

BONE BIOPSY AND CULTURES: Recommendations in Suspected Osteomyelitis

Mickey D. Stapp, D.P.M.

The term osteomyelitis is widely used today as a pyogenic infection of bone marrow and/or bone cortex. Strictly speaking, inflammation of the bone cortex is termed osteitis, and inflammation of the bone and marrow is termed osteomyelitis. Osteomyelitis was first introduced by Nelaton in 1844 to describe infection of bone and marrow.¹ The diagnosis of suspected osteomyelitis is a challenging problem, frequently more difficult than the treatment. Osteomyelitis requires a combination of clinical findings, radiographs, labs, bone culture, and bone biopsy for an accurate diagnosis. Early diagnosis remains vital for successful treatment, and prevention of an acute process from becoming chronic osteomyelitis. Bone culture and biopsy are the definitive and most accurate method of detecting osteomyelitis.

Approximately one-third of all patients with osteomyelitis also have diabetes mellitus.² This high-risk patient population is frequently encountered in podiatric medicine, therefore, pedal osteomyelitis is also frequently seen. In one study of more than 1000 diabetic foot infections, osteomyelitis was the most common initial presentation.³

ETIOLOGY

The etiology of osteomyelitis in the diabetic patient is multifactorial. Diabetic neuropathy, producing loss of normal protective sensation, leads to a breakdown of soft tissue. With repetitive trauma or microtrauma, local tissue edema, inflammation, ulceration, and necrosis occurs. Once the dermal barrier has been violated, a portal for infection is opened. Diabetic angiopathy may cause small areas of gangrene and necrosis-producing environments suitable for bacteria proliferation. Immunopathy, which is present in patients with diabetes, may impair the normal inflammatory reaction to bacterial insult. The autonomic dysfunction impairs vascular response to local tissue damage, resulting in pH changes which produce a favorable bacterial environment.⁴ Any or all of these factors can play a role in the development of diabetic foot osteomyelitis.

CLASSIFICATION

Numerous classification systems have been devised for osteomyelitis. Osteomyelitis has been historically classified as an acute, subacute, or chronic infection of bone based upon the clinical course and histological findings.⁵

In 1970, Waldovogel described a classification system based on pathogenesis. In addition to chronic osteomyelitis, he described three types of acute osteomyelitis: hematogenous osteomyelitis; osteomyelitis secondary to contiguous focus of infection; and osteomyelitis associated with vascular insufficiency.⁶ Cierney and Mader described a clinical staging system for osteomyelitis using both an anatomic classification, and a physiologic classification.⁷ Buckholz described seven types of bone infection: wound induced, mechanogenic infection, physeal osteomyelitis, ischemic limb disease, combinations of 1-4, osteitis with septic arthritis, and chronic osteitis/osteomyelitis.⁸ While each proposed classification system offers a unique look at the disease process, no one system has universal acceptance or offers a treatment method in relation to the disease process.

INDICATIONS

Indications for bone biopsy and culture in suspected osteomyelitis are based on clinical examination, laboratory findings, and radiographic changes. Other diagnostic imaging studies have few advantages in suspected osteomyelitis. The clinical examination, including cardinal signs of inflammation such as edema, erythema and calor, are most important in assessing the severity of an infection. Cellulitis alone is not an indication for surgical debridement or bone biopsy and culture. However, cellulitis in conjunction with an infected non-granulating ulcer is an indication. Surgical debridement with bone biopsy and culture are indicated when any of the following are present: a plantar ulceration exposing nonviable tissue such as cartilage or tendons, an ulcer with

undermining borders, or a draining sinus or an abscess.⁹ Diabetic ulcerations that probe on examination to underlying bone should be assumed to have osteomyelitis present.

Laboratory studies often show a leukocytosis with a shift to the left, an elevated erythrocyte sedimentation rate (ESR), and an elevated glycosylated hemoglobin in an acute infectious process, but all may be normal in chronic osteomyelitis. Laboratory tests are not directly diagnostic of osteomyelitis, and play a more important role in monitoring the response to treatment.

The most important study in determining the indication for bone biopsy and culture in suspected osteomyelitis is radiographic examination. Early bony changes in osteomyelitis include thinning of the cortical bone and the loss of trabeculae in cancellous bone. Soft tissue swelling can often be appreciated radiographically. Periosteal reaction, with resorptive bony changes, occurs as the infection progresses, with bone destruction and joint loss possible in later stages. While it is often stated that radiographic evidence of osteomyelitis is delayed 10 to 14 days from the initial onset of infection, early radiolucency may be appreciated in five to seven days after onset of infection. One may detect early changes with careful inspection, particularly when compared to baseline or previous radiographs. Osseous changes on radiographs, in the presence of soft tissue infection or ulceration, should be presumed to be osteomyelitis, although diabetic osteolysis, spontaneous fracture, reactive periostitis, and neurotrophic joint disease may mimic osteomyelitic changes.¹⁰

Other diagnostic imaging studies offer little to the clinical assessment of the diabetic foot regarding the presence or absence of osteomyelitis.^{9,11} False-positive technetium bone scans can occur with similar bony processes which radiographically mimic osteomyelitic changes. False-negative radiopharmaceutical scans can occur secondary to peripheral vascular disease or local diminished osseous perfusion.

Computed tomography (CT) may detect early signs of acute osteomyelitis, but similar changes occur with aseptic necrosis, osteoporosis, arthrosis, and osteomalacia.¹² Magnetic resonance imaging (MRI) has shown some promise in the diagnosis of acute osteomyelitis by imaging early bone marrow changes. If only an acute osteitis is present, and the marrow is not yet involved, then the accuracy of

the MRI is diminished. MRI would be useful in the diabetic fetid foot with rampant infection, such as necrotizing fasciitis, to demonstrate the extent of involvement.¹¹

BIOPSY TYPES

Once the need for surgical debridement with bone biopsy and culture has been established, one must decide on the type of biopsy which is to be performed. Recall that the goal of surgical debridement is to eliminate all infected and/or necrotic tissue, including bone. It is also important to spare viable skin and soft tissue in order to achieve adequate closure and an optimal functional outcome. If a wound is of questionable viability or grossly infected, then primary closure is not performed. However, a bone biopsy and culture should be obtained. The wound should be packed-open, and the patient returned to the operating room as needed, until granulation occurs. Delayed primary closure can then be undertaken, or the wound may be allowed to close by secondary intention.

A Jamshidi needle, (Perfectum Corp., Hyde Park, NY), can be utilized for either open or percutaneous bone biopsy. The Jamshidi needle is an 11-gauge, 6-inch, bone biopsy needle which is ideal for obtaining a specimen percutaneously or through an ulceration overlying exposed bone. False-negative culture and biopsy results are possible due to a sampling error or an inadequately sized specimen.¹³ Bone trephines are suitable instruments for identifying the presence or absence of osteomyelitic bone. These are often used in obtaining bone biopsies in the midfoot and/or rearfoot, where complete surgical resection of infected bone may leave the patient with a dysfunctional foot. If complete surgical resection of osteomyelitic bone is the goal, then trephines should not be used. A trephine should be chosen based on the size of the bone which is suspect for osteomyelitis. Studies have shown that 2 mm and 7 mm diameter trephines are not significantly different in the percentage of trabecular bone and the surface density of the bone obtained.¹⁴ Therefore, it is recommended that the smallest trephine be used, to prevent further sequelae such as cortical stress risers and delayed healing of the trephined bone.

A bone rongeur or curette may be used in areas of suspicious bone to obtain a diagnosis, if surgical resection is not desired. If only a definitive

diagnosis of osteomyelitis is the surgical goal, and treatment will then consist of long-term antibiotics in an attempt to suppress the bone infection, these instruments will suffice, and may offer the advantage of sparing functionally-needed bone. If the diagnosis of osteomyelitis is made, and further surgical resection of infected bone is warranted, then again the bone rongeur and curette are adequate biopsy instruments.

The majority of bones suspected of having osteomyelitis in the foot are located in the forefoot, thus they are of the long-bone type. Therefore, power instrumentation is suitable for obtaining cylindrical bone specimens for biopsy and culture. In general, the quality of suspicious bone is assessed intraoperatively, and an appropriate level of resection or biopsy is determined. Resection of long tubular bones, (phalanges or metatarsals), is performed until healthy bleeding bone is noted intraoperatively. Once this level is reached, a more proximal cylindrical section of bone can be obtained for separate biopsy, to confirm complete surgical resection of infected bone, or surgical cure of the osteomyelitis.

TIMING

The majority of patients admitted with severe diabetic foot infections have previously been treated with some antibiotics on an outpatient basis. Therefore, it is possible to obtain negative cultures, or cultures of superficial colonizing bacteria only. Such cases require deep cultures of soft tissue and bone for appropriately directed antibiotic therapy. It is important to discontinue the antibiotic 48 to 72 hours prior to obtaining such deep cultures and biopsies, so that residual antibiotics do not retard the growth of the infecting bacteria.¹⁵ If a severe cellulitis, fasciitis, gangrene, or sepsis is present, then it is not necessary to discontinue the antibiotics preoperatively.

The best time to obtain a biopsy and culture of suspicious tissues is at the same time as the incision and drainage, or during the surgical debridement of non-viable tissue. Mackowiak and associates have demonstrated that cultures obtained from draining sinus tracts and soft tissue specimens proximal to osteomyelitic bone frequently fail to demonstrate organisms responsible for the infection of bone.¹⁶

It must be remembered that open biopsy and culture of suspected osteomyelitic bone is a surgical

procedure which risks potential contamination of uninvolved tissues. In addition, the surgical dissection required to obtain the specimens may result in non-healing surgical wounds in patients with compromised peripheral circulation.¹

LOCATION

Controversy exists regarding the best location to obtain a bone biopsy and culture. Most authors believe that an appropriate bone biopsy and culture is best obtained through a clean, open exposure separate from the ulcer or overlying infected soft tissues.^{4,9,11} This reduces the potential risk of implantation of bacteria from the soft tissues into bone during the biopsy and culture process. Biopsy and culture of bone through an ulceration may be indicated in certain circumstances. In a neuropathic diabetic patient with a chronic, non-infected mal-perforans type ulceration which probes to bone, a trephine biopsy or Jamshidi needle biopsy can be used. This can often be performed in a clinic or office setting, without the need for anesthesia. This may establish a definitive diagnosis of osteomyelitis, and then a further surgical and/or medical plan can be laid-out accordingly.

Swab cultures for Gram's stain, aerobic, and anaerobic cultures should be obtained intraoperatively at the same time a bone biopsy and culture is to be obtained. The inaccuracy of swab cultures of ulcers, or draining sinuses, has already been stated. Since the majority of diabetic infections are polymicrobial, the precise identification of bacteria from deep intraoperative swab cultures will aid in choosing the appropriate antibiotics for the soft tissue infection, as well as the bone infection, if present. It has been shown that *Enterococcus* and gram negative bacteria are inadequately identified by swab cultures, and that swab cultures typically only identify about 66 percent of the pathogenic bacteria.¹⁵ Wheat demonstrated that *Proteus* and *Pseudomonas aeruginosa* are frequent anaerobes which are cultured in about one-third of patients with diabetic foot infections.¹⁷

Since swab cultures, even though obtained from deep tissues with open exposure, can fail to identify the pathogenic bacteria, bone cultures should also be obtained. A culture of the advancing edge of infected bone is most accurate for establishing appropriate antibiotics. A bone culture is typically a small section of bone that is

rongeured from the cylindrical wedge of bone removed for biopsy, or a portion of a trephine biopsy that is sent in thioglycolate broth to a microbiology laboratory. Thioglycolate acts as an enrichment broth for bacteria on or within the bone. Gram's stain, aerobic, and anaerobic cultures may then be performed from swabs of the enrichment broth. Bone cultures are also vital in chronic osteomyelitis, since bacteria are not usually seen in blood or local tissues.

EXAMPLES

Digital and Forefoot Infections

It is generally accepted that surgical excision of osteomyelitic bone, combined with intravenous antibiotics, should be instituted whenever bone infection is suspected. With the surgical incision and drainage, radical debridement, or ablative surgery, all necrotic bone, soft tissue and devascularized structures should be excised. All infected bone, and a small portion of apparently uninvolved bone, should be removed. The proximal margin of apparently uninvolved bone should be sent as a separate biopsy to determine if a surgical cure was achieved. Many authors agree that if a surgical cure of the infected bone is accomplished, then a shorter course of intravenous antibiotics is possible.^{4,9,18} It is rarely satisfactory to treat existing osteomyelitis of the forefoot with antibiotics alone. Various circumstances will prohibit the total surgical excision of all infected bone. These include poor surgical candidates, and surgery which might disfigure, destabilize, or cause loss of foot function. In these instances, six weeks of intravenous antibiotics is the standard of care.

Ulcerations, with suspected osteomyelitis at the distal digital tip or tuft of the lesser digits, can be approached through a distal Syme's-type amputation, or distal interphalangeal joint (DIPJ) disarticulation. If the middle phalanx is not suspected of having infection, and the soft tissues are not grossly infected, the wound may be closed with a plantar flap, or a tennis racquet-type incision. The removed bone of the distal phalanx should be sent for both biopsy (microscopic pathologic review) and bone culture in thioglycolate broth. A Jamshidi needle or a small trephine may be used to sample the middle phalangeal head for biopsy only. Removal of the cartilage from the head of the middle

phalanx is recommended prior to closure. If the wound is not ready to be primarily closed at the initial surgery, the cartilage cap should be left intact, providing a better barrier to remaining bacteria. The cartilage should be removed at the time of delayed primary closure, since cartilage is mainly avascular, and necrosis will occur without its normal synovial fluid environment, producing a potential nidus for infection. Curettage of the cartilage in a disarticulation is recommended, since the subchondral bone will provide a better barrier to any remaining bacteria than would a transcortical osteotomy.⁴ Other authors believe that the articular cartilaginous cap of disarticulated joints should remain intact to prevent the invasion of bacteria.¹⁹

Dorsal digital ulcerations with suspected osteomyelitis typically overlie the distal interphalangeal joint (DIPJ) or the proximal interphalangeal joint (PIPJ). They are a result of constant shoe pressure with an underlying contracted digital deformity. Often, a therapeutic and diagnostic arthroplasty at the involved joint is all that is necessary. If radiographs suggest osseous changes only at the joint level, then this will relieve the deformity and provide the surgeon with appropriate bone biopsy and cultures. Both the phalangeal base and the phalangeal head of the resected joint may be sent for biopsy, with a small, rongeured portion from the most obviously-involved bone being sent to microbiology in thioglycolate. A more distal cylindrical wedge, and a more proximal cylindrical wedge, can be removed for pathologic evidence of surgical cure of the osteomyelitis. If the PIPJ is involved, with involvement of the proximal phalanx, an attempt should be made to maintain the base of the proximal phalanx of the central three digits to act as spacers, maintain alignment, and preserve the attachments of the intrinsic musculature. It is common to see a severe hallux abductovalgus deformity after total amputation of the second digit.

Ulcerations occurring at the tip of a hallux, with suggestive radiographic osseous changes in the distal phalanx, may be addressed in a similar manner as a lesser digit. One exception is that since the distal phalanx is substantially larger than a distal phalanx of a lesser digit, a distal Syme's-type amputation may be performed transcortically through the distal phalanx. Again, infected bone must be debrided to apparently clean bone with adequate bleeding. A more proximal cylindrical

wedge of bone can be removed for pathological confirmation of a surgical cure of the osteomyelitis. An ulceration plantar to the hallux interphalangeal joint may be addressed through an interphalangeal joint diagnostic and therapeutic arthroplasty, as described previously for dorsal involvement at the lesser DIPJ and PIPJ.

Ulcerations beneath the metatarsal heads, with radiographically suggestive osteomyelitic changes, offer a unique challenge to the podiatric surgeon. With resection of one or more metatarsal heads, transfer lesions with subsequent ulcerations and possible further osteomyelitis of adjacent metatarsal heads is all too familiar. If no radiographic changes are evident, then a plantar condylectomy of a lesser metatarsal, or a sesamoidectomy of the first metatarsophalangeal joint, may eliminate the underlying bony prominence responsible for the ulceration. This resected specimen should be sent for both biopsy and culture. If radiographic changes are evident, then resection of the metatarsal head should be considered. If only one metatarsal head is involved, an isolated metatarsal head resection may be attempted, with the knowledge that a transfer lesion may occur. If more than one metatarsal head is involved, a pan-metatarsal head resection should be considered for the best functional outcome.

If the digit is also infected, necrotic, or gangrenous, as well as a portion of the corresponding metatarsal, then a ray resection can be performed. A ray resection involves removal of the digit and all or a portion of the metatarsal. A ray resection is usually reserved for the lesser metatarsals, since a first ray resection is not very functional. A ray resection works best for the central or third metatarsal.²⁰ The base of the central three metatarsals should be preserved in ray resections, in order to maintain the inherent stability at the LisFranc joint. If the fifth ray is to be resected, then the entire metatarsal may be removed via disarticulation at the metatarsal-cuboid joint. In a ray resection, a more proximal cylindrical wedge of bone should be obtained and sent as a separate biopsy once clinically apparent involved bone is removed. A bone culture should again be obtained from the most obvious involved bone, generally at the base of the proximal phalanx of the involved digit or the head of the involved metatarsal. Deep soft tissue cultures should be routinely obtained.

Midfoot Infections

Ulcerations plantar to the midfoot, with osseous changes on the radiograph, offer another challenge in the diagnosis of osteomyelitis. Midfoot osseous changes are often due to a Charcot deformity. It is difficult to distinguish between osteomyelitis and Charcot changes on x-ray. Both can produce severe and extensive destructive changes, lysis of bone, and new bone formation. Charcot changes generally do not have significant surrounding osteopenia.⁹ A plantar midfoot exostectomy may be performed through a separate medial or lateral incision, or plantarly with ellipse of the ulceration. The resected bone may be sent for biopsy and culture. If osteomyelitis is diagnosed, then long term antibiotics is often the treatment of choice, in the proper candidate, to maintain a plantigrade functional foot. If the bones and soft tissues distal to the midfoot are involved in the infectious or dysvascular process, then a more proximal amputation (Chopart's or Syme's) may be required. A separate synovial biopsy should be performed. Spicules of bone embedded in synovium is pathognomonic for Charcot deformity.

If osteomyelitis of the midfoot is to be determined or ruled-out before a more aggressive surgery, such as midfoot/rearfoot arthrodesis procedures or a full Charcot reconstruction, then a trephine biopsy is ideally suited. The biopsy should be performed at the most involved bony area, usually the plantar prominence causing the ulceration. A portion of this trephine biopsy should be sent for microscopic review, and a portion in thioglycolate for culture and Gram's stain.

Rearfoot Infections

Suspected osteomyelitis in the calcaneus usually arises from decubitus-type ulcers on the posterior or plantar heel. These are especially difficult to treat and manage, because the plantar fat pad is relatively avascular. A trephine bone biopsy is the simplest way to obtain a diagnosis of osteomyelitis, and appropriate culture of potentially infecting bacteria. If the diagnosis of osteomyelitis is determined, a surgical and medical plan can be devised, based on the patient parameters of lifestyle, ambulation ability, and vascular status.

Exostectomy, partial calcanectomy, and total calcanectomy are options in suspected osteomyelitis of the calcaneus. These are warranted options especially

in the non-ambulatory patient or wheel-chair bound patient, in which transfers from bed to wheelchair, would be more efficient with the use of a functional limb. All resected bone should be sent for microscopic examination and culture. Long-term antibiotics or further surgical intervention can then be determined.

CONCLUSION

The diagnosis of osteomyelitis requires a high index of suspicion, coupled with sound clinical judgement. With radiographic evidence of bony changes in relationship to an ulceration and soft tissue infection or necrosis, bone biopsy and culture should be performed. Accurate bone biopsy and culture are the definitive method for detecting osteomyelitis. When incision and drainage and/or surgical debridement of bone and soft tissue is deemed necessary, all infected and/or necrotic tissues must be excised. Bone should be resected until a level is reached that appears not only clean of infection and erosive changes, but that adequately bleeds when cut. A small portion of apparently uninvolved bone should be removed and sent for separate biopsy. A small portion of the biopsy from the most apparently involved bone should be sent in thioglycolate broth for culture. Generally, the greater the amount of foot salvaged, the greater the function of the foot. With an appropriate surgical cure of osteomyelitis, a shorter course of antibiotics, a shorter hospitalization, and a more functional outcome can be achieved.

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