

Proper Management of Foot Infections in Patients With Diabetes

A superficial foot infection can provide an opportunity for a deep infection to set in.

BY JAMES TAN, MD

One of the most common reasons for hospitalization in diabetic patients is foot infection, with *Staphylococci* and *Streptococci* being the most common organisms for superficial infections. Early and timely intervention for patients with diabetic foot infections can reduce limb loss and save lives.

Among diabetic patients in the United States, foot infection is the leading cause of lower extremity limb loss. To provide optimal management, early recognition is imperative.

Injury as a result of poor fitting footwear or lack of wearing shoes predisposes patients to foot infection. Neuropathy predisposes feet to infections: Autonomic neuropathy causes dry skin, leading to cracking. As skin integrity deteriorates, microbial invasion becomes more likely. With motor neuropathy, foot architecture is altered, changing pressure points as the foot strikes the ground during walking. Sensory loss results in lack of awareness of repeated foot injuries.

Bacteria may invade the foot when the integrity of the skin breaks down due to trauma, infection, paronychia or puncture wounds.

SUPERFICIAL FOOT INFECTIONS

Superficial foot infections (paronychia, infected ingrown toenails, infected shallow ulcers and web spaces between toes) are rarely accompanied by systemic manifestations. Gram-positive cocci are commonly found in superficial infections while gram-negative bacteria or anaerobes are not.

It is common for dermatophytic infections to be found in web spaces. This site of infection provides a nidus for bacterial superinfection, but patients and health care providers often miss its diagnosis due to its anatomic location.

Superinfecting bacteria of the web spaces can enter the deep structures of the foot. Because of its closeness to the digital arterites, tendon joint and bone, infections of these

structures may result in cellulitis, plus in plantar space, gangrene and osteomyelitis.

Cellulitis, dorsal foot phlegmon, deep plantar space infection and infected foot ulcer are typical presentations of deep foot infections. Any deep foot infection can involve the tendon, bone and joints, resulting in limb loss, sepsis and even death. This type of infection commonly begins at the base of a toenail, web space or ulcer, superficially. It then spreads inward to the rest of the foot, often manifesting with swelling and erythema at the base of the toes and distal third of the foot. Swelling may extend even further. Even with this type of involved infection, systemic symptoms are uncommon. If necrotic skin is present, then the arterial supply is impaired.

DIRECT FOOT PENETRATION

Direct penetration of the foot can also result in deep infection. With sensory neuropathy, the patients often cannot feel a puncture from a hypodermic needle, wood splinter or even a nail.

Cellulitis is usually preceded by superficial infection. It may also be a manifestation of a deeper structural infection. Noninfectious inflammatory conditions such as Charcot foot can mimic cellulitis. When soft tissue inflames and includes that neuropathic joint, the joint can be rapidly destroyed along with the bone.

Plantar ulcerations are more commonly found in diabetic patients. When patients present with this type of ulceration, it can be difficult to determine whether the lesion is superficial or deep. Ulceration is the most common precursor to deep foot infection because it provides an avenue to the deep foot spaces. Foot ulcers precede about 75% of foot amputations. While foot ulcers with callus formation are commonly associated with neuropathy, with good vascular supply they are also known as malperforans.

Vascular insufficiency is usually associated with ulcers on

TABLE 1. PATHOGENS ASSOCIATED WITH FOOT INFECTIONS

Foot-infection Syndrome	Pathogen
Cellulitis without an open skin wound	Beta-Hemolytic streptococcus* and <i>S. aureus</i>
Infected ulcer and antibiotic naïve†	<i>S. aureus</i> and Beta-Hemolytic streptococcus*
Infected ulcer that is chronic or was previously treated with antibiotic therapy†	<i>S. aureus</i> , Beta-Hemolytic streptococcus and Enterobacteriaceae
Ulcer that is macerated because of soaking‡	<i>Pseudomonas aeruginosa</i> (often in combination with other organisms)
Long-duration nonhealing wounds with prolonged broad-spectrum antibiotic therapy‡	Aerobic gram-positive cocci (<i>S. aureus</i> , coagulase-negative staphylococci and enterococci) diphtheroids, Enterobacteriaceae, <i>Pseudomonas</i> species, nonfermentative gram-negative rods, and possible fungi
"Fetid foot." extensive necrosis or gangrene, malodorous	Mixed aerobic gram-positive cocci, including enterococci, Enterobacteriaceae, nonfermentative gram-negative rods and obligate anaerobes

*Groups A,B,C and G
† Often monomicrobial
‡ Usually polymicrobial
|| Antibiotic-resistant species (eg, MRSA, vancomycin-resistant enterococci or extended-spectrum Beta-lactamase-producing gram-negative rods are common

Source: Lipsky et al. *Clin Infect Dis* 2004; 39.

the tips of the toes or heels. Neuropathy is associated with ulcers on the sole, especially in areas where repeated pressure injuries occur. Often there is a chronic central ulcer ringed by a halo of hyperkeratinization. If this is left untreated it can lead to deeper infections, progressive tissue necrosis and poor wound healing.

When a physician encounters a chronic nonhealing ulcer, he/she must search underlying osteomyelitis. If the ulcer extends to deeper tissues and is combined with cellulitis, deep-tissue necrosis or systemic toxicity, the infection should be considered moderate to severe and potentially limb or life threatening.

If treated early, the prognosis for infections of this type is typically good. Infection that spreads to the central plantar space is the most serious, and therefore requires drastic surgical intervention. This patient will present with a red swollen foot, and frequently fever, chills, malaise and uncontrolled blood sugar. Complications from this type of an infection include toe gangrene, ischemic necrosis of intrinsic foot muscles, suppurative tendonitis, arthritis and sepsis. If the infection spreads beyond the central plantar space, microorganisms can gain entry to the dorsum of the foot and infection can extend following the flexor tendons.

DIAGNOSIS

Thorough examination of the foot for neuropathy and angiopathy is an important part of the clinical diagnosis. Because sensory neuropathy is the major predisposing factor

to foot infection, an exam for sensory loss, autonomic neuropathy (lack of sweating, dry skin) and motor neuropathy (flattened plantar arch, dorsiflexion hammer toe and splaying of toes) must be done.

The patient should normally be able to feel the monofilament when pressure is applied to the point of buckling. In advanced sensory neuropathy, the patient will not feel pressure when the Achilles is squeezed. A radiographic exam should be done if deformity is suspected. Angiopathy is common in patients with diabetes; therefore vascular status must be determined.

A chronic foot ulcer – no matter its depth – should alert the clinician to investigate for deeper tissue infection, especially osteomyelitis. In elderly patients with osteomyelitis, a common presentation is deep plantar ulcers or ulcers between the toes.

A culture of the infected area directs proper therapy. However, swabbing a superficial ulcer will do no good. If methicillin-resistant *Staphylococcus aureus* (MRSA) is suspected, culture is indicated. Otherwise, samples from the bone and the overlying infected tissues should be obtained.

Traditional radiographs of the foot are cost-effective and should be used initially. Radiography of the foot lacks sensitivity, but when present provides valuable information for management. If osteomyelitis is suspected, clinicians should pay special attention to cortical disruption as a radiographic sign. MRI has become the gold standard in the evaluation of diabetic foot infections.

Probing to bone along with clinical evaluations and radiographic tests may be cost-effective tests for osteomyelitis prior to debridement and definitive bone biopsy.

ANTIFUNGAL TREATMENT

Because superficial fungal infections are common and can predispose patients to bacterial superinfection, these patients should be treated with antifungal agents. For superficial fungal infection with nail involvement, topical agents are generally effective and cheaper than oral agents. Oral agents for tinea pedis should be limited to more extensive or chronic infections that do not respond to topical treatment.

Clinical presentations of diabetic foot infection syndromes and the corresponding pathogens are listed in Table 1. Most superficial infections are caused by gram-positive cocci and culture results are not available. Clinicians must rely on empiric therapy based on previous experience. An oral antimicrobial regimen to treat these bacteria is appropriate.

Clinicians should determine whether an infection is present when an ulcer is detected, noninfected ulcers typically respond well to pressure relief and debridement. When purulence or inflammatory signs are present, infection should be considered. Following pressure relief and debridement, the appropriate antibiotic regimen should be started once appropriate cultures are obtained.

Appropriate footwear is a first line of defense against foot ulcers. Additional therapeutic approaches include hosiery and other pressure-reducing techniques. Patients must learn proper and routine self-care of their feet. Pressure relief remains key to managing neuropathic ulcers, with total contact casting being the gold standard. Successful management is a team approach: Ulcers heal if blood supply is adequate, pressure is relieved from the lesion and infection is properly treated. Hence, multidisciplinary involvement is needed.

DEEP INFECTION TREATMENT

Most deep infections are considered moderate to severe because of the level of involvement and destruction. These patients should be hospitalized and treated with IV antimicrobial agents that eradicate aerobes and anaerobes; surgical intervention may be needed. There are well documented limitations regarding wound management of diabetic foot infections in the literature. However, a regimen with mixed aerobic/anaerobic activities is generally recommended.

There are studies with acceptable results using cefoxitin, carbapenems, and beta-lactam/beta-lactamase inhibitor combinations. These agents have good activity against common infecting organisms and are mainstays of moderate to severe diabetic foot infection treatment.

Cautionary note: Our institution and others have encountered resistance of isolates of the group *B Streptococcus* to

macrolides and clindamycin in vitro.

Recently levofloxacin has been shown clinically effective with activities against gram-positive cocci, gram-negative rods and about three-quarters of anaerobes isolated from the foot. When MRSA is isolated, vancomycin is advised. Linezolid, a newer compound with anti-gram positive activity can be given orally or intravenously, has been reported to achieve excellent response as well (including MRSA). Daptomycin is another new agent with excellent anti-staphylococcal activity.

The main goal if at all possible is to restore function of the foot, namely ability to walk. Surgical intervention, in a timely manner, results in better outcomes and a reduction in limb loss for diabetic patients with deep foot infections, according to studies. This includes early aggressive debridement, bone or digit resection and antimicrobial treatment.

When the bone is not involved in an infection, a 14-day course of treatment is usually adequate. For patients with deep-tissue infection or osteomyelitis and the infected tissues have not been surgically removed, prolonged therapy for 6 to 12 weeks might be needed. While adjunctive therapy such as hyperbaric oxygen and tissue growth factors may be effective, no large-scale clinical evidence is available.

PREVENTION

Early detection of the loss of protective sensation is the biggest factor for preventing lower extremity amputation. The progression of neuropathy and angiopathy with the associated morbidity may be reduced with strict blood sugar control, better patient education and timely intervention on the part of caregivers. Routine foot exams should be performed at every office visit.

Routine foot examinations should include the presence or progression of neuropathy, determining the condition of the pedal pulses, observing for signs of microangiopathy and looking for signs of repeated irritation. Patients should be periodically instructed on things like preventive and regular foot care. Orthotic foot care should be a consideration.

When an ulcer is found, the patient should be instructed to avoid further pressure injury and a consultation with a specialist should be made. In hospitalized patients, limb loss can be avoided by a team approach, including an endocrinologist, general internist, an infectious disease specialist, a foot surgeon and a vascular surgeon. ■

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Tan JS. Current management recommendation for patients with diabetic foot infections. *Infect Dis Clin Pract.* 2005;13:216-223.