines for Authors for a complete description of levels of evidence.

Introduction

Injecting drug abuse (IDA) is a major health problem throughout the world. The World Drug Report 2009 indicated approximately 172 to 250 million persons have used drugs at least once in the past year and 11 to 22 million persons aged 15 to 64 years inject drugs [22]. Illicit drug use in the United States has grown from 3 million persons in 1999 [17] to 20 million persons or 8% of the population older than 12 years of age in 2007 [23].

IDA is associated with increased mortality and morbidity; it has been associated with soft tissue infections at the injection site [1, 8, 9, 19], as well as bone and joint infections [10]. Soft tissue infections at the injection site have been well studied in large series of patients [1, 8, 9, 16, 19, 21], including up to 855 patients [1]. We identified ten clinical series specifically reporting on patients with IDA and infections of the bone and joint [2, 4–7, 11, 13–15, 18]. These

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ten clinical series reported 311 cases total, with the largest series consisting of 45 patients and the most recent series published in 2000. The microbiology of bone and/or joint infections in patients with IDA has been reported with considerable variability in the literature. Older studies from the USA evaluating patients up to 1979 identified *Pseudomonas aeruginosa* as the most common pathogen [7, 11, 14, 18], but more recent studies from the USA and Spain reported *Staphylococcus aureus* as the most common [2, 4–6, 13, 15]. Oxacillin-resistant *S. aureus* (ORSA) infections are an emerging problem in patients with IDA [3]. The existing literature has found rates of ORSA infections that vary from 0 to 36% of all infections but nothing has been reported in the past 10 years. Moreover, only three studies evaluated a series of patients treated in the same institution over a time period of 8 years or more but did not assess changes in resistance patterns [4, 15, 18]. *S. aureus* was not a major pathogen in an early study [18] and two subsequent studies did not report ORSA data [4, 15]. Many of the existing studies have focused on patients with septic arthritis only and the remaining studies have reported on small numbers of patients with osteomyelitis that was hematogenous or contiguous in origin. Furthermore, the microbiology of septic arthritis and osteomyelitis has been compared in only one study with limited numbers [6]. More recent data on the microbiology of these infections, comparing septic arthritis to osteomyelitis, could guide empiric antimicrobial therapy in patients with IDA prior to culture results or after results if cultures were negative, especially given the recent increase of oxacillin-resistant *S. aureus* (ORSA) infections in these patients [3].

We therefore determined (1) the most common pathogen in bone and joint infections in more recent patients with IDA, including patients with hardware-associated infections; (2) the rate of oxacillin resistance in these *S. aureus* infections over a long period of time in a single institution; and (3) differences in the microbiology of septic arthritis versus osteomyelitis.

Patients and Methods

We retrospectively reviewed the paper medical records of patients admitted to the orthopaedic infection ward of our institution from 1998 to 2005 with a history of IDA and concurrent bone and/or joint infection. Admitting diagnosis and patient history in the infection ward brief records were screened to identify eligible patients. Out of 4,725 admissions, we identified 215 patients (154 male, 61 female) with a mean age of 43 years (range, 23–83 years), who had culture results available for review and were included in the study. Culture results could not be retrieved in 17 patients and they were excluded.

No patients were recalled specifically for this study. This study had IRB approval.

Osteomyelitis was present in 127 (59%) patients, septic arthritis in 53 (25%), and both conditions in 35 (16%). Sixty-three of 215 infections (29%) were associated with presence of hardware (54 cases of osteomyelitis and 9 cases of osteomyelitis with adjacent septic arthritis). The diagnosis was based on the presence of positive cultures or on the combination of clinical and laboratory findings, such as drainage from sinus tract, pus aspiration from joint, elevated erythrocyte sedimentation rate and elevated c-reactive protein levels. The lower extremity was most commonly involved (141 patients, 66%), followed by the upper extremity (56 patients, 26%), the spine (nine patients, 4%), and the pelvis (nine patients, 4%). The most common location for osteomyelitis was the tibia (70 patients, 33%) and the most common location for septic arthritis was the knee (30 patients, 14%). All patients who had both septic arthritis and osteomyelitis had contiguous involvement of the bones adjacent to the septic joint with no multifocal involvement of distant sites. Bacteremia was present in 66 patients (31%) and endocarditis was diagnosed in 6 patients (3%). Data on HIV status were available on 79 patients and 13 (16%) of these were HIV positive.

The proportion of ORSA among *S. aureus* infections in the first year of the study was compared to that in the last year of the study using the Fisher's exact test. Patients with osteomyelitis were compared to patients with septic arthritis using the Fisher's exact test for categorical variables (culture results, gender) and the two-sample t-test for continuous parametric variables (age). All tests were two-tailed.

Results

S. aureus was the most common microorganism, identified in 111 (52%) of 215 infections, followed by *S. epidermidis* (42 of 215, 20%) (Table 1). Eighteen of 42 patients with *S. epidermidis* had hardware in place, seven patients had no other organism identified in culture, and in eleven patients organisms other than *S. epidermidis* were also identified. Gram-negative rods were present in 40 (19%) of 215 infections, and of these, *P. aeruginosa* was present in 15 (7%) of 215 infections. Anaerobes were identified in 27 (13%) of 215 infections. Culture results were monomicrobial in 101 (47%) of 215 infections and polymicrobial in 70 (33%) of infections. Cultures yielded no growth in 44 (20%) of 215 infections.

The proportion of ORSA among *S. aureus* infections increased significantly ($p = 0.009$) during the period of the study from 21% in 1998 to 73% in 2005 (Fig. 1).

Patients with osteomyelitis and patients with septic arthritis had differing spectra of organisms (Table 2).

Table 1. Culture results in bone and joint infections in patients with injecting drug abuse

Culture results	Number of infections	Percentage (of 215 infections)
<i>Staphylococcus aureus</i>	111	52%
OSSA	68	32%
ORSA	43	20%
<i>Staphylococcus epidermidis</i>	42	20%
Gram-negative bacteria	40	19%
<i>Pseudomonas aeruginosa</i>	15	7%
Streptococcal species	38	18%
Anaerobes	27	13%
<i>Enterococcus faecalis</i>	16	7%
Fungal organisms	9	4%

OSSA = oxacillin-sensitive *Staphylococcus aureus*; ORSA = oxacillin-resistant *Staphylococcus aureus*.

Fig. 1 A graph shows the progressive increase of ORSA isolates expressed as the percentage of *S aureus* infections during the time period of the study.

Patients with osteomyelitis had a higher prevalence of polymicrobial infections (46% versus 15%, $p < 0.001$), infections due to Gram-negative organisms (24% versus 9%, $p = 0.02$), and anaerobic infections (19% versus 6%, $p = 0.02$) compared to patients with septic arthritis.

Discussion

Limited information exists in the literature regarding bone and joint infections in patients with IDA

Table 2. Comparison of patients with septic arthritis and osteomyelitis

Variable	Patients with osteomyelitis (n = 127)	Patients with septic arthritis (n = 53)	p value
Age*	42.4 (24–70)	43.9 (23–72)	0.34
Male gender	93 (73%)	35 (66%)	0.37
Negative cultures	17 (13%)	11 (21%)	0.25
Polymicrobial infections	58 (46%)	8 (15%)	< 0.001
ORSA	26 (20%)	13 (25%)	0.56
<i>S epidermidis</i>	27 (21%)	7 (13%)	0.22
Gram negative rods	31 (24%)	5 (9%)	0.02
<i>Pseudomonas aeruginosa</i>	15 (12%)	1 (2%)	0.04
Anaerobes	24 (19%)	3 (6%)	0.02

ORSA: oxacillin-resistant *S aureus*.

* Age is presented as: mean (range) in years.

All other variables are presented as: number (%) of patients in each group.

[2, 4–7, 11, 13–15, 18]. Some authors reported *P aeruginosa* as the most common pathogen [7, 11, 14, 18], but others identified *S aureus* as the most common [2, 4–6, 13, 15]. The recent increase of ORSA infections in patients with IDA highlights the potential for progressive changes in the microbiology of bone and joint infections associated with IDA [3]. Knowledge of the microbiology of these infections would help optimize empiric antimicrobial therapy in patients with IDA; therefore, we determined the most common pathogen in bone and joint infections in patients with IDA, the rate of oxacillin resistance in these infections caused by *S aureus*, and compared the microbiology of osteomyelitis versus septic arthritis in these patients.

We acknowledge several limitations. First, it is a retrospective record review and some patients with IDA and with osteomyelitis or septic arthritis may have not been identified. Second, culture results were missing in 17 patients, who were excluded from the study. Third, the identification of eligible patients relied on self-admission of IDA by the patient and some patients may have denied use of illicit drugs for various reasons. Moreover, the exact time frame of IDA was not evident and we cannot differentiate between patients who were actively injecting drugs at the time of admission versus the ones who were not injecting at the time their symptoms developed. Fourth, all testing was performed in a clinical laboratory and no further testing for molecular typing was obtained to differentiate between community-acquired and hospital-acquired ORSA. Finally, when extracting data from records we did not record details of the origin and number of the available intraoperative cultures; therefore, we cannot rule out that the *S. epidermidis* identified in some of our patients without hardware in place is not a contaminant.

Table 3. Literature on musculoskeletal infections in patients with IDA

Authors	Year	Patient number	Time period	Location	Diagnosis	Gram N	PA*	S aureus	ORSA*	Strep	S epi	AN	F	MB	Poly
Kido et al. [11]	1973	32	1969–71	USA	OM: 32	32 (100%)	27 (84%)	0	0	0	0	0	0	0	0
Gifford et al. [7]	1975	10	1970–73	USA	SA: 10	10 (100%)	10 (100%)	0	0	0	0	0	0	0	0
Roca and Yoshikawa [18]	1979	24	1969–78	USA	OM: 14 SA: 10	15 (63%)	14 (58%)	4 (17%)	N/A	2 (8%)	1 (4%)	0	1 (4%)	1 (4%)	3 (13%)
Miskew et al. [14]	1983	35	1976–79	USA	OM: 17 SA: 18	35 (100%)	35 (100%)	0	0	0	0	0	0	0	0
Ang-Fonte et al. [2]#	1985	28 (21 IDA)	1981–82	USA	SA: 21	3 (11%)	0	18 (64%)	7 (25%)	8 (29%)	1 (4%)	0	0	0	2 (7%)
Chandrasekar and Narula [6]	1986	45	1982–83	USA	OM: 7 SA: 33 Both: 5	7 (16%)	5 (11%)	25 (56%)	16 (36%)	14 (31%)	0	1 (2%)	0	0	2 (4%)
Lopez-Longo et al. [13]	1987	37	1982–84	Spain	SA: 37	0	0	27 (73%)	N/A	1 (3%)	0	0	5 (14%)	0	0
Brancos et al. [5]	1991	35	1982–88	Spain	SA: 35	5 (14%)	4 (11%)	27 (77%)	1 (3%)	1 (3%)	0	0	^	^	0
Munoz-Fernandez et al. [15]	1993	31	1981–90	Spain	SA: 31	0	0	17 (55%)	N/A	0	0	0	6 (19%)	2 (6%)	0
Belzunegui et al. [4]	2000	34	1979–99	Spain	SA: 27 OM: 6 Other: 1	2 (6%)	0	25 (74%)	N/A	1 (3%)	1 (3%)	0	3 (9%)	2 (6%)	0
Allison et al. [current study]	2010	215	1998–2005	USA	OM: 127 SA: 53 Both: 35	40 (19%)	15 (7%)	111 (52%)	43 (20%)	38 (18%)	42 (20%)	27 (13%)	9 (4%)	0	70 (33%)

IDA: Injecting drug abuse, OM: Osteomyelitis, SA: Septic arthritis, Gram N: Gram negative organisms, PA: Pseudomonas aeruginosa, ORSA: oxacillin-resistant Staphylococcus aureus, Strep: Streptococci, Staphylococcus epidermidis, AN: Anaerobes, F: Fungi, MB: Mycobacteria, Poly: Polymicrobial, N/A: data not available.

* Please note that the number of Pseudomonas aeruginosa infections is included in the Gram negative infections and that the number of ORSA infections is included in the S aureus infections.

Percentages are calculated with the total number of 28 patients as the denominator. No data were provided specifically for the 21 patients with IDA.

^ Fungal and mycobacterial infections were included in this study.

Our data suggest bone and joint infections associated with IDA are predominantly caused by Gram-positive bacteria, with a progressive increase of ORSA. A considerable proportion of infections are caused by Gram-negative and anaerobic microorganisms. Older studies identified *P. aeruginosa* as the most common pathogen (Table 3). Kido et al. reported that *P. aeruginosa* was the pathogen in 27 (84%) of 32 patients with osteomyelitis or septic arthritis [11]. Roca and Yoshikawa [18] identified *P. aeruginosa* in 14 (64%) of 22 skeletal infections and stated the microbiology of these infections was far less diverse than their anatomic location. Miskew et al. identified *P. aeruginosa* as the pathogen in all 35 bone and joint infections in their series [14]. Similarly, in series of patients with IDA and acute endocarditis, Gram-negative bacteria were the major pathogens [12, 20]. The high rate of *P. aeruginosa* infections in injecting drug abusers has been attributed to contaminated water used for preparation of injection [20]. In contrast, Chandrasekar and Narula [6] reported *S. aureus* was the most common pathogen, identified in 56% (25 of 45) of their patients, whereas *P. aeruginosa* was present in 11% (five of 45). Other studies from the 1980s and later found *S. aureus* present in 55 to 77% of musculoskeletal infections in patients with IDA [2, 4, 5, 13, 15]. We found *S. aureus* was the infecting microorganism in the majority of cases (52%, 111 of 215) with *P. aeruginosa* in only 7% (15 of 215) of infections. The decline in the importance of *P. aeruginosa* in musculoskeletal infections associated with IDA after 1980 has been attributed to the fact that in the 1970s pentazocine, which is soluble in cold water, was a common drug of abuse, whereas in the 1980s heroin became common but required heating of the water, which may have reduced contamination of the water with *Pseudomonas* [10].

After evaluating sensitivities among the *S. aureus* isolates in our series, an alarming increase in oxacillin resistance was documented. From 1998 to 2005, the incidence of oxacillin resistance among *S. aureus* isolates in our series rose substantially from 21% to 73%. Only three of the existing studies documented ORSA bone and joint infections in patients with IDA [6], with considerable variability. Two studies from the USA by Ang-Fonte et al. [2] in 1985 and by Chandrasekar and Narula [6] in 1986 found that ORSA comprised 7 of 18 *S. aureus* infections and 16 of 25 *S. aureus* infections, respectively, but no such data have been reported recently. In contrast, a study from Spain from 1991 reported ORSA in only 1 of 27 *S. aureus* infections [5]. Progressive increase of ORSA in patients with IDA has been demonstrated in soft tissue abscesses [1] and all types of infection overall [3]. A recent study evaluating all types of infections reported, from 2006 to 2008, 49% (18 of 37) of clinical isolates from patients with IDA were ORSA, compared with 7%

(four of 59) in 2000 to 2003 and 0% (zero of 48) in 1999 to 2000.

We found that in patients with osteomyelitis there was a markedly higher prevalence of polymicrobial infections (46% versus 15%), infections due to Gram-negative organisms (24% versus 9%), and anaerobic infections (19% versus 6%) compared to patients with septic arthritis. Chandrasekar and Narula [6] evaluated 7 patients with osteomyelitis and 33 patients with septic arthritis and identified *S. aureus* in 4 of 7 patients with osteomyelitis versus 16 of 33 patients with septic arthritis, and *P. aeruginosa* in none of 7 osteomyelitis cases versus 5 of 33 septic arthritis cases.

Based on our findings, vancomycin should be considered in the empiric antibiotic therapy of bone and joint infections in these patients while waiting for definitive culture results. However, the extensive use of vancomycin has been associated with increasing minimum inhibitory concentrations for ORSA. Empiric coverage for Gram-negative organisms and anaerobes should also be considered, especially in cases of osteomyelitis.

Bone and joint infections in patients with IDA are predominately caused by Gram-positive bacteria. *S. aureus* is the most common pathogen and oxacillin resistance has greatly increased. A considerable proportion of infections, especially osteomyelitis, are caused by Gram-negative and anaerobic microorganisms. This information, in combination with local resistance patterns, will help the treating physician select antibiotics for empiric administration until cultures results are available.

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