Bushehr University of Medical Sciences
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Final Report of Research Project (Thesis of Medical Degree)

The Determination of UBI Scan in Dete tion of Osteomyelitis

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In the name of

Allah

Special thanks to:

My dear wife

&

My advisors,

dear Dr. Vahdat & dear Dr. Asadi

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این طرح با تصویب و حمایت مالی حوزه معاونت پژوهشی دانشگاه علوم پزشکی و خدمات بهداشتی درمانی بوشهر اجرا گردیده است.

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ABSTRACT

Introduction: Imaging can be a useful tool in the setting of suspected osteomyelitis. Currently available techniques such as ultrasonography, CT, and MRI are anatomically oriented. Despite being highly sensitive and sophisticated, these modalities lack specificity for infection. Recently, antimicrobial peptides have been proposed as new agents to distinguish bacterial infections from sterile inflammatory processes and ubiquicidin (UBI) 29-41 is one of them that has showed interesting results for infection detection in previous studies. The aim of this study was to determine the UBI scan accuracy in detection of osteomyelitis and comparison of it with other modalities.

Methods: Twenty patients (mean age=48.90 years) with suspected osteomyelitis were included in this study. After evaluation of each patient by history taking, physical exam, and proper laboratory tests, other processes include bone probing, wound culture, simple X-ray, bone MRI, and UBI scan were done for them. Preliminary diagnosis of osteomyelitis was acquired according to clinical and paraclinical data and confirmed by patient's fallow up.

Results: In current study, 17 cases had osteomyelitis in UBI scan and it showed accuracy of 100% in detection of osteomyelitis, compared with accuracy of 90% for three phase bone scan.

Conclusion: 99mTc-UBI 29-41 is a proper choice for detection of osteomyelitis, regarding the fast imaging with high sensitivity, specificity, and accuracy.

Key Words: Osteomyelitis; Ubiquicidin; 99mTc-UBI; Antimicrobial peptides; Infection detection

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INTRODUCTION

OSTEOMYELITIS:

Osteomyelitis is infection localized to bone [1]. Osteomyelitis can occur as a result of hematogenous seeding, contiguous spread of infection to bone from adjacent soft tissues and joints, or direct inoculation of infection into the bone as a result of trauma or surgery. Hematogenous osteomyelitis is usually monomicrobial, while osteomyelitis due to contiguous spread or direct inoculation is usually polymicrobial.

In long bone hematogenous osteomyelitis, the most common site of infection is in the metaphysis.

In the setting of osteomyelitis, inflammatory exudate in the marrow leads to increased intramedullary pressure, with subsequent extension of exudate into the bone cortex where it can rupture through the periosteum. If this occurs, the periosteal blood supply is interrupted, leading to necrosis. The resulting pieces of separated dead bone (known as sequestra) can be visualized radiographically. New bone formation that forms in areas of periosteal damage is known as an involucrum. In some cases, a sequestrum can evolve into an involucrum as it is encased with new bone growth. Occasionally, pus may exist in an opening (cloaca) of involucrum.

Acute osteomyelitis is infection in bone prior to development of sequestra. In some forms of infection, development of sequestra is relatively slow (such as vertebral osteomyelitis), while in others the development of sequestra occurs relatively rapidly (such as osteomyelitis in the setting of prosthetic devices or compound fractures) [2]. Following formation of sequestra, the infection is considered chronic osteomyelitis; other

hallmarks of chronic osteomyelitis include formation of an involucrum, local bone loss, and sinus tracts (if there is extension of infection through cortical bone).

DIABETIC FOOT INFECTIONS:

Diabetic foot infections are associated with substantial morbidity and mortality [3]. Important factors for development of diabetic foot infections include neuropathy, peripheral vascular disease, and hyperglycemia. In the setting of sensory neuropathy there is diminished perception of pain and temperature, so delays in injury presentation are common.

Evaluation for osteomyelitis is an important consideration in the management of diabetic foot infections. The following factors increase the likelihood of osteomyelitis in patients with diabetic foot infections [4-7].

Patients with diabetic foot infections should have initial evaluation with conventional radiographs. Those with one or more of the above factors whose radiographs are indeterminate for osteomyelitis should undergo magnetic resonance imaging (MRI); such imaging is especially useful to guide decision-making regarding bone biopsy and choice and duration of antimicrobial therapy.

The following factors increase the likelihood of osteomyelitis in patients with diabetic foot infections:

- Grossly visible bone or ability to probe to bone
- Ulcer size larger than 2 x 2 cm
- Ulcer depth >3 mm
- Ulcer duration longer than 1 to 2 weeks

- ESR >70 mm/h

Patients with diabetic foot infections should have initial evaluation with conventional radiographs. Those with one or more of the above factors whose radiographs are indeterminate for osteomyelitis should undergo magnetic resonance imaging (MRI). Such imaging is especially useful to guide decision-making regarding bone biopsy and choice and duration of antimicrobial therapy.

APPROACH TO IMAGING MODALITIES IN OSTEOMYELITIS:

INTRODUCTION-Imaging can be a useful tool in the setting of suspected osteomyelitis, particularly for supporting a presumed clinical diagnosis, delineating the extent of disease, and planning therapy.

However, interpretation of imaging findings can be a diagnostic challenge. The sensitivity of radiographs for detecting of acute osteomyelitis is limited. MRI and nuclear medicine studies can have limited specificity in the setting of confounding bony pathology, although both have high negative predictive value for osteomyelitis.

PATHOPHYSIOLOGY - In the setting of osteomyelitis, inflammatory exudate in the marrow leads to increased intramedullary pressure, with subsequent extension of exudate into the bone cortex where it can rupture through to the periosteum. If this occurs, the periosteal blood supply to the bone is interrupted, leading to necrosis. The resulting fragments of isolated dead bone (known as sequestra) can be visualized radiographically.

Acute osteomyelitis refers to infection in the bone prior to development of sequestra. In some forms of infection, development of sequestra is relatively slow (such as vertebral

osteomyelitis), while in others the development of sequestra occurs relatively rapidly (such as osteomyelitis in the setting of prosthetic devices or compound fractures) [8]. Following formation of sequestra, the infection is considered chronic osteomyelitis. Other hallmarks of chronic osteomyelitis include involucrum (reactive bony encasement of the sequestrum), local bone loss, and sinus tracts (extension of infection through cortical bone).

RADIOGRAPHS - Conventional radiographs are relatively inexpensive and readily available; they may suggest a diagnosis of osteomyelitis, exclude other pathology, or provide clues for other conditions . Radiographs can be useful for demonstrating findings of chronic osteomyelitis; characteristic findings include cortical erosion, periosteal reaction, mixed lucency and sclerosis [9,10]. Other findings may include sequestra (devitalized bone with radiodense appearance) and soft tissue swelling (particularly when osteomyelitis is accompanied by cellulitis or abscess). In the setting of orthopedic hardware, findings of osteomyelitis may include fracture nonunion, or periprosthetic lucency indicative of hardware loosening.

Radiographs are limited by their sensitivity and specificity[11]. This is particularly true in early infection, when imaging findings may be subtle or radiographically absent [12]. While nonspecific soft tissue changes can be seen as early as three days, osseous changes attributable to osteomyelitis may not be visible on radiographs in the first one to two weeks of infection. The earliest osseous change may simply be regional osteopenia, a subtle and non-specific finding [13]. In addition, radiography may be insufficient to distinguish osteomyelitis from other processes such as Charcot arthropathy and, on

occasion, fracture [14]. Following trauma, radiographic findings of architectural distortion, osteopenia due to disuse, and normal fracture healing may be difficult to distinguish from osteomyelitis [15].

MAGNETIC RESONANCE IMAGING (MRI) - MRI is sensitive for the detection of acute osteomyelitis and demonstrates abnormal marrow edema as early as three to five days following onset of infection [16,17]. To now it is the best modality available for obtaining detailed images delineating the extent of cortical destruction characteristic of osteomyelitis as well as bone marrow and soft tissue inflammation (such as in the setting of cellulitis or myositis) [18,19]. Gadolinium contrast-enhanced MRI is also useful for demonstrating sinus tracts, fistulas, and abscesses.

In light of its sensitivity, MRI also has a high negative predictive value for osteomyelitis: an MRI with no evidence for osteomyelitis is typically viewed as good evidence for having excluded osteomyelitis if clinical signs or symptoms have been present for 1 week [8]. The sensitivity of MRI is similar to that of radionuclide studies [8].

Although MRI is sensitive for detection of bone marrow edema associated with osteomyelitis, a bone marrow edema pattern on MRI is a nonspecific finding that can also be seen with a variety of different pathologies, such as contusion, fracture, postsurgical change, Charcot arthropathy, osteonecrosis, adjacent arthritis, or neoplasm. Thus, given the extensive differential diagnosis of a bonemarrow edema pattern, establishing the correct diagnosis depends on the clinical setting and on any additional imaging findings. Moreover, if infection co-exists with additional pathology that can cause a bone marrow

edema pattern, MRI cannot reliably distinguish between marrow changes attributable to infection and those attributable to other pathology [20].

In addition, MRI may overestimate both the extent and duration of infection. Reactive marrow edema may co-exist with true marrow infection, leading to an imaging abnormality that is larger than the area of actual infection. Bone marrow changes may also persist for weeks to months after osteomyelitis begins to respond to therapy. Such findings can lead to more aggressive treatment than necessary.

MRI is especially useful for evaluation of osteomyelitis in the foot (particularly in the setting of diabetes) and in the vertebrae (given its excellent depiction of the adjacent spinal cord).

To now MRI was the preferred modality for evaluation of osteomyelitis in the setting of diabetic foot ulcers [12, 21]. MRI is the modality of choice for delineating the anatomy of the spinal cord and the adjacent osseous and soft tissues. In vertebral osteomyelitis, findings on T1-weighted images include decreased signal intensity in the disk and adjacent vertebral bodies and loss of endplate definition [22]. Findings on T2-weighted images include increased signal intensity in the disk and adjacent vertebral bodies. Following intravenous administration of gadolinium, there is enhancement of the disk, adjacent vertebral bodies, and involved paraspinal and epidural soft tissue [23]. Some patients may not be candidates for MRI, including those with cardiac pacemakers, implanted insulin pumps, or other devices. Even some metallic implants that are MRI-compatible may obscure a region of interest due to metallic susceptibility artifact, if the metal lies near a site of suspected infection.

COMPUTED TOMOGRAPHY (CT) - Computed tomography (CT) is the modality of choice in circumstances where MRI imaging cannot be obtained. CT is useful for assessing cortical and trabecular integrity, periosteal reaction, intraosseous gas, and the extent of sinus tracts [12, 15, 24-27]. It is the most useful modality to evaluate for presence of osseous sequestra, and it can provide excellent anatomic delineation of adjacent soft tissues [8].

However, as with MRI, metallic hardware can give rise to artifact that may degrade image quality and limit diagnostic capability.

NUCLEAR MODALITIES - Nuclear imaging can be a useful diagnostic alternative to MRI, although the findings must be interpreted with caution. Nuclear imaging tends to be more reliable for evaluation of acute infection than chronic infection given its sensitivity for detecting evidence of inflammation.

The most common nuclear imaging studies used in the assessment of osteomyelitis are the three phase bone scan, gallium scan, and tagged white blood cell scan. Other less commonly used nuclear modalities include bone marrow scans, scans utilizing radiolabeled antigranulocyte antibodies, and radiolabeled antibiotics.

Three phase bone scan - Three phase bone scans uses a radionuclide tracer that accumulates in areas of bone turnover and increased osteoblast activity (such as technetium-99m bound to a phosphorus containing compound) [28]. Scans are performed using a gamma camera at three points following tracer injection: immediately after injection (blood flow phase), 15 minutes after injection (blood pool phase), and four hours after injection (osseous phase).