Review Article

The imaging of osteomyelitis

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Abstract: Osteomyelitis is an important cause of morbidity and mortality in children and adults. Imaging plays a crucial role in establishing a timely diagnosis and guiding early management, with the aim of reducing long-term complications. Recognition of the imaging features of osteomyelitis requires a good understanding of its pathogenesis. In this review, the key imaging findings in osteomyelitis are correlated with the underlying pathological processes. There is a particular emphasis on magnetic resonance imaging (MRI), which is the best available imaging modality owing to its high sensitivity for detecting early osteomyelitis, excellent anatomical detail and superior soft tissue resolution. However, other modalities such as nuclear medicine and computed tomography (CT) are also useful in many clinical contexts, and will also be described in this review.

Keywords: Musculoskeletal; infection; radiology; magnetic resonance imaging (MRI)

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Introduction

Osteomyelitis is inflammation of the bone marrow secondary to infection, which can progress to osteonecrosis, bone destruction and septic arthritis. It is an important cause of permanent disability in both children and adults worldwide (1). Osteomyelitis has a bimodal age distribution with peak incidences in children under 5 and adults over 50 years of age (2). Two epidemiological studies conducted in the United States within the last decade have demonstrated an increase in the incidence and severity of acute osteomyelitis in children, linked to the increasing prevalence of methicillin-resistant Staphylococcus Aureus (MRSA) (3,4).

The typical clinical presentation of osteomyelitis with pain, erythema and oedema of the affected part is non-specific and can be caused by a multitude of other diseases (5). Poor feeding and irritability may be the only symptoms present in infants. Serum inflammatory markers may be normal, especially in neonates and patients with chronic osteomyelitis (6). For these reasons, imaging plays an integral role in establishing the diagnosis of osteomyelitis and characterising the extent of disease spread. The importance of imaging goes beyond making the initial diagnosis as radiologists are able to perform image-guided abscess aspirations and bone biopsies to direct further management, and follow-up scans are often required during the course of treatment to ensure resolution of infection (7).

This article provides an overview of the imaging of osteomyelitis, focusing on the correlation between radiological features and the underlying pathological processes. The pathogenesis of acute and chronic osteomyelitis will be described, together with a summary of key age-related differences in the patterns of disease. This is followed by a review of the imaging features of osteomyelitis on plain radiography, magnetic resonance imaging (MRI), nuclear medicine, computed tomography (CT) and ultrasound. There will be a particular emphasis on MRI because it is the imaging modality of choice for the investigation of suspected osteomyelitis in current evidence-based guidelines (8).

Pathogenesis

An understanding of the pathogenesis of osteomyelitis is essential for recognition and interpretation of its imaging findings. Osteomyelitis arises from infection with a variety of microorganisms via different mechanisms. The progression of disease from acute to chronic stages produces a constellation of pathological features that can vary according to the age of the patient.

Staphylococcus aureus is the causative organism in up to 80% of cases of osteomyelitis. Most of these cases involve community-acquired MRSA strains. MRSA infection is associated with an increased incidence of extra-osseous disease, greater number of surgical interventions and longer hospital stays (4). One postulated cause for the increased severity of osteomyelitis in these patients is the production of a toxin known as Panto-Valentine leukocidin (PVL) by MRSA strains (3).

Other common pathogens include *Staphylococcus epidermidis* and *Enterobacter* species. Certain organisms predominate in specific clinical settings, such as *Salmonella* species in sickle-cell patients and *Pseudomonas* or *Klebsiella* in intravenous drug users. Fungal osteomyelitis most commonly occurs in immunocompromised patients (9).

It is important to be aware of an aseptic form of osteomyelitis known as chronic recurrent multifocal osteomyelitis (CRMO) that primarily affects children and adolescents. Blood cultures and bone biopsies in CRMO do not yield any microbial growth and there is no response to antibiotics. While the aetiology of CRMO has not been firmly established, an autoimmune cause has been postulated and there is a known association with inflammatory bowel disease (10).

Routes of disease spread

Three main routes for spread of osteomyelitis have been described; these are haematogenous, contiguous and direct inoculation (11).

Haematogenous spread

Blood-borne organisms, usually bacteria, are deposited in the medullary cavity and form a nidus of infection. In long bones, the region which is most predisposed to infection is the metaphysis, because it has a large supply of slow-flowing blood. This creates an ideal environment for bacteria to accumulate and proliferate (2). The metaphysis is also prone to infection because there is discontinuity in the endothelial lining of the metaphyseal vessel walls. The gaps in the metaphyseal vessels allow bacteria to escape from the bloodstream into the medullary cavity. In flat bones, the equivalent regions where infection tends to originate are the bony-cartilaginous junctions (12).

Contiguous spread

Infections originating from soft tissues and joints can spread contiguously to bone. This often occurs in the context of vascular insufficiency, such as in patients with diabetes mellitus or peripheral vascular disease. There is a diminished immune response secondary to poor perfusion of the infected region. In these patients, the lower extremities are most commonly affected as there is associated peripheral neuropathy, which predisposes to repeated microtrauma (13).

Direct inoculation

Direct seeding of bacteria into bone can occur as a result of open fractures, insertion of metallic implants or joint prostheses, human or animal bites and puncture wounds (13).

Acute and chronic osteomyelitis

Osteomyelitis can be divided into acute and chronic stages (*Figure 1*). The duration of disease determines what imaging findings are seen in osteomyelitis.

Acute osteomyelitis

In osteomyelitis secondary to haematogenous spread or direct inoculation, bacterial proliferation within the bone induces an acute suppurative response. There is accumulation of pus within the medullary cavity leading to raised intramedullary pressure and vascular congestion, which can disrupt the intraosseous blood supply. Reactive bone and hypervascular granulation tissue may form around the intramedullary pus, giving rise to a well-circumscribed intraosseous abscess, also known as a Brodie's abscess (14).

The rise in intramedullary pressure may eventually lead to rupture of the bony cortex, producing a cortical defect known as a cloaca, the Latin term for 'sewer'. Intramedullary pus can spread outward through the cloaca and form a subperiosteal abscess. This causes elevation of the periosteum and disrupts the periosteal blood supply to the bone (14). Continual accumulation of pus in the subperiosteal space leads to rupture of the periosteum and spread of infection to soft tissues through a channel between the bone and skin surface known as a sinus tract. In up to 1% of patients who have persistent draining sinus tracts, squamous cell carcinoma may

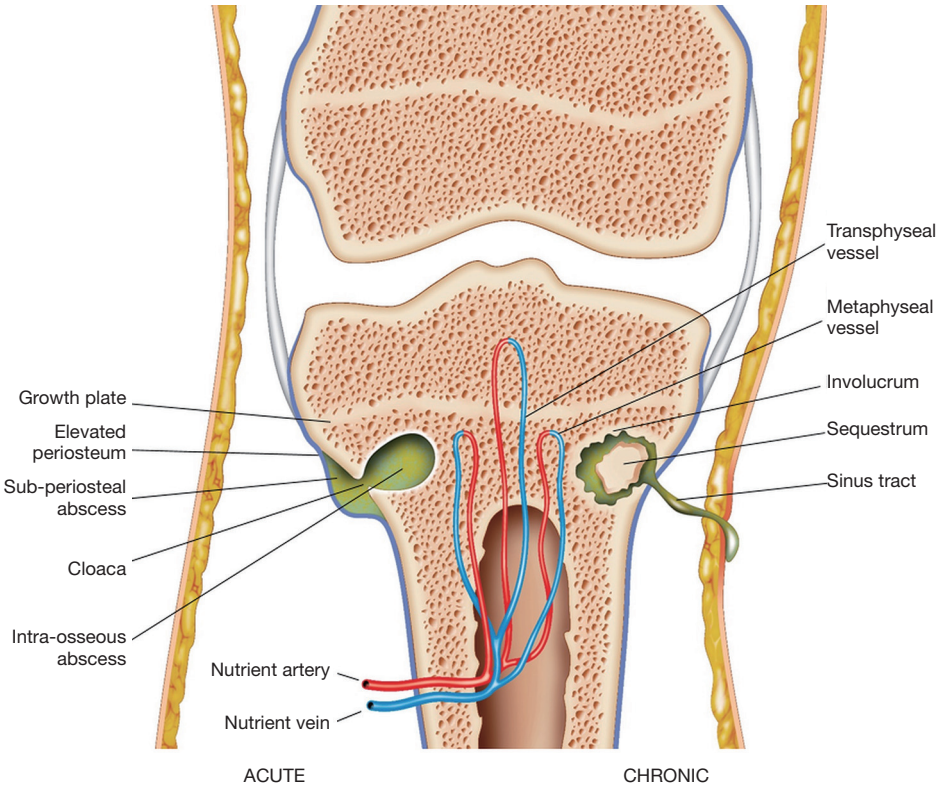

Figure 1 The pathogenesis of osteomyelitis. Metaphyseal vessels contain slow-flowing blood, predisposing to bacterial proliferation. Hence, the metaphysis is a common site for haematogenous osteomyelitis. The growth plate forms a barrier between the metaphyseal and epiphyseal vessels in children over 18 months of age. However, in infants under 18 months and in adults, transphyseal vessels are present which provide a route for infection to communicate between the metaphysis and epiphysis. In acute osteomyelitis, a collection of pus becomes surrounded by granulation tissue and reactive bone, forming an intraosseous abscess. Raised intramedullary pressure secondary to accumulation of pus leads to rupture of the cortex, creating a defect known as a cloaca, which drains pus from the bone to the surrounding tissues. This can cause a subperiosteal abscess with elevation of the periosteum, as well as soft tissue abscesses. In chronic osteomyelitis, disruption of the intraosseous and periosteal blood supply leads to formation of a necrotic bone fragment, known as a sequestrum, which is surrounded by pus and granulation tissue. A reactive shell of new bone forms around the sequestrum and is known as an involucrum. A sinus tract, which drains pus from bone to the skin surface, may be present in both acute and chronic osteomyelitis.

develop in the epithelial lining of the tract (15).

In osteomyelitis secondary to contiguous spread from soft tissue infections, the direction of infection is essentially the reverse to that of haematogenous osteomyelitis.

Chronic osteomyelitis

If the acute infection is inadequately treated, there will be progression of disease to chronic osteomyelitis. The pathological features of chronic osteomyelitis are a result of osteonecrosis, caused by disruption of the intraosseous and periosteal blood supply during the acute stage of disease. A fragment of dead infected bone becomes separated from viable bone and is known as a sequestrum. The bacteria within the devascularised sequestrum are protected from antibiotics and the endogenous immune response, thus forming a nidus for chronic infection which may persist for many years (1). In an attempt to wall off the sequestrum, an inflammatory reaction characterised by osteoclastic resorption and periosteal new bone formation occurs. The sequestrum becomes surrounded by pus, granulation tissue and a reactive shell of new bone known as an involucrum. The involucrum may have a cloaca through which the pus or sequestrum can be discharged (14).

Age-dependent differences

There are several important age-dependent differences

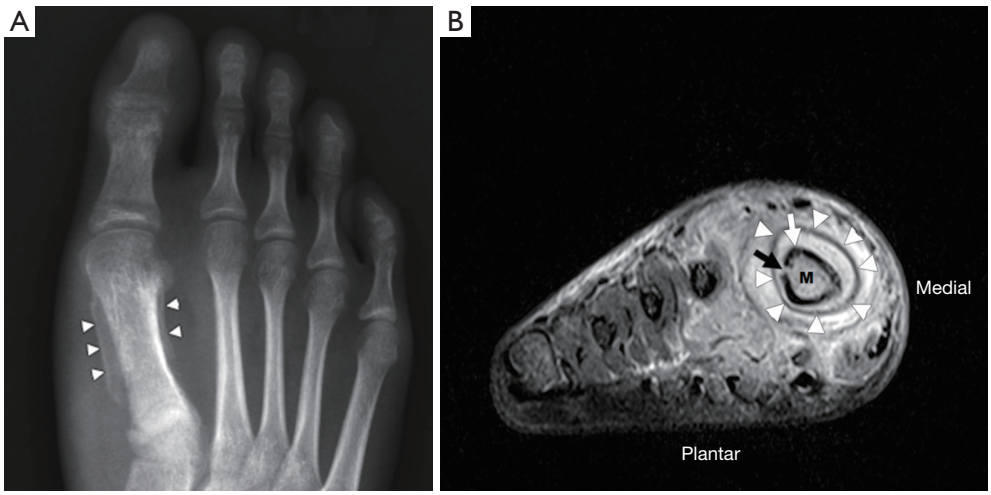

Figure 2 Osteomyelitis in the right foot of a 63-year-old male. (A) The dorso-plantar radiograph shows a periosteal reaction around the 1st metatarsal diaphysis (white arrowheads); (B) short axis coronal short-tau inversion recovery (STIR) image of the same patient demonstrating marked soft tissue oedema surrounding the 1st metatarsal. The periosteum (white arrowheads) is separated from the cortex (white arrow) by high signal material representing pus. There is a defect in the cortex (black arrow), known as a cloaca, that allows pus to drain from the medullary cavity into the subperiosteal space. Compared to the other metatarsals, the medulla (M) of the 1st metatarsal has high signal, consistent with bone marrow oedema.

in the pathophysiology of osteomyelitis that explain the imaging findings seen in infants, children and adults.

Mechanism of infection

Haematogenous spread is the predominant mechanism of infection in children and usually causes long bone osteomyelitis (2). In adults, haematogenous spread is less common and when it does occur, usually leads to vertebral osteomyelitis. Adult osteomyelitis is most commonly caused by contiguous spread from soft tissue infections or direct inoculation (13).

Intraosseous vascular anatomy

During skeletal maturation, there are changes in intraosseous vascular anatomy that determine the pattern of osteomyelitis spread in different age groups. In infants below 18 months of age, metaphyseal and epiphyseal vessels anastomose via transphyseal vessels that perforate the growth plate. These transphyseal vessels allow infection to spread from the metaphysis, where osteomyelitis commonly originates, to the growth plate, epiphysis and joint space. This may result in slipped epiphyses, growth impairment and joint destruction. In children older than 18 months of age, the growth plate ossifies and forms a barrier between the metaphysis and epiphysis, limiting the spread of infection from the metaphysis (12). In adulthood, the growth plate is reabsorbed, removing the barrier between the metaphyseal and epiphyseal vessels. These vessels reanastomose, once again allowing spread of infection into the epiphysis and joint space (14).

Subperiosteal abscess formation

Subperiosteal abscesses are more common in children than in adults for two main reasons. In children, the cortical bone is thinner and more easily ruptured, leading to spread of infection from the medullary cavity to the subperiosteal space (16). The periosteum in children is also more loosely attached to the surface of the cortex and is easily separated, allowing accumulation of pus beneath the periosteal layer as a subperiosteal abscess (2).

Plain radiography

Plain radiography has low sensitivity and specificity for detecting acute osteomyelitis. As many as 80% of patients who present in the first two weeks of infection onset will have a normal radiograph (2). Bone marrow oedema, which is the earliest pathological feature, is not visible on plain films. The features of acute osteomyelitis that may be visible include a periosteal reaction secondary to elevation of the periosteum (*Figure 2*), a well-circumscribed bony lucency representing an intraosseous abscess (*Figure 3*) and soft

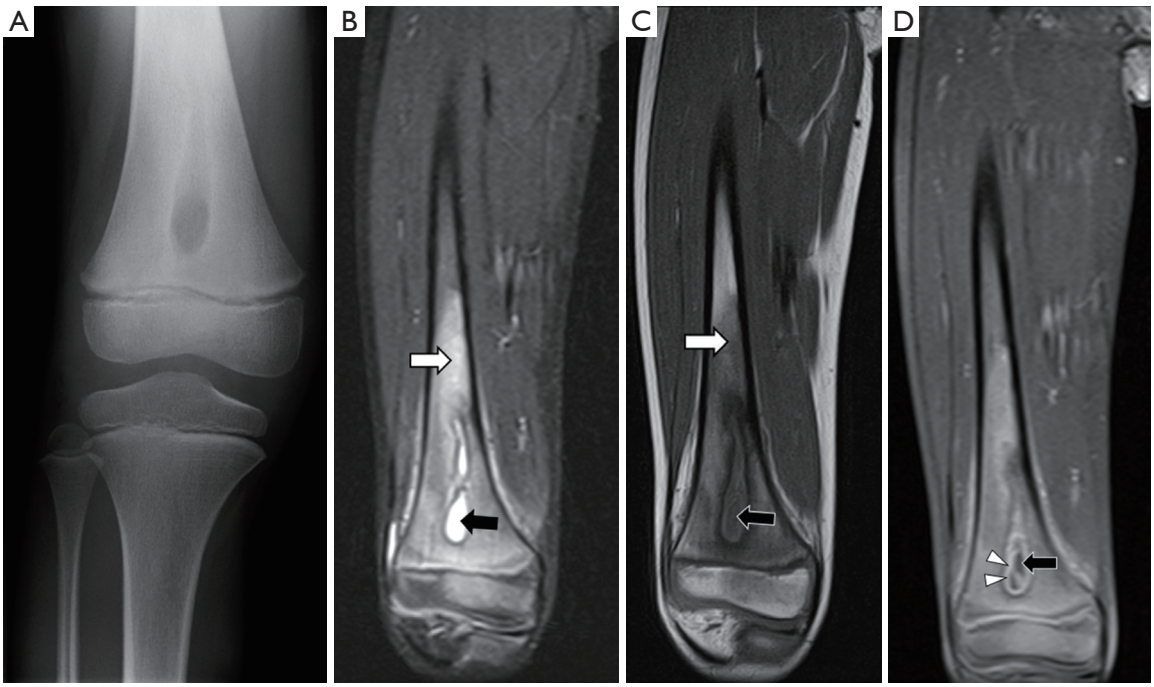

Figure 3 A 6-year-old girl with no history of trauma presents with pain and swelling in her right knee. (A) The anteroposterior radiograph shows a well-circumscribed lucent lesion with sclerotic margins in the right distal femur metaphysis, suspicious for an intraosseous abscess; (B) coronal STIR image of the right femur shows that the lesion is within the medullary cavity and has high signal (black arrow). The bone marrow of the distal diaphysis and metaphysis has diffuse high signal (white arrow) compared to the mid-diaphysis, representing bone marrow oedema; (C) coronal T1W image shows that the intraosseous lesion has central heterogeneous low signal (black arrow). The bone marrow of the distal diaphysis and metaphysis has diffuse low signal consistent with oedema (white arrow). Note the distinct margin between normal and abnormal marrow, suggestive of bone marrow oedema due to osteomyelitis rather than reactive osteitis; (D) coronal fat-suppressed T1W image after administration of intravenous contrast shows that the lesion has central low signal (black arrow) and peripheral enhancement (white arrowheads). The central low signal represents pus and the peripherally enhancing areas represent hypervascular granulation tissue. This confirms an intraosseous abscess. Its location in the metaphysis is characteristic for haematogenous osteomyelitis.

tissue swelling. However, none of these findings are specific to osteomyelitis and can also be seen in stress fractures, bone tumours or soft tissue infections (5).

In chronic osteomyelitis, a sequestrum may be visible on plain radiographs as a focal sclerotic lesion with a lucent rim (*Figure 4*). An involucrum can be seen as thickened and sclerotic bone surrounding the sequestrum. There can also be marked cortical destruction, a disorganised trabecular pattern and ill-defined bony lucencies. These findings of chronic osteomyelitis are best demonstrated with CT (17).

Despite its limitations, plain radiography should still be the first-line imaging test in suspected osteomyelitis, as it is useful for excluding other differentials such as fractures. Plain radiographs are also useful for assessing the progression of disease, by comparing changes seen on follow-up films with the initial radiograph (6).

Magnetic resonance imaging

MRI has emerged as the imaging modality of choice for diagnosing osteomyelitis because of its excellent anatomical detail, high sensitivity for detecting early infection and lack of ionising radiation (17). The protocols and pulse sequences used in the evaluation of osteomyelitis will be described, followed by the MRI findings in acute and chronic osteomyelitis (*Table 1*).

Magnetic resonance imaging (MRI) protocols

In suspected osteomyelitis, the affected area is imaged in axial, sagittal and coronal planes using multiple pulse sequences. A pulse sequence is a set of parameters that highlights different tissue characteristics. The typical

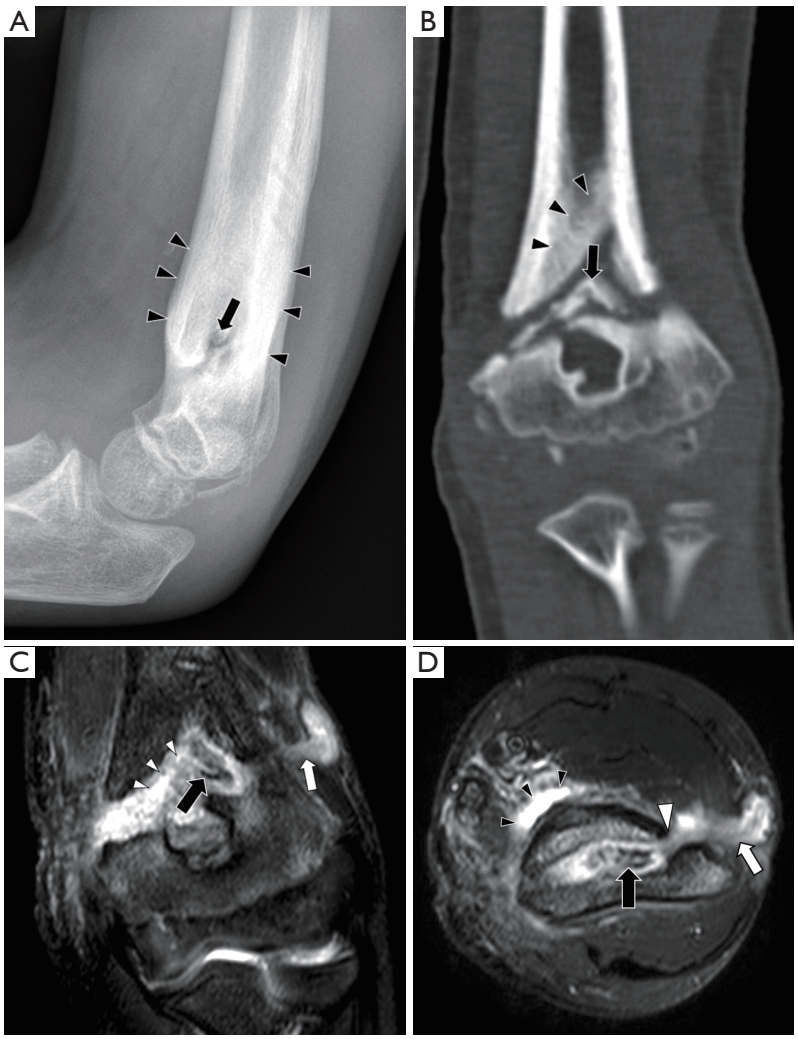

Figure 4 Chronic osteomyelitis in a 9-year-old boy with a non-united left distal humerus fracture. (A) The lateral radiograph shows marked periosteal thickening (black arrowheads) and a central sclerotic lesion with a lucent rim (black arrow); (B) coronal CT with bone windows shows a sclerotic fragment of bone which is separate from the rest of the humerus (black arrow), consistent with a sequestrum. Cortical thickening is also noted (black arrowheads); this represents an involucrum which is a result of periosteal new bone formation. These findings were not present on initial images taken at the time of the fracture; (C) coronal STIR image shows the low signal sequestrum (black arrow) surrounded by high signal pus and granulation tissue (white arrowheads). There is a sinus tract draining pus to the skin surface (white arrow); (D) axial fat-suppressed T2 image demonstrates that the pus surrounding the sequestrum (black arrow) communicates with the sinus tract (white arrow) via a cloaca (white arrowhead). There is also a soft tissue fluid collection anteromedial to the humerus (black arrowheads). (*Images courtesy of Dr. Asif Saifuddin, Royal National Orthopaedic Hospital, Stanmore*).

sequences used in the evaluation of osteomyelitis are as follows:

- T1-weighted (T1W) sequences provide good anatomical detail and enable delineation of the medulla, cortex, periosteum and soft tissues. On T1W images, fluid has low signal (appears dark), abscesses have low to intermediate signal and fat has high signal;
- Fluid-sensitive sequences include T2-weighted (T2W), fat-suppressed (FS) and short-tau inversion recovery (STIR) sequences. These all display fluid as high signal and are useful for detecting infection and inflammation, which cause an increase in tissue fluid content. Fat on T2W images has variable signal but

Table 1 A summary of the key terms used to describe the pathological processes in osteomyelitis and their MRI signal characteristics

Key term	Pathological process	MRI signal		
		T1	T2	T1 + C
Bone marrow oedema	Accumulation of pus within the medullary cavity, leading to vascular congestion	Low	High	High
Intraosseous abscess	Formation of reactive bone and granulation tissue around intramedullary pus	Low	High	Peripheral enhancement
Subperiosteal abscess	Accumulation of pus beneath elevated periosteum	Low	High	Peripheral enhancement
Cloaca	A cortical defect that allows pus to drain between bone and soft tissue	Low	High	Low
Sinus tract	A channel, lined with granulation tissue, that allows pus to drain between bone and the skin surface	Low	High	Peripheral enhancement
Sequestrum	A separated fragment of necrotic bone that is surrounded by pus, granulation tissue and an involucrum	Low	Low	Peripheral enhancement

MRI, magnetic resonance imaging.

is generally less bright than on T1W images. In fat-suppressed and STIR sequences, the signal from fat is decreased, increasing the visibility of inflammatory changes and fluid collections. Fat suppression can be applied to 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. PD images provide good anatomical detail but with less tissue contrast compared to T1W images (9).

Indications for intravenous gadolinium contrast

Gadolinium is a contrast agent that causes enhancement of tissues according to their degree of vascularity. This enhancement is best assessed on FS-T1 sequences (17). When investigating suspected osteomyelitis, there are various clinical contexts in which gadolinium is useful. If a possible abscess or sinus tract is seen, post-contrast FS-T1 sequences will allow further characterisation, as will be described later in the article (2). Contrast is also indicated in suspected epiphyseal infection because the unenhanced images may appear normal. Contrast administration is essential for differentiating an abscess from a phlegmon, which is a solid inflammatory mass (5). Overall, there is a low threshold for gadolinium administration and we routinely obtain post-contrast sequences for patients with suspected osteomyelitis at our institution. However, it is important to note that intravenous gadolinium is contraindicated in patients with impaired renal function because of the risk of nephrogenic systemic fibrosis.

Magnetic resonance imaging (MRI) findings in acute osteomyelitis

Bone marrow oedema is the earliest feature of acute osteomyelitis seen on MRI and can be detected as early as 1 to 2 days after the onset of infection (2). The normal marrow has high T1 signal due to fat within the medulla. In acute osteomyelitis, the bone marrow becomes congested with fluid and pus, producing low signal on T1W images and high signal on fluid-sensitive and post-contrast sequences (*Figures 2*,*3*,*5*,*6*). Comparison with marrow signal in adjacent or contralateral bones can be useful for detecting oedema (5).

Intraosseous and subperiosteal abscesses will have low signal on T1W images and high signal on fluid-sensitive sequences. A thin rim of intermediate T1 signal is seen surrounding the abscess, representing hypervascular granulation tissue. On post-contrast FS-T1 images, the peripheral granulation tissue will enhance while the central pus-filled cavity remains low in signal intensity (*Figures 3*,*5*). This pattern of peripheral enhancement is known as the penumbra sign and can help differentiate an abscess from a phlegmon (17). A phlegmon, which is a solid inflammatory mass, would demonstrate more heterogeneous enhancement instead of the discrete peripheral enhancement seen with abscesses (18). This distinction is important because an abscess usually requires more immediate intervention with aspiration or surgical decompression (19).

The sinus tract is seen as a linear fluid-filled structure

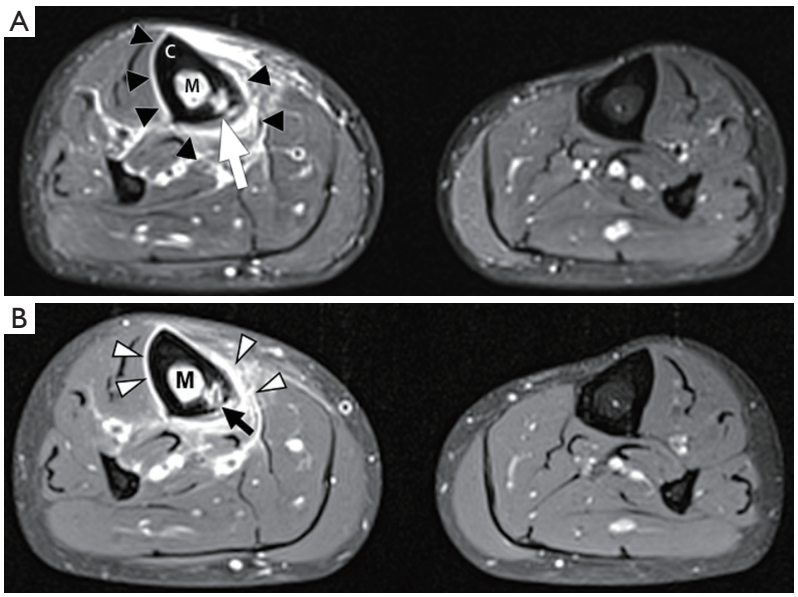

Figure 5 Osteomyelitis in the right tibia of a 44-year-old male. (A) Axial STIR image of both legs. There is high signal in the medullary cavity of the right tibia (M) compared to the normal low signal medulla of the left tibia. This could represent either bone marrow oedema or an intramedullary abscess. There is also circumferential periosteal elevation and high signal (black arrowheads), suggesting a periosteal reaction with a possible subperiosteal abscess. Within the tibial cortex (C), there is a focal area of high signal intensity (white arrow), suspicious for an intraosseous abscess; (B) axial fat-suppressed T1W image following intravenous contrast. The cortical lesion (black arrow) has central low signal and peripheral enhancement, confirming the suspicion of a cortical abscess. There is uniform enhancement of the bone marrow (M) and periosteum (white arrowheads), consistent with bone marrow oedema and a periosteal reaction. The absence of central low signal in these regions excludes intramedullary and subperiosteal abscesses.

extending from bone to the skin surface (*Figures 4*,*6*). As with abscesses, sinus tracts are lined by hypervascular granulation tissue and will also demonstrate peripheral enhancement after intravenous contrast (17).

An additional finding to note in acute osteomyelitis is periostitis, which is seen as elevation of the low-signal periosteum off the cortical surface and corresponds to the periosteal reaction seen on plain radiographs (*Figures 2*,*5*,*6*).

Magnetic resonance imaging (MRI) findings in chronic osteomyelitis

The sequestrum can be difficult to visualise on MRI. It appears dark on all sequences because it is a fragment of necrotic bone that has very few protons available to produce an MR signal. However, the sequestrum is surrounded by hypervascular granulation tissue so it will have peripheral enhancement on post-contrast sequences, making it more conspicuous (*Figure 4*) (17). The involucrum is seen as a thickened shell of bone around the sequestrum which displays either normal signal or oedema (9).

A cloaca can be seen in both acute and chronic osteomyelitis as a cortical defect that drains pus from within the medulla to the surrounding soft tissues. It is most easily seen on fluid-sensitive sequences because the draining pus within it will have high signal (*Figures 2*,*4*) (9).

Magnetic resonance imaging (MRI) sensitivity and specificity

MRI has very high sensitivity for the detection of osteomyelitis; a normal MRI virtually excludes osteomyelitis (5). However, this high sensitivity means that MRI can overestimate the severity of infection. Abnormalities on MRI may also persist even after the infection has begun to resolve (20). The MRI findings should always be correlated with the clinical and biochemical picture to avoid unnecessary or overly aggressive treatment.

The specificity of MRI for diagnosis of osteomyelitis, as quoted in the literature, is usually less than the sensitivity (5). This is because the MRI appearances of osteomyelitis may be

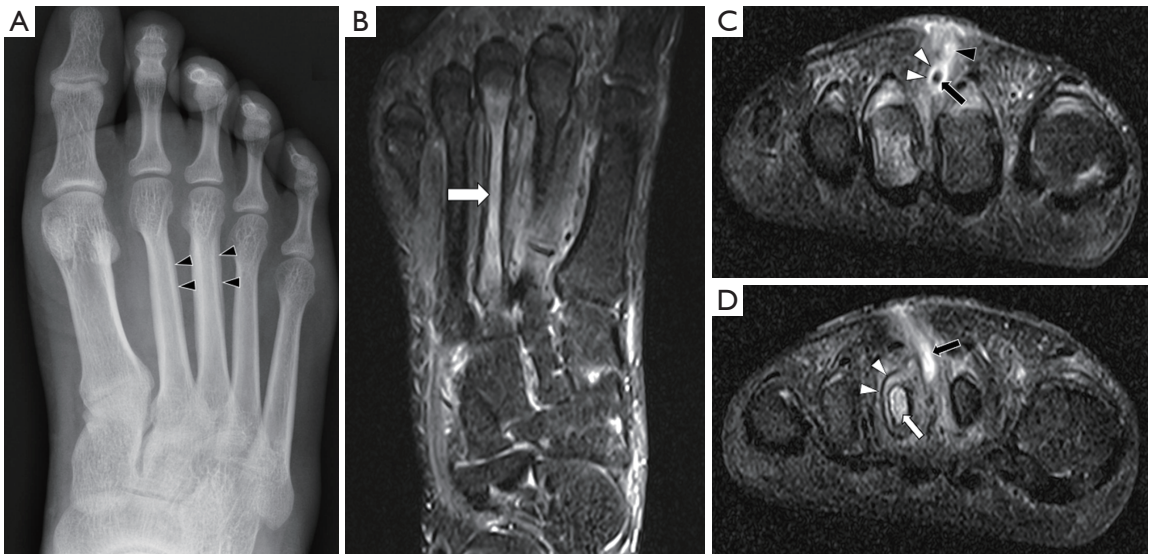

Figure 6 A 16-year-old female who stepped on a wooden splinter 2 months earlier, now presents with right foot pain and purulent discharge from the puncture wound. (A) The dorso-plantar radiograph shows sclerosis of the 2nd and 3rd metatarsals, with surrounding periosteal reaction (black arrowheads). The wooden splinter is radiolucent; (B) coronal STIR image shows high signal in the medulla of the 3rd metatarsal (white arrow), consistent with bone marrow oedema; (C) axial STIR image shows that the splinter (black arrow) has become embedded in the 2nd intermetatarsal space. It is surrounded by a high signal fluid collection (white arrowheads) which communicates via a sinus tract (black arrowhead) to the skin surface; (D) axial STIR image at a more distal level showing bone marrow oedema (white arrow), periosteal elevation (white arrowheads) and a sinus tract extending from the bone to the skin surface (black arrow).

similar to other pathologies such as neuropathic arthropathy, malignancy and trauma. As always, the clinical presentation and biochemical findings should be taken into consideration. However, there are several key imaging features which can help distinguish osteomyelitis from other pathologies; these are discussed in the following section on differential diagnosis.

Differential diagnoses on magnetic resonance imaging (MRI)

Highly suggestive features of osteomyelitis on MRI are a peripherally enhancing intraosseous lesion, a non-enhancing sequestrum and a sinus tract. The presence of intra and extramedullary fat globules, seen as foci of high T1 signal, is a less common finding of acute osteomyelitis but which is nonetheless highly suggestive (21). A proposed aetiology for the presence of these fat globules is increased intramedullary pressure causing extrusion of medullary fat. Bone marrow oedema and periostitis are more equivocal features which are often seen in other pathologies.

Depending on the clinical context, the following differentials may be considered when investigating suspected osteomyelitis:

- Reactive osteitis—reactive osteitis occurs secondary to trauma, cellulitis, pressure sores or inflammatory arthropathy and produces high marrow signal on fluid-sensitive sequences. To distinguish between reactive osteitis and osteomyelitis, the corresponding T1W images should be carefully scrutinised. In reactive osteitis, the marrow can have intermediate T1 signal or poorly demarcated areas of low T1 signal in a subcortical distribution. In acute osteomyelitis, the marrow is invariably of low T1 signal and appears darker and more well-demarcated compared to reactive osteitis, with an intramedullary distribution (18,19);
- Neuropathic arthropathy—neuropathic arthropathy, or Charcot's joint, can cause soft tissue and marrow changes which mimic osteomyelitis. The distribution of the abnormalities is key to differentiating these two entities. Neuropathic arthropathy usually affects multiple bones in a periarticular distribution, while osteomyelitis typically affects single bones in weight-bearing areas such as the 1st metatarsophalangeal joint and calcaneus. Marrow oedema adjacent to soft tissue inflammation is also typical of osteomyelitis (18,22);

- Malignancy—on serial MRIs, osteomyelitis tends to cause more rapid destructive change compared to malignant bone tumours (17). Abscesses demonstrate peripheral rim enhancement whereas tumours usually enhance heterogeneously (23);
- Langerhans cell histiocytosis (LCH)—when it affects long bones, LCH tends to be centered on the diaphysis while haematogenous osteomyelitis tends to originate in the metaphysis (5);
- Osteoid osteoma—an osteoid osteoma is a benign tumour which is seen as an oval lucent lesion with a densely sclerotic center. It may appear similar to a sequestrum. Osteoid osteomas are usually round whereas sequestra are irregularly shaped. On post-contrast sequences, osteoid osteomas will enhance avidly while sequestra do not enhance. Osteoid osteomas are not associated with bone destruction or soft tissue inflammation (17);
- Stress injuries—bones which undergo repetitive stress may demonstrate marrow oedema with periosteal reaction, similar to osteomyelitis. However, unlike osteomyelitis, the signal abnormality is confined to bone in stress injuries and there is no inflammatory change in the surrounding soft tissue (17).

Once osteomyelitis has been established as the most likely diagnosis based on the MRI findings and clinical history, treatment with empirical antibiotics would be commenced. If the patient fails to respond to antibiotics, a bone biopsy specimen may be required so that a definitive diagnosis can be made on microbiology and histology.

Magnetic resonance imaging (MRI) contraindications and limitations

Despite the many advantages of MRI, there are circumstances where it may not be feasible. The presence of a permanent pacemaker or intracranial aneurysm coils is an absolute contraindication. In patients with metallic prostheses, the usefulness of MRI is decreased because of susceptibility artefact, although metallic artefact suppression techniques are now available for reducing this limitation (9). Infants and young children may require sedation or general anaesthesia before they can undergo an MRI scan. Cost and lack of accessibility remain important considerations in many parts of the world. Hence, it is important to have an understanding of alternative modalities for assessing suspected osteomyelitis.

Nuclear medicine

Nuclear medicine studies involve intravenous administration of a radionuclide, which emits radiation that is detected by a gamma camera. This allows assessment of abnormal bone metabolism, which in osteomyelitis manifests as areas of increased radionuclide uptake. The most commonly performed radionuclide studies for diagnosing osteomyelitis are the triple-phase, gallium and white cell scans, which are described individually in this section together with a newer technique, ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET). In general, nuclear medicine studies have very high sensitivity in the detection of osteomyelitis and allow imaging of the whole skeleton to look for multiple sites of infection (24). However, nuclear medicine studies are limited by poor specificity and anatomical localisation. If there is an abnormal result, further confirmation with MRI or bone biopsy is usually required before a diagnosis of osteomyelitis can be established. Newer targeted radionuclides can increase the specificity of nuclear medicine studies and hybrid imaging techniques such as single photon emission computed tomography-CT (SPECT-CT) provide more anatomical information than conventional techniques (*Figure* 7) (25,26).

Triple-phase bone scan

In a triple-phase bone scan, technetium-99m-labelled MDP (Tc^{99m}-MDP) is injected intravenously followed by image acquisition in three phases: the angiographic, tissue and osseous phases (27). Tc^{99m}-MDP is a radiopharmaceutical that localises to areas of increased osteoblastic activity and is useful for differentiating osteomyelitis from cellulitis. In osteomyelitis, there is high tracer uptake in all three phases. In cellulitis, there is high uptake only in the first two phases (24).

Triple-phase bone scans have high sensitivity for detecting osteomyelitis in non-violated bone, even in the early stages of infection. However, their specificity is lower when bone has been violated—for instance in trauma, malignancy or previous surgery. These can all cause increased osseous uptake, making differentiation from osteomyelitis difficult. A combined white cell and marrow scan, described later in this section, is a better test for investigating suspected osteomyelitis in violated bone. Triple-phase scans are also difficult to interpret in suspected vertebral osteomyelitis because of overlying vascular structures. If these scans are equivocal, further imaging with other tracers such as gallium and labelled white cells can be

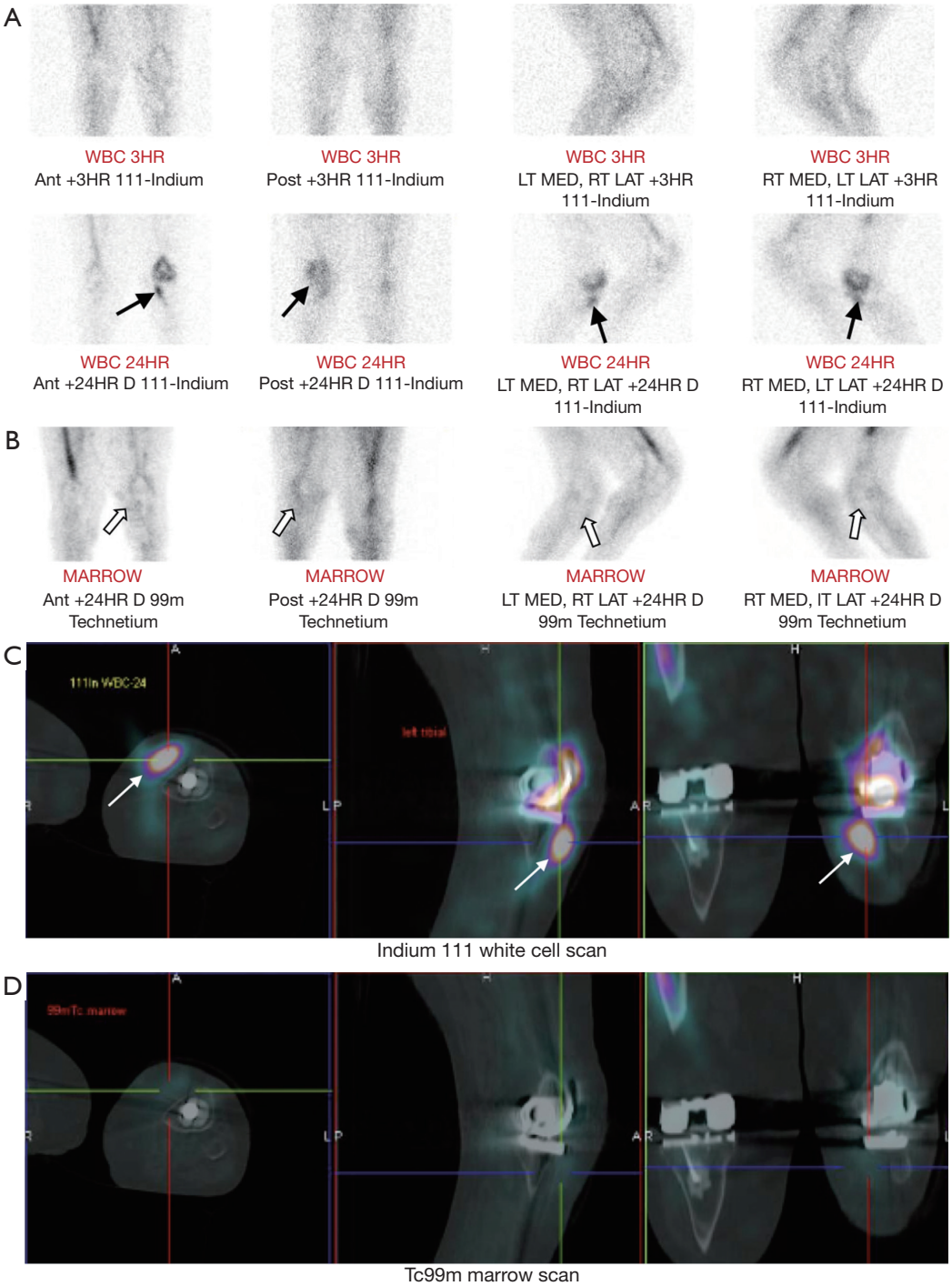

Figure 7 Suspected periprosthetic infection in a 72-year-old male with history of bilateral total knee replacements. A combined white cell and marrow scan was performed. (A) Indium 111-labelled white cell scan of the knees demonstrates accumulation of radiolabelled white cells in the left knee between the 3-hour and 24-hour images (black arrows); (B) the technetium 99m-labelled bone marrow scan provides a baseline map of physiological white cell uptake. No tracer uptake is seen in the left knee (white arrows). The discordance between the white cell and marrow scan demonstrates that the white cell uptake is likely to be due to a focus of infection; (C,D) hybrid SPECT/CT imaging fuses functional and anatomical information to enable more accurate localisation of the focus of infection. The discordance between the white cell (white arrows) and marrow scans is again demonstrated, suggestive of periprosthetic infection.

performed to obtain a more definitive diagnosis (24).

Gallium scan

Gallium-67 is a radionuclide that binds to acute phase reactants such as transferrin and accumulates in areas of infection and inflammation. Gallium scans have higher specificity than triple-phase scans and these two tests are often combined when investigating suspected vertebral osteomyelitis. Osteomyelitis is likely if there is greater tracer uptake in the gallium scan compared to the triple-phase scan. Conversely, if the gallium scan is normal, then osteomyelitis is unlikely, regardless of the bone scan findings (24,26). The main limitation of gallium scans are that they take 48–72 hours to complete, necessitating multiple visits to the nuclear medicine department (22).

White cell scans

The combined white cell and marrow scan is the current study of choice for investigating suspected osteomyelitis in violated bone. In white cell scans, the patient's white blood cells are labelled with a radionuclide, either Indium-111 or Tc^{99m}-HMPAO, then returned to the patient intravenously. Increased white cell uptake is seen in areas of infection. However, normal bone marrow also takes up white cells in a variable distribution. To differentiate between infection and physiological marrow uptake, the white cell scan is combined with a bone marrow scan that uses Tc^{99m}-labelled colloid. The bone marrow scan provides a map of physiological white cell uptake that is then compared to the white cell scan. Any discordance in white cell uptake between the two studies indicates a focus of infection (*Figure 7*) (24).

Fluorodeoxyglucose positron emission tomography (FDG-PET)

Fluorine-18 fluorodeoxyglucose (^{18}F-FDG) is a positron-emitting radiopharmaceutical that localises to hypermetabolic tissues that have high glucose uptake. FDG-PET has been shown to have the highest sensitivity of all the radionuclide techniques in the detection of chronic osteomyelitis. This is because FDG accumulates in activated macrophages, which are the predominant cell type found in chronic infection (28).

Computed tomography

Computed tomography is more widely available than MRI and image acquisition is less time-consuming. CT has good spatial resolution and can demonstrate clearly the anatomical relationship between areas of infection and important structures such as the spinal cord or major vessels. Hence, percutaneous aspirations and biopsies are often performed under CT guidance to avoid damage to these structures. CT has superior bony resolution to MRI and is better at demonstrating osseous changes such as cortical destruction, periosteal reactions and sequestrum formation. As with plain radiographs, the sequestrum on CT appears as a sclerotic lesion with a lucent rim (*Figure 4*). Intramedullary gas is an ancillary sign of osteomyelitis that is also best seen on CT (9).

However, the evaluation of osteomyelitis with CT is limited by its poorer soft tissue resolution compared to MRI. CT is unable to demonstrate bone marrow oedema, which means that a normal CT does not exclude early osteomyelitis. Other limitations of CT are ionizing radiation exposure and image degradation by streak artefact when metallic implants are present (7). Despite these limitations, CT remains a useful alternative when MRI is unavailable or contraindicated.

Ultrasound

Ultrasound is of limited use in the diagnosis of osteomyelitis, as it cannot assess bone. Ultrasound is also an operator-dependent technique and can be challenging with larger patients. However, it can be useful for detecting soft tissue or subperiosteal collections, especially in children, although an MRI will still be required for a more thorough assessment. Subperiosteal abscesses are seen on ultrasound as periosteal elevation with an underlying fluid collection. Soft tissue oedema is seen as areas of hypervascularity around the affected bone on colour Doppler (2). If a collection is seen, the dynamic nature of ultrasonography makes it useful for guiding needle aspiration (*Figure 8*) (29).

Summary

Imaging plays a central role in the diagnosis and management of osteomyelitis; a summary flow chart for imaging modality choice is provided in *Figure 9*. 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

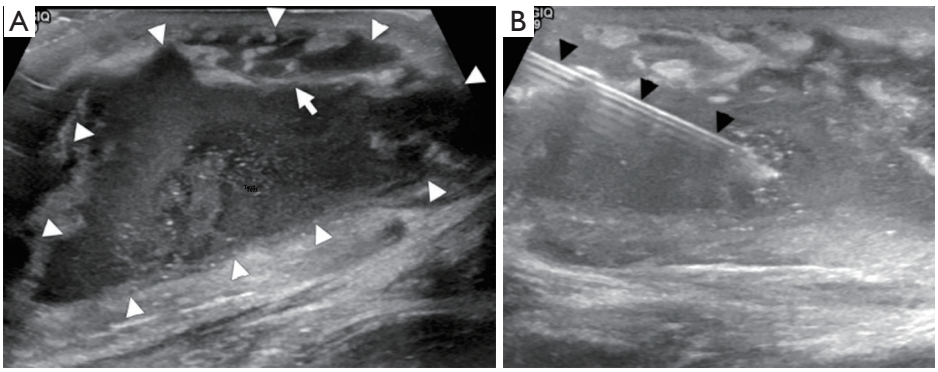

Figure 8 Osteomyelitis may be associated with soft tissue collections which can be seen on ultrasound. (A) Transverse section ultrasound image demonstrating a well-defined complex fluid collection which has an irregular thick wall (white arrowheads) and a hyperechoic septation (white arrow); (B) percutaneous needle aspiration of the fluid collection was performed (black arrowheads). Culture of the aspirate grew Staphylococcus aureus.

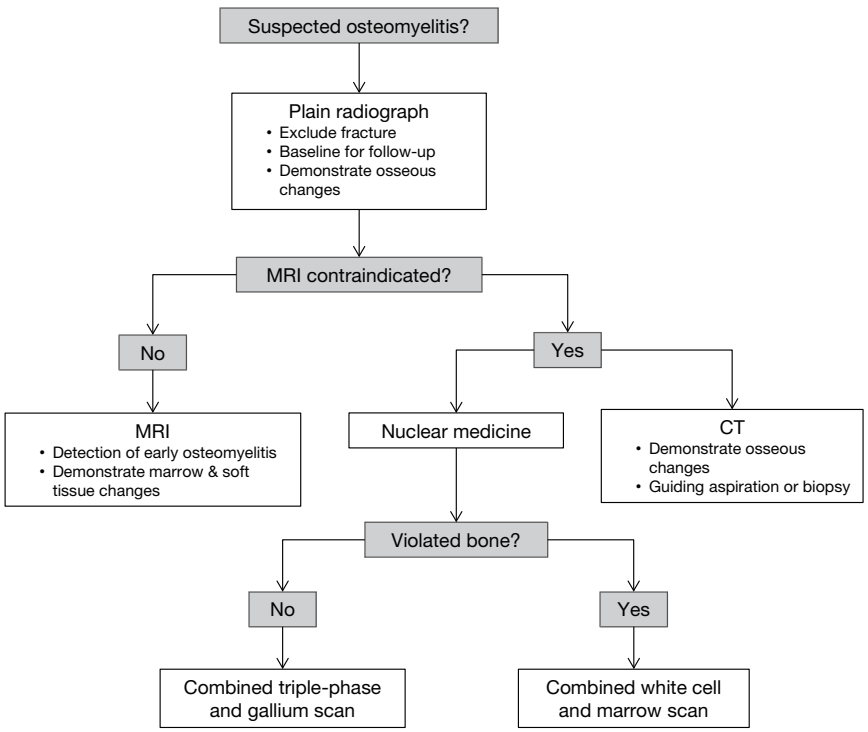

Figure 9 Flow chart for imaging modality choice in osteomyelitis. A plain radiograph should always be obtained first to exclude fractures. Unless contraindicated, an MRI should then be performed as it is the best currently available modality for establishing the diagnosis of osteomyelitis. If MRI is contraindicated, CT or nuclear medicine studies can be obtained, although these tests are of limited sensitivity and specificity compared to MRI.

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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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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