[46] Achermann Y, Vogt M, Leunig M, Wüst J, Trampuz A. Improved diagnosis of periprosthetic joint infection by multiplex PCR of sonication fluid from removed implants. J Clin Microbiol. 2010;48:1208–1214. doi:10.1128/JCM.00006-10.
[47] Holinka J, Bauer L, Hirschl AM, Graninger W, Windhager R, Presterl E. Sonication cultures of explanted components as an add-on test to routinely conducted microbiological diagnostics improve pathogen detection. J Orthop Res. 2011;29:617–622. doi:10.1002/jor.21286.
[48] Shen H, Tang J, Wang Q, Jiang Y, Zhang X. Sonication of explanted prosthesis combined with incubation in BD bactec bottles for pathogen-based diagnosis of prosthetic joint infection. J Clin Microbiol. 2015;53:777–781. doi:10.1128/JCM.02863-14.
[49] Yano MH, Klautau GB, da Silva CB, Nigro S, Avanzi O, Mercadante MT, et al. Improved diagnosis of infection associated with osteosynthesis by use of sonication of fracture fixation implants. J Clin Microbiol. 2014;52:4176–4182. doi:10.1128/JCM.02140-14.
[50] Portillo ME, Salvadó M, Trampuz A, Siverio A, Alier A, Sorli L, et al. Improved diagnosis of orthopedic implant-associated infection by inoculation of sonication fluid into blood culture bottles. J Clin Microbiol. 2015;53:1622–1627. doi:10.1128/JCM.03683-14.
[51] McDowell A, Patrick S. Evaluation of nonculture methods for the detection of prosthetic hip biofilms. Clin Orthop Relat Res. 2005:74–82.
[52] Tzeng A, Tzeng TH, Vasdev S, Korth K, Healey T, Parvizi J, et al. Treating periprosthetic joint infections as biofilms: key diagnosis and management strategies. Diagn Microbiol Infect Dis. 2015;81:192–200. doi:10.1016/j.diagmicrobio.2014.08.018.
[53] Panousis K, Grigoris P, Butcher I, Rana B, Reilly JH, Hamblen DL. Poor predictive value of broad-range PCR for the detection of arthroplasty infection in 92 cases. Acta Orthop. 2005;76:341–346.
[54] Gomez E, Cazanave C, Cunningham SA, Greenwood-Quaintance KE, Steckelberg JM, Uhl JR, et al. Prosthetic joint infection diagnosis using broad-range PCR of biofilms dislodged from knee and hip arthroplasty surfaces using sonication. J Clin Microbiol. 2012;50:3501–3508. doi:10.1128/JCM.00834-12.

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QUESTION 3: What is the optimal method to perform bone biopsy (method, location, imaging use) for patients with foot and ankle infections?

RECOMMENDATION: A bone biopsy should generally be performed in a percutaneous fashion, particularly in cases where surgical debridement is not considered necessary.

If surgical debridement is considered necessary, then an open biopsy can be performed as part of the debridement.

Percutaneous biopsy should be performed under sterile conditions by an interventional radiologist or other physician trained in image-guided techniques.

The location of the biopsy will depend upon the clinical and radiographic evaluations, with a goal of maximizing the yield of the biopsy while minimizing the risk of injury to surrounding and/or overlying soft tissue structures.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Infection in the foot and ankle bone or soft tissues can be associated with significant morbidity and even mortality. Prompt diagnosis and treatment are paramount. Often, diagnosis can be made based on a combination of clinical examination, radiographic imaging and laboratory data. Bone biopsy is considered the gold standard for the diagnosis of osteomyelitis [1–5].

Bone biopsy can be particularly helpful when the clinical exam, radiographic imaging and laboratory data are not clearly confirmatory of an underlying infection. Additionally, a bone biopsy can allow for identification of the infecting organism(s), and therefore allow for a more tailored treatment regimen. It can also exclude rarer causes of bone disease, such as malignancy or osteonecrosis [6,7].

A percutaneous bone biopsy is generally preferable to an open biopsy, particularly in cases where surgical debridement is not considered necessary. Percutaneous techniques are less invasive, less costly and are associated with less morbidity [7–10]. A percutaneous bone biopsy should be carried out under image guidance, generally either fluoroscopy or computed tomography (CT) and should be performed by an interventional radiologist or other physician trained on image-guided techniques. Image guidance allows for specimens to be obtained from specific targeted areas. The choice of imaging technique used to guide the biopsy depends on the anatomic location, availability and practitioner preference. Fluoroscopy can be used for more superficial lesions and allows for real-time guidance. Its main limitation is its two-dimensional nature. CT guidance provides visualization of not only osseous structures but also important soft tissue structures, such as neurovascular structures, within a three-dimensional framework. Its main limitation is the increased radiation exposure in comparison to fluoroscopy. There are reports in the literature regarding magnetic resonance (MR) guided percutaneous bone biopsies, but the availability of MRI-compatible instruments and accessories limits its use [11,12].

The choice of anatomical region to perform a biopsy will depend on the state of the overlying soft tissues and the radiographic findings. The goal should be to increase the yield of the biopsy while minimizing potential risk to nearby soft tissue structures. In general, more superficial areas of concern are targeted. If multiple areas of concern exist, one will also want to prioritize the site which is likely to provide the highest diagnostic yield. The procedure should be performed under sterile conditions to reduce the risk of contamination of skin flora. If possible, multiple samples should be obtained utilizing multiple trajectories within the bone to increase the diagnostic yield of the procedure.

REFERENCES

[1] Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJG, Armstrong DG, et al. 2012 infectious diseases society of america clinical practice guideline for the diagnosis and treatment of diabetic foot infections. J Am Podiatr Med Assoc. 2013;103:2–7.
[2] Lipsky BA, Aragón-Sánchez J, Diggle M, Embil J, Kono S, Lavery L, et al. IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. Diabetes Metab Res Rev. 2016;32 Suppl 1:45–74. doi:10.1002/dmrr.2699.
[3] Berendt AR, Peters EJG, Bakker K, Embil JM, Eneroth M, Hinchliffe RJ, et al. Diabetic foot osteomyelitis: a progress report on diagnosis and a systematic review of treatment. Diabetes Metab Res Rev. 2008;24 Suppl 1:S145–161. doi:10.1002/dmrr.836.

[4] Leffler SG, Chew FS. CT-guided percutaneous biopsy of sclerotic bone lesions: diagnostic yield and accuracy. AJR Am J Roentgenol. 1999;172:1389–1392. doi:10.2214/ajr.172.5.10227522.
[5] Lipsky BA. Osteomyelitis of the foot in diabetic patients. Clin Infect Dis. 1997;25:1318–1326.
[6] Howard CB, Einhorn M, Dagan R, Yagupski P, Porat S. Fine-needle bone biopsy to diagnose osteomyelitis. J Bone Joint Surg Br. 1994;76:311–314.
[7] Ng C, Gishen P. Bone biopsies. Imaging. 2000;12:171–177.
[8] Berning W, Freyschmidt J, Ostertag H. Percutaneous bone biopsy, techniques and indications. Eur Radiol. 1996;6:875–881.
[9] Carrasco CH, Wallace S, Richli WR. Percutaneous skeletal biopsy. Cardiovasc Intervent Radiol. 1991;14:69–72.
[10] Fraser-Hill MA, Renfrew DL, Hilsenrath PE. Percutaneous needle biopsy of musculoskeletal lesions. 2. Cost-effectiveness. AJR Am J Roentgenol. 1992;158:813–818. doi:10.2214/ajr.158.4.1546598.
[11] Gogna A, Peh WCG, Munk PL. Image-guided musculoskeletal biopsy. Radiol Clin North Am. 2008;46:455–473, v. doi:10.1016/j.rcl.2008.04.014.
[12] Gupta S. New techniques in image-guided percutaneous biopsy. Cardiovasc Intervent Radiol. 2004;27:91–104.

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QUESTION 4: What is the best method to differentiate acute Charcot foot from acute infection?

RECOMMENDATION: Differentiation between acute Charcot neuroarthropathy (CN) and acute infection/osteomyelitis is complex and requires multiple (>1) diagnostic criteria. These criteria include an emphasis on the presence of neuropathy, history and physical examination. The absence of skin wounds and resolution of swelling/erythema with elevation makes the likelihood of infection very low.

In unclear cases, laboratory testing, histological examination and culturing of bone specimens, scintigraphy, and imaging, especially magnetic resonance imaging (MRI), may be of benefit.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

At initial presentation, acute infection comprising of cellulitis and osteomyelitis (OM) and CN may be difficult to differentiate. However, it is important for the clinician to make an accurate diagnosis, as correct treatment largely determines outcome as both present a substantial risk of limb amputation and mortality.

Physical features can provide essential clues to the diagnosis. The "probe-to-bone" test, which tests whether the underlying bone is palpable via a probe inserted into a wound, has demonstrated sensitivity ranging from 38 to 95%, specificity ranging from 84 to 98%, and a positive predictive value ranging from 53 to 97% for the diagnosis of osteomyelitis [1–6]. In their study of 1,666 consecutive diabetic patients, Lavery et al. demonstrated that a positive probe-to-bone test increases the probability of OM greater than 50%, whereas a negative test is a strong predictor of absence of infection [3]. The test, however, has shown to have a high variability when performed by inexperienced clinicians, but this intra-observer variability was demonstrated to decline with experience [7].

In terms of other physical features, CN typically affects the midfoot and lacks associated skin breakage, whereas OM is more frequently found in the forefoot and is often accompanied by soft tissue infection or ulcer [8,9]. Additionally, while it is possible to contract OM through hematogenous spread, the vast majority of cases are spread directly via a soft tissue infection or ulcer. A wound size > 4.5 cm^2 is associated with a three times higher chance of underlying OM [10]. However, others have suggested that both ulcers of size > 2 cm^2 and depth > 3 mm are also significant [11,12]. White blood cell (WBC) counts, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) are often utilized for work-up of infection. Some investigators have concluded that elevated ESR (> 70 mm/h) is strongly associated with OM [11–14].

A further benefit of ESR is that, while levels of the other inflammatory markers drop rapidly once antimicrobial treatment begins, ESR remains elevated for longer periods of time, therefore making it useful in monitoring treatment efficacy. Interleukin (IL)-6 has also been suggested as a marker for diagnosis of OM and monitoring treatment in preliminary studies [15,16]. However, these inflammatory markers are nonspecific and may be elevated by various other factors. Given that many patients with histologically proven OM may present with a normal WBC count, hematologic studies alone are not reliable for diagnosis of OM [11–14].

Bone culture alone is reported to have a sensitivity of 92% and a specificity of 60% in diagnosing OM in diabetic feet [17]. Bone samples can be obtained by percutaneous biopsy or during surgery [12,18]. However, bone specimens may often yield false-positive or false-negative results. Histologic analysis is suggested to be important in preventing these undesirable results, as several studies have shown that 40 to 60% of histologically proven cases of OM at surgery or biopsies of foot and ankle had negative cultures [19–22]. Therefore, standard criteria for the diagnosis of OM should be a positive culture with histopathologic evidence of infection in bone specimen [23].

Radiographic signs of infection, such as demineralization, periosteal reaction and cortical destruction, may not appear until two to three weeks after onset and require a loss of 40 to 50% bone mass to detect the difference [8,24]. The accuracy of plain radiography for early diagnosis is 50 to 60% with a sensitivity of 60% and a specificity of 80% [25,26]. Therefore, more advanced imaging is needed for diagnosis of acute osteomyelitis.

Magnetic resonance imaging (MRI) is suggested to be an effective modality to aid in early diagnosis [27,28]. A previous meta-analysis has shown that the sensitivity of MRI to diagnose OM in the foot and ankle is 90% sensitive and 79% specific [29]. In a meta-analysis of 16 studies, MRI performance was superior to that of technetium ^{99m}Tc bone scanning, plain radiography, and WBC studies. The sensitivity for the diagnosis of OM was found to be 90% while specificity was 85% [30]. MRI was better able to identify the extent of the involved area, whereas WBC bone scan may have better performance in differentiating OM from CN, especially in patients with metal implants [23,24].

While chronic CN shows low intensity in both T1- and T2-weighted images, both acute OM and acute CN show low signal on T1-weighted images and hyperintensity on T2-weighted images with contrast enhancement. However, these are common markers in both infective and neuropathic disease, making differentiation