ICONOGRAPHIC REVIEW

Pitfalls in osteoarticular imaging: How to distinguish bone infection from tumour?

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Abstract In this article examining pitfalls in osteoarticular imaging we examine the differential diagnosis of osteomyelitis from bone tumours. We describe the different features which differentiate these two types of disease in radiology and CT and MRI scanning.

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The appearances of bone infection and bone tumour are often similar on imaging. The differential diagnosis of osteoarticular infection includes above all malignant tumours but also some benign, inflammatory tumours (osteoid osteoma osteoblastoma) and pseudo-tumours (eosinophilic granuloma). The clinical and laboratory context does not always discriminate between these and the diagnosis is occasionally only obtained on histological examination. This confusion can lead to delays in treatment and inadequate management.

We describe here the imaging appearances of osteomyelitis, specifically those of subacute osteomyelitis. It is estimated that 50% of cases in children are initially confused with tumour [1].

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Definitions

Three pathways of infection of bone by pathogenic organisms can be distinguished: haematogenous, direct (after trauma or surgery) or contiguous infection (joint or soft tissue infection). The term osteomyelitis is usually reserved for bone infection due to haematogenous spread (centrifugal extension). Osteitis is a generic term combining bone infections with a breach in the bone cortex from the outset (centripetal extension). Septic osteoarthritis is a combination of septic arthritis with co-existent bone infection [2].

Acute, sub-acute and chronic osteomyelitis can be considered separately. The criteria for length of infection (acute = less than one month, sub-acute = one to three months, chronic = more than three months) are arbitrary and vary according to the author. Histologically, acute infection is suppurative and not contained; sub-acute infection is suppurative and contained (abscess) whereas chronic infection is variably suppurative and associated with healing bone remodelling [2].

Clinical and laboratory features

Acute osteomyelitis is found predominantly in children and classically presents as pain, features of infection, local swelling and loss of function. It is usual to find an acute phase reaction with leukocytosis and raised C-reactive protein. Blood cultures are positive in almost half of cases. The organism most often isolated is *Staphylococcus aureus* (in 90% of cases).

These signs are not specific as they can be present in some pseudotumours and inflammatory tumours such as Ewing’s sarcoma [3]. They are often absent or less pronounced in sub-acute or chronic osteomyelitis and in infants. The diagnosis is particularly difficult in a non-febrile child in a context of injury [4].

Radiographic and CT scan appearances

Radiographs are always essential in the acute phase [5], although offer poor sensitivity, in the region of 37% with a specificity of 73% in the study by Tumeh et al. [6]. CT scans are particularly useful in the sub-acute or chronic phase [7].

Chronology of radiological changes

Initially, radiographs are normal. They may then show successive swelling of the soft tissues (early), bone demineralisation (after seven days), a periosteal reaction (after 15 days), and trabecular and cortical osteolysis (after three weeks) [8].

The duration of an infection is an important factor where this can be assessed reliably from repeated films. Rather schematically according to Greenspan [9], Ewing’s sarcoma requires approximately four to six months, osteomyelitis four to six weeks and eosinophilic granuloma only around ten days to produce the same amount of bone destruction.

Radiological signs

The radiological signs of osteomyelitis involve a variable combination of trabecular and then cortical osteolysis with sequestrum, a periosteal reaction and soft tissue abnormalities (collections, fistulae).

Osteolysis

Osteomyelitis preferentially affects the metaphyses and epiphyses of lower limb, long bones. Osteolysis is due to the inflammatory reaction and septic necrosis in the bone layers. It is characterised initially by a zone of bone demineralisation with blurred edges (Fig. 1), and then extends to the cortex, taking on a moth-eaten or porous appearance. These are types IC, II and III of the Lodwick classification [10]. Trabecular and cortical osteolysis can be examined in far more detail by CT scanning. This can show a non-specific increase in bone marrow density due to the inflammatory infiltrate [7]. Finally, the occasional presence of gas (Fig. 2) or fat-fluid levels in the bone marrow cavity is very specific for osteomyelitis outside of a context of trauma [11,12].

Periosteal reaction

A periosteal reaction is present in more than 50% of cases of acute, sub-acute or chronic osteomyelitis. It usually occurs earlier and is more clearly visible in children who have an active periosteum, which is poorly adherent to bone. It needs to be ossified in order to be visible (Fig. 3), although can be seen more early on CT scanning than by radiographs.

The periosteal reaction can be unilamellar, plurilamellar ("onion skin") or compact. It is relatively non-specific and has many causes: physiological (premature infants), fracture, osteosarcoma or eosinophilic granuloma for a unilamellar periosteal reaction, Ewing’s sarcoma or osteosarcoma for a plurilamellar reaction and fracture or osteoma for a compact periosteal reaction. A spiculated...
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**Figure 2.** Gas present in the bone marrow cavity indicating reactivation of chronic osteomyelitis.

**Figure 3.** Compact periosteal reaction associated with sub-acute tibial osteomyelitis.

**Figure 4.** Sequestrum appearance in sub-acute tibial osteomyelitis. Note also the bone reaction which surrounds the focus of infection ("involucrum").

Sequestrum

Sequestrum is a fragment of dead bone surrounded by granulation tissue and is seen in more than fifty per cent of cases of chronic osteomyelitis. It appears on radiographs as a dense, often irregular fragment with a surrounding clear zone (Fig. 4). It is important to diagnose as it is firstly very suggestive of infection and secondly represents a reservoir of organisms, which are not readily accessible to antibiotics, and often requires surgical excision. The sensitivity of this sign to diagnose infection is poor with radiographs but better for CT scans [6,7]. It is not entirely specific as it is also seen in eosinophilic granuloma, fibrosarcoma and can occasionally be confused with a calcified nidus of osteoid osteoma [14].

Soft tissue abnormalities

The fatty planes, which are visible on radiography are classically abolished by infection and displaced by tumours. Collections and fistulae are invisible on radiography unless fistulography is performed. The first line investigation to examine a subperiosteal or juxta-osseous collection is ultrasound. Bone and soft tissues can be studied in great detail by MRI. Failing this, a CT scan with contrast injection and multi-planar reconstructions can be used for a rapid urgent patient assessments [15].

Soft tissues calcifications or ossifications are rare in osteoarticular infection due to the classic pyogenic organisms and are more suggestive of a neoplastic (osteosarcoma) or pseudo-neoplastic (circumscribed myositis ossificans) process. On the other hand it is a characteristic finding in tuberculosis and is also seen in hydatid disease and fungal infections.

Clinical-radiological features and differential diagnosis

Acute osteomyelitis

The diagnosis is suggested from clinical evidence (infection, metaphyseal pain) and laboratory findings (acute inflammatory reaction, positive blood cultures). Initial radiography
is normal. Ultrasound can be used to investigate for subperiosteal abscesses and guide aspiration puncture [18]. The initial changes in bone marrow signal can only be seen on MRI (see below).

Sub-acute osteomyelitis

This is the most difficult situation, which raises the problem of the differential diagnosis from tumour. We propose that the Gledhill and Rombouts classification [16,19] be used as the basis for description. Type 1 refers to the appearances of a single osteolytic lesion, which may or may not be surrounded by a reactive bony reconsolidation line which spares cortical bone. The most classical form of this is the Brodie abscess (Fig. 5) [16]. This is usually found in the metaphysis and may extend to the epiphysis along the epiphyseal cartilage. It is usually 1 to 5 cm in diameter and is ovoid or funicular along the long axis of the bone. A periosteal reaction or appearances of sequestrum are typically absent. Diaphyseal forms of disease have been described to have far more variable appearances which may include cortical thickening or a periosteal reaction and contains sequestrum [17]. The main differential diagnoses are eosinophilic granuloma and osteoid osteoma (Fig. 6). Type 2 refers to a zone of metaphyseal osteolysis with cortical destruction. The main

![Figure 5. Brodie's abscess of the radial metaphysis (type 1 sub-acute osteomyelitis). Note the epiphyseal extension through the growth cartilage, which is far easier seen on CT.](image)

![Figure 6. Sub-acute tibial osteomyelitis (type 3 sub-acute osteomyelitis). Osteoid osteoma and stress fractures can be excluded by a CT scan.](image)
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Figure 7. Brodie’s abscess of the femoral head (type 1 sub-acute osteomyelitis). The presence of bony sequestrum is atypical and raises the possibility of osteoid osteoma.

differential diagnoses are osteosarcoma and an aneurysmal cyst. Type 3 involves thickening of the diaphyseal cortex caused by a compact periosteal and an endosteal reaction. The differential diagnosis includes osteoid osteoma (Fig. 7) and fatigue fractures or stress reactions. CT scans are very useful to look for abnormalities which are not visible on radiographs. Type 4 refers to a plurilamellar diaphyseal periosteal reaction. The main differential diagnosis is Ewing’s sarcoma (Fig. 8).

Other forms exist including epiphyseal disease imitating chondroblastoma or a giant cell tumour (Fig. 9) [20] and “metaphyseal equivalent” forms which affects the flat bones (ilium) or short bones (calcaneum, vertebra) immediately next to the epiphyseal cartilage [21].

Chronic osteomyelitis

Healing bone changes predominate in the chronic stage of osteomyelitis and episodes of reactivation are common.

Figure 8. Plurilamellar femoral periosteal reaction (type 4 sub-acute osteomyelitis). The differential diagnosis is Ewing’s sarcoma.

Chronic suppuration may be present, the classical complication of which, which is seen in 1% of cases, is squamous cell carcinoma developing from epithelial metaplasia in the sinus tract [22].

MRI appearances

MRI is extremely useful for early diagnosis of acute osteomyelitis with sensitivities and specificities of between 60 and 100% depending on the study. The lowest values were obtained from studies performed without injection of contrast medium whereas values of over 90% have
been achieved from the most recent work. MRI was previously performed second line after bone scintigraphy and is now performed directly after radiographs and ultrasound.

**MRI signs**

**Abnormal bone marrow signal**

Abnormalities in bone marrow signal are initially due to the oedema, exsudate, the presence of inflammatory cells and bone ischemia and then reflect the formation of collections and bone healing. The trabecular bone signal abnormalities in acute osteomyelitis are homogeneous, poorly delineated, low or normal intensity on T1 and increased intensity on T2 (oedema), simultaneously involving the bone marrow cavity, cortical bone and the adjacent soft tissues. The signal abnormalities are better delineated, greatly reduced intensity on T1 and increased intensity on T2 (collection) in sub-acute osteomyelitis, occasionally with reduced intensity sequestrum on T1 and T2 (Fig. 10). Signal abnormalities in chronic osteomyelitis are heterogeneous and involve a combination of reduced intensity T1 and increased intensity T2 areas and reduced intensity T1 and T2 areas (sclerosis) [23].

![Figure 10](image1.png)

**Figure 10.** a: weighted T2 MRI appearances of sequestrum and b: periosteal reaction correlated with CT scan findings.

![Figure 11](image2.png)

**Figure 11.** Acute osteomyelitis of the humeral metaphysic (same patient as in Fig. 1). The necrosis and early intra-osseous collection are clearly seen after injection of contrast medium (a). On the T1-weighted sequence (b), fat can be seen in the focus of osteomyelitis.
The periphery of the bone collections can be highlighted by injecting contrast medium, making them easier to detect (Fig. 11) [24].

The signal abnormalities seen with oedema are a sensitive but relatively non-specific sign of osteomyelitis. Some signs which are variably present are more specific for the diagnosis.

Fat globules (acute osteomyelitis)

Acute osteomyelitis causes septic necrosis of the bone marrow, releasing fat particles which sediment with pus to form fat-fluid levels inside or outside of the bone [12]. The presence of fat in soft tissues (Fig. 12) is believed to be due to the fat passing through the Haversian canals and is an indirect sign of a breach in cortical bone [25].

Davies et al. [26] have studied the presence of fat in a focus of osteomyelitis. This sign is found in acute osteomyelitis (Fig. 11) and is due either to persistent normal bone marrow within the oedema or to linear or to globular clumps of necrotic bone marrow.

Penumbra sign (Brodie’s abscess)

The target appearance of the Brodie’s abscess on MRI was initially described by Marti-Bonmati et al. [27]. Four concentric layers are seen: the centre (pus) which is reduced in intensity on T1 and increased intensity on T2, the internal ring (abscess wall) which is of normal intensity on T1 and increased intensity on T2, the external ring (reactive sclerosis) which is reduced in intensity on T1 and T2 and the periphery (bone oedema) which is reduced in intensity on T1 and increased on T2.

The penumbra sign (Fig. 13) described on T1-weighted sequences represents the internal ring which has a relatively high density signal compared to the other layers of the target. Histologically, this represents the granulation tissue surrounding all abscess cavities (in bone, soft tissues or any other organ) and appears to be due to the presence of paramagnetic free radicals produced by activated macrophages. The penumbra sign is more apparent when the granulation tissue is young and represents direct annular uptake of contrast. It appears to be very specific (99%) for abscess although its sensitivity varies from 27% to 75% depending on the study [28,29].

The double line sign described on T2-weighted sequences is less useful. It represents the internal ring (increased intensity) and external ring (reduced intensity). Its visibility depends on the window used and offers a sensitivity of only 22% [28].

Periosteal reaction and sequestra

The periosteal reaction is often missed on MRI although it can be seen before ossification and therefore earlier than on a CT scan. The target appearance on a T2-weighted sequence (Fig. 14) represents the periosteal lamellae separated by granulation tissue [30]. The sequestra appear as reduced intensities on all sequences.

Soft tissue abnormalities

Sequences with contrast medium injection and abolition of the fat signal or useful to delineate collections and fistula tracts within inflammatory changes [31].

Texture sign (soft tissue mass)

It is not always easy to distinguish between inflammatory or neoplastic changes in a soft tissue mass. Classically, inflammation is diffuse and crosses the fascias whereas tumour forms a well defined mass which preserves the fascia. The texture sign proposed for use in following up treated sarcomas can also be used. A visible muscular framework in a T1-weighted sequence supports inflammatory changes when

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**Figure 12.** Fat present in soft tissues confirming the diagnosis of sub-acute osteomyelitis in a bone lesion with soft tissue mass. The presence of sequestrum (b) is also suggestive.
signal abnormalities are present on a T1-weighted sequence [32].

**Differential diagnosis by MRI**

In the acute phase, the problem that arises with osteomyelitis is the differential diagnosis with bone oedema, which can have many causes (trauma, necrosis, algodystrophy, inflammatory joint disease, tumour, etc.). We will pay particular attention to the aggressive presentation of benign inflammatory bone tumours (osteoid osteoma, osteoblastoma and chondroblastoma), eosinophilic granuloma and stress fractures which cause bone and soft tissue oedema that is often disproportionate to the size of the lesion [33]. In these situations, careful examination of radiographs is essential and a scan targeted on the abnormal area can occasionally reveal subtle abnormalities (nidus, fracture line, stress reaction).

The differential diagnosis between osteomyelitis and bone oedema as a reaction to neighbouring septic arthritis or cellulitis is also difficult. Bone would appear to take up contrast medium less intensely than soft tissue in cellulitis with reactive bony oedema, whereas contrast uptake appears to be equivalent in osteomyelitis [24]. Bone oedema as a reaction to septic arthritis appears to be less intense on T1 sequences than in osteomyelitis [34].

An additional approach may be to use a contrast media containing supermagnetic iron particles (SPIO) which shorten the T1 and particularly T2 relaxation time. After intravenous injection these particles are taken up by the reticulo-endothelial cells and accumulate in macrophages and fibroblasts in the inflamed area. These contrast media could help to delineate inflammatory reactions and distinguish them from neoplastic disease [35,36].

**Disclosure of interest**

TM is a consultant for Arthrosis.

**References**

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