Rheumatology 2007;46:1116–1121
Advance Access publication 27 April 2007
doi:10.1093/rheumatology/kem058

Diagnosis of gout by ultrasound

R. G. Thiele and N. Schlesinger[1]

Objectives. To establish the usefulness of ultrasonography (US) for diagnosing gout and to determine whether there are sonographic features that are characteristic for gout but not for other arthropathies.
Methods. We retrospectively compared joint images of gout patients with matching images from patients with other rheumatic conditions. Images of 37 joints of 23 patients with monosodium urate (MSU) crystal-proven gout were reviewed. MSU crystals were identified in at least one joint in each patient. Our control group had 23 randomly selected patients with 33 examined joints with rheumatic conditions other than gout.
Results. Specific diagnostic features included a hyperechoic, irregular band over the superficial margin of the articular cartilage described as a double contour sign in 92% of gouty joints and in none of the controls ($P < 0.001$); hypoechoic to hyperechoic, inhomogeneous material surrounded by a small anechoic rim, representing tophaceous material, was seen in all gouty metatarsophalangeal (MTP) joints, in all metacarpophalangeal (MCP) joints and in none of the controls ($P < 0.001$); erosions adjacent to tophaceous material were seen in 65% of MTP joints and in 25% of MCP joints. One erosion was seen in a MTP joint in a control patient with psoriatic arthritis.
Conclusions. US can detect deposition of MSU crystals on cartilaginous surfaces ($P < 0.001$) as well as tophaceous material and typical erosions. US may serve as a non-invasive means to diagnose gout.

Key words: Gout, Gouty arthritis, Tophi, Ultrasonography, Diagnostic imaging.

Introduction

Gout is one of the commonest forms of inflammatory arthritis. The prevalence appears to be rapidly increasing worldwide [1]. It is mediated by the crystallization of uric acid within the joints [2]. Urate crystals are deposited predominantly in the superficial portions of the articular cartilage [3]. These characteristic cartilaginous deposits are not readily demonstrated with conventional diagnostic imaging including roentgenography, computed tomography (CT) or magnetic resonance imaging (MRI).

Imaging modalities such as plain roentgenography, MRI and bone scintigraphy can provide helpful diagnostic clues. However, disadvantages include lack of specificity (bone scan, MRI), considerable cost (MRI) and the inability to assess early soft tissue changes such as effusion, early erosions, synovial hypertrophy and hypervascularity or small tophi (roentgenography). Typical well-defined, 'punched out,' periarticular erosions with overhanging edges are not seen radiographically until 6–12 yrs after the initial acute attack [4, 5]. The most reliable method of diagnosis is invasive needle aspiration and identification of crystals on polarizing microscopy [6]. However, many physicians do not perform synovial fluid analysis, and therapy is often initiated with an assumed diagnosis [7].

Ultrasound has recently been identified as a promising new imaging modality for gout [8]. The aim of our study was to determine whether there are sonographic features that are characteristic for gout, but not for other arthropathies, which would help provide an early, non-invasive diagnostic tool.

Rheumatology Division, Department of Medicine, Cooper University Hospital, Camden and [1]Rheumatology Division, Department of Medicine, UMDNJ/RWJMS, New Brunswick, NJ, USA.

Submitted 29 December 2006; revised version accepted 9 February 2007.

Correspondence to: R. Thiele, Department of Medicine, Allergy/Immunology & Rheumatology Division, University of Rochester School of Medicine and Dentistry, 601 Elmwood Avenue, Box 695, Rochester, NY 14642, USA.
E-mail: ralf_thiele@urmc.rochester.edu

Methods

Patients

In our Rheumatology division, we routinely perform diagnostic musculoskeletal ultrasonography (US) of all patients when the diagnosis is unclear. In this retrospective study, all musculoskeletal US studies that were performed from November 2003 through December 2004 were reviewed (500 studies). Approval by our Institutional Review Board (IRB) was obtained. Informed consent was waived by the IRB as this was considered a diagnostic procedure for patient benefit.

Studies of 37 symptomatic joints of 23 patients were found. In all gout patients, the diagnosis was established through aspiration of synovial fluid from at least one joint and subsequent crystal analysis with polarizing microscopy. The disease duration was greater than six months in all but one patient. To identify distinguishing sonographic features of gout, these images were compared with sonographic images of joints of patients with diseases other than gout. Thirty-three matching, symptomatic joints of 23 randomly selected patients were examined in the comparator group. The disease phenotypes represented in this group are detailed in Table 2.

Ultrasonographic evaluation

US studies were performed with a high-frequency, linear transducer (10 lb, 5–10 MHz, footprint 40×9 mm, GE Medical Systems, Milwaukee, WI) on a GE Logic 3 ultrasound machine. The ultrasound scans were obtained applying published guidelines for musculoskeletal ultrasound in rheumatology. Images are oriented so that proximal is on the left and distal is on the right side [9].

Cartilage of the humeral head was examined in maximal internal rotation from an anterior, transverse, short axis view. The humero-radial joint was examined from a volar, long axis view centred over the joint line. Metacarpophalangeal (MCP) joints were examined from dorsal and volar in long and short axes. In addition, MCP joint number two was visualized from a radial aspect and MCP joint number five was visualized from an ulnar aspect. Femoral cartilage was visualized in a suprapatellar, long and short axis view with the knee in maximal flexion. First metatarsophalangeal (MTP) joints were examined in long and

short axes from a dorsal, plantar and medial aspect. All studies were performed in a dynamic fashion, scanning across the joints in a medial-lateral sweep for long axis views and proximal-distal sweep for short axis views. Joints were also gently led through range of motion, with the probe kept steady. Representative still images and cine-loops were saved and stored on the hard drive of the ultrasound machine.

A rheumatologist certified in musculoskeletal ultrasound (RT) performed the examination, which takes an experienced sonographer 5–15 min per joint area. A second rheumatologist, who was blinded to the patients' diagnoses (NS), reviewed all the joint ultrasound images after a short instruction period. The US images were randomly chosen images of gouty joints juxtaposed to joint images of controls. Saved images were reviewed side by side on a computer screen, with one image of a gouty joint juxtaposed to one image of a control per screen. The review by the blinded rheumatologist included assessment of the existence of a hyperechoic band over anechoic cartilage (double contour sign), presence of tophi, joint effusions and erosions. A double contour sign, typical tophi or a combination of both were considered diagnostic.

Statistical analysis

Fisher's exact test was used to compare the results between the group with monosodium urate (MSU) crystal-proven gout and the group with rheumatic conditions other than gout. *P*-values <0.05 were considered significant.

Results

Demographics of patients with gouty arthritis and involved joints are summarized in Table 1.

Demographics of patients in the control group, their underlying diseases as well as involved joints are summarized in Table 2.

Serum urate (SU) levels during the 6 months preceding the sonographic examination were available for 21 of the 23 gout patients. In 19 patients, SU levels had exceeded 6.8 mg/dl within this time (mean: 11.2 mg/dl) (Table 1).

Ultrasound findings seen in the joints of our study patients were the following: a hyperechoic, irregular band over the superficial margin of the articular cartilage of the metatarsal heads, metacarpal heads, femoral condyles and humeral head was seen in 34 (92%) of the gouty joints and in none of the controls ($P < 0.001$, Fisher's exact test) (Figs 1 and 2).

Hypoechoic to hyperechoic, inhomogeneous material often surrounded by a small anechoic rim, representing tophaceous material, was seen in all gouty MTP joints ($n = 23$), often medial or dorsal to metatarsal heads or proximal phalanges (Fig. 3), in all gouty MCP joints ($n = 4$) and in none of the controls ($P < 0.001$, Fisher's exact test). Tophi often had a characteristic sonographic appearance of 'wet sugar clumps' (Figs 3 and 4). No tophi were seen in the shoulder, elbows or knees.

We distinguished formed tophi, which we found to be often oval shaped, intraarticular bodies and amorphous aggregates of tophaceous material from a distinct layer of hyperechoic material over anechoic hyaline cartilage and hyperechoic bone (double contour sign). We found this layer to be bound to the underlying hyaline cartilage since it moved with bone and cartilage during a real-time, dynamic examination. Formed tophi did not move with bone and cartilage upon range of motion. In two of the MTP joints of gout patients, small, hyperechoic particles distributed along the synovial inner lining of the joint capsule were observed. In both patients, these particles measured <1 mm in size. These particles may represent synovial microtophi, since we found them only in joints with gout proven by aspiration and polarizing microscopy (Fig. 3).

There appeared to be a characteristic distribution of tophaceous material in first MTP joints. Lining of hyaline cartilage with tophaceous material was observed dorsally, medially and from the plantar aspect (Figs 1 and 2). Hyperechoic microparticles were observed in the dorsal proximal recess of the synovial membrane, more amorphous material in the central area of the joint space, and formed, oval shaped tophi riding on the hyaline cartilage of the metatarsal head, impinging on (and eventually eroding into) the proximal phalanx (Fig. 3). Formed tophi were also frequently observed medial to the metatarsal head (Fig. 4).

Erosions were defined as breaks in the hyperechoic outline of the bony cortex, seen in two perpendicular planes, following the OMERACT criteria [10]. Erosions adjacent to tophaceous material were seen in 15 of 23 (65%) MTP joints and 1 of 4 (25%) MCP joints. One erosion was seen in a MTP joint in a control patient with psoriatic arthritis. No erosions were seen in the shoulder, elbows or knees.

TABLE 1. Demographics of patients with MSU crystal-induced arthritis and involved joints

Patient	Age	Sex	Palpable tophi on exam	Creatinine (mg/dl) within last month	Maximal serum urate (mg/dl) within last six months	Most recent serum urate (mg/dl) within last month	Race	Joint
1	61	F	No	2.0	9.1	5.1	African American	MCP 3
2	33	M	No	1.2		9.2	Caucasian	MTP 1 R+L
3	52	M	Yes	1.1		9.7	Asian	Humero-radial, MTP 1, knee R+L
4	78	F	No				African American	MTP 1
5	83	F	Yes		11.2	8.1	African American	MTP 1
6	72	M	Yes	1.8	12.9	10.2	Hispanic	MTP 1
7	54	M		1.0		11.9	Asian	MTP 1 R+L
8	70	M	No	0.9		9.4	Caucasian	MTP 1
9	88	F	Yes	1.3		11.9	Caucasian	MCP 5, humero-radial, knee R+L
10	82	M	Yes	2.0	11.0	4.2	Caucasian	MTP 1
11	76	M	Yes	1.2		8.9	Caucasian	MTP 1
12	38	M	No	1.6		12.4	Hispanic	Humero-radial
13	78	M	Yes	1.6		6.1	Caucasian	MCP 2, shoulder
14	58	M	Yes	1.1	9.4	3.2	African American	MTP 1
15	49	M	No	1.5	12.3	11.0	Caucasian	MTP 1, knee
16	64	F	No	0.9		5.6	African American	MTP1 R+L
17	44	M	No	1.0		9.5	Hispanic	MTP 1
18	53	M	No	1.7	13.0	5.0	Caucasian	MCP 2
19	44	M	No				Caucasian	MTP 1 R+L
20	33	M	No	1.3		13.5	Caucasian	Knee, humero-radial
21	46	F	No	1.5	10.5	6.8	Caucasian	MTP 1
22	54	M	No	1.0		8.3	Caucasian	MTP 1 R+L
23	68	M	Yes	1.0	11.6	10.0	Caucasian	MTP 1 R+L

TABLE 2. Demographics of patients in the control group, their underlying diseases and involved joints

Patient	Age	Sex	Race	Joint	Diagnosis
1	84	F	Unknown	Knee	Pyrophosphate arthropathy
2	46	F	Caucasian	MTP 1 R+L	Retrocalcaneal bursitis
3	40	M	Caucasian	R ankle, L knee	Inflammatory oligoarthritis
4	30	F	African American	R elbow	Sarcoidosis
5	63	F	Caucasian	MTP 1 L	RA
6	56	M	Hispanic	Elbow	Lateral epicondylitis
7	42	F	Asian	Knee	OA
8	54	F	Caucasian	MTP	FMS
9	31	F	Caucasian	MTP	FMS
10	74	M	Caucasian	Knee	OA
11	43	M	Caucasian	MTP	Psoriatic Arthritis
12	80	M	Caucasian	Knee	Muscle Fibre Tear
13	66	F	Caucasian	Shoulder, Knee	Bursitis, Tendinitis
14	35	F	Caucasian	Elbow	FMS
15	?	F	Caucasian	Knee	Pyrophosphate arthropathy
16	64	F	Caucasian	Knee	OA
17	41	M	Caucasian	Elbow	OA
18	57	M	Hispanic	MTP	Psoriatic Arthritis
19	62	F	Caucasian	Knee	OA
20	87	F	Caucasian	Knee	Pyrophosphate arthropathy, OA
21	37	F	Caucasian	Knee	FMS
22	68	M	Caucasian	MTP	OA
23	48	F	Caucasian	Elbow	RA

OA: Osteoarthritis; RA: Rheumatoid Arthritis; FMS: Fibromyalgia

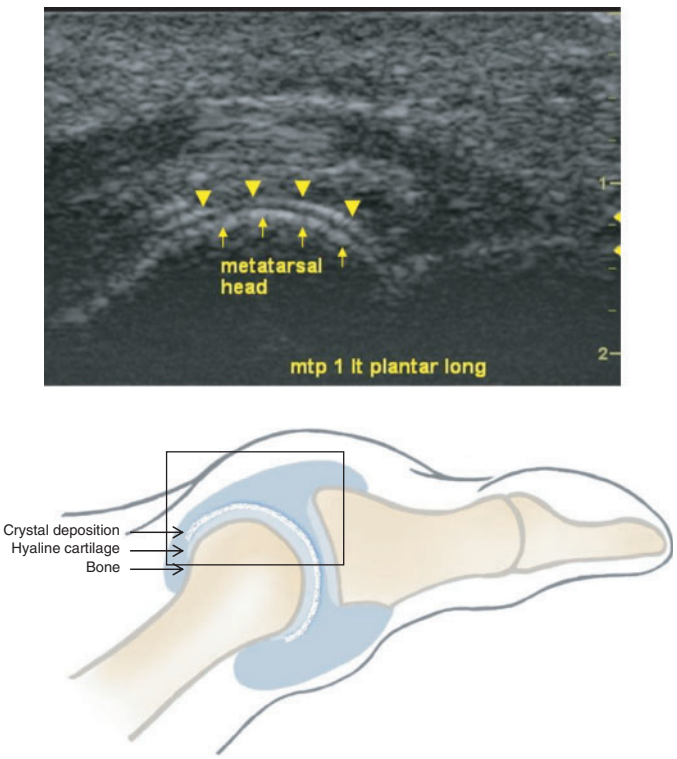

FIG. 1. Ultrasonographic finding in longstanding hyperuricaemia: outline of metatarsal head (arrows), slightly irregular echogenic deposition (arrowheads) on hyaline cartilage (anechoic line paralleling bony contour of metatarsal head).

Martel reactions (overhanging margins) [11] were observed as delicate, egg-shell-like bony protrusions in one MTP and in one MCP joint. They appeared to overlie invading tophi, with the anechoic rim that surrounds the tophus separating overhanging bone and tophus (Fig. 3).

Synovial hypertrophy in gout patients appeared sonographically as a concentric thickening of the synovial membrane (Fig. 2). Villous hypertrophy, as seen in rheumatoid synovium, was not observed. Hypervascularized synovial tissue was detected by power Doppler exam in two MTP joints of patients without clinical signs of acute gout. This was also seen in one control patient with psoriatic arthritis. We found no evidence for hypertrophic synovial tissue invading subchondral bone in gout patients.

Fluid collections were seen in 17 of 23 (74%) MTP joints of gout patients and 8 of 11 (73%) MTP joints of controls.

The second rheumatologist, blinded to patient diagnosis, was able to correctly identify 36 of 37 (97%) images of gouty joints when these were juxtaposed to joint images of controls.

Discussion

The first descriptions of gout can be traced to the dawn of recorded medical history. Still, questions remain regarding the diagnosis of gout [12]. Demonstrating the presence of MSU crystals in aspirated joint fluid or tophus is considered the gold standard [6].

Over the past few years, there has been a growing interest in US in rheumatology [13–15]. Advantages include: lack of radiation, low cost, repeatability, patient friendliness, multiplanar imaging capability, high resolution, dynamic assessment and its efficacy as a method of guidance for invasive procedures. The physics of US makes it an ideal tool to detect crystalline material in soft tissues. It has long been used to detect calcified gallstones and uric acid renal stones. US visualizes tissues as acoustic reflections. Crystalline material found in gouty joints reflects ultrasound waves more strongly than surrounding tissues such as unmineralized hyaline cartilage or synovial fluid and can thus be readily distinguished. Ultrasonographic investigation, in this study, could detect deposition of MSU crystals on cartilaginous surfaces, as well as tophaceous material and typical erosions. We found the double contour sign exclusively in gout ($P < 0.001$, Fisher's exact test). This band had a slightly irregular surface. This seems to represent crystalline precipitates of MSU; it was not seen in control patients. This sonographic finding is consistent with older histopathological studies that showed a particular predilection for uric acid to crystallize on the surface of hyaline cartilage [3]. Chondroitin sulphates and phosphatidylcholine, constituents of hyaline cartilage, have been reported to foster crystallization of uric acid *in vitro* [16].

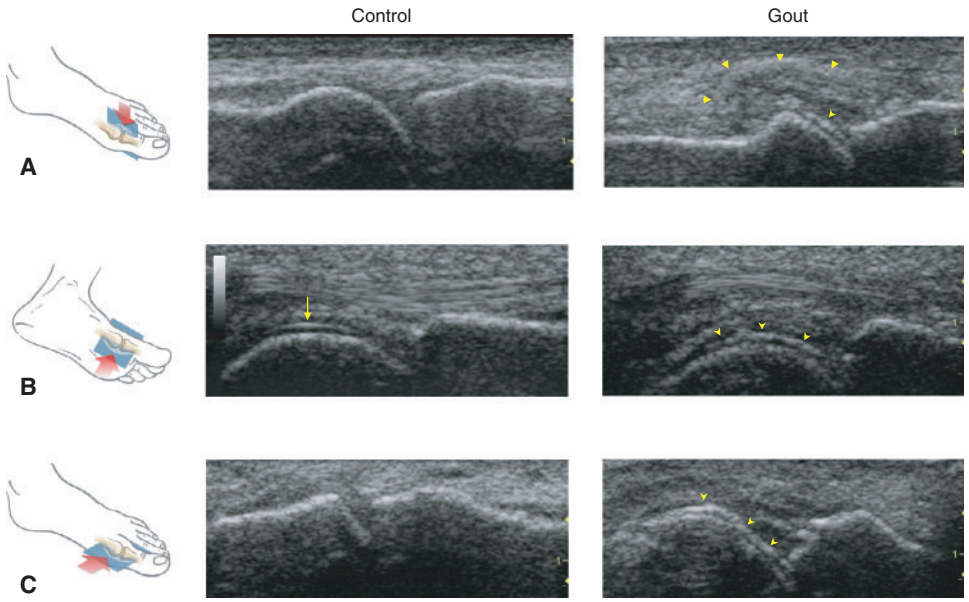

FIG. 2. Comparison of findings in first MTP joints in controls and gout patients. (**A**) Dorsal longitudinal view. A distended joint capsule is seen in the gout patient. The synovial lining is thickened (closed arrowheads). A hyperechoic, irregular line is seen paralleling the hyperechoic bony contour and the anechoic hyaline cartilage of the metatarsal head (open arrowhead). (**B**) Plantar longitudinal view. In the control patient, an interface reflex artefact is seen on the apex of the hyaline cartilage of the metatarsal head (arrow). In contrast, an irregular, thicker band is seen covering the hyaline cartilage in the gout patient (open arrowheads). This band is not limited to the area of perpendicular incidence of sound waves (open arrowheads). (**C**) Medial longitudinal view. A band of hyperechoic material (open arrowheads) parallels bony contour and cartilage in the gout patient. This is not seen in the control.

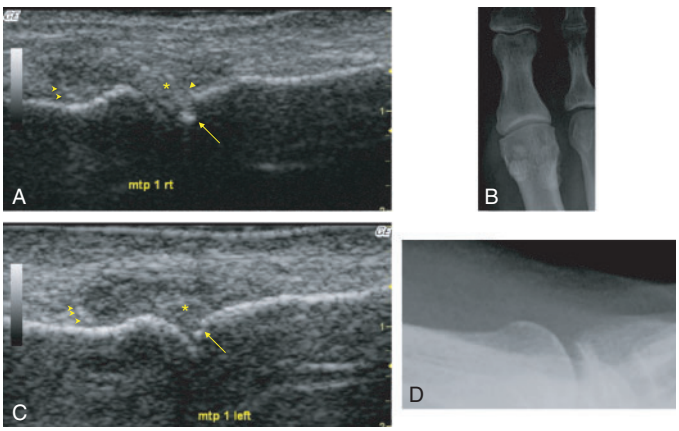

FIG. 3. Comparison of ultrasound images and conventional radiography: Images A/B and C/D, respectively, were taken of the same patients, on the same day. Both patients had an acute gout attack on the day the images were taken. Synovial fluid aspiration and polarizing microscopy were performed at the time of the ultrasound study. Distension of the joint capsule is seen in images A and C. No meaningful soft tissue characterization is possible in the radiographs B and D. An oval-shaped tophus is seen in image A (asterisk). A faint tophus is seen in image C (asterisk). There is early erosion of both tophi into the proximal, dorsal aspect of the proximal phalanx in both patients (arrow). No break in the cortical contour of the proximal phalanx is seen in the radiographs B and D. An early Martel reaction (overhanging edge) is seen in sonogram A (closed arrowhead). Small hyperechoic particles are seen in the synovial lining of the proximal cul-de-sac of the joint capsule in both sonograms. The particle size was <1 mm in both patients (open arrowheads).

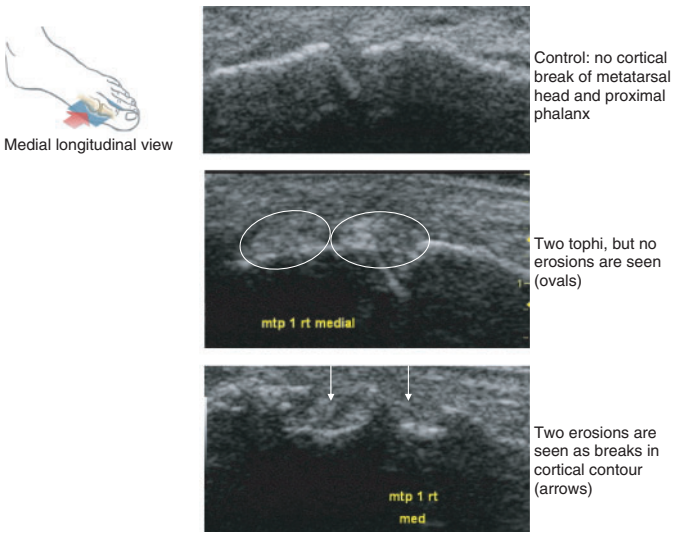

FIG. 4. Sonographic appearance of tophi and erosions. Medial longitudinal view of first metatarsal-phalangeal joint (schematic illustration). Top: control. Outline of metatarsal head and proximal phalanx interrupted by joint space. Middle: two oval-shaped tophi (white ovals) are seen adjacent to bone and joint space. They have a typical hypoechoic to hyperechoic, inhomogenous appearance of 'wet sugar clumps'. A fine anechoic (black) seam is seen surrounding the tophi. Bottom: erosions are seen in typical locations at metatarsal head and proximal phalanx (arrows).

Remarkably, the ultrasonographic findings in the cohort of gout patients were clearly distinct from those in three pseudogout patients in the comparator group. In contrast to gout, calcium pyrophosphate crystals tend to aggregate in the centre of both hyaline and fibrous cartilage [17–19]. In hyaline cartilage, this material forms a layer that parallels the bony cortex. Sonographically this appears as a hyperechoic, irregular line embedded in anechoic appearing hyaline cartilage. Chondrocalcinosis can thus be readily distinguished from gout (Fig. 5). Ultrasound was found to be more sensitive in the detection of hyaline cartilage calcifications when compared with conventional radiography [20].

Effusions were less specific for gout. The frequent finding of small fluid collections in first MTP joints is in keeping with previous sonographic studies [21, 22]. The finding that first MTP joints contain more free fluid than other MTP joints or MCP joints may be due to increased mechanical stress and hydrostatic pressure. This may support the theory that gout attacks in this

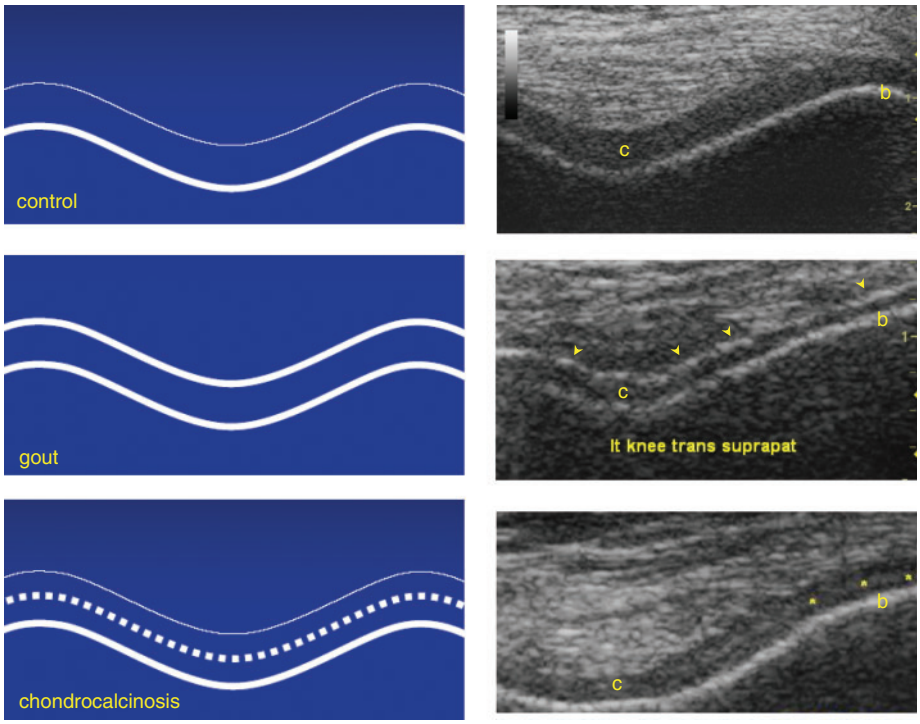

FIG. 5. Comparison of sonographic appearance of normal control, gout and chondrocalcinosis in knee joints. Suprapatellar, transverse view in flexion. Schematic illustrations on left. Top: anechoic (black) layer of hyaline cartilage (c) overlying bony contour of distal femur (b). Middle: double contour sign. Hyperechoic (bright), slightly irregular layer of crystal deposits (open arrowheads) overlying anechoic hyaline cartilage (c) and bony contour of distal femur (b). This patient had crystal-proven, untreated gouty arthritis. The hyaline cartilage is thin in this 88-yr-old individual. Bottom: hyperechoic, crystalline material (asterisks) is layered in the centre of the anechoic hyaline cartilage (c). This layer parallels the outline of the bony cortex (b). Calcium pyrophosphate crystals were found on aspiration.

joint are due to nocturnal reabsorption of this fluid, leading to increased MSU concentrations.

How can the differential distribution of formed tophi, unformed tophaceous material and microtophi in first MTP joints hypothetically be explained? With range of motion, unformed material shifts within the joint capsule. In the dorsal compartment of the MTP joint, tophaceous material meets the flexible proximal cul-de-sac and is being pushed against the synovial lining where it may form microaggregates. Distally, joint capsule and extensor tendon are firmly attached to the proximal phalanx. With dorsiflexion, tophaceous material is impacted against the ungiving proximal dorsal margin of the proximal phalanx. Since tophi are known to form on pressure points [23], this appears to foster consolidation in this location. Similarly, flexion and expansion of the joint capsule at the medial compartment with range of motion will impact unformed tophaceous material against metatarsal head and proximal phalanx and foster consolidation to formed tophi here (Figs 3 and 4).

In vitro, gouty tophi are surrounded by an inflammatory reaction, a rim of macrophages, lymphocytes and large foreign body giant cells [24]. This may explain our *in vivo* finding of an anechoic rim surrounding tophi. Sonographically, tophi (but not invading synovial tissue) were closely associated with bony erosions. The inflammatory cells surrounding tophi seemed to attack bone if contact was made. This may also be an explanation why tophi can erode completely into bone.

US was found to be more sensitive in detecting bony erosions in rheumatoid arthritis when compared with radiography [25–29]. Although we did not systematically compare ultrasound findings with conventional radiography in all patients in this study, it seems likely that ultrasound can also detect erosions in gout with greater sensitivity than radiography. In support of this hypothesis, two examples of early gouty erosions detected by sonography but not by conventional radiographs are shown (Fig. 3). If left untreated, visible tophi develop years after a first gout attack [30]. With US, we found tophaceous material in joints affected by the first attack (Fig. 3).

Some limitations of our study should be mentioned. First, it is not known how long hyperuricaemia must be present before crystalline precipitate can be seen sonographically. All but one patient had disease duration of greater than six months. At least 19 of the 23 gout patients had elevated levels of SU within the 6 months preceding the ultrasonographic examination, suggesting undertreatment. It is possible that early cases of gout would be missed. Future studies may address the utility of our findings in newly diagnosed patients. Secondly, it is not known how quickly these precipitates dissolve after normouricaemia is achieved with treatment. Longitudinal studies may shed light on this question. Thirdly, since this is a retrospective study, it is unclear how many cases of gouty arthritis will be recognized if the examiner is unaware of the patient's final diagnosis. This issue is partially resolved in this study by review of all images by the second investigator who was blinded to the patient's diagnosis, and yet assigned the sonographic image to the correct diagnostic group in 36/37 cases.

In patients with typical clinical signs and the double contour sign, hypoechoic to hyperechoic, inhomogeneous material surrounded by a small anechoic rim, representing tophaceous material and erosions adjacent to tophaceous material on US, it may be possible to make a diagnosis of gouty arthritis and begin treatment without performing a needle aspiration of the acutely inflamed joint or suspected tophus.

The importance of accurate diagnosis and treatment of gout should not be underestimated for a number of reasons: the likely need for lifelong therapy, reduction of co-morbidities associated with hyperuricaemia, in particular, cardiovascular and renal disease as well as progressive functional loss. The diagnostic potential of US as a readily available, non-invasive tool therefore

merits further investigation. In this study, we found that US may serve as a non-invasive means to diagnose gout.

Acknowledgements

We would like to thank Professor Peter C. Taylor and Professor Marc Feldmann for their kind review and constructive criticism.

The authors have declared no conflicts of interest.

References

1 Zaka R, Williams CJ. New developments in the epidemiology and genetics of gout. Curr Rheumatol Rep 2006;8:215–23.
2 Choi HK, Curhan G. Gout: epidemiology and lifestyle choices. Curr Opin Rheumatol 2005;17:341–45.
3 Sokoloff L. The pathology of gout. Metabolism 1957;6:230–43.
4 Peh WC. Tophaceous gout. Am J Orthop 2001;30:665.
5 Buckley TJ. Radiologic features of gout. Am Fam Physician 1996;54:1232–8.
6 McCarty DJ, Hollander JL. Identification of urate crystals in gouty synovial fluid. Ann Intern Med 1961;54:452–60.
7 Chen LX, Schumacher HR. Gout: can we create an evidence-based systematic approach to diagnosis and management? Best Pract Res Clin Rheumatol 2006;20:673–84.
8 Liote F, Ea HK. Gout: update on some pathogenic and clinical aspects. Rheum Dis Clin North Am 2006;32:295–311.
9 Backhaus M, Burmester GR, Gerber T *et al.* Guidelines for musculoskeletal ultrasound in rheumatology. Ann Rheum Dis 2001;60:641–9.
10 Wakefield RJ, Balint PV, Szkudlarek M, Filippucci E, Backhaus M, D'Agostino MA *et al.* Musculoskeletal ultrasound including definitions for ultrasonographic pathology. J Rheumatol 2005;32:2485–7.
11 Martel W. The overhanging margin of bone: a roentgenologic manifestation of gout. Radiology 1968;91:755–6.
12 Schlesinger N, Baker DG, Schumacher HR, Jr. How well have diagnostic tests and therapies for gout been evaluated? Curr Opin Rheumatol 1999;11:441–5.
13 Balint P, Sturrock RD. Musculoskeletal ultrasound imaging: a new diagnostic tool for the rheumatologist? Br J Rheumatol 1997;36:1141–2.
14 Wakefield RJ, Gibbon WW, Emery P. The current status of ultrasonography in rheumatology. Rheumatology (Oxford) 1999;38:195–8.
15 Grassi W, Filippucci E, Busilacchi P. Musculoskeletal ultrasound. Best Pract Res Clin Rheumatol 2004;18:813–26.
16 Burt HM, Dutt YC. Growth of monosodium urate monohydrate crystals: effect of cartilage and synovial fluid components on in vitro growth rates. Ann Rheum Dis 1986;45:858–64.
17 Reginato AJ, Schumacher HR, Martinez VA. The articular cartilage in familial chondrocalcinosis. Light and electron microscopic study. Arthritis Rheum 1974;17:977–92.
18 Bjelle AO. Morphological study of articular cartilage in pyrophosphate arthropathy. (Chondrocalcinosis articularis or calcium pyrophosphate dihydrate crystal deposition diseases). Ann Rheum Dis 1972;31:449–56.
19 Grassi W, Lamanna G, Farina A, Cervini C. Sonographic imaging of normal and osteoarthritic cartilage. Semin Arthritis Rheum 1999;28:398–403.
20 Ptasznik R. Ultrasound in acute and chronic knee injury. Radiol Clin North Am 1999;37:797–830.
21 Koski JM. Ultrasonography of the metatarsophalangeal and talocrural joints. Clin Exp Rheumatol 1990;8:347–51.
22 Schmidt WA, Schmidt H, Schicke B, Gromnica-Ihle E. Standard reference values for musculoskeletal ultrasonography. Ann Rheum Dis 2004;63:988–94.
23 German DC, Holmes EW. Hyperuricemia and gout. Med Clin North Am 1986;70:419–36.
24 Rosenberg AE. Bones, Joints, and Soft Tissue Tumors. In: Kumar V *et al.* eds. Robbins and Cotran Pathologic Basis of Disease, Elsevier, 2005;1311–14.
25 Grassi W, Filippucci E, Farina A, Salaffi F, Cervini C. Ultrasonography in the evaluation of bone erosions. Ann Rheum Dis 2001;60:98–103.
26 Wakefield RJ, Gibbon WW, Conaghan PG *et al.* The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis: a comparison with conventional radiography. Arthritis Rheum 2000;43:2762–70.
27 Backhaus M, Kamradt T, Sandrock D *et al.* Arthritis of the finger joints: a comprehensive approach comparing conventional radiography, scintigraphy, ultrasound, and contrast-enhanced magnetic resonance imaging. Arthritis Rheum 1999;42:1232–45.
28 Weidekamm C, Koller M, Weber M, Kainberger F. Diagnostic value of high-resolution B-mode and doppler sonography for imaging of hand and finger joints in rheumatoid arthritis. Arthritis Rheum 2003;48:325–33.
29 Szkudlarek M, Narvestad E, Klarlund M, Court-Payen M, Thomsen HS, Ostergaard M. Ultrasonography of the metatarsophalangeal joints in rheumatoid arthritis: comparison with magnetic resonance imaging, conventional radiography, and clinical examination. Arthritis Rheum 2004;50:2103–12.
30 Hench PS. The diagnosis of gout and gouty arthritis. J Lab Clin Med 1936;22:48–55.