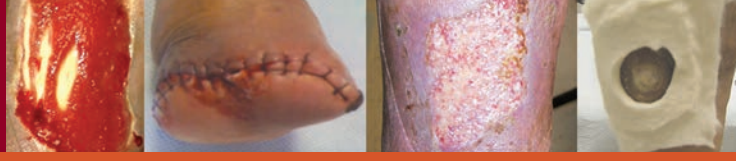

Diagnosing Osteomyelitis

Here are the current trends.

BY PATRICIA KIM, DPM AND BARRY ROSENBLUM, DPM

Foot infections and osteomyelitis are the leading cause of hospitalizations among diabetic patients in the U.S. today. Among the sixteen million patients with diabetes in the U.S., more than 15% develop foot ulcers at some point in their lifetime.[1] Diabetic amputations alone are responsible for greater than 60% of lower extremity related amputations.[2] Five-year survival of below-knee amputees ranges from 15% to 40%, indicating high morbidity and mortality rates. Prevention of diabetic foot ulcers from undergoing conversion to infection—to osteomyelitis—to minor amputation to major amputation is one of the most prevalent scenarios seen in podiatry clinics.

In treating diabetic foot ulcers, today's podiatrist is armed with an arsenal of tools and therapies in diagnosing osteomyelitis. While some modalities are becoming more refined with time, other newer therapies are emerging to aid in earlier diagnosis and preventative treatment. It is important to utilize a combination of diagnostic tools clinically and surgically in the diagnosis of osteomyelitis.

Clinical Treatment

Clinically, diabetic foot ulcers are typically treated on a weekly basis with regular debridements and/or adjuvant therapies including growth factors, hyperbaric oxygen therapy, and negative pressure therapy. Although an ulcer may appear uninfected, i.e., lacking any purulent drainage, ascending lymphangitis, or systemic signs of illness, suspicion for osteomyelitis is warranted when an ulcer does not show any signs of improvement after four to six weeks of continued treatment.[3] Impaired healing is caused by the disruption of the natural wound-healing phases with chronicity of the inflammation phase and a propagation of leukocytic activity.

A clinician must also assess whether a patient's vascular status is adequate to rule out any other causes for a non-healing ulceration, such as peripheral arterial disease. The presence of exposed bone or ulcer larger than 2cm2 also increases the risk of the presence of osteomyelitis.[4]

It is important to utilize a combination of diagnostic tools clinically and surgically in the diagnosis of osteomyelitis.

A recent study showed that regardless of whether an ulcer is infected or a patient has an elevated white blood cell count, risk factors for osteomyelitis can include ulcers that probe to bone, a prior history of wounds, recurrence and multiple wounds.[5] Infection or elevated white blood cell count is more indicative of cellulitis or active infection rather than a harbinger of osteomyelitis.

Diagnosing Osteomyelitis

Diagnosing osteomyelitis relies both on what is seen clinically as well as corroborating it to other evidence such as imaging. The probe-to-bone test has long been used as an initial clinical indicator of osteomyelitis prior to when no other tests have been performed. Other tests have shown that in an infected wound, "a positive probe-to-bone test is highly suggestive of osteomyelitis, but a negative test does not exclude the diagnosis; conversely, in the case of an apparently uninfected foot wound, a positive probe-to-bone test is not specific for osteomyelitis, but this diagnosis is unlikely if the probe-to-bone test is negative."[6]

Grayson's article in 1995 illustrated that the probe-to-bone test could accurately diagnose osteomyelitis in an infected pedal ulcer, eliminating the need for specialized radionuclide and roentgenographic tests.[7] Articles in response to Grayson's original article argued that although the probe-to-bone test was highly sensitive as well as specific, the positive predictive value was inflated as the study population was already at high risk for osteomyelitis. Other research showed that the positive predictive value was relatively low (0.57), while the negative predictive value was high (0.98) indicating that a negative probe-to-bone test could be used to exclude the diagnosis of osteomyelitis.[8] The probe-to-bone test is useful in aiding in diagnosis of osteomyelitis, but should not be used as a sole modality; instead it should be used in conjunction with other tests.

While imaging alone shows low sensitivity for diagnosis of osteomy-

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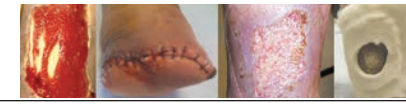

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elitis, when used in conjunction with the probe-to-bone test, patients can be more confidently diagnosed.[9] Osteomyelitic changes to bone such as periosteal reaction and cortical destruction seen in active osteomyelitis and involucrum, sequestrum, and cloaca in chronic osteomyelitis can be seen on plain radiographs but may take several weeks to appear with an up-to-two-week time lag.

Serial plain radiographs are recommended as they may have greater sensitivity and specificity with progressive changes documented if isolated but also can have low accuracy in the presence of other conditions such as Charcot arthropathy.

Research for other imaging such as FDG PET/CT imaging has emerged as alternatives to plain radiographs. A prospective article showed that FDG PET/CT imaging had high sensitivity, specificity, and accuracy (100%, 92%, 95% respectively) in the diagnosis of pedal osteomyelitis. It was able to identify foci in acute infections which were localized on PET/CT imaging which differentiated between osteomyelitis and soft tissue infection.[10] Although plain CT is best for calcified structures, it still remains relatively insensitive for bone marrow pathologies or soft tissue pathology. Other nuclear medicine imaging should be used in problematic cases wherein MRI specificity is decreased as seen in neuropathic feet or in cases with infected hardware.

MRI

MRI is presently considered the imaging modality of choice as it has high spatial resolution; sensitivity has been reported as ranging between 80% to 100%.[11] It is able to demonstrate soft tissue edema extent as well as abscesses and other drainable fluid collections. Although hematogenous spread is the most common cause of osteomyelitis outside of the foot, contiguous spread of infection from the skin and soft tissue is typically the most common cause of diabetic foot osteomyelitis.[12] A soft tissue abscess increases the likelihood that the edema in underlying bone marrow is osteomyelitis. On T1-weighted images, osteomyelitis will demonstrate low signal in the bone marrow and high signal on T2-weighted images.[13] Although it is useful in aiding in the diagnosis of osteomyelitis, especially if plain radiographs are negative, a highly skilled radiologist is necessary for a comprehensive read. Infected bone marrow edema can be marrow edema due to other causes such as neuropathic arthropathy. In some cases, MRI may also be contraindicated in a patient or unavailable for the clinician to use in certain areas.

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Superficial swabs are sometimes collected to aid in narrowing pathogens affecting limbs afflicted with osteomyelitis. A retrospective study from 2006 followed 76 patients with 81 episodes of osteomyelitis comparing initial superficial swabs with surgical percutaneous bone biopsies. Superficial swabs had isolated pathogens that were predominantly staphylococci and gram-negative bacilli. Concordance between swab and bone biopsy specimens was only 22.5%, indicating that superficial swabs did not reliably identify bone bacteria.[14]

Bone Biopsies

Bone biopsies remain the gold standard in the diagnosis of osteomyelitis. There has been some debate as to whether histopathology or microbiology is better in increasing the likelihood of an accurate diagnosis. While a multitude of pathogens are found in osteomyelitic bone, S. aureus remains the most common; Staphylococcus epidermidis and Escherichia coli are also frequently found. Samples may either be collected percutaneously through non-affected skin or as part of an operative procedure. Obtaining intra-operative samples are not without pitfalls; skin flora or contiguous tissue may contaminate cultures or misrepresent the number of infecting pathogens. Antibiotics should be held at least 48 hours prior to bone biopsy to maximize yield from the cultures.[15]

Microbiological Tests

Microbiological tests may have false-negative results due to operator-related complications, missing the osteomyelitic site, low levels of pathogenic organisms, or prior antibiotic therapy.[16] Histopathologically, osteomyelitic bone does not have a standardized definition or classification, and there are few studies which attempt to qualify characteristics of osteomyelitic bone samples.[17] Osteomyelitis can only be considered proven if a reliably obtained bone specimen grows one or more pathogens; the specimen should also show acute or chronic inflammation, bone death, and/or reparative responses.[18] If both microbiology and histology are obtained with a well-obtained bone culture, there is an increased likelihood of accuracy of diagnosis of osteomyelitis.

Studies have shown that bone culture-guided antibiotic regimen led to better outcome versus antibiotic regimen without any culture guidance.[19] In the patient where surgical resection of all infected bone has occurred, a shorter duration of oral antibiotics is usually indicated. This may range from five to 15 days depending on the appearance of the site intra-operatively.[20] When residual infected bone remains despite surgical intervention, therapy of choice remains a longer course of intravenous antibiotics ranging from four to eight weeks. There has been minimal research indicating a specific regimen that adequately treats osteomyelitis, including route, therapy, or duration of treatment. Antibiotic treatment should be halted once all modalities have been evaluated, including resolution of the ulcer, improvement of soft tissue infection, and radiographic improvement.

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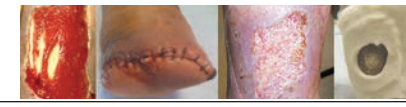

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Non-surgical Treatment of Osteomyelitis

Non-surgical treatment of osteomyelitis is only indicated in certain individuals with vascular compromise such as limb ischemia, lack of surgical target, localization of infection to forefoot or minimal soft tissue loss, or the patient and his or her healthcare team decide that surgical intervention would be more detrimental or carried a higher risk than appropriate.[21] In cases such as these, long-term intravenous antibiotics are the preferred method of treatment with serial imaging, blood marker evaluation (i.e., ESR), and close evaluation. Several studies of nonsurgical management of osteomyelitis illustrated that surgical versus nonsurgical treatment has similar long-term results; two of the studies were able to identify several factors associated with failure of non-surgical treatment. These included lower transcutaneous oxygen tension, high serum creatinine, more severe signs of infection with gangrene and necrosis, and pyrexia.[22]

In the foot and ankle, diabetes can lead to vascular disease, arthritic diseases, and soft tissue and osseous infections; pedal infections alone account for hospitalizations of 20% of diabetic patients while the incidence of amputations are ~40% higher in diabetic patients versus non-diabetic patients.[23] The early diagnosis of pedal osteomyelitis remains a combination of available modalities. This includes radiographic imaging, clinical assessment, and surgical cultures. After bone infection is appropriately diagnosed, long-term intravenous antibiotics as well as surgical debridement demonstrate ~51% to 86% success rates.[24] In summary, an early and accurate diagnosis of osteomyelitis may lead to enhanced limb salvage. **PM**

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