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QUESTION 4: Should treatment of diabetic foot osteomyelitis be based on bone biopsies?

RECOMMENDATION: Yes. Bone biopsies play both a crucial diagnostic and interventional role in the management of diabetic foot infection. While bone biopsies are not required in every case of diabetic foot infection, their most important role is in guiding accurate antibiotic treatment, as they provide more accurate microbiological information than superficial soft tissue samples in patients with diabetic foot osteomyelitis.

LEVEL OF EVIDENCE: Moderate

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

RATIONALE

Diabetic foot infections of the skin and soft tissue can lead to contiguous spread to underlying bone, resulting in osteomyelitis. Where a diabetic foot ulcer fails to heal with no other apparent reason or when exposure of bone is observed, osteomyelitis should be suspected. Plain radiography has demonstrated to have poor sensitivity in detecting osteomyelitis in the early stages [1].

Moreover, plain radiography and other imaging modalities do not identify pathogenic organisms, and, thus cannot guide antibiotic therapy. Despite the ease of obtaining superficial wound swab cultures, the cultured organisms are polymicrobial and do not correlate well with bone biopsy cultures and, therefore, should not be used to guide antibiotic therapies [2–6]. A single retrospective multicenter cohort study reported that the rate of infection resolution was significantly higher in the group for whom the choice of antibiotic regimen was based on bone culture versus those based on wound swab culture (82% vs. 50%, p = 0.02) [7].

Bone biopsies taken for microbiological and histopathological analysis are the gold standard for a definitive diagnosis of osteomyelitis [8–10]. A specimen can be obtained either transcutaneously through uninfected skin or as part of an operative procedure following debridement. Bone biopsies play both a crucial diagnostic as well as interventional role in the management of diabetic foot infection. While bone biopsies are not required in every case of diabetic foot infection, their most important role is in guiding accurate antibiotic treatment.

A positive microbiological result is where one or more pathogens from a reliably-obtained bone specimen is cultured [11]. It has shown to give a sensitivity of 92% and specificity of 60% in diagnosing diabetic foot osteomyelitis [12]. Reliable and accurate identification of the causative pathogens in diabetic foot infections is important, as prolonged antimicrobial therapy is tailored according to microbiological susceptibility profile. Most diabetic foot osteomyelitis cases are polymicrobial, with *Staphylococcus aureus* being the most commonly isolated pathogen (50% of cases). Other frequently isolated organisms include coagulase-negative staphylococci, *Enterobacteriaceae*, aerobic streptococci and *Pseudomonas aeruginosa* [8,13,14]. Contamination of contiguous wound colonizing flora and skin commensals may give a false positive result, whereas prior antibiotic therapy, patchy infectious involvement or inability to culture fastidious organisms may yield false-negative results [11].

Positive histological findings include aggregates of inflammatory cells (neutrophils, lymphocytes, histiocytes and plasma cells), erosion of trabecular bone, marrow changes (fat necrosis, edema, fibrosis and reactive bone formation) [11,15,16]. Other causes of inflammation may give false-positive histological results, whereas sampling errors can give a false-negative result. Histological analysis may have better sensitivity than bacteriological cultures, as the latter is often performed under flawed conditions. However, a study by Meyr et al. has questioned the statistical reliability of the histopathologic diagnosis of diabetic foot osteomyelitis using bone biopsies, quoting a 41% of clinically significant disagreement between different pathologists, falling short of what would be expected of a “reference standard” [16]. This highlights the controversy in histopathological patterns and findings that pathologists use as a reference to establish a diagnosis of osteomyelitis [15,17,18].

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