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Review Article

IMAGING IN OSTEOMYELITIS

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Abstract:

Introduction: Osteomyelitis by definition is a secondary inflammation affecting the bone marrow. as the infection progress it can develop to osteonecrosis, septic arthritis and the destruction of bones . It is considered one of the leading causes of permanent disabilities bot children and adults around the world. The most common between children under the age of 5 and adolescences older than 50 years. Typically, osteomyelitis is presented by pain, edema and erythema of the affected part of the body. The goal of this manuscript is to review the currently available imaging modalities that are used for the management, diagnosis and treatment of osteomyelitis.

Aim of work: In this review, we will discuss the currently available imaging modalities that are used for the management, diagnosis and treatment of osteomyelitis

Methodology: We did a systematic search for Imaging in osteomyelitis using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

Conclusions: Imaging has a crucial role in the diagnosis and management of osteomyelitis. Plain radiographs should ideally be obtained first to exclude other pathologies such as fractures. MRI is the best imaging modality for establishing the diagnosis of osteomyelitis as it can demonstrate bone marrow oedema, confirm the presence of abscesses and delineate extraosseous disease spread. The triple phase bone scan has high sensitivity for detecting acute osteomyelitis in non-violated bone. CT allows visualisation of osseous changes such as sequestrum formation and also for guiding aspiration and biopsy.

Key words: Imaging, X-ray, CT scan, MRI, osteomyelitis

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INTRODUCTION:

Osteomyelitis by definition is a secondary inflammation affecting the bone marrow. As the infection progress it can develop to osteonecrosis, septic arthritis and the destruction of bones. It is considered one of the leading causes of permanent disabilities bot children and adults around the world [1]. The most common between children under the age of 5 and adolescences older than 50 years [2]. During the last decade, studies in the United States reported an increase in the incidence and severity of acute osteomyelitis among, and suggested the association between this increase and the increase in the of methicillin-resistant Staphylococcus Aureus infections (MRSA) [3].

Typically, osteomyelitis is presented by pain, edema and erythema of the affected part of the body. Such symptoms are not specific to osteomyelitis and could be caused by a lot of other causes [4]. In infants, osteomyelitis is presented only with irritability and poor feeding. Inflammatory markers in the serum could be normal, especially in neonates and patients with chronic osteomyelitis [5].

Because of this causes, imaging have a very important role the diagnosing and assessing the severity and spread of osteomyelitis. Furthermore, imaging plays a very important role in performing guided biopsies, abscess aspiration and the follow-up scans required during the treatment to ensure the complete resolution of the infection [6].

The goal of this manuscript is to review the currently available imaging modalities that are used for the management, diagnosis and treatment of osteomyelitis, and the association between the different radiological features and the underlying etiology. The pathophysiology of acute and chronic osteomyelitis will also be described, together with summarizing the key age-related differences in the patterns of this condition. This will be followed by a thorough review of the imaging features of osteomyelitis on x-ray, magnetic resonance imaging, nuclear medicine, computed tomography and ultrasound. There will be a special focus on MRI techniques because it is the modality of choice for investigating and assessing suspected osteomyelitis cases in most current evidence-based guidelines [7].

METHODOLOGY:

We did a systematic search for Imaging in osteomyelitis using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We

only included full articles.

The terms used in the search were: Imaging, X-ray, CT scan, MRI, and osteomyelitis

Pathogenesis

Osteomyelitis can be caused by various organisms and mechanisms. The course of the disease and its progression from acute into chronic phase produces can cause different symptoms and pathological findings according to the age of the affected person. In 80% of the cases, osteomyelitis is caused due to an infection with staphylococcus aureus, mostly with community-acquired MRSA strains. MRSA caused osteomyelitis is associated with higher incidence of extra osseous manifestations, increased possibility of surgical interventions and an extended hospital stays. The severity of MRSA caused osteomyelitis can be due to the effects Panto-Valentine leukocidin toxin (PVL) produced by MRSA bacteria.

Osteomyelitis can be caused by many other pathogens such as Staphylococcus epidermidis and Enterobacter strains. Some bacterial organisms are associated with existence of specific conditions. Salmonella species are predominant in sickle-cell anemia patients and intravenous drug addiction is associated with Pseudomonas or Klebsiella infections. Osteomyelitis due to fungal infection is commonly seen in immune-compromised patients ⁸.

Chronic recurrent multifocal osteomyelitis (CRMO) is an aseptic form of osteomyelitis seen in children and adolescents, it is associated with no microbial growth and there is no effect of antibiotics on it. The etiology of CRMO is not known yet, but the established associations with inflammatory bowel disease suggest an autoimmune cause [9].

Mechanism of infection

In children, a blood born infection is the most common cause of long bone osteomyelitis. The most common cause of osteomyelitis in adults is infectious spread from soft tissue infection; it can be also caused by direct inoculation. Blood born infections are less common in adults and mostly associated with vertebral osteomyelitis [10].

Plain radiography

Plain radiography does not play an important role in the diagnosis of acute osteomyelitis. Is it has low sensitivity and specificity. 80% of osteomyelitis patients presented in the first two weeks of infection have a normal radiographic finding. The first pathological feature of acute osteomyelitis is bone marrow oedema, and it cannot be seen on plain radiographic films. Acute osteomyelitis clinical

findings that can be detected with plain radiography are soft tissue swelling, periosteal reaction caused by the elevation of the periosteum and a well-circumscribed bony lesion representing an intraosseous abscess. However, these findings are not specific to osteomyelitis and can be detected in many other conditions like fractures, bone tumors and many infections in soft tissues. Sequestrum can be seen in cases of chronic osteomyelitis as a focal sclerotic lesion with a lucent rim. Involucrum is sclerotic thick bone tissue that can be seen around the sequestrum. Chronic osteomyelitis can also be presented with cortical destruction, disorganization of the trabecular pattern and ill-defined bony lucencies¹¹. Despite the limited information offered by plain radiography, it must still be the first line imaging test when osteomyelitis is suspected, to excluding other differential diagnosis like fractures. It also plays an important role in the follow up of the disease by comparing the initial radiographic films with the follow-up radiographs.

Magnetic resonance imaging

MRI is considered to be the imaging test of choice in diagnosing osteomyelitis, as it offers images with detailed anatomy, it is highly sensitive in detecting early bone infections and it does not come with the disadvantages of ionizing radiations [11].

The protocols used in Magnetic resonance imaging of osteomyelitis (MRI) recommend for the area with suspected infection to be imaged in three plans; axial, sagittal and coronal using a sequence of multiple pulse. A pulse sequence is defined as the set of parameters used to highlight the difference in tissue characteristics. Typical, the sequences used in evaluating osteomyelitis are:

- T1-weighted (T1W) sequences provide anatomically detailed images and enable the delineation of the medulla, cortex, periosteum and other soft tissues. On T1W images, fluids appear dark as they have low signal, abscesses have low to intermediate signal and fat has high signal.
- T2-weighted (T2W) sequences are characterized with a high sensitivity for fluids, as well as fat-suppressed sequences (FS) and short-tau inversion recovery sequences (STIR). All of these sequences display fluids as high signal and have a great role in the detection of inflammations and infections, which can increase the tissue fluid content. Fat on T2W images has variable signal but have generally less brightness than T1W images. In fat suppressed and STIR sequences, the signal from fat is decreased, increasing the visibility of inflammatory changes and

fluid collections. The technique of suppressing fat signals can be used in T1, T2 or proton density-weighted sequences. STIR sequences are more commonly used as the fluid-sensitive sequence in an osteomyelitis MRI protocol, as they are generally more sensitive than fat-suppressed sequences in demonstrating fluid;

- Proton density-weighted (PD) sequences are intermediately weighted between T1 and T2. The images produced by the PD sequences are characterized with high anatomical accuracy but with less contrast between different tissues than T1W images.

Indications for intravenous gadolinium contrast

Gadolinium is a contrast agent that can enhance the quality of tissue images according to the vascularity of these tissues. Such enhancement is best recorded on FS-T1 sequences (17). In cases with suspected osteomyelitis, gadolinium can be of many useful uses. In cases with the possibility of developing sinus tracts or abscess, post-contrast FST1 sequences is used for further characterization. Contrast can also be used in patients with suspected epiphyseal infection as the unenhanced images may not be able to detect any findings. Contrast materials are essential in the differentiation between abscess and, solid inflammatory mass like phlegmons. Generally, post contrast sequences are done in patients with suspected osteomyelitis as there is a low threshold for gadolinium administration. However, it is a must to note that gadolinium contrast is contraindicated in patients with impaired renal function due to the high risk of nephrogenic systemic fibrosis.

In magnetic resonance imaging (MRI) the earliest sign of acute osteomyelitis is the oedema of bone marrow. It can be detected in the first two days after the onset of the infection. Normal bone marrow is characterized with high T1 signal due to its high medullary fat content. In cases of acute osteomyelitis, bone marrow produces low signal on T1W images and high signal on fluid-sensitive and post-contrast sequences due to the congestion with fluid and pus. Images of congested bone marrow are better to be compared with normal adjacent tissue or tissue from the contralateral in order to detect the edema and congestion.

Intraosseous and subperiosteal abscesses produce images with low signal on T1W and high signal on fluid-sensitive sequences. The hyper vascular granular tissue surrounding the abscess will appear as a thin rim of intermediate T1 signal is on post-contrast FS-T1 images, as it will be enhanced while

the central pus-filled cavity will continue to have low in signal intensity.

The mentioned peripheral enhancement can be helpful in differentiating between abscesses and phlegmon, it is called the penumbra sign. Solid inflammatory masses like phlegmons, would be characterized with more heterogeneous enhancement unlike abscesses where discrete peripheral enhancement is seen [12]. This differentiation has marked clinical importance as an abscess requires immediate aspiration or surgical intervention [13]. Sinus tracts are seen as linear structures filled with fluid material extending from bone up to the surface of the skin. Sinus tracts are lined by granular hyper vascular tissue and this will appear as peripheral enhancement after contrast.

Periostitis can be seen in acute osteomyelitis as an elevation of the low-signal periosteum from the cortical surface, it corresponds to the periosteal reaction seen on plain radiographs.

In magnetic resonance imaging (MRI) the earliest sign of chronic osteomyelitis are sequestrum, involucra and cloaca; sequestrum is difficult to observe on MRI images, it appears dark on all sequences as it has very few protons available to produce an MR signal because it is a necrotic bone material. However, the sequestrum is surrounded by hyper vascular granular that will have peripheral enhancement on post-contrast sequences, which makes it appear more clear. The involucrum is usually seen around the sequestrum as a thickened shell of bone.

Cloaca formation can be seen both in acute and chronic osteomyelitis. It appears as cortical defect draining pus in the surrounding soft tissues from the medulla. Usually it is seen on fluid-sensitive sequences as the draining pus within it will have high signal.

MRI images are highly sensitive and specific for osteomyelitis detection; normal findings on MRI will exclude the possibility of osteomyelitis. However, the high sensitivity of MRI can exaggerate the severity of the infection. Furthermore, abnormal findings can still appear even after the resolution of the infection [14]. Thus, MRI findings should always be checked and with clinical examination and biochemical tests in order to avoid unnecessary or over aggressive treatment.

The appearances of osteomyelitis on MRI images

could be similar to other pathologies like neuropathic arthropathy, many malignancies and traumas so it is important to perform clinical examination and biochemical tests and take its results into consideration.

Differential diagnoses on magnetic resonance imaging (MRI)

Peripherally enhancing, intraosseous lesion, a non-enhancing sequestrum and a sinus tract are highly suggestive of osteomyelitis. Intra and extra medullary fat globules, can be seen as foci of high T1 signal in cases of osteomyelitis [15]. Fat globules could be due to the increased intramedullary pressure which can cause extrusion of medullary fat. Bone marrow oedema and periostitis are signs of less importance that could be seen in other pathologies. The following differentials may be considered when investigating suspected osteomyelitis:

- **Reactive osteitis**

This can occur secondary to trauma, cellulitis, pressure ulcers or inflammatory arthropathy. On MRI images it usually produces high marrow signal on fluid-sensitive sequences. To be able to differentiate between cases of reactive osteitis and cases of osteomyelitis, the T1W images must be carefully scrutinized. In cases of reactive osteitis, the marrow may have moderate T1 signals or poorly demarcated sites of low T1 signal within a subcortical distribution. On the other hand, in acute osteomyelitis, the marrow is almost always low of low T1 signal and is seen darker and highly well-demarcated when compared with reactive osteitis, with an intramedullary distribution;

- **Neuropathic arthropathy:**

Cases of neuropathic arthropathy, which is also known as Charcot's joint, can lead to the development of soft tissue and changes in the marrow which will mimic cases of osteomyelitis. This distribution of present abnormalities is the main key in the process of distinguishing the differences between these two entities. Neuropathic arthropathy usually impacts several bones in a periarticular distribution, whereas osteomyelitis classically impacts single bones located in weightbearing sites like the first metatarsophalangeal joint and calcaneus. Marrow edema that is near the soft tissue inflammation is also classical in cases of osteomyelitis;

- **Malignant neoplasms:**

On serial MRI images, cases of osteomyelitis usually tend to lead to more rapid destruction when compared to bone cancers. Abscesses are usually demonstrative of the presence of peripheral rim enhancement while cancers classically improve

heterogeneously [16];

- Langerhans cell histiocytosis:

When it attacks long bones of the body, LCH often tends to be centered in the diaphysis whereas haematogenous osteomyelitis classically tends to originate in the metaphysis;

- Osteoid osteoma:

Osteoid osteoma is known to be a benign neoplasm that is seen as an oval lucent lesion with a densely sclerotic center. It can appear like a sequestrum. Osteoid osteomas are often rounding while sequestra are shaped in an irregular manner. On postcontrast sequences, osteoid osteomas will usually show avid enhancement whereas sequestra will not enhance. Osteoid osteomas are not correlated with the development of bone destruction or soft tissues inflammation;

- Stress injuries:

Bones that undergo continuous stress might show marrow edema with periosteal reaction, which is similar to cases of osteomyelitis. However, in contrast to osteomyelitis, the abnormality in signals is limited to the bone in stress damage and there is no inflammatory change in the peripheral soft tissue. Once osteomyelitis has been confirmed as the diagnosis based on findings found on MRI and obtained clinical history, treatment with empirical antimicrobials should be initiated. If the patient does not respond to antimicrobials treatment, a bone biopsy sample might be needed so that a definitive diagnosis could be assured based on microbiology and histology.

Nuclear medicine

Nuclear medicine studies are done by the intravenous administration of a radionuclide, which emits radiations to be detected by a gamma camera. This allows the assessment of bone metabolism. In the case of osteomyelitis areas of increased radionuclide uptake are observed. The triple-phase, gallium and white cell scans are the most commonly performed nuclear tests in the case of osteomyelitis. Nuclear medicine studies have are very sensitive to osteomyelitis, it allow scanning the whole skeleton in order to search for multiple infection sites¹⁷. However, nuclear medicine studies have poor specificity and poor anatomical localization of the detected lesions. Thus, further confirmatory MRI image or bone biopsies are needed in case of any abnormal findings before establishing the diagnosis. Newer techniques like targeted radionuclides and single photon emission computed tomography-CT (SPECT-CT) can increase the specificity of nuclear medicine studies and provide more detailed anatomical information than normal conventional

techniques [18].

Triple-phase bone scan

In a triple-phase bone scan, technetium-99m-labelled MDP (Tc99m-MDP) is administered by intravenous injection, then a three phase image acquisition is performed in angiographic, tissue and osseous phases[19]. Tc99m-MDP localizes to bone areas with high osteoplastic activity. It has a clinical importance in differentiating osteomyelitis from cellulitis. In osteomyelitis, there is high tracer uptake in all three phases. In cellulitis. A triple-phase bone scan is highly sensitive in detecting osteomyelitis, even in the early stages. However, the specificity of triple-phase bone scan is lower in cases of trauma, malignancy or previous surgeries. As this conditions could increase the osseous activity in the bone tissue, that mimics the appearance of osteomyelitis in the scan. In this case a combined white cell and marrow scan can be used to detect osteomyelitis. In cases of suspected vertebral osteomyelitis Triple-phase scans have less importance because of the highly vascular surrounding tissues. Further imaging with gallium and labelled white cells should be done establish a diagnosis.

Ultrasound

Ultrasound imaging have limited use diagnosing osteomyelitis, as it cannot assess the state bone tissue. However, it can be useful in the detection of subperiosteal collections which can be seen as periosteal elevation with an underlying fluid collection, especially in children, in this case an MRI scan should be performed in order to establish the diagnosis. Soft tissue oedema is seen as areas of hypervascularity around the affected bone on color Doppler. If a collection is seen, ultrasonography can be useful in performing a needle guided aspiration [20].

CONCLUSIONS:

Imaging has a crucial role in the diagnosis and management of osteomyelitis. Plain radiographs should ideally be obtained first to exclude other pathologies such as fractures. MRI is the best imaging modality for establishing the diagnosis of osteomyelitis as it can demonstrate bone marrow oedema, confirm the presence of abscesses and delineate extraosseous disease spread. If MRI is contraindicated or unavailable, nuclear medicine studies and CT are useful alternatives. The triple phase bone scan has high sensitivity for detecting acute osteomyelitis in non-violated bone. For violated bone, a combined white cell and bone marrow scan is the current study of choice. CT allows visualisation of osseous changes such as sequestrum formation and

also for guiding aspiration and biopsy.

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