

Difficult diagnosis of gout: the benefit of dual energy computed tomography, initial experience in routine clinical practice

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Abstract

Gout, one of the most common inflammatory arthritides in humans, is still difficult to diagnose in challenging situations, when fluid for arthrocentesis or an apparent tophus are absent and, for example, an infection as differential diagnosis has to be ruled out. Dual energy computed tomography (DECT) is an established tool for detection and characterisation of uric acid stones in the urinary tract and has recently been used to detect and display urate deposits. Our first experiences with DECT as a diagnostic tool in routine clinical practice show, that DECT is a promising imaging technique which allows the detection of monosodium urate deposits and benefits the routine diagnosis of tophaceous gout particularly in diffuse soft tissue swelling of the limbs, without the possibility of needle aspiration. However, DECT does not seem suitable to detect dissolved urate crystals, neither *in vitro* nor *in vivo*.

Introduction

Gout is one of the most common forms of inflammatory arthritis in humans, its prevalence and incidence is increasing worldwide.¹

Usually gout is not difficult to diagnose if either the typical picture of podagra or an acute arthritis of other regions than the big toe with detection of uric acid crystals in synovial fluid aspiration is present. However, gout can present with extensive soft tissue swelling far beyond one joint, without sufficient synovial fluid for arthrocentesis in the examined joints. It is well documented, that there is a large variability in the location of urate deposits from the superficial portions of the articular cartilage to the soft tissue and bone.

However, in the absence of fluid or apparent tophus, diagnosis may be difficult particularly when pronounced soft tissue swelling dominates the clinical picture.

Diagnostic advances in the field of gout have been long outstanding. Serum urate levels can be either elevated, normal or even lowered during gouty attack and are not useful for diagnosis. The characteristic, well defined, *punched out*, periarticular erosions with overhanging edges on plain radiography are most often not seen until 6 or more years after the initial presentation. Magnetic resonance (MRI) can provide helpful diagnostic information,² but is expensive and like traditional computed tomography (CT) lacks specificity. Ultrasonography (US) has recently gained ground as a very helpful imaging modality in diagnosis of gout provided the characteristic features are present.³ Advantages of US include the absence of ionising radiation, low cost, easy availability, and its usefulness in guiding aspiration. It does, however, require an experienced sonographer and high resolution equipment.

Dual-source computed tomography (DSCT) was developed to permit better temporal resolution in cardiac imaging.⁴ Using the dual energy mode, it has shown its performance in other applications including the detection and characterisation of uric acid stones in the urinary tract.⁵ The DECT-examination requires a scanner with dual-energy capabilities. There is no need for additional intravenous contrast medium and thus, DECT-scans are possible in patients with severely impaired renal function. Usually, the two scan-energies are set to 140 kV and 80 kV. Based on these two imaging series, different crystals with different absorption characteristics can be distinguished using several commercially available software modalities. These software tools allow for colour-coded discrimination of urate crystal deposits as well as several other crystal types. A study involving 20 patients with tophaceous gout and 10 controls with other arthritic conditions showed, that dual energy CT scans using a renal stone colour coding program effectively produced obvious colour displays for urate deposits, identified subclinical urate deposits and were in addition able to measure the tophus volume.⁶ Generally, DECT is able to detect very small-sized crystal deposits, but interestingly only deposits >2 mm in size are causing symptoms.⁷ The quantification of tissue urate burden with dual energy CT during urate lowering therapy may help monitoring the success of the initiated urate lowering therapy.⁸ There is evidence that DECT can serve as a problem-solving tool in the presence of challenging clinical presentations.⁹

Investigation is required to establish whether DECT is a reliable diagnostic tool in routine clinical practice.

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Case Report #1

This 77 year-old man was admitted to our hospital because of coronary heart disease. On admission painful redness and swelling in the region of the left lateral aspect of the ankle joint was present (Figure 1A).

The patient reported the onset of these symptoms 3 days prior to admission. Laboratory results revealed increased uric acid. Ultrasound examination showed no effusions, neither in the first metatarsophalangeal joint nor in the ankle or the surrounding soft tissue. As there was no possibility for needle aspiration, the differential diagnosis of gout or soft tissue infection remained unanswered. Due to the urgent need for coronary examination a dual energy CT of the left foot and ankle was performed and confirmed the presence of small urate deposits in the lateral-dorsal aspect of the hind foot as well as the first metatarsophalangeal joint (Figure 1B).

Thus, gout seemed more likely than an infectious process. Treatment with oral prednisone was established and the coronary angiography was performed. Four days of low dose steroid treatment led to complete regression of the inflammatory swelling.

Case Report #2

A 50-year-old man with a 10-year history of systemic lupus erythematosus (SLE), was under

drug therapy comprising mycophenolat-mofetil, hydroxychloroquin and prednisone. Repeated episodes of synovitis in the context of his SLE involved most frequently the finger and knee joints. One year previously, he had begun to suffer recurrent episodes of pain and swelling of the left ankle joint. An MRI was performed and revealed little effusion of the upper and lower ankle joint and signs of flexor hallucis longus-tendovaginitis. Needle aspiration was attempted but arthrocentesis did not produce enough fluid for laboratory examination. After steroid injection in the upper as well as the lower ankle joint, all symptoms rapidly decreased and the patient was able to walk without pain. Five months later the patient presented with a relapse of pain and swelling of the left ankle, additionally there was severe pain and swelling in the right foot. Ultrasound showed absence of effusion in the upper and lower ankle joint as well as in the foot. DECT was performed and revealed the presence of uric acid deposits in multiple regions on the left and in the big toe on the right (Figure 2). Therefore the diagnosis of gout was made and an allopurinol therapy was initiated.

Case Report #3

A 59-year-old man was admitted after he recently developed swelling of his left index finger. He was under treatment with allopurinol for microscopically proven gout of the lower limbs (podagra and knee joints) for 2 years. His medical situation was complicated by advanced vasculopathy in the context of chronic kidney disease and atherosclerosis, leading to finger- amputation (1st finger on the right and 3rd on the left). No fluid could be detected by clinical and ultrasound examination, therefore DECT of the left hand was carried out. DECT shows uric acid deposits in all remaining fingers (Figure 3). Low-dose allopurinol as well as low dose steroid therapy was initiated.

Case Report #4

An 87-year-old female patient presented to the internal medicine clinic with a 7-day history of diarrhoea and acute renal insufficiency. She had bilateral swelling of the feet with pronounced redness of the second toe on both sides and the fifth on the left (Figure 4A).

Since ultrasound revealed no fluid, DECT was performed of both feet. Multiple small urate deposits in the soft tissue around the joints including the tip of the second and fifth toes were seen (Figure 4B). After one week of low dose steroid treatment the inflammatory swelling had disappeared.

Case Report #5

The patient, a 51-year-old man with a history of established, polyarticular, tophaceous gout for 16 years was seen for aspiration of a left knee effusion. Before synovial aspiration, DECT was done and demonstrated large deposits in the ligaments and the lateral recessus suprapatellaris (Figure 5).

No urate signal was detected in the rest of the

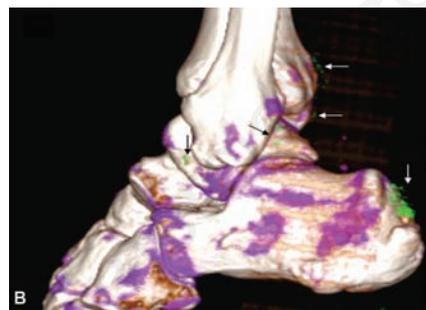


Figure 1. A) Swelling of the whole foot and localised reddish oedema in the region of the left lateral aspect of the ankle joint; B) DECT demonstrating small deposits of uric acid (green) in several areas of the hindfoot (arrows).

joint space. The aspirate showed inflammatory fluid (6690 mononuclear cells/uL) with numerous of bi-refringent monosodium urate crystals intra- and extracellularly.

Case Report #6

This 52-year-old man suffered of persistent hyperuricaemia and frequent arthritis flares of

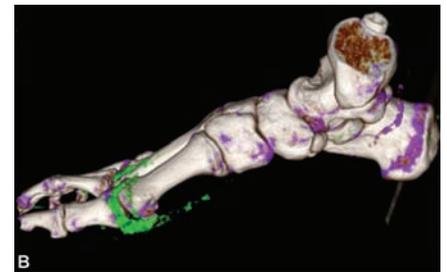
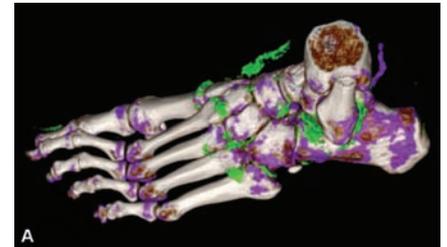


Figure 2. A) DECT dorsal view of the left foot showing uric acid deposits accentuated in and around the tarsal joints. B) DECT medial view demonstrating deposits at the MTP-I joint.



Figure 3. DECT showing the three dimensional distribution of uric acid deposits in the left hand. A) dorsal view, B) palmar view, C) radial view.

proven gout involving ankle and knee joints. On his most recent presentation to the emergency department, needle aspiration of the right knee joint produced 20 mL of a whitish synovial fluid (Figure 6A). Microscopic examination confirmed the presence of masses of monosodium urate crystals even before centrifugation (Figure 6B). Examination of the tube with synovial fluid in an upright position by DECT didn't show a urate signal (Figure 6C).

Discussion

The accurate diagnosis of gout is important for several reasons. First, in the acute situation crystal-induced arthritis and septic arthritis are the most important differential diagnoses. Second, the need for long-term drug treatment in gout requires an established diagnosis. Needle aspiration remains the gold

standard for the diagnosis of gout because negatively bi-refringent monosodium urate crystals can be reliably recognised under polarising microscopy and gram staining as well as culture can be performed in the same aspiration. Furthermore, intra-articular corticosteroid injection is a very effective treatment of the acute attack and it is reasonable to administer them immediately following joint aspiration when gout appears likely and when synovial fluid has been obtained for analysis.

However in difficult situations like excessive swelling of peripheral soft tissue and absence of accessible fluid or tophus, there is a need for a specific and sensitive imaging tool.

DSCT is known to detect cardiovascular plaque and, using the dual energy mode, to analyse the composition of urinary stones through identification of uric acid. DECT has recently been shown to be able to specifically identify uric acid deposits outside the urogenitary tract.

In our experience, as briefly demonstrated in our case-series, DECT is a promising imaging technique, which allows the detection of monosodium urate deposits in clinically unexpected locations. It also shows the extent of the deposits in a clearly three-dimensional way. This performance makes it a very helpful tool in the situation of an acute swollen limb without the possibility of needle aspiration.

As demonstrated in this initial *experiment* of case 6, DECT seems unsuitable to detect dissolved urate crystals in synovial fluid. This is demonstrated by the *in vitro* DECT-examination of a tube filled with synovial fluid with high concentration of monosodium urate monohydrate crystals (Figure 6). This might be also true for *in vivo* examinations of gouty arthritis without tophaceous deposits as demonstrated in the fifth case (Figure 5).



Figure 4. A) Oedematous swelling of both feet, pronounced redness (dactylitis) mainly of the second toe. B) DECT demonstrating among others (only one plane shown) small urate deposits in the first tarso-metatarsal joint and the second and fifth toe on the left.

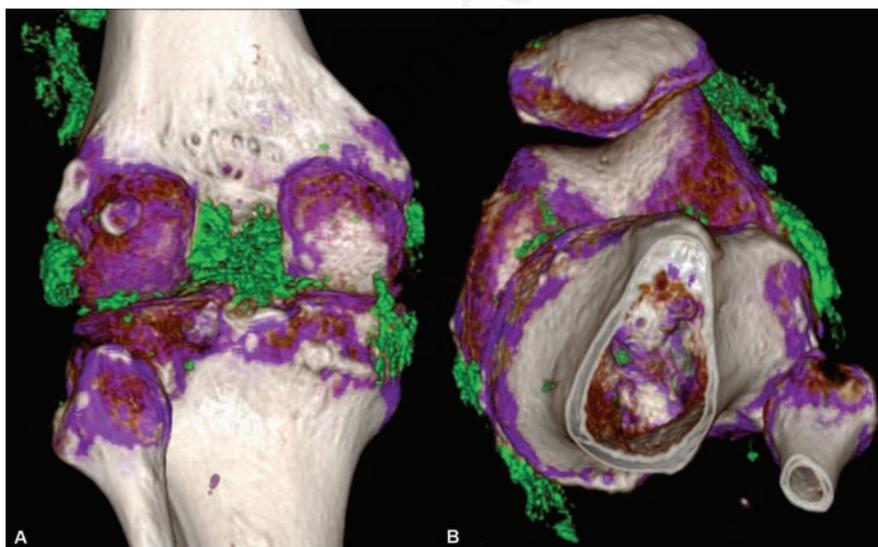


Figure 5. DECT-examination in a 51-year old man with polyarticular tophaceous gout and acute gonarthrosis on the left (proven by synovial fluid analysis after DECT-examination). A) DECT, dorsal view from distal demonstrating deposits in the medial and lateral collateral ligaments, the cruciate ligament and the lateral aspect of the recessus suprapatellaris. B) DECT, axial view.

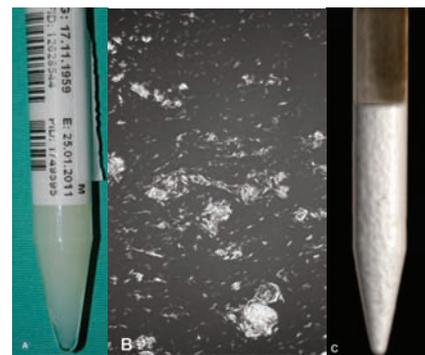


Figure 6. Synovial fluid from the knee joint of a 52-year old man with established polyarticular gout. A) Synovial fluid macroscopic view, B) microscopic examination without centrifugation, C) DECT.

Conclusions

Based on our first experiences, DECT benefits the routine diagnosis of tophaceous gout particularly in diffuse soft tissue swelling of the limbs, without the possibility of needle aspiration. DECT seems unsuitable to detect dissolved urate crystals in synovial fluid. Further benefit consists in the monitoring of treatment response. The short examination time and the non-invasivity are advantages, the need for dual-energy capabilities in CT-scan and the radiation dose are negative aspects.

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