Arthritis due to deposition diseases: differential diagnosis in conventional radiology

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Learning objectives

The purpose of this article is to describe the typical imaging findings on plain film of deposition diseases arthropathies, differentiating them according to their radiographic appearance and body segments most commonly affected by the substance deposition.

Background

Arthritis due to deposition diseases are an increasingly prevalent variety of inflammatory arthritides that occur in response to several systemic biochemical disorders.

These conditions lead to joint deposition of different types of metabolites that can be seen in conventional radiography through calcium precipitation, articular surface deformities, periarticular inflammation and soft tissue swelling.

Arthritis due to deposition diseases primarily include gout, calcium pyrophosphate deposition disease (CPPD) and basic calcium phosphate hydroxyapatite deposition disease (HADD). Less common causes of joint deposition-related entities include ochronosis and hemocromatosis.

Other diseases with joint affection through metabolite deposition such as cholesterol crystal arthropathy, Charcot-Leyden crystals deposition, Wilson disease and xanthine or cysteine deposition arthropathy are very rare and therefore not developed here.

These conditions share similarities in their radiographic features, but they also have distinctive characteristics, either by the type of lesions they cause or the skeletal segment involved. In fact, although deposition-induced arthropathies can potentially show late widespread involvement throughout the skeleton (particularly gout), they initially present with a specific distribution, involving a particular joint to the detriment of another.

Findings and procedure details

Gout

Clinical presentation
Gout (or gouty arthritis) develops as a result of deposition of crystals of monosodium urate in various connective tissues and joints, either as a result of an inborn metabolic error leading to the increase of uric acid in the blood (primary gout) or secondary to a dietary excess of purines or a disease causing increased production/decreased excretion of uric acid (secondary gout).

Although the risk of gout increases with the degree and duration of hyperuricaemia, high levels of uric acid in the blood are not an essential requirement for the diagnosis of gout. In fact, its presence even in a patient with arthritis does not necessarily establish the diagnosis. The definitive diagnosis of gout requires aspiration of synovial fluid from an affected joint and examination under polarising light microscopy to look for typical monosodium urate crystals.

The clinical manifestations (and imaging findings) of gout depend on whether the patient suffers from acute or chronic gout.

Acute gout is an acute inflammatory arthritis more common in men than women and occurs typically between the third to sixth decades. Typically the gout attack happens suddenly, frequently awaking the patient from sleep. The joint becomes extremely painful, hot and swollen, making impossible for the patient to bear weight on it.

Chronic gout can appear as a result of recurrent acute attacks and is characterized as a chronic deforming arthritis associated with soft tissues masses (tophi) created by the deposition of urate crystals. The tophi appear especially in the peri-articular areas as a mass filled with a soft material.

**Sites of involvement**

Acute gout is characterized by monoarticular affection, typically of the first metatarsophalangeal joint (also referred as podagra). Only in about 10% of the cases the initial presentation is polyarticular with sparing of the 1st metatarsophalangeal joint. Chronic gout involves more frequently the feet (any of the metatarsophalangeal joints may be involved), ankles and knees, and less often the hands (without preferential involvement of a joint) and elbows (mainly the olecranon bursa).

**Imaging findings**

Only about half the patients with gout manifest radiographic bone changes (and secondary gout does not usually produce any).
The imaging findings differ upon where the urate crystals are deposited. When deposited in the cartilage, the radiographic picture will be that of a typical osteoarthritis, with joint space narrowing, sclerosis and osteophytosis. These findings cannot be distinguished from osteoarthritis secondary to any other etiology.

When deposited in soft tissue, the imaging findings are consistent with chronic tophaceous gout, with punched-out erosions ("mouse bite" like erosions) with sclerotic borders and overhanging edge of cortex (Fig. 1).

![Fig. 1: Anteroposterior and lateral view of the right hand in diffuse tophaceous (*) gout showing punched-out erosions (star) and overhanging edge of the cortex (arrows).](image)

References: Radiology Department, Coimbra University Hospital - Coimbra/PT

The tophi are pathognomonic for gout disease (Fig. 2-4). Typically the mineralization and joint space are preserved.
Fig. 2: Anteroposterior and lateral view of the left hand in tophaceous gout of the 3rd proximal interphalangeal joint. Calcium has precipitated with the urate crystals, giving density to the tophi (*). The joint spaces are globally preserved.

References: Radiology Department, Coimbra University Hospital - Coimbra/PT
Fig. 3: Lateral and anteroposterior view of the left elbow in a patient with gout showing soft tissue swelling in the expected location of the olecranon bursae (*), consistent with olecranon bursitis.

References: Radiology Department, Coimbra University Hospital - Coimbra/PT
**Fig. 4**: Lateral view of the left knee in a patient with previous diagnosis of gout showing prepatellar soft tissue swelling, consistent with pre-patellar bursitis (*).

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**Calcium pyrophosphate deposition (CPPD) disease**

**Clinical presentation**

CPPD crystal deposition is the most common crystal arthropathy and its prevalence increases with age. The calcium pyrophosphate deposition in both hyaline and fibrous cartilage (chondrocalcinosis) is associated with many metabolic disorders, but in most cases there is no significant association between CPPD and the underlying disease.

The clinical presentation of CPPD crystal deposition is very heterogeneous, varying from asymptomatic (the most common presentation) to acute or chronic arthritis.

A pseudogout form (more common in men) is characterized by acute episodes of mono-articular synovitis (very often the knee), with acute pain, swelling and warmth in the affected joint.

A common type of CPPD crystal deposition resembles osteoarthritis, but has a distinctive distribution within the skeleton and the individual joint, affecting the wrists, elbows and shoulders, joints not typically involved in osteoarthritis.

The pseudorheumatoid arthritis form with sub-acute inflammatory polyarthritis is much less common and differs from rheumatoid arthritis because of the presence of degenerative features, absence of rheumatoid factor and typical marginal erosions on the hands or feet x-rays and presence of chondrocalcinosis. However, like in gout, diagnosis confirmation is made with demonstration by polarising light microscopy of typical crystals of CPPD after aspiration of synovial fluid from an affected joint.

**Sites of involvement**

Calcium pyrophosphate deposition disease mostly affects the knees, hands, wrists (typically in the triangular fibrocartilage, hyaline cartilage or in the ligament between the lunate and the triquetrum) and hips, in decreasing order of frequency. Less common joints involved are the shoulder and elbow.
Imaging findings

The classical radiographic finding in CPPD crystal deposition disease is chondrocalcinosis. In fact, radiographic diagnosis of the disease can be made when chondrocalcinosis is found in two or more areas in the skeleton (Fig. 5-6).
Fig. 5: Anteroposterior view of the knees in a patient with CPPD crystal deposition disease demonstrating typical bilateral distribution of wedge-shaped chondrocalcinosis (arrows). Unlike most CPPD crystal deposition cases, this patient has asymmetric joint space narrowing (arrowhead).

References: Radiology Department, Coimbra University Hospital - Coimbra/PT
Fig. 6: Anteroposterior view of the hand in a patient with CPPD crystal deposition disease, showing chondrocalcinosis of the triangular fibrocartilage of the wrist (arrow).

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Osteoarthritic changes like subchondral new bone, cysts and osteophyte formation and joint space narrowing are also frequent.
Typically the findings are bilateral and joint space loss is usually uniform. When asymmetric, in case of knee involvement, the medial tibiofemoral compartment narrowing is more frequent than the medial tibiofemoral compartment.

In the hands, the arthropathy is usually confined to the second and third metacarpophalangeal joints, sparing the interphalangeal joints.

In the hips, the acetabular labrum fibrocartilage and the hyaline cartilage paralleling the femoral head are typically involved.

**Basic calcium phosphate hydroxyapatite deposition disease (HADD)**

*Clinical presentation*

Although associated with many systemic diseases (like renal osteodistrophy, hipervitaminosis D and collagen vascular diseases), the hydroxyapatite deposition disease frequently is idiopathic.

The deposition of hydroxyapatite is a very frequent cause of tendinitis and bursitis, in most cases involving the shoulder. Besides deposition in the bursa and tendon sheaths, calcium hydroxyapatite deposits can also be found in the muscles and less often in the intra-articular space, where it is associated with a highly destructive arthritis (the Milwaukee shoulder).

Shoulder pain is the classical symptom of patients suffering from HADD and hydroxyapatite can be found in almost half the shoulders radiographed for omalgia.

*Sites of involvement*

The joint most frequently affected is the shoulder. Other less common sites of involvement are the hip (in the gluteal insertions into the greater trochanter and surrounding bursa), wrist (most often in the flexor carpi ulnaris), elbow (in the lateral epicondyle in the common extensor tendon, in the medial epicondyle in the common flexor tendon and posteriorly in the olecranon in the triceps tendon) and neck (in the longus colli muscle).

In the shoulder, it is possible to identify the actual tendon where the hydroxyapatite deposit is by changes in rotation of the humerus on the radiograph. In most cases, the deposit is found over the greater tuberosity on external rotation, corresponding to the supraspinatus tendon.
**Imaging findings**

The classical finding in HADD is a periarticular calcification, in most cases around the shoulder. If not easily identified at an early stage, over time this calcification becomes well-defined, denser and homogeneous (Fig. 7).

![Fig. 7](image)

**Fig. 7**: Anteroposterior view of the right shoulder in external (a) and internal (b) rotation. There is a amorphous well circumscribed calcification in the proximity of the greater tubercle of the humerus (arrows). These changes are related to a calcific deposit in the supraspinatus muscle in a patient with hydroxyapatite deposition disease.

**References**: Radiology Department, Coimbra University Hospital - Coimbra/PT

The presence of the calcification may lead to soft tissue swelling, and in cases of intra-articular deposition, joint effusion can be found.

**Hemochromatosis**

**Clinical presentation**

Primary (or hereditary) hemochromatosis is a metabolic disorder characterized by a systemic iron overload. Before the disease causes organ damages (in the pancreas, liver, heart, endocrine glands and skin), joint pain is the first cause of the degradation of the quality of life of patients suffering from hemochromatosis.
The arthropathy of hemochromatosis (reported in 24 to 80% of affected patients) is almost identical to that of CPPD crystal deposition, and chondrocalcinosis is frequently observed. This finding can be explained by the fact that iron inhibits pyrophosphatase activity in the cartilage, leading to the precipitation of CPPD crystals.

**Sites of involvement**

Hemochromatosis initially involves the hands and wrists and then the knee and hip. With the disease progression there is widespread involvement throughout the skeleton.

**Imaging findings**

Hemochromatosis arthropathy is hardly differentiated from that of CPPD crystal deposition. As in CPPD joint involvement, chondrocalcinosis (Fig. 8) is a frequent finding in hemochromatosis and osteoarthritic changes (uniform joint space loss, sclerosis and subchondral new bone and cysts formation) in an uncommon distribution for primary osteoarthritis are also seen.
Fig. 8: Anteroposterior view of the knee shows chondrocalcinosis (arrow) in a patient with previous diagnosis of hemochromatosis.

References: Radiology Department, Coimbra University Hospital - Coimbra/PT

However, subtle differences allow the differentiation of both conditions. In hemochromatosis the "beak-like" osteophytes are frequent (Fig. 9), there is preferential involvement of the second and third metacarpophalangeal joints in the hand and the common carpometacarpal, midcarpal and the first carpometacarpal compartments in the wrist and the disease progression is slower.

Fig. 9: Anteroposterior view of the left shoulder of a patient with previous diagnosis of hemocromathosis. There is a typical "beak like osteophyte" (arrow) of the humeral head and a glenoid subchondral cyst (*).

References: Radiology Department, Coimbra University Hospital - Coimbra/PT
**Ochronosis**

*Clinical presentation*

Ochronosis is due to a congenital defect in homogentisic acid oxidase, leading to homogentisic acid accumulation which deposits in collagen as a dark pigment that leads to chondrocyte death and matrix degradation.

Although intra-articular calcification usually is observed, it is due to calcium hydroxyapatite and not to this ochronotic pigment, since it is non-radiodense.

*Sites of involvement*

Mostly the lumbar spine but also the sacroiliac joints, knee, hip and shoulder.

*Imaging findings*

Radiographic findings of ochronosis are not evident until the fourth decade. The spinal radiographic changes include disc degeneration at multiple levels with calcification or vacuum phenomenon, diffuse osteoporosis and extensive subchondral sclerosis. The osteophytes tend to be small (Fig. 10).
Fig. 10: Lateral view of the lumbar spine showing slight loss of disc height, subchondral sclerosis, intervertebral disc vacuum phenomenon (arrow) and evidence of calcification (arrowheads) and at multiple levels.

References: Radiology Department, Coimbra University Hospital - Coimbra/PT

Spinal involvement usually precedes the peripheral ochronotic osteoarthritis. The most commonly involved joint outside the spine is the knee, and it is characterized by bilateral symmetrical distribution, absence of chondrocalcinosis (because CPPD crystals are not able to deposit in the cartilage since it is destroyed by the ochronotic pigment) and uniform loss of joint space (if isolated, typically occurs at the lateral tibiofemoral compartment). Like in the spine, osteophytes are usually insignificant.

Images for this section:
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Conclusion

Conventional radiology frequently plays an important role in the differential diagnosis of deposition diseases arthropathies and can potentially allow assessment of disease progression and treatment response.

Personal information

References