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QUESTION 5: Is there a role for percutaneous bone sampling (biopsy) for microbiological diagnosis of septic arthritis/osteomyelitis (OM)? If so, when should this be performed?

RECOMMENDATION: Yes. Percutaneous bone sampling (biopsy) is very safe and cost-effective and can be obtained from any site under the guidance of fluoroscopy or computed tomography (CT). It has a low sensitivity for microbiological diagnosis of OM that can be enhanced by the addition of histopathological examination. Literature suggests that bone sampling should be performed before initiating empirical antibiotic therapy.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 88%, Disagree: 7%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

OM is described as inflammation of the bone marrow and adjoining bone and is usually related with cortical and trabecular destruction. It can be caused by bacteria, fungi and a variety of other organisms [1]. Prompt identification and treatment of OM is necessary since undiagnosed cases can result in chronic pain, amputation and death. Even though clinical symptoms, inflammatory serological markers and imaging, such as magnetic resonance imaging (MRI), play an essential role in reaching a diagnosis of OM, the most important aspect of diagnosis relies on isolation of the infective organism from the infection site [2–4]. Pathogen identification and determination of its antibiotic susceptibility are paramount for successful treatment with antimicrobial therapy. Blood cultures may also be positive in a small number of patients with OM, which can guide antimicrobial therapy, so definite diagnosis and suitable therapy depend on tissue samples collected through bone biopsy [4].

Although surgical biopsy is also an option for confirming the diagnosis, percutaneous biopsy with fluoroscopic or computed tomography (CT) guidance has been proven to be a more reasonable, faster and more cost-effective modality with fewer complications [5,6]. The first percutaneous vertebral bone biopsy was performed by Ball in 1934. The use of image guidance was first seen with radiography in 1949, fluoroscopy in 1969, CT in 1981, MRI in 1986 and CT fluoroscopy in 1996 [6].

Literature review from the 1990's and early 2000's stated the accuracy of a percutaneous biopsy of vertebral lesions guided with CT or fluoroscopy ranged from 88% to 100% [6]. The recent and most comprehensive retrospective review done by Sehn and Gilula reported that 63 of 113 cases were positive when samples were tested histologically (55.7%) and only 28 of the 92 cases were positive when samples were investigated microbiologically (30.4%). Culture and/or pathology review was positive in 73 (64.6%) of the 113 cases. Pathology review along with culture of biopsy specimen supported a diagnosis of OM in 64.6% of investigated cases. However, the age of the participants ranged from 1 to 92 years [7]. This is in contrast to the study done in the 1990s and early 2000s [6].

Ballah et al. reported that there were 26 biopsies performed, 21 out of 26 biopsies were diagnostic (81%); 2/26 (8%) were false-negative extracting nonlesional tissue, 2/26 (8%) were nondiagnostic and 1/26 (4%) were technically unsuccessful. The diagnoses were as follows: 12/26 biopsies (46%) were OM; 3/26 (11%) biopsies were Langerhans cell histiocytosis; 3/26 biopsies (11%) were normal bone; 2/26 (8%) biopsies were malignant tumors and 1/26 (4%) biopsies were osteoblastoma. Of 12 children with OM only 3 had a positive culture; 9/12 (75%) children had a negative culture. They did not report any p-value or confidence interval. They concluded that percutaneous CT guided vertebral bone biopsy is safe in children with a high degree of diagnostic accuracy [8].

A systematic review and meta-analysis of 7 studies (later excluded 2 studies) indicated that image-guided percutaneous needle aspiration biopsy has a high specificity (99.9%) and, therefore, is quite effective when positive. However, it has low sensitivity (52.2%) and can miss a substantial proportion of patients. Image-guided spinal biopsy had a diagnostic odds ratio (DOR) of 45.50 (95% confidence interval [CI], 13.66–151.56), a likelihood ratio of positive test (LRP) of 16.76 (95% CI, 5.51–50.95), a likelihood ratio of negative test (LRN) of 0.39 (95% CI, 0.24–0.64), a sensitivity of 52.2% (95% CI, 45.8–58.5) and a specificity of 99.9% (95% CI, 94.5–100). The results of this study strengthen

the importance of image-guided percutaneous spinal biopsy [9].

Wu et al. observed that out of 41 (age range 3 to 82 years) histologically positive cases of OM, 14 (34%) cases were positive at culture. The proportion of positive culture results in confirmed cases of OM on the basis of histology was low. Patients who were on antimicrobial therapy in a 24 hour period of the biopsy, 24% had a positive culture, and the patients who were not on antibiotics had a 42% culture positivity rate. Larger prospective studies are required to investigate this finding further. They also advised or requested physicians to hold antibiotics for at least 24 hours before the biopsy [10].

Rankine et al. performed a retrospective study on 20 patients who had percutaneous spinal biopsies, with 8 out of 20 patients (40%) on antibiotics before the biopsy. An organism was isolated in 8 out of 20 cases (40%). Out of 8 patients on antibiotics, an organism was isolated in only 2 cases (25%). The result of the biopsy helped to modify the treatment in 7 of the 20 patients (35%). They also suggested that spinal biopsy should be done before starting antibiotic and a sample should be sent for both microbiology and histopathology [11].

Ng et al. reviewed the histopathological, cytological and microbiological results of patients who underwent bone and para-osseous biopsies between July 1977 and March 1996. The 502 biopsies were taken from 477 patients (age range for male patients was 5-86 years and for female patients was 2-86 years). Tumors were reported in 40% of the biopsies and infection in 16%. The latter study confirms the importance of bone biopsy in confirming diagnosis of infection and also detecting the presence of neoplasm, a differential diagnosis that needs to be born in mind when encountering pediatric patients suspected of infection. A bone biopsy can be taken from any site under the guidance of fluoroscopy or CT [12].

In conclusion, our extensive search of the literature has revealed one study evaluating the role of bone biopsy in children with the remainder of the studies being performed in an adult population. Based on the available evidence, we recommend that percutaneous bone biopsy under fluoroscopic or CT guidance is a reasonable, fast and cost-effective modality for diagnosis of OM and differentiating infection from neoplasm. It carries low complication rate but the ability of this test to isolate the infective organism in OM remains low. The above studies suggest that percutaneous bone biopsy shows high specificity but low sensitivity in microbiological diagnosis of OM but the combining results of microbiological examination with histological evaluation of the samples enhances the sensitivity. Literature also suggests that bone biopsy should be performed before initiating empirical antibiotic therapy in order to increase its yield for isolation of the infective organism.

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QUESTION 6: Is there any role for polymerase chain reaction (PCR) or molecular testing in pediatric musculoskeletal infection (PMSI)?

RECOMMENDATION: PCR may be a useful diagnostic adjunct with the potential to expedite a preliminary diagnosis of PMSI in comparison to the use of microbiological culture alone. Furthermore, PCR can enable pathogen identification in cases where the organism is indolent, fastidious or difficult to culture. However, data remains sparse and further research is needed to standardize molecular techniques, minimize contamination and explore emerging molecular methods that are primer-independent.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 2%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

The diagnosis of musculoskeletal infection is typically based on pertinent clinical findings, synovial fluid analysis and a positive gram stain or culture confirming the microbial identity of a pathogen [1]. Although culture results are used to identify the infecting organism and determine antimicrobial sensitivity, culture is often limited by sampling methodology, processing issues, early antibiotic administration, and/or the presence of hard to culture organisms [2–4]. PCR and other molecular techniques have been investigated to a limited