Microorganisms Associated with Osteomyelitis of the Foot and Ankle

Christy M. King, DPM, FACFAS[1], Francesca M. Castellucci-Garza, DPM, MS[2], Matthew D. Doyle, DPM, MS[2], Craig J. Nimick, DPM, AACFAS[3], Mitzi L. Williams, DPM, FACFAS[4]

[1]Attending Staff and Residency Director, Kaiser San Francisco Bay Area Foot and Ankle Residency Program, Oakland, CA
[2]Resident, Kaiser San Francisco Bay Area Foot and Ankle Residency Program, Oakland, CA
[3]Attending Staff, Kaiser Foundation Hospital, Redwood City, CA
[4]Attending Staff, Kaiser San Francisco Bay Area Foot and Ankle Residency Program, Oakland, CA

Statement of Purpose

Osteomyelitis of the foot and ankle can be difficult to treat, cause a considerable amount of morbidity and lead to great financial costs. The morbidity associated with osteomyelitis is dependent on several factors, including the infecting organisms, overall health of the patient and location of the infection. The purpose of this study was to evaluate the microorganisms associated with osteomyelitis of the foot and ankle in patients with various comorbidities.

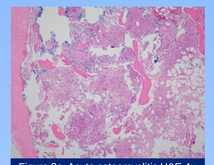

Figure 2a. Acute osteomyelitis H&E 4x.

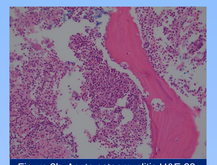

Figure 2b. Acute osteomyelitis H&E 20x.

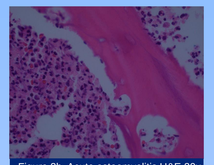

Figure 2b. Acute osteomyelitis H&E 20x.

Methodology & Hypothesis

This study was approved by the Kaiser Permanente Northern California Institutional Review Board. A retrospective study was conducted of 302 patients with osteomyelitis of the foot and ankle. Data was obtained by reviewing medical records from patients within the Kaiser Permanente Northern California region. The study reviewed 151 patients who were diagnosed with osteomyelitis in 2005 and another 151 patients who were diagnosed with osteomyelitis in 2010, giving the study 80% power to detect statistical significance. The diagnosis of foot and ankle osteomyelitis was used to identify the study cohort, and subjects were identified by ICD codes (730.07, 730.17, 730.20, 730.27, 730.97).

The surgical pathology report was used to confirm the diagnosis of osteomyelitis and bone culture reports were used to confirm the organism or organisms involved. The use of antibiotics prior to obtaining a bone culture was also recorded. Patients that had received antibiotics within two weeks of the bone culture were documented as having had antibiotics.

Comorbidities of each patient were recorded which included diabetes mellitus, peripheral vascular disease, rheumatoid arthritis, chronic kidney disease and Charcot arthropathy. Location of osteomyelitis was also recorded as either forefoot, midfoot, or rearfoot.

Our analyses included descriptive statistics to describe the demographic and clinical characteristics of the cohorts 2005 and 2010. We performed chi-square tests for comparison of categorical variables, T-tests for continuous variable and multivariate regression modes for determining predictors for acquisition of MRSA as an organism causing osteomyelitis.

We hypothesized that the incidence of MRSA in osteomyelitis of the foot and ankle would increase from 2005 to 2010.

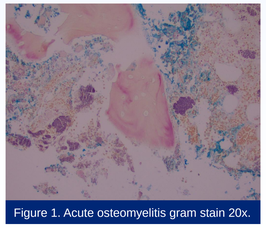

Figure 1. Acute osteomyelitis gram stain 20x.

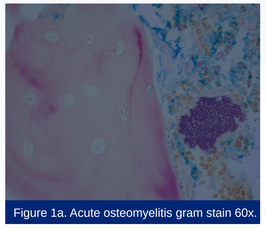

Figure 1a. Acute osteomyelitis gram stain 60x.

Literature Review

Osteomyelitis can present a challenge to physicians. The severity of osteomyelitis can depend on a variety of factors, including etiology, pathogenesis, extent of bony involvement, duration, and health of the host (1-3).

A variety of imaging techniques have been used to evaluate and identify osteomyelitis. Radiographs are a simple method to evaluate osseous abnormalities but evidence of osteomyelitis on radiographs is not visible for 10-14 days (4). In a study by Ertugrul et al., labeled leukocyte scanning had a sensitivity of 91% and specificity of 60% while MRI had a sensitivity of 78% and specificity of 60% in the diagnosis of osteomyelitis (5). The definitive method to identify osteomyelitis is bone biopsy with 95% sensitivity and 99% specificity (4).

It is important to obtain a bone biopsy to allow for proper identification of the pathogenic microorganism so that antibiotic treatment can be directed appropriately. While bone biopsies are the gold standard in pathogenic identification, swabs of cultures have also been used to attempt to identify causative organisms. However, studies have shown a poor relationship between the agreement of bone biopsy and culture swab results. A study by Lavery et al. looked at 36 patients with soft tissue culture and operative bone cultures and found that there was an exact match in 13% of the cases (6). Similarly, Senneville et al. evaluated swabs and bone cultures in 76 patients and found identical identification of microorganisms in 17.4% of patients (7). Additionally, they found that there was a higher concordance with Staphylococcus aureus (42.8%) as compared to gram-negative bacilli (28.5%) and Streptococci (25.8%), revealing that even the concordance rates can change depending on the involved microorganism (7).

The literature evaluating the causative organism in contiguous osteomyelitis in patients without diabetes is scant. Much of the literature evaluating the microorganisms involved in osteomyelitis relates to patients with diabetes mellitus. In most studies Staphylococcus aureus is the most common organism followed by aerobic gram-positive cocci and aerobic gram-negative rods (4-7). Staphylococcus aureus accounts for 26.4-60% of the cases of diabetics with osteomyelitis, and MRSA occurred in 9.6-24% of those infections (5-8). Streptococcus had a wide range of occurrence, from 12-61% and gram-negative organisms were found in 18.4-50% of cases of osteomyelitis (6-7). Anaerobic bacteria have been found in 4.8-14% of the cases (6,7,9) and the occurrence increases as the duration of the lesion increases (4). Polymicrobial infections are also common, shown to occur in 15-31.8% of cases (4,5,7).

Results

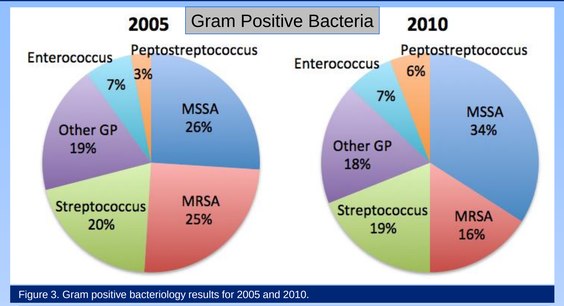

Figure 3. Gram positive bacteriology results for 2005 and 2010.

There was a noticeable increase in the proportion of MSSA infections and a decrease in MRSA infections from 2005 to 2010. The percentage of other gram positive bacteria remained relatively the same.

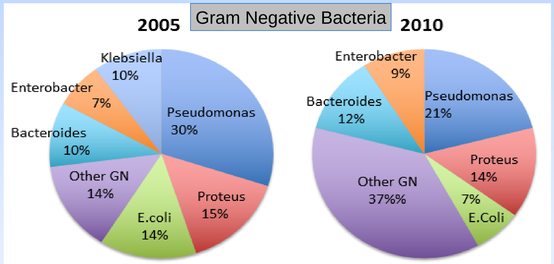

Figure 4. Gram negative bacteriology results for 2005 and 2010.

There was a noticeable decrease in the percentage of Pseudomonas and E. Coli infections while there was a noticeable increase in other gram negative bacteria from 2005 to 2010.

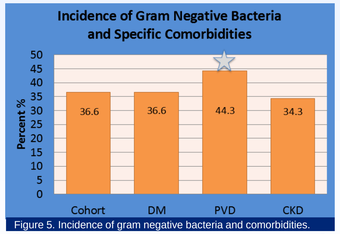

Figure 5. Incidence of gram negative bacteria and comorbidities.

Patients with peripheral vascular disease were shown to have a statistically significantly higher incidence of gram negative bacteria when evaluating the cohort as a whole - odds ratio 2.1, 95% confidence interval 1.3 to 3.6, p-value 0.003.

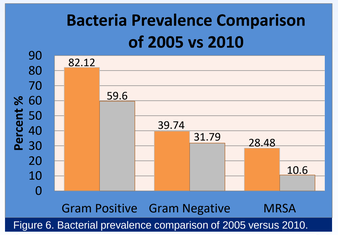

Figure 6. Bacterial prevalence comparison of 2005 versus 2010.

Comparing 2005 to 2010 there was:
- A significant decrease in the incidence of gram positive bacteria from 2005 to 2010 (p-value < 0.001).
- A decrease in the incidence of gram negative bacteria (p-value 0.48).
- A significant decrease in the incidence of MRSA (p-value < 0.001).

Results continued

Three hundred and two patients were included in the study, 151 from each year. The cohort consisted of 213 males and 89 females with an average age of 64.1± 12.9. Comorbidities included: diabetes mellitus (n=254), peripheral neuropathy (n=240), peripheral vascular disease (n=149), end stage renal disease on dialysis (42), Charcot arthropathy (n=23), rheumatoid arthritis (n=6), and HIV (n=1). Osteomyelitis was predominantly found in the forefoot (n=263), followed by the rearfoot (n=32) and then the midfoot (n=7). There was no significant difference noted in location of osteomyelitis from 2005 to 2010. A significant increase in the use of antibiotics prior to obtaining bone cultures was found between 2005 to 2010 (p-value < 0.0001).

Figures 3 and 4 show the comparison of bacteria found in bone cultures between the two years. Figure 5 shows the incidence of gram negative bacteria between specific comorbidities. Figure 6 represents the bacterial prevalence comparison between 2005 and 2010.

Analysis & Discussion

While there are studies that evaluate the pathogenic microorganisms that cause contiguous osteomyelitis in diabetic patients, the number of cases reviewed is low, and the microorganisms involved can vary widely between studies. Also, the literature evaluating the pathogenic organism in osteomyelitis of patients with other comorbidities is minimal.

Between the years 2005 and 2010 our data shows that gram positive bacterial infections predominate. Interestingly, we found a significantly decreased incidence of MRSA infections and increased incidence of MSSA infections during this time period. This is consistent with the recent literature (10,11).

In the current study we also found a significantly higher incidence of gram negative bacteria in patients with PVD. This can potentially be attributed to the local environment of the host as well as the slower healing time in patients with PVD and hence a likely increased duration of the wound.

A thorough knowledge of microorganisms associated with osteomyelitis may help dictate surgical treatment, guide antibiotic therapy and promote antibiotic stewardship to decrease the incidence of multi-drug resistance. The results of this research may assist physicians with their choice of antibiotics to initiate in empiric therapy and the specific management of osteomyelitis.

References

1. Calhoun JH, Manring MM, Shirtliff M. Osteomyelitis of the long bones. Semin Plast Surg 23(2):59-72, 2009.
2. Waldvogel FA, Medoff G, Swartz MN. Osteomyelitis: A review of clinical features, therapeutic considerations and unusual aspects. N Engl J Med 282:198-206, 1970.
3. Cierny G III, Mader JT, Penninck JJ. A clinical staging system for adult osteomyelitis. Clin Orthop Relat Res 414:7-24, 2003.
4. Lipsky BA. Osteomyelitis of the foot in diabetic patients. Clin Infect Dis 25(6):1318-1326, 1997.
5. Ertugrul MB, Baktiroglu S, Salman S, Unal S, Aksoy M, Berberoglu K, Calangu S. The diagnosis of osteomyelitis of the foot in diabetes: microbiological examination vs. magnetic resonance imaging and labeled leukocyte scanning. Diabet Med 23(6):649-653, 2006.
6. Lavery LA, Sariaya M, Ashry H, Harkless LB. Microbiology of osteomyelitis in diabetic foot infections. J Foot Ankle Surg 34(10):61-64, 1995.
7. Senneville E, Melliez H, Beltrand E, Legout L, Valette M, Cazaubiel M, Cordonnier M, Caillaux M, Yazdanpanah Y, Mouton Y. Culture of percutaneous bone biopsy specimens for diagnosis of diabetic foot osteomyelitis: concordance with ulcer swab cultures. Clin Infect Dis 42(1):57-62, 2006.
8. Armstrong EP, Rush DR. Treatment of osteomyelitis. Clin Pharm 2(3):213-224, 1983.
9. Raff MJ, Melo JC. Anaerobic osteomyelitis. Medicine 57(1):83-103, 1978.
10. Acree ME, Morgan E, David MZ. S.aureus infections in Chicago, 2006-2014: Increase in CA MSSA and decrease in MRSA incidence. Infect Control Hosp Epidemiol 38:1226-1234, 2017.
11. Dantes R, Mu Y, et al. National burden of invasive methicillin-resistant staphylococcus aureus infections, United States, 2011. JAMA Intern Med 173(21):1970-1978.