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Hematogenous Septic Ankle Arthritis

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Abstract Ankle infection is a serious problem with limited published information on microbiology and associated morbidities. We describe the laboratory findings, microbiology, and occurrence of adjacent osteomyelitis in patients with hematogenous septic ankle arthritis. We retrospectively reviewed 30 patients with hematogenous septic arthritis of the ankle admitted over a 10-year period. Twenty-two patients were male and eight female. The mean age was 46 years (range, 23–67 years). C-reactive protein and erythrocyte sedimentation rate were elevated in all patients, but the peripheral white blood cell count was elevated in only 47% of patients. Staphylococcus aureus (S. aureus) was the most common pathogen, isolated in 13 (54%) of the 24 patients with positive cultures; four of these isolates (four of 24; 17% of positive cultures) were oxacillin-resistant. Four (17%) of the 24 patients with positive cultures had a mycobacterial infection. We identified adjacent osteomyelitis in 30% of patients, which was considerably associated with the presence of patient comorbidities. S. aureus is the most common pathogen in septic ankle arthritis and empiric antibiotic therapy is recommended. Adjacent osteomyelitis may be present and a high index of suspicion is necessary in patients with comorbidities.
Level of Evidence: Level III, diagnostic study. See the Guidelines for Authors for a complete description of levels of evidence.

Introduction

Septic arthritis is a serious and potentially debilitating condition. According to one report septic arthritis has an annual incidence of two to 10 per 100,000 individuals, although that study did not report data on the incidence of ankle septic arthritis [6]. Untreated joint infection can lead to irreversible destruction of articular cartilage, disability, systemic sepsis and death [3, 4, 7]. A retrospective study of septic arthritis in the United Kingdom reported 23.8% of patients had considerable loss of function in the affected joint and 11.5% of patients died as a result of their illness [18].

The value of laboratory examinations in the diagnosis of septic arthritis remains uncertain, especially for peripheral white blood cell count [4, 9]. Synovial fluid analysis for cell count, Gram stain, and culture is the fundamental diagnostic tool for septic arthritis [15]. Staphylococci and streptococci are identified in the literature as the offending organisms in the majority of joint infections [1, 2, 4, 5, 8]. However, most of the studies report primarily patients with knee and hip infection and include only a small number of patients with ankle or other joint infection [4, 12]. In a review by Newman [11] of 134 patients reported over a 30-year period in the United Kingdom (1944–1973), only 7% of the cases of septic arthritis involved the ankle. Vispo Seara et al. [17] reported 88 patients with septic arthritis, of which only three (3.4%) had ankle infection. Stutz et al. [14] reviewed their experience with 76 patients with septic

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arthritis, and reported five (7%) had an infected ankle. Few recent studies specifically address ankle sepsis [8, 16]. The study by Lee et al. [8]. reported Staphylococcus aureus (S. aureus) was the most common organism causing ankle sepsis in their series of 23 adults and six children. Thordarson et al. [16] identified Staphylococcus epidermidis as the most common pathogen in their nine patients; all of their patients had had previous ankle surgery. The coexistence of osteomyelitis with septic arthritis has been described in only two studies [13, 19]. Perlman et al. [13] reported in 10 pediatric patients with osteomyelitis in bones adjacent to the ankle, four had involvement of the ankle. Only one study [19] evaluated the presence of adjacent osteomyelitis in adult patients with septic knee arthritis and reported 85% of these patients had comorbidities. No study, to our knowledge, has examined this relationship in adult patients with septic arthritis of the ankle.

We aimed to answer the following questions regarding septic ankle arthritis: (1) What is the sensitivity of common laboratory findings (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and synovial white blood cell (WBC) count? (2) What are the offending pathogens? (3) What is the occurrence of adjacent osteomyelitis in patients with hematogenous septic ankle arthritis? and (4) Is adjacent osteomyelitis more common in patients with comorbidities?

Materials and Methods

We retrospectively identified all adult patients (older than 18 years) with a discharge diagnosis of ankle infection from January 1996 to December 2005. We defined infection as a synovial culture growing a microorganism or an aspiration of the joint showing a white blood cell count greater than 50,000 with findings of frank purulence at surgery. Patients were classified by the criteria described by Newman [11] as patients with an organism isolated from the joint, patients with an organism isolated from elsewhere, or patients who had no organism isolated but histologic or radiographic evidence of infection or turbid fluid aspirated from the joint. Patients with previous surgery to the ankle were excluded. With this definition we identified 30 patients with ankle sepsis. Twenty-two patients were male and eight female. The mean age was 46 years (range, 23–67 years). None of the patients had a history of an acute fracture. Three patients reported a "twisting" injury to the ankle within 2 weeks of admission but did not seek medical care for this. Twelve (40%) of 30 patients had comorbidities: eight of the 30 patients (27%) had diabetes mellitus, three patients (10%) were intravenous drug abusers, and one patient received corticosteroids and methotrexate. None of the patients was known to be HIV-infected. The study was approved by our Institutional Review Board.

We reviewed patient charts and specific information was collected in each case using a standardized form; no patients were seen in followup for this study. Symptoms and physical findings were extracted from the admitting physician's notes. We recorded laboratory values from each patient at the time of admission, including systemic white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). Joint aspirate WBC count and differential as well as culture results were collected. All patients had aerobic, anaerobic, fungal and mycobacterial cultures of synovial fluid aspirates or specimens obtained at the time of surgery. The presence of concurrent osteomyelitis adjacent to the affected ankle was evaluated based on plain radiographs and MRI.

Twenty-six of 30 patients (87%) reported ankle pain and 21 patients (70%) reported swelling around the ankle. Ten patients (33%) had a history of fever before presentation and five patients (17%) were febrile on admission.

To address the question as to whether adjacent osteomyelitis is more common in patients with comorbidities (such as diabetes mellitus, intravenous drug use and immunosuppresion), we compared patients who had concurrent osteomyelitis of the affected joint and those without concurrent osteomyelitis for the presence of comorbidities using Fisher's exact test.

Results

Of the 16 patients who had a synovial fluid WBC count performed, 13 had an elevated count ($\geq$ 50,000/mm^3). There was no evidence of crystals in the synovial fluid of any patient (Table 1).

Twenty-four of the 30 patients (80%) had an organism isolated from the joint fluid. Seventeen of the 30 patients (57%) had a single organism isolated from cultures of the synovial fluid; seven patients (23%) had two organisms. Six patients (20%) had no growth on cultures. Therefore, a total of 31 microbes were isolated from 24 patients (Table 2).

S. aureus was the most common pathogen; only four of these isolates were oxacillin-resistant. Streptococci were the next most common organisms. Overall, Gram-positive cocci were isolated in 20 (83%) of 24 culture-positive cases (two patients had infection with both S. aureus and streptococcus). No isolates of Neisseria gonorrhea were identified. The patient who grew Coccidioides immitis was Filipino and had a history of Addison's disease.

Four patients had infection with Mycobacterium tuberculosis; three were from Latin America and one from Armenia. Two patients had a monomicrobial infection with

Table 1. Patient characteristics

	Total	Adjacent osteomyelitis	No adjacent osteomyelitis
Number	30	9	21
Age	46 years (range 23–67)	45 years (range 33–62)	45 years (range 23–67)
Comorbidities present	11 (37%)	4 (44%)	7 (33%)
Mean ESR	82 (range 23–140)	84 (range 53–107)	81 (range 23–140)
Mean CRP	16.9 (range 0.9–37.8)	17.0 (range 0.9–36.9)	16.8 (range 1.3–37.8)
Mean peripheral WBC	10.8 (range 2.1–24.1)	11.7 (range 6.8–15.7)	10.6 (range 2.1–24.1)
Synovial fluid WBC performed	16/30 (53%)	5/9 (56%)	11/21 (53%)
Synovial fluid WBC count	Mean = 108,782	Mean = 120,449	Mean = 103,479
	Median = 71,364	Median = 70,909	Median = 71,818
	(range 12,200–292,000)	(range 20,700–311,000)	(range 12,200–292,000)
Organism cultured	23/30 (77%)	9/9 (100%)	14/21 (67%)

Table 2. Relative frequency of causative microorganisms for 24 culture-positive patients with hematogenous septic ankle

Organism	Number (%) of total (31) isolates	Percentage of culture-positive patients*
Staphylococcus aureus	13 (42%)	54%
Oxacillin-susceptible S. aureus	9 (29%)	38%
Oxacillin-resistant S. aureus	4 (13%)	17%
Streptococci	9 (29%)	38%
Beta-hemolytic streptococci	4 (13%)	17%
Other streptococci	5 (16%)	21%
Gram-negative rods	3 (10%)	8%
Other		
Mycobacterium tuberculosis	4 (13%)	17%
Coccidioides immitis	1 (3%)	4%
Aspergillus spp.	1 (3%)	4%

* Because seven patients had two organisms isolated, this column does not add up to 100%.

Mycobacterium tuberculosis. One of these had a history of unspecified polyarthritis and had been treated with corticosteroids and methotrexate for 3 years. He also had a history of tuberculous arthritis in his knee 2 years before this admission; the specifics of his previous treatment were not available. The other patient had a history of tuberculous arthritis of the elbow diagnosed 2 weeks before admission. Of the two patients with polymicrobial infections with M. tuberculosis, one had no history of illness and grew both M. tuberculosis and Enterobacter cloacae from the ankle. The other patient had a history of psoriasis and had a corticosteroid injection into the ankle 3 weeks before presentation; she grew both M. tuberculosis as well an Aspergillus species.

Concurrent osteomyelitis adjacent to the infected ankle occurred in nine of 30 patients (30%). Plain radiographs of the ankle suggested the presence of osteomyelitis in two of the patients at presentation. Fifteen of the remaining 28 patients had an MRI of the ankle performed and seven of those showed evidence of osteomyelitis. Three of the nine patients had osteomyelitis involving two bones, resulting in 12 sites. The tibia was involved in five patients, the fibula in three, and the calcaneus, talus, navicular, and cuboid in one case each. Comparison of patients with and without adjacent osteomyelitis demonstrated a higher ($p = 0.01$) presence of one of the three comorbidities in patients with adjacent osteomyelitis: comorbidities were present in seven (78%) of nine patients with osteomyelitis compared with five (24%) of 21 patients without osteomyelitis.

Discussion

The current study, which to our knowledge is the largest case series of adult septic ankles in the literature, addressed the laboratory findings, microbiological features and the presence of adjacent osteomyelitis in patients with septic arthritis of the ankle joint.

We note several limitations. We retrospectively review only medical records and since it was not a prospective series not every patient had an MRI. The number of patients with adjacent osteomyelitis may be underestimated because an MRI was not performed in all patients with a septic ankle. Long-term follow up was not available to assess the possibility of later development of osteomyelitis.

There is little evidence to suggest which laboratory values are most useful in diagnosing septic arthritis. The absence of a raised WBC count is not sufficient to rule out joint infection [10]. In our patient population less than half of the patients with septic ankle arthritis had an elevated WBC on admission. The elevation of nonspecific markers of inflammation such as ESR and CRP has been associated with septic arthritis [2, 4, 5]. Our data support these notions, because every patient in our study had an elevated ESR and CRP levels on admission.

Staphylococci and streptococci are the most common causative organisms of septic arthritis [1, 2, 4, 5]. In 2000, Lee et al. [8] reported, among a cohort of 29 adults and children diagnosed with septic ankles, S. aureus was the most common offending organism. This was true in our study as well; S. aureus was the most common isolate in our adult patient population (n = 13) and streptococci were the second most common (n = 9). Overall, Gram-positive cocci were isolated from 83% (20 of 24) of culture-positive cases. Therefore, empiric antibiotic therapy should cover against Gram-positive cocci in all patients with septic ankle arthritis. In our series, oxacillin-resistant S. aureus was present in 17% of culture-positive cases, suggesting vancomycin may be preferable as empiric coverage until culture results become available.

Four cases of infection of the ankle with M. tuberculosis were identified in our patient population. Although tuberculous joint sepsis is a rare clinical finding, the LAC + USC Medical Center serves an area of very high tuberculosis prevalence relative to many other areas of the United States. Aspergillus infection of the joint is also a very rare phenomenon. The patient infected with Aspergillus species in our sample had a very low WBC count (2.6), indicating possible immune dysfunction. A history of steroid injection to the affected ankle 3 weeks before hospital admission also provides a possible vehicle of entry for the organism. Coccidioides immitis was cultured from one patient of Filipino origin with a history of treated Addison's disease. This patient lived in Los Angeles, an area endemic for Coccidioides infection. Our findings underscore the importance of sending specimens for aerobic, anaerobic, mycobacterial, and fungal cultures.

In 2000, Perlman et al. [13] demonstrated 33% of pediatric patients with osteomyelitis had septic joint involvement adjacent to the affected bone and 40% of pediatric patients with osteomyelitis in bones adjacent to the ankle had involvement of the ankle. Our result of 30% reveals a similar rate of concurrence between sepsis of the ankle and osteomyelitis in adult patients. We found an association between adjacent osteomyelitis and the presence of comorbidities, supporting a previous study on septic knee arthritis [19]. Therefore, a higher degree of suspicion for adjacent osteomyelitis should be assigned to patients with comorbid conditions.

CRP and ESR appear sensitive indicators for septic arthritis of the ankle, in contrast to the peripheral WBC count. S. aureus is the most common pathogen, but atypical pathogens may be present, especially in patients coming from endemic areas. Adjacent osteomyelitis may be present in septic arthritis of the ankle, especially in compromised patients.

We confirmed that for infectious arthritis of the ankle as for other joints, the most common organism is S. aureus, followed by streptococci. Adjacent osteomyelitis occurred in 30% of the patients who presented with septic ankle arthritis. Patients with septic ankle arthritis, especially those with comorbid conditions, should have screening performed for adjacent osteomyelitis.

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