



RESEARCH ARTICLE

Clinical and Ultrasonic Characteristics of 100 New Crystal Proven Gouty Patients in a Rheumatology Clinic

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Abstract

Objectives: A 30-years-old study reported gout to be oligo- or polyarticular in 40% of cases presenting to a rheumatology clinic. The prevalence of gout has increased markedly since and presently gout has become the most prevalent inflammatory joint disease. Furthermore, specific Ultrasound (US) changes in gout have been described in recent years. The aim of this study was to register the clinical characteristics of gout patients diagnosed presently in a rheumatology clinic and the prevalence of gout specific US findings.

Methods: Data from consecutive new crystal proven gout patient fulfilling the 2015 gout classification criteria at diagnosis were analyzed in an observational study.

Results: Hundred patients (88 males (62.1 ± 13.1 (SD) years), 12 females (74.1 ± 6.9 years)) were included. Disease duration was 8.6 ± 6.9 years; disease pattern was monoarticular/oligoarticular/polyarticular/tophaceous in respectively 18/37/25/20 patients. Podagra ever was found in 74%. Symptoms from upper extremities were present in 47%. Disease severity was positively associated to disease duration and serum-urate.

US signs of urate deposition was found in 84% (79/94) of patients Double Contour (DC) sign in 69/94 (73%), Intrasynovial Hyperechoic (ISHE) areas in 64/94(68%). DC sign was associated to serum-urate while ISHE areas was associated to disease severity and disease duration.

Conclusion: Patients presenting to a rheumatology clinic and diagnosed with crystal proven gout have in most cases long disease duration and display complex clinical characteristics. Specific US findings are very common in gout. It is considered that ISHE areas to determine gout severity whereas DC sign to determine the response to treatment could be used. The study indicates that US is a useful and noninvasive diagnostic tool in gout to determine disease severity and response to treatment.

Introduction

Gout is a painful and disabling rheumatic disease caused by hyperuricemia induced articular and juxta articular deposition of sodium urate crystals. It usually affects middle aged and elderly patients with predominance in males. Typically, gout presents as an intermittent monoarthritis in the foot or ankle, but with prolonged and insufficiently treated hyperuricemia gout may develop into polyarticular disease [1].

In a study, more than 30 years ago 40% of new gout patients presenting to a hospital rheumatology clinic had oligo- or polyarticular disease [2]. Since then the prevalence of gout has increased worldwide [3], and gout is presently the most prevalent inflammatory joint disease in USA and Western Europe [4,5]. It is not known whether the increased prevalence of gout is accompanied by an altered clinical presentation.

Characteristic Ultrasound (US) changes associated with gout have been described in recent years [6]. These findings still need further validation [7], but US may be helpful in finding appropriate locations for joint and tissue puncture to obtain material for microscopic diagnosis and maybe in the future US may facilitate non-invasive diagnostics of gout.

The aims of this study were to describe the clinical characteristics of gout patients diagnosed presently in a rheumatology clinic and register the prevalence of gout specific US findings.

Methods

Patients referred to a hospital rheumatologic clinic or attending hospital acute ward with arthritis that might be due to gout were examined clinically and when applicable with US of symptomatic joints and the metatarsophalangeal joints and the knees. US investigation was done and registered by the author before diagnostic punctures and microscopy. Caution was made to differentiate the double contour sign from the cartilage interface sign and intracartilaginous calcifications. Intrasynovial Hyper-Echoic (ISHE) areas were registered when characteristic soft contoured more than 1 mm large intrasynovial hyperechoic elements were seen [6]. Tophi, defined as heterogeneous hyperechoic elements often surrounded by a small anechoic rim, were registered as ISHE areas.

As well patients with as without acute attacks were seen. Joint distribution of arthritis symptoms within the last 6 months was registered as were the occurrence of podagra ever, disease duration, medication history, and serum-urate. Patients with joint effusions had ar-

throcentesis, while patients without joint effusion but with clinical tophi or US signs of urate deposits were punctured with sterile technique, in order to obtain tissue specimens for microscopic examination for urate crystals [8]. Patients with a positive monosodium urate crystal confirmation were diagnosed with gout in accordance with the 2015 Gout Classification Criteria [9] and prospectively included in an observational study.

The associations between disease severity (defined progressively as monoarthritis, oligoarthritis (2-4 joints), polyarthritis, or tophaceous gout), disease duration, serum-urate and US signs of urate deposits were calculated with Spearman's 2-tailed non-parametric correlation test.

Results

100 consecutive patients with crystal proven gout were included during October 2012 to March 2015. See [Table 1](#) for characteristics and results. Only a minority (18%) of patients presented with monoarthritis while the majority (82%) presented with oligo-, polyarticular, or tophaceous gout. Nearly half the patients (47%) had

Table 1: Clinical characteristics at presentation of 100 new crystal proven gout patients.

Males, n = 88, age, mean ± SD	62.1 ± 13.1 years	
Females, n = 12, age, mean ± SD	74.1 ± 6.9 years	
Disease duration, mean ± SD	8.6 ± 6.9 years	
<i>Disease pattern</i>	<i>Disease duration, mean ± SD</i>	
• Monoarticular disease (n = 18)	1.5 ± 6.2 years*	
• Oligoarticular disease (n = 37)	6.8 ± 6.9 years*	
• Polyarticular disease (n = 25)	11.3 ± 6.6 years*	
• Tophaceous disease (n = 20)	12.3 ± 8.1 years*	
Podagra ever (n = 100)	74%	
Urate Lowering Treatment ever (n = 100)	42%	
Urate Lowering Treatment at entry (n = 100)	15%	
<i>Distribution of affected joints</i>		
Metatarsal-phalangeal joints (n = 100)	63%	
Midfoot/ankles (n = 100)	57%	
Knees (n = 100)	57%	
Hands/wrists/elbows (n = 100)	47%	
<i>Ultrasonic findings</i>	Double contour	ISHE
All (n = 94)	73%	68%
Monoarticular (n = 18)	50%	38%†
Oligoarticular (n = 36)	75%	64%†
Polyarticular (n = 21)	76%	84%†
Tophaceous (n = 19)	74%	100%†
<i>Serum-Urate</i>		
With ULT (Allopurinol) (n = 15), mean ± SD	7.7 ± 1.7 mg/dl (0.46 ± 0.10 mmol/l)	
Without ULT (n = 85), mean ± SD	8.9 ± 1.9 mg/dl (0.53 ± 0.11 mmol/l)	
• Monoarticular (n = 15)	8.4 ± 1.7 mg/dl (0.50 ± 0.10 mmol/l)#	
• Oligoarticular (n = 34)	8.7 ± 1.7 mg/dl (0.52 ± 0.10 mmol/l)#	
• Polyarticular (n = 22)	9.3 ± 2.2 mg/dl (0.55 ± 0.13 mmol/l)#	
• Tophaceous (n = 14)	9.8 ± 1.7 mg/dl (0.58 ± 0.10 mmol/l)#	

ULT: Urate Lowering Therapy; ISHE: Intra-Synovial Hyper-Echoic areas; *Spearman's ρ : 0.466, $P < 0.001$. †Spearman's ρ : 0.400, $P < 0.001$. #Spearman's ρ : 0.247, $P < 0.05$.

symptoms from the upper extremities. Disease severity was positively correlated to disease duration and p-urate.

US findings of ISHE areas were correlated to disease severity and disease duration (Spearman's ρ : 0.237, $P = 0.02$), while US findings of DC signs were not. Contrarily DC signs were correlated to s-urate in patients not on ULT (Spearman's ρ : 0.314, $p < 0.01$), while the correlation between s-urate and ISHE areas did not reach level of significance.

Discussion

The study presents a cross sectional sample of patients with crystal proven gout diagnosed in a rheumatology clinic. The clinical features show that gout often is a clinically complex and progressive entity correlated to disease duration and p-urate.

The majority of patients presented with oligoarticular- or polyarticular arthropathy in many cases both in the lower and/or upper extremities. Compared to the results of a similar study thirty years earlier [2] more patients had oligo- and polyarticular disease (82% vs. 40%). Disease durations were comparable (7.4 vs. 7.2 years), while the patients in the present study were older (64.4 vs. 60.9 years), and included women, which might explain some of the differences [10]. The two studies though were different regarding nationality, healthcare settings, and racial distribution of patients, and direct comparison over time must be done with caution.

One in four gout patients did not experience podagra, which has been described earlier [11]. Consequently, attempts to diagnose gout on typical clinical characteristics with intermittent monoarthritis of the lower extremities in combination with measurement of s-urate measurements that may show normal values during gout flares, may miss the diagnosis in many cases [12]. Diagnostic joint puncture and microscopic examination for urate crystals are usually not done in general practice [5,12,13]. Thus, many physicians may concentrate solely on the management of acute arthritic manifestations without diagnosing gout and thus not initiate or adhere to ULT due to diagnostic uncertainty [14].

Reports on the joint involvement at onset of gout patients in primary care have not been found, but it must be assumed that the majority of patients initially present with intermittent monoarthritis [1,13]. The patients in the present hospital based study may represent a selected subgroup of patients with longer-standing and more severe disease than most patients seen in primary care. But all patients included were referred from primary care or attending emergency ward independently, and they thus represent patients of short to long disease duration that until presenting to rheumatology care had been in general practice care without receiving sufficient treatment. A survey of 7443 British gout pa-

tients from primary care, where 72% were symptomatic within the last year, showed a mean disease duration of 81.4 months (6.8 years) [5] which is comparable to the findings in this study. It thus seems plausible to assume that many gout patients in primary care live with long standing disease without proper ULT and subsequently develop oligo- and polyarticular disease that later may obscure the diagnosis of gout and explain some of the diagnostic and therapeutic failings registered [15].

US investigation was done before diagnostic punctures and microscopy. The ultrasonic interpretation was in that sense unbiased to the subsequent diagnosis of gout or not. The US findings of ISHE areas in the majority of patients confirm gout as a urate deposition disease, and the occurrence of ISHE areas was significantly correlated to disease duration and disease severity. The DC sign was significantly correlated to p-urate, which is in concordance with other studies describing DC in asymptomatic hyperuricaemic patients [16]. In a previous report DC sign was significantly correlated to s-urate but ISHE areas were not investigated [17]. According to the present study, ISHE areas might be considered to determine gout severity whereas the DC sign might be useful in evaluating treatment response. Further studies are needed to verify this. However, this study indicates that US is a useful, noninvasive diagnostic tool in gout to determine disease severity and response to treatment.

In conclusion, the study shows that gout in many cases is a complex progressive widespread disease with a significant correlation to disease duration and s-urate. Early diagnosis and early treatment with ULT is recommended to prevent gout from developing into complicated disease with high load of monosodium-urate deposits. Experiences from several countries have demonstrated that gout is insufficiently treated in primary care [5,18-20] and it may prove cost effective if rheumatology specialists to a higher degree assumed the task of diagnosing gout patients and initiate treatment.

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