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Original article

Ultrasound and clinical features of hip involvement in patients with gout



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ABSTRACT

Objectives: To investigate the prevalence of the ultrasound findings indicative of monosodium urate crystal deposits at the hip joint in patients with gout and to explore the association between the ultrasound findings and the clinical and serological features.

Methods: Bilateral ultrasound assessment of the hip joint was carried out in 40 consecutive patients with gout, diagnosed according to the latest Gout American College of Rheumatology/European League Against Rheumatism classification criteria, and 25 disease controls. Ultrasound evidence of crystal deposits was obtained using the Outcome Measures in Rheumatology definitions: hip intra-articular aggregates and/or tophi, and “double contour” sign over the hyaline cartilage of the femoral head.

Results: The ultrasound examination revealed crystal deposits in at least one hip in 17 out of 40 patients (42.5%) with gout, and in 2 out of 25 disease controls (8.0%) ($P=0.0029$). Aggregates, tophi, and “double contour” sign were found in at least one hip in 13 (32.5%), 6 (15.0%) and 6 (15.0%) out of 40 patients with gout, respectively. A moderate association between disease duration ($P=0.004$, $R_{pb}=0.442$), number of gouty “attacks” in the previous year ($P=0.029$, $R_{pb}=0.346$), presence of subcutaneous tophi ($P=0.037$, $V=0.330$) and ultrasound crystal deposits was found.

Conclusion: Our results indicate that detecting monosodium urate crystals by ultrasound is common at hip joint in patients with gout.

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1. Introduction

Gout is a crystal arthropathy characterized by monosodium urate (MSU) crystal deposition in joints and surrounding soft tissues [1].

The gold standard for the diagnosis of gout is the identification of MSU crystals in the synovial fluid analysis [2]. Over the few last years, ultrasound (US) has proven to be a fast, safe and accurate imaging technique in the detection of MSU crystal deposits, inflammatory and structural changes both at joint and tendon levels [3,4]. The US “double contour” (DC) sign has been included in the latest gout American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria [5].

Gout affects mainly the peripheral joints of the lower limb, especially the first metatarsophalangeal (MTP) joint, ankle and knee [6]. However, no joint is exempt, including the rare involvement of spine, pubic symphysis and sacroiliac joints [7–10].

Hip involvement in patients with gout is considered uncommon and it has been described only in a few case reports [11–19].

In a recent preliminary US study, our group found a considerable burden of MSU crystal deposits at the hip joint in a group of patients with gout, raising the hypothesis that hip involvement in gout might be underestimated [20].

The objectives of this study were to investigate the prevalence of the US findings indicative of MSU crystal deposits (aggregates, tophi and DC sign) at the hip joint in patients with gout, in comparison with a group of disease controls, and to explore the association between the US findings and the clinical and serological features.

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2. Methods

2.1. Patients

Consecutive patients with gout, diagnosed according to the 2015 ACR/EULAR classification criteria [5], and age/body mass index (BMI)/sex-matched controls, diagnosed with other rheumatic diseases according to the international diagnostic/classification criteria, were enrolled [21–25].

All the patients were recruited from the outpatient clinic of the “Clinica Reumatologica” of the “Carlo Urbani” Hospital, Jesi, Ancona, Italy.

The required inclusion criteria for patients with gout were either a positive synovial fluid analysis for MSU crystals and/or presence of subcutaneous tophi at the physical examination. Exclusion criteria for patients with gout and disease controls were: prior diagnosis of other crystal related arthropathies, such as calcium pyrophosphate deposition disease, previous surgical procedures and/or pronounced injuries of the hip, and hip synovitis at the time of the evaluation. Patients with hip synovitis at the time of the evaluation were excluded as the presence of joint effusion may generate an image of pseudo “double contour” enhancing the echogenicity of the cartilage superficial margin. Disease controls with hyperuricemia and/or with family history of gout were excluded.

Local ethics committee approval was not obtained as all patients underwent clinical and US examination per our local protocols. All patients gave their informed consent before entry into the study for the anonymous analysis of the data. No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

2.2. Clinical examination

A clinically experienced rheumatologist collected the demographic (age, gender, height and weight), clinical (family history of gout, disease duration, number of gouty “attacks” in the previous year, previous episodes of hip inflammatory involvement) and laboratory (synovial fluid analysis, serum urate level, C-reactive protein and erythrocyte sedimentation rate) data of all patients. Comorbidities (congestive heart failure, chronic kidney disease, dyslipidemia, hypertension, type II diabetes and metabolic syndrome) and use of medications (urate-lowering treatments, colchicine and diuretics) were also investigated. Previous episodes of gouty “attacks”, including those involving the hip, were identified according to the definitions for the symptomatic and “typical” episodes provided in the ACR/EULAR classification criteria for gout [5]. The BMI was calculated for each patient. The same rheumatologist also performed the physical examination mainly aimed at the detection of subcutaneous tophi.

2.3. Ultrasound examination

Each patient underwent a bilateral hip US exam. The hip US exam was carried out by a rheumatologist with seven years of experience in musculoskeletal US (A.D.M.), blind to patients’ clinical data, using a My Lab Twice US machine (Esaote S.p.A. Genoa, Italy), working with a linear (3–13 MHz) or, when necessary, a convex probe (2–7 MHz). The lower frequency probe (2–7 MHz) was used to assess overweight and obese patients in which higher frequency probes were not appropriate to examine deep structures, such as the hip.

During the US exam, the patients were placed on the examination bed lying in supine position with the lower limb in external rotation (heels together, toes apart). The hip joint was scanned with both longitudinal and transverse views [26]. The following

abnormalities were investigated: hip intra-articular tophi and/or aggregates, DC sign over the hyaline cartilage of the femoral head.

According to the Outcome Measure in Rheumatology definitions [27], the US elementary lesions of gout were identified as follows:

- aggregates: “highly reflective heterogeneous hyperechoic foci that may generate posterior acoustic shadow”;
- tophi: “a circumscribed, inhomogeneous, hyperechoic and/or hypoechoic aggregation (which may or may not generate posterior acoustic shadow), which may be surrounded by a small anechoic rim”;
- DC sign: “abnormal hyperechoic band over the superficial margin of the articular hyaline cartilage, which may be either irregular or regular, continuous, or intermittent”.

2.4. Statistical analysis

Results are reported as mean ± standard deviation (SD) for quantitative variables. Results for qualitative variables are expressed as frequency and corresponding percentage.

The correlation between the US findings and the clinical and serological variables was assessed. Chi-square test and Cramer’s V were used to correlate the US findings with the categorical and/or ordinal variables (gender, previous episodes of hip synovitis, presence of subcutaneous tophi and synovial fluid analysis positive for MSU crystals). Point-biserial correlation (Rpb) was used to evaluate the correlation between the US findings and the quantitative variables (age, BMI, disease duration, serum urate levels and number of gouty “attacks” in the previous year). *P*-value was set at <0.05 for significance.

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) software (version 24.0 for Mac, Chicago, Illinois, USA).

3. Results

Eighty hips, in 40 patients with gout, and 50 hips, in 25 disease controls, were evaluated.

Forty-nine patients (29 patients with gout and 20 disease controls) were assessed using a linear probe whereas the remaining 16 patients (11 patients with gout and 5 disease controls) were studied using a convex probe. The group of disease controls was made up of 7 patients with rheumatoid arthritis, 6 patients with psoriatic arthritis, 5 patients with hip osteoarthritis (OA), 5 patients with ankylosing spondylitis and 2 patients with rheumatic polymyalgia.

Table 1 illustrates the main demographic, clinical and serologic features of the patients with gout and disease controls.

Table 2 illustrates the prevalence and distribution of the US findings indicating MSU crystal deposits at the hip joint in patients with gout and disease controls.

In patients with gout, aggregates were identified as isolated findings in 11 out of 13 hips (84.6%) and in association with tophi and/or DC sign in the remaining 2 hips (15.4%). Tophi were detected as isolated findings in 4 out of 7 hips (57.1%) and in association with aggregates and/or DC sign in the remaining 3 hips (42.9%). DC sign was detected as isolated findings in 4 out of 7 hips (57.1%) and in association with aggregates and/or tophi in the remaining 3 hips (42.9%).

There was a moderate association between the US findings and the disease duration (*P* = 0.004, *Rpb* = 0.442), the number of gouty “attacks” in the previous year (*P* = 0.029, *Rpb* = 0.346) and the presence of subcutaneous tophi (*P* = 0.037, *V* = 0.330). No correlation was found between the US findings and the other variables that had been considered.

Table 1
Demographic, clinical and serological data of the patients with gout and disease controls.

	Gout	Gout with hip US MSU deposits	Gout without hip US MSU deposits	Controls
Male/Female	39/1	17/0	22/1	23/2
Age (years)	67.0 ± 12.5	68.9 ± 9.5	65.5 ± 14.4	59.7 ± 13.1
Disease duration (years)	10.5 ± 10.1	15.6 ± 9.1	6.7 ± 9.2	8.8 ± 13.5
BMI (kg/m ²)	27.7 ± 5.0	28.2 ± 3.6	27.3 ± 5.9	28.6 ± 3.5
Subcutaneous tophi	16 (40.0%)	10 (58.8%)	6 (26.1%)	0
History of hip inflammatory involvement	11 (27.5%)	5 (29.4%)	6 (26.1%)	8 (32.0%)
Family history of gout	20 (50.0%)	10 (58.8%)	10 (43.5%)	0
Gouty “attacks” in the previous year	28 (70.0%)	15 (88.2%)	13 (56.5%)	–
Number of gouty “attacks” in the previous year	2.4 ± 2.9	3.5 ± 3.4	1.5 ± 2.2	–
Laboratory data				
Serum urate level (mg/dL)	6.3 ± 1.7	6.0 ± 1.4	6.5 ± 1.9	5.4 ± 1.1
ESR (mm/h)	22.2 ± 14.6	23.9 ± 15.3	21.5 ± 14.2	24.3 ± 13.8
CRP (mg/dL)	1.2 ± 1.1	1.2 ± 1.1	1.1 ± 1.1	1.4 ± 1.6
MSU crystals in the synovial fluid analysis	31 (77.5%)	11 (64.7%)	20 (87.0%)	–
Therapy				
Urate-lowering drugs	35 (87.5%)	15 (88.2%)	20 (87.0%)	0
Colchicine	22 (55.0%)	9 (52.9%)	13 (56.5%)	0
Diuretics	9 (22.5%)	4 (23.5%)	5 (21.7%)	4 (16.0%)
Comorbidity				
Metabolic syndrome	16 (40.0%)	6 (35.3%)	10 (43.4%)	4 (16.0%)
Type II diabetes	11 (27.5%)	5 (29.4%)	6 (26.1%)	3 (12.0%)
Hypertension	17 (42.5%)	7 (41.1%)	10 (43.5%)	7 (28.0%)
Hypercholesterolemia	16 (40.0%)	6 (35.3%)	10 (43.5%)	8 (32.0%)
Congestive heart failure	6 (15.0%)	3 (17.7%)	3 (13.0%)	3 (12.0%)
Chronic kidney disease	6 (15.0%)	2 (11.8%)	4 (17.4%)	2 (8.0%)

BMI: body mass index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; MSU: monosodium urate; US: ultrasound.

Table 2
Prevalence and distribution of the US findings indicative of MSU crystal deposits at the hip joint in patients with gout and disease controls.

US findings indicative of MSU crystal deposits	Patients			Hips		
	Gout	Controls	P-value	Gout	Controls	P-value
In at least one hip	17 (42.5%)	2 (8.0%)	0.0029	22 (27.5%)	2 (4.0%)	0.0008
Aggregates	13 (32.5%)	2 (8.0%)	0.0226	13 (16.3%)	2 (4.0%)	0.0334
Tophi	6 (15.0%)	0	0.0421	7 (8.8%)	0	0.0315
DC sign	6 (15.0%)	0	0.0421	7 (8.8%)	0	0.0315
In both hips	5 (12.5%)	0	0.0658	–	–	–

MSU: monosodium urate; DC: double contour; US: ultrasound.

Percentages refer to the total number of patients (gout = 40 patients, disease controls = 25 patients) and hips (gout = 80 hips, disease controls = 50 hips), respectively.

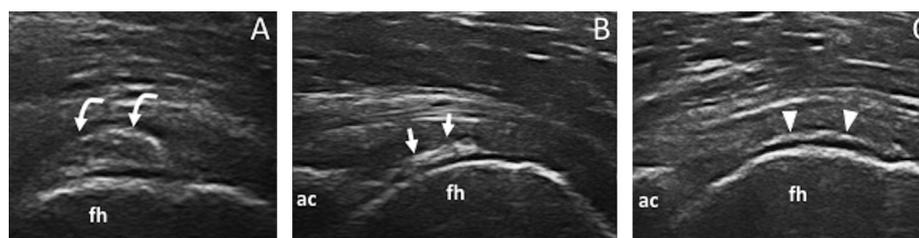


Fig. 1. US findings indicative of MSU crystal deposits at the hip joint in patients with gout. A. The US transverse scan of the hip shows an intra-articular tophus (curved arrows). B. and C. The US longitudinal scans of the hip reveal an intra-articular aggregate (arrows) and the DC over the hyaline cartilage of the femoral head (arrowheads), respectively. Legend: ac: acetabulum; fh: femoral head.

One or more US findings indicative of MSU crystal deposits were found in 5 out of the 16 hips reported as previously involved in the patient's medical history (31.3%) and in 14 out of the 64 hips without a clinical history of previous inflammatory involvement (21.9%).

Representative US patterns of hip involvement in patients with gout are shown in Fig. 1.

4. Discussion

Most of the US studies that evaluated patients with gout are focused on the knee and first MTP joint [4,28–30]. To the best of our knowledge, this is the first imaging study that explored the prevalence of MSU crystal deposits at the hip joint in a group of patients with gout.

The prevalence of US crystal deposits was significantly higher in patients with gout than in disease controls: 17 out of 40 patients with gout vs 2 out of 25 disease controls ($P=0.0029$).

Hip involvement is considered uncommon in gout and may raise diagnostic challenge. We found MSU crystal deposits in 42.5% of the patients including those without a previous medical history of hip inflammatory involvement. Aggregates were the most common US findings detected, followed by tophi and DC sign of the femoral head's cartilage, with a prevalence ranging from 32.5% to 15.0% and to 15.0%, respectively. The detection of “subclinical” crystal deposits in anatomic areas uncommonly involved in gout, such as the hip, is relevant from a clinical point of view as it provides a more comprehensive assessment of the disease burden.

Until now, hip involvement in patients with gout has been described only by a few case reports [11–19]. A case of inaugural

attack at the hip in a patient with gout was documented by Daboiko et al. [12]. Hip tophaceous gout has been reported in association with hip OA [13] and also as a cause of hip fracture [14]. Several case reports described hip involvement in patients with gout developed after hip arthroplasty [15–17].

In our study, a significant association between the US findings and disease duration, number of gouty “attacks” in the previous year and presence of subcutaneous tophi was found. This result is in line with what had been shown in many of the above-mentioned case reports, where hip inflammatory symptoms were described in subjects with chronic tophaceous gout, polyarticular involvement or long-standing disease [14,18,19].

In conclusion, we believe that the hip should be included among the joints to explore by US in patients with suspected gout for a tailored patient’s management approach. The prevalence of MSU crystal deposits at the hip joint in patients with gout appears to be higher than expected, suggesting that hip involvement in patients with gout may be not as rare as generally perceived.

Disclosure of interest

Andrea Di Matteo has received speaking fees from Grünenthal. Emilio Filippucci has received speaking fees from AbbVie, Bristol-Myers Squibb, Celgene, Roche and Union Chimique Belge Pharma. Fausto Salaffi has received speaking fees from Roche, AbbVie, Eli Lilly, Janssen and Merck Sharp and Dohme Italia. Walter Grassi has received speaking fees from AbbVie, Celgene, Grünenthal, Pfizer and Union Chimique Belge Pharma.

The other authors declare that they have no competing interest.

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