

The Foot as a Primary Site for Distant Metastatic Infection

Localized foot infection can lead to generalized sepsis under certain conditions. Two diabetic patients who suffered from infected foot ulcers, even after treatment with debridement and appropriate antibiotics, developed distant site infection. Another diabetic patient developed a distant site abscess from a chronic foot infection, for which he initially sought no medical treatment. Evaluation revealed that one patient had a psoas muscle abscess, one a renal abscess, and one an epidural abscess. All three patients were treated aggressively for their infections. One recovered fully, while two expired from septic complications associated with their illnesses. These case histories, along with the chronology of the development of sepsis from a foot infection, are presented.

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In order to understand generalized sepsis, the entry of pathogenic bacteria into the circulation must be explained. Bacteremia is defined as the presence of bacteria in the bloodstream without systemic infection (1). It can be caused by: infections involving vascular canulas used in parenteral therapy; diagnostic or therapeutic manipulations of the mouth, respiratory, genitourinary or gastrointestinal tracts; dissemination of localized infection; or surgery on infected tissues (2).

Bacteremia may follow infection in a primary site; for example, a foot abscess. As bacteria multiply, they can spread to a contiguous region and enter the bloodstream by direct extension, through venous channels, or lymphatic drainage. Metastatic foci in distant sites can develop and form distinct abscesses. Target organs include the lung, kidney, heart, or bone (2). The vertebral bodies, posterior elements of the spine, epidural space, intervertebral disc, and the paraspinal soft tissues are all potential sites for infection from blood borne organisms (3). The pelvic veins drain directly into the spinal venous plexus, and this is cited as the explanation of frequent metastasis of infections to the spine and pelvic area (3).

Generalized sepsis is the presence of pathogenic bacteria in the systemic circulation, which release endotoxins and numerous mediators that produce cellular damage sufficient to cause systemic illness (1). Fever, chills, prostration, pain, headache, confusion, nausea, or diarrhea are all possible symptoms of septicemia. Diagnosis is based on physical findings and positive blood cultures, and should be treated by appropriate antibiotics. Septic shock can occur during an episode of septicemia when bacterial toxins are released in the bloodstream causing hypotension, fever, tachycardia, tachypnea, renal failure, confusion, or coma. The causative agents are usually Gram negative bacteria (2). Gram positive bacteria can also cause septicemia, however, not as commonly.

The diabetic patient is particularly susceptible to bacteremia or sepsis and can be considered immunocompromised. Neutrophil dysfunction in phagocytosis and chemotaxis may allow a localized infection to progress to a more serious form of sepsis (4). According to Wheat, diabetic patients are predisposed to Gram negative sepsis and group B streptococcal bacteremia in particular (5).

Figure 1 diagrams the pathogenesis of sepsis from a diabetic foot ulcer. Pressure causes loss of skin integrity leading to ulceration. Damaged tissues can become contaminated with sufficient numbers of bacteria to lead to localized infection. This infection may be reversible by host defenses or with appropriate medical care. If unresolved, the infection can result in cellulitis, which is an acute diffuse type of inflammation with little or no suppuration. This is also reversible with appropriate care. Local infection with or without cellulitis can extend to the bone causing osteomyelitis.

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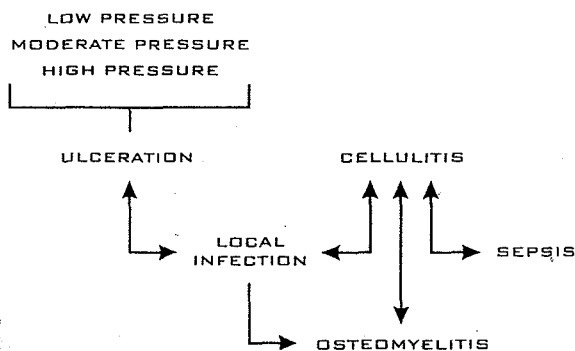


Figure 1. Evolution of sepsis from a diabetic foot ulcer.



Figure 2. Seriously infected foot that could lead to metastatic infection.

This is not usually reversible without excision of the infected bone. Cellulitis or osteomyelitis can become suppurative, while bacteria multiply and invade the circulation. Generalized sepsis can then occur as described earlier. Aggressive medical and surgical care is necessary to reverse this condition (2).

Renal disease is a frequent complication of diabetes. Patients who suffer from the end stage form of renal disease may undergo transplantation as an alternative to dialysis. These people are not only compromised by their diabetes, but also require immunosuppressive therapy to prevent rejection of the transplanted organ. They have a lymphopenia, their response to some antigens is diminished, and they have a decreased inflammatory response. They are susceptible to dangerous, opportunistic viral, fungal, and protozoan invasion. Infection is the leading cause of death in these patients (2). They require special consideration beyond that usually given to other diabetics.

In diabetics, the most common sources of bacteremia are infections of the skin and subcutaneous tissues (6). Most septic processes usually start as a minor break in the skin frequently occurring on the toes or plantar surfaces of the foot (7). Figure 2 is a foot with an extensive dorsal and plantar abscess that could lead to septicemia. The pathogens are usually a mixture of aerobes and anaerobes with some of the most common being *Staphylococcus aureus*, *Escherichia coli*, *Bacteroides fragilis*, and *Pseudomonas aeruginosa* (4, 8, 9). While severe diabetic foot infections are usually polymicrobial in nature, the bacteremia associated with them is commonly monomicrobial (10). Hematogenous spreading of the local foot infection to another site can occur. As these bacteria multiply and toxic products are released, septicemia or shock can develop (2).

To prevent septicemia and its complications, diabetic foot infection must be managed aggressively. The most important element in controlling the lower extremity infection is adequate drainage. If any abscesses are formed, they must be opened and debrided. Cultures for aerobic and anaerobic organisms should be taken

from the deep tissues intraoperatively. Daily soaks or dressing changes may be performed to promote drainage and maintain a clean environment. Due to the mixed nature of infections in the diabetic foot, a broad spectrum antibiotic should be used initially. Consultation with an infectious disease specialist is beneficial. When the results of the cultures are available, the patient should be started on the antibiotic most effective for the organisms identified, unless gross clinical improvement is evident. *In vitro* sensitivity studies are not always indicative of the *in vivo* action of antimicrobial agents. Care should be taken to prescribe the safest, most economical drug available which can be expected to reach therapeutic concentrations. If there is any question of the presence of osteomyelitis, antibiotic therapy should be continued for 6 weeks (11). A high index of suspicion for metastatic spread of infection is necessary to recognize involvement of distant organs in patients who are not responding as expected. The following three cases illustrate how foot infection can be associated with serious dissemination of septic disease.

Case 1

A 66-year-old white female was admitted to the hospital for an infected right foot ulcer. Fever, malaise, and chills had been present for 1 week. The patient's history was positive for cardiac arrhythmia, hypertension, diabetes mellitus, and Charcot arthropathy of the right foot. Physical examination revealed collapse of the inner longitudinal arch and an ulceration measuring 2.5 cm. in diameter on the dorsolateral aspect of the mid-foot. A sinus tract extended to the plantar surface. Purulent drainage was noted. Cellulitis was localized around the ulceration. Pulses were palpable. Laboratory studies revealed erythrocyte sedimentation rate: 121 mm./hr.; white blood count; 17,300/cubic cm.; serum albumin: 2.8 mg./dl. Cultures of the wound and blood were positive for *S. aureus*.

Initially, the patient was started on parenteral ampicillin/sulbactam. Because of the presence of extensive bone destruction and evidence of deep abscess formation, an open Chopart amputation was performed. Complete drainage of the infection was obtained. Based on infectious disease service consultation, antibiotic coverage was changed to Nafcillin.

Approximately 2 days after surgery, the patient remained febrile with an elevated white blood cell count. Normally, one could expect the patient to defervesce after incision and drainage. Another focus of infection was suspected and a Gallium bone scan was ordered. Results revealed increased uptake in the lumbar spine (Fig. 3). Magnetic resonance imaging confirmed the presence of a psoas muscle abscess associated with L1 and L2 vertebral body infection. The general surgery service operated to drain the psoas abscess, and the patient's condition improved. Culture and sensitivity tests identified the same organism that was found in the foot. Intravenous nafcillin was administered for approximately 4 weeks. During that time, the foot amputation site was primarily closed and a tendo achillis lengthening was performed.

The patient was discharged on oral antibiotics for approximately 4 more weeks and subsequently resolved all evidence of infection. She returned to active community ambulation on her operated foot relying on high top athletic shoes with a soft filler for footwear. She has remained free from complications for over 3 years.

Case 2

A 56-year-old white male diabetic who had undergone renal transplantation was first seen as an outpatient with a localized foot ulcer on the hallux. With conservative care, this lesion healed. His medical history included coronary artery disease, treated by coronary artery bypass grafting, hypertension, and chronic transplant rejection. He was on immunosuppressive therapy including prednisone, Imuran®, and cyclosporine.

The patient developed progressive neuropathic changes at the level of the midtarsal and tarsometatarsal articulations. He ultimately developed an ulceration beneath the first metatarsocuneiform articulation. The ulcer was controlled as an outpatient by local debridement, daily cleansing, dressing changes and the use of limited weightbearing. Custom molded shoes with an accommodative plastizote liner were prescribed.

The patient remained stable for some time, but an episode of increased ambulation led to worsening of the ulcer and the development of localized cellulitis. Because of his numerous risk factors, especially immunosuppression, he was admitted to the hospital for administration of parenteral antibiotics. His condition

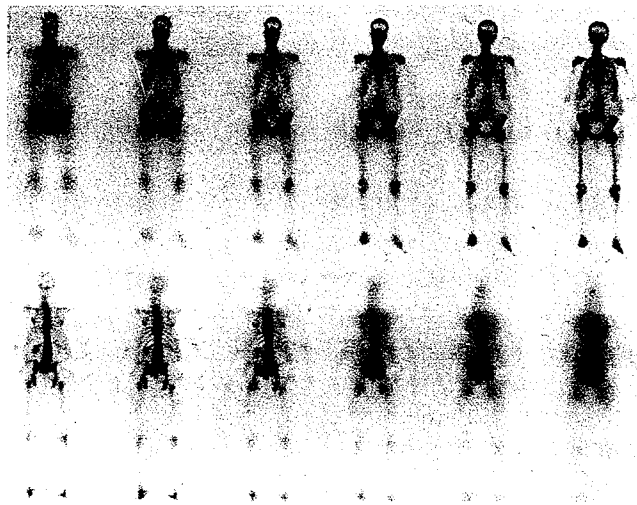


Figure 3. Gallium scan indicating vertebral body involvement and psoas abscess.

stabilized and he was discharged only to be readmitted several weeks later for another bout of cellulitis.

X-rays revealed destructive changes throughout the midfoot. Because of the history of Charcot joint, a definitive diagnosis of osteomyelitis was impossible to confirm without a biopsy. However, it was highly suspected. Although the patient had an ankle-brachial artery index consistent with a good prognosis for healing a local debridement, a more aggressive Syme's amputation was advocated because of the patient's immunocompromised state. It was hoped that the more proximal procedure would be more likely to heal without complication.

A stage I Syme's amputation was performed, and the immediate postoperative course was uneventful. However, during the first 6 weeks after surgery, a progressive dehiscence developed and the patient was rehospitalized. Despite the fact that cartilage on the distal tibia was retained at the time of surgery, destructive changes were noted in the bone. This was treated with debridement, local wound care consisting of whirlpool and dressing changes, and parenteral antibiotics. Wound cultures revealed the presence of methicillin-resistant *S. aureus*. Vancomycin was started on the recommendation of the infectious disease service. A central venous catheter was inserted and the patient was discharged on home intravenous (I.V.) antibiotic therapy.

The patient was re-admitted approximately 2 weeks later for wound infection. Cultures grew methicillin resistant staphylococcus and *Klebsiella pneumoniae*. Treatment consisted of local wound care and I.V. antibiotics. The acute infection was stabilized and the patient was discharged.

Four days later he was re-admitted with chills and fever. Shortly after admission the patient suffered a

respiratory arrest. He was transferred to intensive care. Neither pulse nor blood pressure could be maintained. Resuscitation was attempted, but was unsuccessful. Postmortem examination revealed the presence of *E. coli* and *Proteus aeruginosa* in the residual limb, blood, and transplanted kidney. *P. vulgaris* was found in the residual limb and transplanted kidney. *Candida albicans* was grown in blood culture and from the kidney specimen taken at postmortem examination. Septic shock was considered the immediate cause of death.

Case 3

A 51-year-old male was transferred from a community hospital for treatment of a diagnosed cervical spine epidural abscess. The patient was ventilator dependent on transfer and was placed in intensive care. His past medical history was remarkable for poorly controlled insulin dependent diabetes mellitus, hypertension, and chronic renal insufficiency. The patient's admission history was significant for a long-standing right foot ulceration with associated draining and swelling for 4 weeks' duration, and recent development of a febrile illness. With the onset of fever, he became lethargic and noticed progressive upper and lower extremity weakness that eventually made him bedridden. Prior to admission, bowel and bladder functions were apparently lost. Upon admission, the cranial nerves were found to be grossly intact, motor function from the fifth cervical spinal segment distally was absent.

The patient was afebrile with vital signs stable. He was treated initially by the community hospital for Gram positive (*S. aureus*) sepsis, diagnosed per blood cultures, with Vancomycin and Aztreonam. Prior to transfer, he underwent a lumbar puncture and a computerized tomographic scan of the head, which were negative. Magnetic resonance imaging of the cervical spine region revealed an epidural abscess from C1 to C6, a C4-C7 disc herniation and C4-C5 osteomyelitis.

His lower extremity examination revealed a lateral/plantar ulceration 1 cm. in diameter that tracked deep to bone. Gross edema and localized erythema were noted with significant purulent discharge from the site. Pulses were palpable. Radiographs revealed a substantial plantar exostosis with marked midtarsal dislocations consistent with Charcot arthropathy. Osteomyelitis could not be ruled out.

The infectious disease service was consulted on admission and concurred that the two acute processes required immediate systemic antibiotics and surgical debridement. The recommendation was to change antibiotic coverage to nafcillin and ceftizoxime for empiric coverage of probable polymicrobial infection originating from the diabetic foot infection. The patient was taken to the operating room where he underwent debridement of the epidural abscess, a C3-C6 discec-

tomy, and a C4-C6 corpectomy with iliac crest bone graft fusion. At the same setting, he underwent an incision and drainage of his right foot and lower leg with excision of the prominent tarsal bone.

He tolerated both procedures well and remained afebrile postoperatively. Intraoperative cultures revealed *S. aureus* from the distal right leg and *S. aureus*, *Bacterium* Sp., and *Corynebacterium* Sp. from the right foot wound. Cultures from the epidural abscess revealed no growth. Pathology results from bone specimens from the foot and C4-C5 spine were consistent with acute and chronic osteomyelitis.

Following infectious disease service recommendation, the patient was placed on nafcillin for definitive antibiotics. Based on the fact that the foot infection was the only premorbid condition, identical bone pathologic destructive processes and intraoperative findings, it was believed that the C-spine infection represented metastatic spread of the preceding foot infection.

The patient experienced a relatively unremarkable postoperative course and his surgical sites healed with local wound care. Neurologic function was never regained below the C5 level, and he was discharged to an extended care facility, ventilator-dependent, in stable condition. Six months later he developed pulmonary complications and expired.

Summary

Generalized sepsis can occur as a result of a foot infection. This is especially true in the debilitated or immunocompromised patient. Persisting signs of septicemia in spite of thorough treatment of a foot infection, or physical status changes, such as onset of neurologic deficits, may suggest another focus of infection. Appropriate systems review, physical examination, x-rays or a gallium scan may provide clues to the location of such a lesion.

Prevention of generalized sepsis may be possible through aggressive treatment of the primary infection. This treatment should consist of appropriate antibiotics, debridement, drainage, and local care. Although limb salvage can be accomplished even in seriously infected extremities, consideration should be given to aggressive high amputation in patients who present with serious immunodeficiencies. The persistence of necrotic or infected tissue in these patients constitutes a significant risk of generalized sepsis. This risk must be considered before embarking on a prolonged course of limb salvage therapy that may have limited prospects for success. Because septicemia can have disastrous effects in these patients, the advantage of complete ablation of infected tissue by amputation below, through, or above the knee should be given due consideration.

The possibility of metastatic infection should be considered when a compromised patient presents with a

foot infection, along with other significant complaints or unexplained abnormalities in the physical examination. Inadequate response to appropriate treatment of foot infection may also suggest metastatic spread of infection. Thorough evaluation, along with consultation to the appropriate service regarding findings and complaints in other organ systems, is essential. Three case studies were presented to emphasize that lower extremity infections are not always isolated events, and, in rare instances, can be the primary source of serious generalized sepsis.

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