Imaging in ischemia of bone – A pictorial essay

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Abstract
Ischemia of bone is not uncommon and is not recognized clinically unless it is acute. Ischemia of bone marrow in shafts of long bones goes by the name of infarction and is well recognized. Ischemia of epiphysis, small bones and subarticular ends of bones goes by the name of avascular necrosis and ischemia of cortical bone goes by the name of Osteosclerosis. The imaging features of these three entities are described with differential diagnosis wherever necessary.

Keywords: bone infarction; avascular necrosis; osteosclerosis; hemoglobinopathies; Gaucher's; radiation therapy; chronic osteomyelitis

Introduction
Ischemia of bone includes medullary infarction, cortical ischemia and osteonecrosis of the articular margins. Bone infarction is a term used to refer to bone marrow necrosis within the metaphysis or diaphysis of a long bone. Necrosis is a type of cell death due to irreversible cell injury. Bone ischemia also includes cortical bone sclerosis and avascular necrosis by the way of collapse of articular ends of bones, small bones of hands and feet and ossification centres [1]. The causes of these are many and are listed in Table 1.

Of these, the common entities include steroids and other non-steroidal pain killing drugs, alcoholism, trauma and systemic disorders including hemoglobinopathies, Gaucher disease, Gout, collagen vascular disorders, etc. [2].

Bone infarction involves the bone marrow of long bones.
Bone ischemia that occurs in systemic disorders such as hemoglobinopathies is shown as sclerosis of the cortical bone on conventional films with infarcts. Ischemia of the physeal region results in shortening of the bone such as seen in trauma, sickle cell anemia, radiation therapy, etc.

**Table 1: Associated lesions and causes of Ischemia of bone:**

- Idiopathic
- Trauma
- Hemoglobinopathies, e.g. sickle cell disease
- Gaucher disease
- Collagen vascular disorders including Lupus
- Behçet’s disease
- Corticosteroid excess (both endogenous and exogenous)
- Alcohol
- Radiotherapy
- Chemotherapy for lymphoma
- Pancreatitis
- Gout
- Infection
- Renal transplant
- Diabetes
- Caisson disease
- Fibrous dysplasia

Osteonecrosis involves the epiphysis, small bones of the hands and feet, articular margins of long bones in adults and ossification centres in children. Radiographically there are several stages in bone marrow infarction and avascular necrosis. Plain films may be normal initially but MRI demonstrates classical findings in the bone marrow and in osteonecrosis.

Pathologically, the blood supply to a section of bone is interrupted and an infarct forms. The infarct includes a central necrotic core which is surrounded by a hyperemic ischemic zone. With time collagen granulation tissue becomes layered around the necrotic core. Demarcation between the normal surrounding marrow, the ischemic zone, and the necrotic core accounts for many of the radiographic appearances of bone infarcts. Calcification occurs eventually due to saponification of fat in necrotic areas. Investigations mainly include conventional radiology and MRI. An interesting observation is the presence of gas in post traumatic osteonecrosis of the vertebral body and it goes by the name of Kummell disease. Similarly gas emboli producing osteonecrosis in bones is noted in Caisson disease. Other methods of imaging are included in Table 2.

**Table 2: Imaging methods.**

- Conventional radiographs
- CT
- MRI
- Nuclear bone scanning
- PET CT

**Imaging features and discussion**

Conventional radiology is the initial investigation and the infarct can be missed in early stages, where CT and MRI will help. Radionuclide scanning is non-specific but identifies the location of the lesion. In acute ischemia, radionuclide scan is cold and as reparative changes take place, it becomes hot. PET scan shows the different changes better (Figure 1).

**Figure 1a-c:** Bone infarcts, (a) conventional, (b) MRI, (c) PET scan.

**Imaging features of bone infarction**

On conventional radiography, a significant delay occurs between the onset of infarct and development of radiographic signs. In acute infarct, the findings may simulate acute osteomyelitis such as seen in children with osteolysis and periosteal reaction. It is
better noted in Sickle Cell Dactylitis (Figure 2a,b). In the spine, cup-like deformities are noted with a "step off" density in the middle-third of the depressed articular plate (Figure 2c). This is called Raynold’s Phenomenon representing the site of infarction of bone. MRI at this time identifies the lesion. Early in the course of disease a bone infarct may develop as an area of rarefaction and, later, may have a mixed, osteolytic and sclerotic pattern. With healing, the lesion becomes well demarcated, with a serpiginous or linear zone of calcification and ossification. The calcified peripheral zone is called fibroosseous membrane and this is specific for bone infarct.

CT: CT would outline the mineralized portion of the infarct (Figure 3).

MRI features are as follows:

An important feature in differentiating bone infarct from other medullary lesions is that the central signal usually remains that of normal marrow. The marrow is not replaced.

T1 shows serpiginous peripheral low signal due to granulation tissue and to lesser extent sclerosis, peripheral rim may enhance post gadolinium and central signal usually that of marrow (Figure 4).

T2 shows double-line sign: hyperintense inner ring of granulation tissue and a hypointense outer ring of sclerosis, absence of double-line sign does not exclude bone infarct and central signal usually that of marrow.

Radionuclide bone scan shows no uptake (cold spot) in the early stage where blood supply is absent, and shows mildly increased uptake at periphery during acute phase.

Differential diagnosis: (1) Enchondroma: chondroid matrix, central marrow signal is absent, (2) Healing non-ossifying fibroma: usually cortically oriented and is not medullary, (3) Lipoma: well circumscribed fatty lesion with varying degrees of
calcification, (4) Brodie's Abscess: Penumbra effect of the border.

**Figure 4a,b:** Infarct, well demarcated peripheral rim.

**Figure 4c:** Enchondroma, note the arc-like and circular calcifications

**Figure 5a:** Avascular necrosis head of femur – Crescent sign.

**Figure 5b-d:** Crescent sign in osteonecrosis with collapse of fragment. (c) Snowcap sign.

**Idiopathic**

Osteonecrosis of femoral head or otherwise called avascular necrosis (AVN) is defined as bone death of the adult femoral head owing to ischemia. Majority of the times, the etiology may not be established. The plain radiographic features follow a sequence with the Crescent sign (Figure 5a) to start with, followed by osteoporosis, osteosclerosis, cystic changes, collapse of femoral head and secondary osteoarthritic changes (Figure 5b-e). It may be bilateral (Figure 5f). Another sign which is characteristic of avascular necrosis of the head of the femur is Snowcap sign which is on the top of the necrotic area (Figure 5c) [3]. There is classification of the stages of osteonecrosis of the femoral head, the details of which are not included in this article.

Osteonecrosis (ischemic necrosis) of the proximal epiphysis of the femur is called Perthe's disease and is common in boys aged between 4-8 years. Bilateral involvement is not uncommon (Figure 6). There is classification regarding the stages of Perthe's disease, the details of which are not included in this article.
Trauma

Osteonecrosis of the knee is necrosis of unknown origin affecting predominantly the medial condyle of the distal femur in adults. On occasion the lateral condyle is also involved. It may be associated with trauma or any other cause such as SLE (Figure 7) [4].

The exact mechanism of osteonecrosis depends primarily on the predisposing cause. In trauma, interruption of arterial supply to bone (e.g., scaphoid fracture, fracture neck of femur) is noted (Figure 8a-d).

Keinbock’s disease is osteonecrosis of the lunate bone either due to trauma or some other reason. Very often the exact cause could not be established. There are five stages in the radiological spectrum, the details of which are not included here. The ultimate
result is dense collapsed lunate bone (Figure 8e,f) [5].

Kümmell disease or vertebral osteonecrosis is generally noted in cases of osteoporosis, whatever the cause maybe. Gas bubbles are demonstrated in plain films as well as in CT or MRI (Figure 8g,h) [6].

Spontaneous multifactorial adult onset osteonecrosis of the tarsal navicular occurs in adults between 40 and 60 years of age. Plain radiographic features can include comma-shaped deformity due to collapse of the lateral part of the bone and medial or dorsal protrusion of a portion of the bone or the entire navicular bone. The disease may be bilateral or asymmetric and associated with pathologic fractures (Figure 9) [7].

**Hemoglobinopathies**

Hemoglobin SC (HbSC) disease, although a sickle cell disease subtype, with similarities to the classic condition, should ideally be considered as a distinct pathological entity (Figure 10) [8].

**Gaucher’s disease**

Gaucher’s disease is a rare familial disturbance of the cellular metabolism in the reticulo-endothelial cells and histiocytes, characterized by an accumulation and retention of the cerebroside keratin. Marrow packing by Gaucher cells causing medullary hypertension and intrasosseous venous occlusion is noted [9]. Proliferation of endosteal bone is another finding. Compromised blood supply will result in bone infarction at both subarticular and diaphyseal sites (Figure 11).
Collagen vascular diseases including lupus
The body's immune system attacks its own tissues such as seen in Lupus. In many of the collagen vascular disorders, vasculitis with arterial occlusion is noted (Figure 12) [10].

Behcet's disease
Behcet's disease is a multisystem disease characterized by recurrent oral and genital ulcers, relapsing uveitis, mucocutaneous, articular, gastrointestinal, neurologic, and vascular manifestations. Rheumatologic manifestations may also occur in Behcet's disease, and arthritis and arthralgia are the most common musculoskeletal findings followed by enthesopathy, avascular necrosis, myalgia, and myositis [11]. Although the main pathology of Behcet's disease has been known to be the underlying vasculitis, the etiology and exact pathogenesis of the disease are still unclear. Vasculitis causing arterial occlusion is noted.
Corticosteroid excess (both endogenous and exogenous)

Endogenous steroids are involved in a large number of physiologic processes, including modulating immune function, behavior, cardiovascular function, growth, metabolism, and inflammatory responses. In regional anesthesia and pain medicine, exogenous glucocorticosteroids (GCS) are some of the most common pharmacologic agents in clinical use. These potent intermediate to long-acting GCS are now used to promote predominantly anti-inflammatory effects on target tissues [12]. Fat cell enlargement causing medullary hypertension and intraosseous venous occlusion is noted (Figure 13).

Alcohol

Alcohol induced osteonecrosis is part of the differential diagnosis in patients with history of alcohol abuse and diffuse bone pain. Usually patients have a longer than 10 year history of alcohol abuse prior to the development of osteonecrosis. The femoral head is the commonest site involved; however, involvement of the long bones is also seen [13]. Fat embolism secondary to coexisting hyperlipidemia has been postulated as a possible...
cause of osteonecrosis in alcoholics. Fatty emboli causing arterial occlusion is also noted (Figure 14).

Radiotherapy
Osteoradionecrosis (ORN) refers to a severe delayed radiation-induced injury and is characterized by bone tissue necrosis and failure in healing [14]. There is some overlap with the term Radiation osteitis. Direct injury to vascular supply leading to occlusion is noted (Figure 15a,b).

Chemotherapy
Single or multiple infarcts are not uncommon in therapy of lymphomas and other myeloproliferative disorders (Figure 15c,d) [15].
Pancreatitits
Sporadic cases of intramedullary fat necrosis associated with bone destruction have been reported in conjunction with acute and subacute pancreatitis, traumatic pancreatitis, and pancreatic carcinoma [16].

Gout
The radiographic manifestations of bone ischemia and the possible mechanism of infarction in gout are monosodium crystal deposits in small vessels [17].

Infection
In chronic osteomyelitis, sequestrum is a common observation which is a dead bone and an example of ischemic bone (Figure 16) [18]. The increased bone density in the sequestrum is partly due to ischemia and mostly due to collapsed trabeculae.

Renal transplant
It is not uncommon to observe bone necrosis in patients who had organ transplant therapy particularly renal transplant. Besides the classical findings of osteonecrosis, infarcts also may be seen (Figure 17) [19]. Some of the necrotic cases are attributed to steroid and other immunotherapy.

Diabetes
In chronic diabetes, bone infarcts are noted either due to arteriosclerosis/ microvascular disease or sub-clinical trauma [20]. The imaging characteristics are the same as in other entities (Figure 18).

Caisson disease
The etiopathology of Caisson disease: accumulation of nitrogen gas in blood vessels. These act as emboli and produce bone ischemia, infarction and osteonecrosis. This phenomenon is noted in deep
sea drivers who are removed too rapidly from a high pressure environment, less frequently from low pressure environments such as in high altitude flying. The entire syndrome has been called Decompression sickness (Figure 19) [21].

Figure 19: Caisson disease, bone infarction and osteonecrosis.

Fibrous dysplasia

Fibrous dysplasia associated with avascular head of the femur is extremely rare. But it has been reported in adults, but its association with Perthe's is being described for the first time (Figure 20).

Figure 20: Fibrous dysplasia associated with Perthe’s disease of femoral head

Conclusion

Bone ischemia and its imaging forms an interesting part of radiology where the ischemia manifests in increased density of bone in traumatic and infective diseases, collapse in different stages in osteonecrosis, and bone infarcts in long tubular bones. The identification by imaging methods is important. Each one of the above entities gives a different spectrum. There are numerous causes of ischemia but few imaging methods which include conventional, MRI and nuclide scan. The article is profusely illustrated with classical examples.

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Conflicts of interest

Author declares no conflicts of interest.

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