The Advanced Imaging of Gouty Tophi

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Gout is a metabolic disorder in which there is hyperuricemia caused by an increase in production or a decrease in excretion of uric acid. Long-lasting hyperuricemia causes the deposition of monosodium urate crystals in the joints and soft tissues, triggering gouty arthritis and, if not properly treated, the formation of gouty tophi. The diagnosis of gout is usually based on clinical presentation and laboratory examinations, long before any abnormality can be demonstrated with imaging. Radiography is the primary imaging modality used in the initial evaluation of gouty arthritis. Ultrasonography, CT, MRI, and nuclear medicine are seldom necessary. Occasionally a tophus has an unusual presentation and simulates neoplasm or infection prompting the utilization of cross-sectional imaging for further evaluation and surgical planning. Cross-sectional imaging is also used in areas that are difficult to visualize on radiographs such as spine, sacroiliac joints, and soft tissues.

Introduction

The diagnosis of gout is usually based on the clinical presentation and laboratory values. The demonstration of the presence of monosodium urate (MSU) crystals in the joint fluid or tophus remains the gold standard for the diagnosis of gout [1]. Typically the diagnosis of gout is made clinically, long before any abnormality can be demonstrated with imaging. Radiography remains the primary imaging modality used in the initial evaluation of gouty arthritis. Advanced imaging, such as ultrasonography, CT, MRI, and nuclear medicine, is seldom necessary. Occasionally a tophus has an unusual presentation and simulates neoplasm [2] or infection [3–5] prompting the utilization of cross-sectional imaging for further evaluation and surgical planning. Cross-sectional imaging is also used in areas that are difficult to visualize on radiographs, such as the spine, sacroiliac joints, and soft tissues [6].

Radiography

The radiographic manifestations of gout are well known and have remained unchanged. During initial gouty attacks radiographs are normal or show only soft tissue swelling and joint effusion, with normal joint spaces and bone mineralization. In the intercritical phase radiographs are normal.

Radiographic changes of tophaceous gout do not appear until several years after the first attack, usually more than 10 years later, and only if appropriate treatment has not been instituted. Characteristic radiographic changes of tophaceous gout include well-defined, punched out erosion with overhanging edges, preservation of the joint space, lack of periarticular osteopenia, soft tissue nodules, asymmetric involvement, and intraosseous calcifications.

Erosions in gout may be intra-articular, para-articular, or extra-articular. Intra-articular erosions start from the margin of the joint and extend toward the center. Para-articular and extra-articular erosions are the result of tophi eroding into bone; usually the tophi are visible on radiographs as dense soft tissue nodules, occasionally calcified. Gouty erosions are well defined, "punched out," often with a thin sclerotic border. An additional characteristic feature of gouty erosions is the presence of an overhanging edge, a thin bony margin at the periphery of the erosion that extends into the soft tissues and partially covers the tophus. This overhanging edge is caused by a gradually expanding tophus eroding the cortex with concomitant new periosteal bone formation trying to contain the tophus. The joint space is often remarkably well preserved until late in the disease. No periarticular mineralization is preserved, but with progression of the disease, disuse osteoporosis may develop. The intraosseous calcifications are the result of intraosseous tophi that are calcified and are present in approximately 6% of patients with tophaceous gout [7]. Calcifications are more common when there is alteration of the calcium metabolism associated with renal disease.

Few studies have discussed radiographic changes in tophi during gout hyperuricemia treatment and whether radiographs can be used in monitoring effectiveness in clinical trials. In a study of 39 patients treated for gout, over a 10-year period, no correlation existed between radiographic changes and mean serum urate concentrations. This may be due to the fact that, as tophi take years to build up, they may take years to dissolve even with appropriate therapy [8]. Another explanation is poor

patient compliance with treatment. In another report of 10 patients, radiographs demonstrated regression of osseous tophi in all patients when proper treatment was instituted and serum concentration was maintained below 5.6 mg/100 mL (0.30 mmol/L)[9].

Computed Tomography

Computed tomography can demonstrate the extent of joint and bone involvement by gout, but it is rarely used as the primary imaging modality, except for evaluating areas that are difficult to visualize on radiographs, such as the spine [10••,11,12], sacroiliac joints [13], and soft tissues [6]. As helical multi-slice scanners become more readily available, the increased scanning speed and multiplanar capabilities may result in increased use of CT in the diagnosis and assessment of gouty arthritis [14••]. On CT, tophi have a mean attenuation of 160–170 Hounsfield units, which is less than that of calcifications and more than that of soft tissues. Calcium deposits have an attenuation of approximately 450 Hounsfield units [15••]. However, tophi may contain calcifications and the distinction of tophi from other calcified lesions may be difficult. CT is useful in differentiating tophi from other soft tissue masses such as xanthomas [16] or rheumatoid nodules [17], which have a lower attenuation than tophi.

Magnetic Resonance Imaging

Magnetic resonance imaging is used as the primary imaging modality only in the rare cases of gout involving the spine. Otherwise MRI is not used for the diagnosis or management of patients with gout. Most MRI exams in patients with gout are obtained for unrelated reasons. As with conventional radiographs, the typical radiographic manifestations of marginal and para-articular erosions of gout may be demonstrated with MRI. MRI may show cartilage sparing, typical of the disease. Characteristically, tophi have homogeneous low signal intensity, similar to muscle on T1-weighted images [18]. On T2-weighted images, the signal characteristics of tophi vary from homogeneous high signal intensity [18,19] to homogeneous low signal intensity [4,20,21]. However, signal intensity on the T2-weighted images may be heterogeneous due to urate crystals or calcium deposition, making distinction from neoplasm difficult in a patient without clinically diagnosed gout. The variability in signal intensity on T2-weighted images could be due to differences in calcium concentration within a tophus. Hemosiderin deposition in a tophus has also been reported as a cause of low signal on T2-weighted images [16]. The pattern of enhancement is variable from intense homogeneous to peripheral and heterogeneous enhancement [15••]; near homogeneous enhancement is the most common pattern. The enhancement of the tophus is likely caused by hypervascularity of the affected synovium and the hypervascular granulation tissue surrounding the tophus [18].

Although the MR appearance of tophi is nonspecific, the diagnosis of gout should be considered when a mass has heterogeneous low to intermediate signal intensity on T2-weighted images, especially if the mass erodes adjacent bones [18]. MRI can demonstrate extra-articular deposition of MSU in bones [22,23], tendons [24], and bursae [23]. In my experience MRI has been useful in distinguishing ulcerated tophi from non-healing ulcer due to osteomyelitis. In ulcerated tophi, the tophus and underlying bone have low to intermediate signal intensity on the T2-weighted images (Fig. 1), whereas in non-healing ulcer due to osteomyelitis the underlying bone has high signal intensity on T2-weighted images.

Ultrasonography

Ultrasonography is rarely used for imaging patients with gout. Ultrasonography is helpful in detecting small joint effusion and is used in directing joint aspirations [25] and biopsies. The joint effusion in gout has been described as a "snow-storm" with multiple mildly heterogeneous echoic spots [26]. On ultrasonography, tophi most often appear as heterogeneous hypoechogenic masses of high attenuation with some shadowing and hyperechogenic surrounding [15••]; occasionally tophi may contain calcifications that appear hyperechoic with acoustic shadowing [27]. Ultrasound can demonstrate cortical bone erosions adjacent to tophi. With color Doppler vascularity can be frequently seen surrounding the tophus [7].

Nuclear Medicine

Nuclear medicine is rarely used in the evaluation of patients with gout. Skeletal scintigraphy using Tc 99m phosphate compounds may be helpful in surveying the extent, severity, and distribution of gouty arthritis [28,29], but is not specific. Increased uptake on all three phases of a bone scan is present with gout and may mimic osteomyelitis [29]. Labeled leukocyte scintigraphy during an acute gouty arthritis shows accumulation of labeled leukocyte in the affected joints in a pattern indistinguishable from septic arthritis, but after treatement and remission of the acute attack, labeled leukocyte scintigraphy return to normal [30]. On PET with 18F-fluoro-2-deoxy-D-glucose (FDG) a gouty tophus was reported as having moderately increased uptake but less than the uptake expected in malignant tumor [31].

Distribution

Foot and ankle

The most characteristic site of involvement is the first metatarsophalangeal joint. Erosions are frequently seen in the dorsal and medial surfaces of the fist metatarsal head and less frequently in the first proximal phalanx. The other joints of the foot, the metatarsophalangeal, interphalangeal, tarsometatarsal, and intertarsal joints,

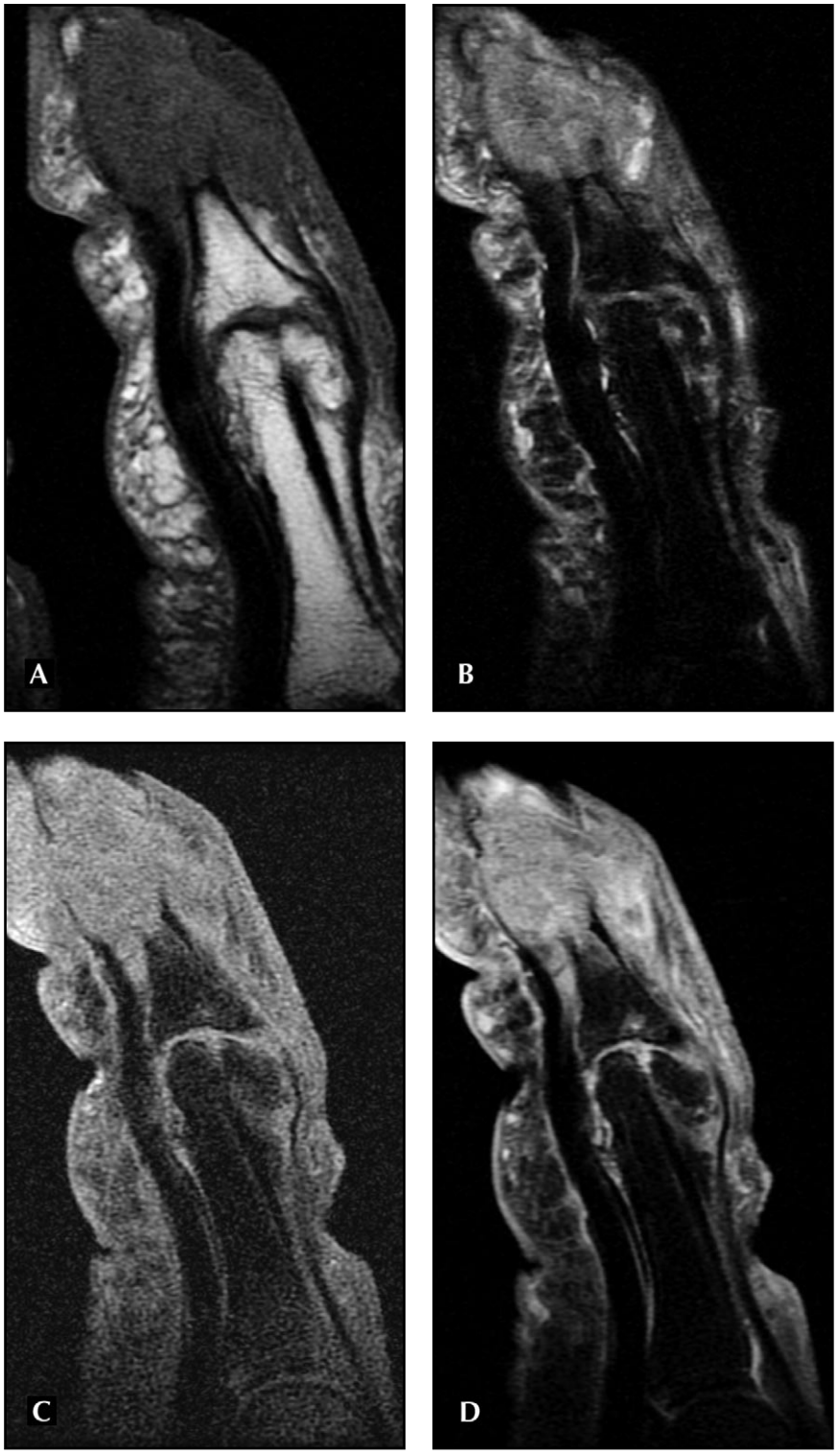

Figure 1. An 88-year-old man with a painful, swollen finger treated with antibiotics for the presumed diagnosis of cellulitis, presented with increased swelling and drainage of his finger over the previous 2 days. MRI was obtained to exclude osteomyelitis. **A,** Sagittal T1-weighted image, **B,** Sagittal T2-weighted fat-suppressed image, **C,** sagittal T1 fat-suppressed image, **D,** T1 sagittal fat-suppressed, contrast-enhanced, T1-weighted image demonstrate a tophus centered in the distal interphalangeal joint of the index finger. This mass, which extends proximally and distally to include the middle and distal phalanx, is a tophus; it has low signal on T1-weighted image **A,** intermediate signal on T2-weighted image **B,** and has diffuse enhancement on the contrast-enhanced image **D** when compared to corresponding unenhanced image **C**. There is no bone marrow edema to suggest osteomyelitis. After treatement with allopurinol and colchicine the drainage stopped and the pain and swelling improved.

are also frequently involved. Isolated involvement of the ankle joint is rare. Radiographs are usually sufficient; occasionally MRI is obtained to evaluate for tendon rupture [24], nerve entrapment [32], or infection [5].

Hand and wrist

The hand and wrist are also commonly affected, usually with bilateral but asymmetric articular and soft tissue abnormalities. In the hand, the joints most commonly involved in decreased order of frequency are the distal interphalangeal joints, the proximal interphalangeal joints, and the metacarpophalangeal joints. In the wrist, erosions can be present in the intercarpal and carpometacarpal joints. Tophi are a rare cause of carpal tunnel syndrome. MR imaging is the study of choice in the pre-operative investigation to evaluate the presence,

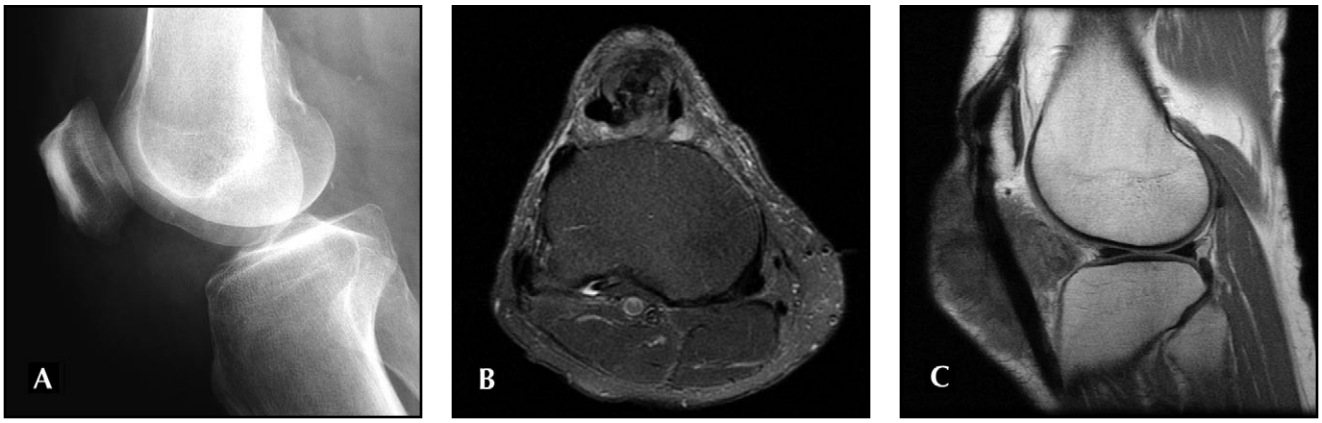

Figure 2. A 63-year-old male with knee pain, locking, and inability to fully extend the knee. **A)** Lateral radiograph of the knee shows nonspecific increased density in the region of the Hoffa fat pad. **B)** Axial T2-weighted fat-suppressed MR image and **C)** Sagittal proton density MR image demonstrate a large mass centered in the patellar tendon extending posteriorly in the Hoffa fat pad and anteriorly in the subcutaneous tissue, with signal characteristic typical of a tophus.

location, and complexity of gouty lesions in patients with carpal tunnel syndrome [33].

Elbow

In the elbow the most common presentation is soft tissue swelling caused by olecranon bursitis [34,35] or soft tissue tophi. Joint involvement may be present, but it is less common.

Knee

In the knee, marginal erosions of the tibia and or femur, with sparing of the joint space are typical, but isolated lesions of the patella have been reported [35,36]. Intraosseous lesions in the patella and femur may be confused with neoplasms. Intraosseous lesions in the patella may also predispose to pathologic fractures.

Intra-articular and periarticular tophi limiting knee joint range of motion are a rare but important cause of walking disability in gout patients. Although most patients do not display visible subcutaneous tophi over the knee on physical examination, the differential diagnosis should consider intra-articular tophi. MRI is valuable in this clinical setting [37] as radiographs may not demonstrate intra-articular tophi (Fig. 2). Rarely, gout of the knee can present as a Baker cyst [38].

Spine

Although spine manifestations of gout are very rare, there has been an increase of reports of gout involving the spine. Bony erosions and secondary proliferative osseous changes are the prominent but nonspecific feature of spinal gout on plain films [39]. In the spine gout can cause erosions of the posterior elements, facets, and vertebral bodies; disc space narrowing; and vertebral subluxation [10••]. CT is helpful in delineating bone and soft tissue changes and in showing tophi. MRI is the modality of choice to evaluate the spinal canal. Involvement of the disc space can simulate discitis [4]. Tophi in the spinal canal can be mistaken for an epidural abscess [3,40] or can cause spinal canal stenosis and myelopathy [41].

Other joints

Sacroiliac joints, hip, and shoulder are uncommon sites of involvement, and usually other sites are also affected. For the evaluation of the sacroiliac joints CT and MRI are useful, as the sacroiliac joints are difficult to visualize on radiographs.

Conclusions

The diagnosis of gout is based on clinical presentation and laboratory examinations. Radiography remains the primary imaging modality used in the initial evaluation of gouty arthritis. Ultrasonography, CT, MRI, and nuclear medicine are seldom necessary. The use of cross-sectional imaging is limited to areas that are difficult to visualize on radiographs such as spine, sacroiliac joints, and soft tissues. Occasionally a tophus has an unusual presentation and can simulate a neoplasm or infection, prompting the utilization of cross-sectional imaging for further evaluation and surgical planning.

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have been highlighted as:

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