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Has the clinical spectrum of gout changed over the last decades?

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ABSTRACT

Objective. *To evaluate if the clinical spectrum of gout has changed over the last decades, a cohort of 107 patients was studied in relation to the date of disease onset and of presentation to our Institution.*

Methods. *The structured questionnaires of 107 consecutive patients with gout seen between 1989 and 2009 were retrospectively reviewed. Patients were divided into two subgroups according to the year of the first acute arthritis attack: (a) patients with gout onset dating back to 1967–2001, and (b) patients with gout of later (2002–2009) onset. The patients were also subdivided according to the date of their first admission to our Institution: 1989–2006 and 2007–2009 admissions.*

Results. *The male to female ratio changed from 11.3 in the patients who had the first attack before 2002 to 2.4 in the second onset group (p=0.02). A family history of gout was slightly more frequent in the second subgroup (22.7% vs. 6.4%, p=0.05). The mean number of acute attacks was higher in patients seen before 2002 (p=0.01). Synovial fluid was examined more frequently in the subgroup visited for the first time after 2006 (p=0.001).*

Conclusions. *Our data indicating that the patients' sex ratio has changed over time, with women more frequently affected, could be of importance to clinicians who often believe that gout is a disease affecting males only. The increased utilisation of synovial fluid analysis suggests a closer attention to the disease in recent years. Clinicians should be aware that gout is increasingly affecting women.*

Introduction

Gout is one of the most common inflammatory rheumatic diseases, with 1.4% prevalence in the general population (1). This disease, caused by the intra- and extra-articular deposition of crystals of monosodium urate (MSU), is the most frequent form of arthritis in man.

According to the recent literature, gout seems to be changing its clinical spectrum, for it is now more frequently polyarticular, involves the hand, affects a wide range of age groups, and its incidence is increasing in women. Arromdee *et al*. demonstrated a statistically significant increase in the incidence of primary gout in the study of two cohorts separated by 20 years (1977-78 and 1995–96) (2). This study also showed a change in presentation of gout, with a decrease of the classical podagra and a shift to monoarthritis of other joints, including the hands, or to poliarticular arthritis (2). In a prospective cohort study including a follow-up of 52 years, an increased incidence of gout was found in women (3). The relevance of various risk factors in women failed to show any major differences, except for the fact that women with low level of uric acid have less risk of gout in comparison to males with similar levels. In a descriptive analysis based on a U.S administrative claims database in the years 1990-1999, Wallace *et al*. observed an increased prevalence of gout in the overall population, mostly in the over 75-year age group. A change in the male to female ratio was noted in this study, from 4:1 at baseline to 3:1 at the end of the considered period (4). A contrasting view was suggested by Elliot *et al*. who described a decrease in the prevalence of gout, associated to a higher use of allopurinol. The study was based on data collected from the UK general practitioners database (5) in a retrospective study from 1994 to 2007. In a study based on data from the UK General Practice Research Data Base in the years 1990–1999, the incidence of gout was relatively stable over time, with a prevalence of 1.4% among 24,000 subjects, with a male to female ratio of 3.6:1 (1).

To test the hypothesis that the clinical characteristics of gout have changed over time, we studied a cohort of 107 patients, divided according to the years of disease onset and of admission to our Institution.

Patients and methods

The structured questionnaires of 107 consecutive patients with gout seen at our Institution between 1989 and 2009 were retrospectively reviewed. Gout was diagnosed according to the preliminary ACR criteria (6). The follow-

Table I. Results of the comparison between the two groups.

	First attack			First visit		
	<2002	≥2002	*p*	<2007	≥2007	*p*
Age (years)	65.1 ± 12	61.7 ± 17.8	0.31	61.8 ± 12.1	64.6 ± 17.2	0.35
Sex	45M, 4F	31M,13F	0.02	52M, 7F	38M, 10F	0.31
Sex ratio	M:F 11.3	M:F 2.4		M:F 7.4	M:F 3.8	
Presence of familiarity (%)	6.4	22.7	0.05	12.1	17	0.66
Number of attacks	6 (1-90)	3 (1-30)	0.01	4 (1-90)	4 (1-48)	0.91
Tophi (%)	40.4	22.7	0.11	30.5	32.6	0.98
Chronic renal insufficiency (%)	19.1	24.4	0.71	18.6	19.1	0.85
Diuretics use(%)	34.8	35.6	0.89	35.6	34.8	0.9
Colchicine use (%)	65.2	59.5	0.74	61	57.1	0.85
Serum uric acid (mg/dL)	8.30	8.70	0.63	8.5	8.45	0.74
Number of involved joints	2 (1-12)	2 (1-6)	0.65	2 (1-12)	2 (1-6)	0.54
Monoarthritis (%)	48.9	45.5	0.9	45.8	50	0.82
Arthritis I MTP (%)	53.2	47.7	0.75	52.5	52.2	0.87
Wrist arthritis at onset (%)	8.5	0	0.14	6.8	0	0.2
Wrist arthritis during follow-up (%)	21.3	12.2	0.39	15.5	15.9	0.83
Number of ACR criteria fulfilled	6.3 ± 2	6.0 ± 2	0.5	5.8 ± 1.9	6.4 ± 1.9	0.11
Synovial fluid aspiration at onset (%)	6.4	13.3	0.45	5.1	12.8	0.29
Synovial fluid examination at onset (%)	0	6.7	0.22	1.7	4.3	0.85
Synovial fluid examination during follow-up (%)	23.9	17.1	0.6	7	34.9	0.001

ing data were collected, as previously reported (7): (a) demographic data including age, gender and family history of gout and psoriasis; (b) history of present or previous comorbidities, including diabetes mellitus, hypertension, renal or gallbladder stones, renal insufficiency, cardiovascular or cerebrovascular ischaemic events, hyperlipemia, and psoriasis; (c) medications, including urate lowering agents (allopurinol, sulphinpirazone), anti-inflammatory agents (colchicine, NSAIDs, corticosteroids), and diuretics; (d) clinical features of arthritis including time from the first attack, number of attacks, number and type of involved joints, presence of tophi; and (e) serum uric acid concentrations, ESR and C-reactive protein. The ethics committee of the University of Genova granted approval for the review of the patients' medical data.

Patients were divided according to the date of the first acute arthritis attack (median 2001) into two subgroups, patients with gout onset between 1967 and 2001, and patients with gout onset between 2002 and 2009. The patients were further subdivided into two groups (1989–2006 and 2007–2009) according to the date of their first admission to our Institution (median 2006).

Means were compared with the Student's *t*-test when data were normally distributed and with the Kruskall Wallis test when they were not parametrical. Categorical data were compared by the Fisher's exact test. The variables resulting significant in univariate analysis were entered in a multiple regression model. All statistical calculations were performed with MedCalc version 9.6.4.0 (Belgium).

Results

The 107 patients with gout had a mean age of 63.2±14.6 years; 90 of them (84.1%) were males. The year of the first attack could be established in 92 (86%) patients.

The results of the comparison between groups are shown in Table I. The male to female ratio changed from 11.3 in the patients with gout onset up to 2001 to 2.4 in those with later onset gout (p=0.02). No difference of male to female ratio was observed according to the date of the first admission. A family history of gout was slightly more frequent in the subgroup with recent disease onset (22.7% *vs*. 6.4%, p=0.05). The number of acute gouty attacks was higher in patients with gout onset up to 2001 [median 6 (1–90) *vs*. 3 (1–30); p=0.01].

Synovial fluid was examined during follow-up in 34.9% of the patients who were first admitted in 2007–2009, and in 7% of those admitted in 2002–2006 (p=0.001). The occurrence of synovial fluid aspiration and examination on first admission was not different among groups.

In multiple regression, after exclusion of number of acute attacks from the model because this significant difference was explained by the longer exposure time in the group with longer disease duration, both gender (p=0.023) and familial history (p=0.032) predicted the dependent variable of date of the first attack.

Discussion

Our results highlight a few changes that occurred in the clinical presentation of gout, and others that are related to a changing attitude toward the disease. The main finding of this study is that female gout has nearly doubled in patients with recent onset of gouty arthritis in comparison with patients with earlier onset. In the same period, the familial history of gout became more frequent.

On the contrary, the number of acute attacks was higher in the first cohort, which is not surprising in view of the longer time interval that elapsed since disease onset. Synovial fluid analysis increased significantly in patients who were first admitted in 2007–2009, probably as a result of a wider diffusion of the EULAR guidelines (8, 9) and of a renewed interest in the disease. When compared with a previous description of a large cohort of British patients with gout seen in the sixties (10), the following differences were observed. The percentages of women seen in both the first (13.5%) and second (23.6%) period of our study are higher than the 9.7% observed in the UK. This may be related to the fact that our observation is more recent and that incidence and awareness of female gout has increased over time (3). The classical localisation of arthritis in the 1st MTP joint was seen in 76% of UK patients and in 50% of Italian ones. A positive

family history of gout was observed in 36% of UK patients and 16% of Italian patients. Finally, tophi were seen in 21.2% of UK patients and in 32.7% of Italian ones. Taking into account the different periods of the two studies, it is likely that differences are due to changes in ascertainment of gout rather than true modifications of the occurrence of the disease and of its manifestations. As an example, gout was defined as the occurrence of arthritis and hyperuricaemia in the first study, whereas we applied the preliminary ACR criteria. In our study, there was no significant change in the localisation of gout over time, an observation that could be related to the overall low frequency of 1st MTP involvement in this study in comparison with other studies (10).

There are a few caveats that should be considered in our study. The periods of observation have been chosen on the basis of a statistical consideration, since the median years (2001 for disease onset, and 2007 for first admission) were used as cut-off. This approach has the advantage of comparing cohorts of similar size, but is not based on a specific cut-off as, for example, the date of publication of guidelines. Therefore the results obtained are relevant to these particular time intervals and could not reflect the behaviour of the disease in other settings. However, the change in male to female ratio is consistent with previous studies (4).

In conclusion, our data suggest that the only relevant feature of gout that has changed in the considered period of time is the patients' sex ratio. The increased utilisation of synovial fluid analysis suggests a closer attention to the disease in recent years. Clinicians should be aware that gout is increasingly affecting women.

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