Original Paper

Clinical Evolutive Aspects and Physical Rehabilitation in Patients with Chronic Gout

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ABSTRACT: Gout is a metabolic disease caused by a disturbance of the metabolism of purines. Urate hyperproduction, primary or secondary to other diseases, leads to hyperuricemia found in most of the gout patients. In the advanced diseases stages, the patients presents secondary arthrosis with the subchondral sclerosis and outbreaks of osteophytes. The extra-articular manifestations (renal, biliary) are quite frequent and sometimes invalidating.

KEYWORDS: *Gout, hyperuricemia, secondary arthrosis, renal disease.*

Introduction

The term gout represents a heterogenous group of diseases characterized by [1-5]:

-The increase of serum uric acid concentration (>7 mg/dL in men and > 6 mg/dl in females)

-Recurrent episodes of characteristic acute arthritis, with deposits of monosodium urate crystals on polymorphonuclear neuthrophils found in the synovial liquid. [1,2, 6-9]

-Aggregated deposits of monosodium urate (tophi), localized in the joints and around the distal joints, which will lead to severe deformities after a period of time. [10-12]

-Tubular, interstitial and vascular kidney injury [12-14]

-Urate renal lithiasis [10, 11]

-Vesicular lithiasis

-Hyperuricemia, which is the necessary condition of the gout onset, can be primary or secondary. The mechanisms of hyperuricemia are either the increased production of uric acid (10%) or the decreased renal excresion of the uric acid (in 90% of all cases) [1-4, 15, 16].

The possible causes are presented in table 1:

Table 1. The main causes of the hyperuricemia and gou t[1-12]

The increase production of uric acid	The decrease of uric acid excretion
PRIMARY GOUT Idiopathic (unknown molecular defects) the increase of de novo purine biosynthesis -hypoxanthine-guanine phosphoribosyl transferase deficiency complete= Lesch-Nyhan syndrome, partial= Kelly-Seegmiller syndrome -the increase of pyrophosphate 5 phosphoribosyl synthetase activity	**PRIMARY GOUT** the decrease of tubular secretion
SECONDARY GOUT the increase of de novo purine biosynthesis through the ATP degradation -glycogenoses(tipe I, III, V, VII) -tissue hypoxia (respiratory insufficiency) -alchool intake -metabolic myopathy the increase of the nucleic acids turnover -myeloproliferative and lymphoproliferative syndromes, multiple myeloma, secondary polyglobulia, pernicious anemia, certain hemoglobinopathies and thalassemia -infectious mononucleosis -certain carcinomas -psoriasis excessive purine intake	**SECONDARY GOUT** the increase of tubular reabsorption: conditions associated with the extracellular volume decrease: -dehydratation -diabetes insipidus -diuretics the decrease of renal functional tissue (CKI) the decrease of tubular secretion -conditions associated with the increase of β-hydroxybutyrate and acetoacetate levels (diabetic ketoacidosis and inanition) -conditions associated with hyperlactacidemia (acute ethanol ingestion) unknown mechanisms -Pb nephropathy, polycystic kidney -cyclosporine, aspirin, pirazinamide

The gout generally goes through four clinical stages: asymptomatic hyperuricemia, acute gout arthritis, the intercritical period and chronic tophaceous gout. Gouty nephropathy (through the deposit of monosodium urate crystal at the interstitial level) and the obstructive uropathy (through the formation of uric acid crystals within the collector tubes, thus blocking the kidney flow) appear during each stage with the exception of the first stage. [1-11]

Patients and method

In this paper we conducted a retrospective study on a group of 48 gout patients admitted in the Physiotherapy and Clinical Rehabilitation Clinic, Emergency County Hospital of Craiova, during the period 2011-2012. Patients were men aged between 35 and 72 (average 51.19 years, standard deviation 11.01 years).

We have recorded:

family history: diabetes, obesity, ischemic cardiopathy or gout

personal pathological history: kidney disorders, hematological disorders (myeloproliferative and lymphoproliferative syndromes, multiple myeloma, secondary polyglobulia and chronic hemolytic anemias), carcinomas, psoriasis, chronic tissue hypoxia (cardiac or respiratory failure), long term use of drugs (diuretics)

associated diseases: diabetes, renal lithiasis

alimentation habits, alcohol intake and the chronic Pb poisoning

Because most of the patients address the hospital either during acute flares of gouty arthritis either with chronic tophaceous gout, accompanied or not by the uric nephrolithiasis, the examination of the affected joints included the localization and the order of the joints impairment, the triggering factors, the evolution of the inflammatory process, the intercritical period and the localization of the tophi.

Laboratory data included: complete blood count, urea, creatinine and serum uric acid, blood glucose level and a lipid panel. The inflammatory level was explored through: ESR, fibrinogen, reactive protein C, electrophoresis. The impairment of the kidney function was evaluated through: urine test, Addis count, urine cultures, creatinine clearance and renal ultrasound.

The diagnosis was established mainly based on the clinical findings (inflammatory joint phenomenon found to an overweight or obese, dyslipidemic patient, sometimes with family aggregation on which laboratory tests were added for revealing the hyperuricemia and eventually the renal impairment). The examination of the synovial liquid was performed to only 12 patients from the studied group (25%) and it showed monosodium urate crystals. The affected joints radiography was used for the exclusion of other rheumatic diseases.

Results and discussions

All 48 patients were men. The average age was 51.18 years, with values between 35 and 72 years, the maximum prevalence being between 40 and 60 years. The patients were approximately uniform distributed between rural population (22 patients, 45.83%) and urban population (26 patients, 54.16%).

Among those 48 patients, 18 (37.5%) suffered from acute gout arthritis, 14 (29.16%) were during the intercritical period and 16 (33.33%) patients were diagnosed with chronic tophaceous gout. Overall, 22 (45.83%) presented renal impairment (gouty nephropathy) and renal calculi were revealed by ultrasonography in 16 (33.33%) patients.

A family history of obesity was observed in 8 patients (16.66%), while 12 patients (25%) presented a history of gout, which can indicate the possible presence of some metabolic anomalies characteristic to the primary gout (hypoxanthine-guanine phosphoribosyl transferase deficiency and the increase of pyrophosphate phosphoribosyl synthetase, X linked inherited) or the genetic predisposition (gout associated with the glucose-6-phosphatase deficiency found in the glycogenosis tipe 1, autosomal recessive inherited , or the gout and the nephropathy which are autosomal dominant transmitted as familial urate nephropathy).

A large number of patients were chronic alcohol consumers (36 patients, 75%), which represents one of the important factors determining hyperuricemia both by the increase of *de novo* purine biosynthesis due to the increase of ATP degradation and also by hyperlactacidemia (competitive tubular secretion between lactic acid and uric acid) [14, 16, 17] and eventually through Pb nephropathy due to a chronic not professional Pb intoxication. Twelve patients (25%) presented hepatic steatosis as a consequence of chronic alcohol consumption.

Two patients presented psoriasis, which can produce secondary hyperuricemia through the increase of the nucleic acids turnover, leading to

the appearance of secondary gout. In both patients, the beginning of the joint damage was more than 10 years back, to the level of right ankle and right hallux. It is hard to affirm if the hallux injury was due to the psoriatic rheumatism or to an acute gout flare. Anamnesis revealed the fact that 8 years back, the cutaneous lesions characteristic to the psoriasis appeared at the elbow level, the upper part of the thorax and calf. The actual episode consisted on the right knee and right ankle joint affectation.

We did not find other conditions which generates hyperuricemia, a fact which can be explained by the large time period which is necessary for the asymptomatic hyperuricemia to initiate the gout arthritis or nephrolithiasis (20-30 years).

Regarding the frequency, the affected joints were: hallux (36 patients, 75%), knee (28 patients, 58.33%), elbow (20 patients, 41.66%), ankle (16 patients, 33,33%), interphalangeal (14 patients, 29.16%), tarsotarsal (4 patients, 8.33%) and radiocarpal (4 patients, 8.33%) (figure 1).

The results of the laboratory explorations performed on the study group are presented in table 2.

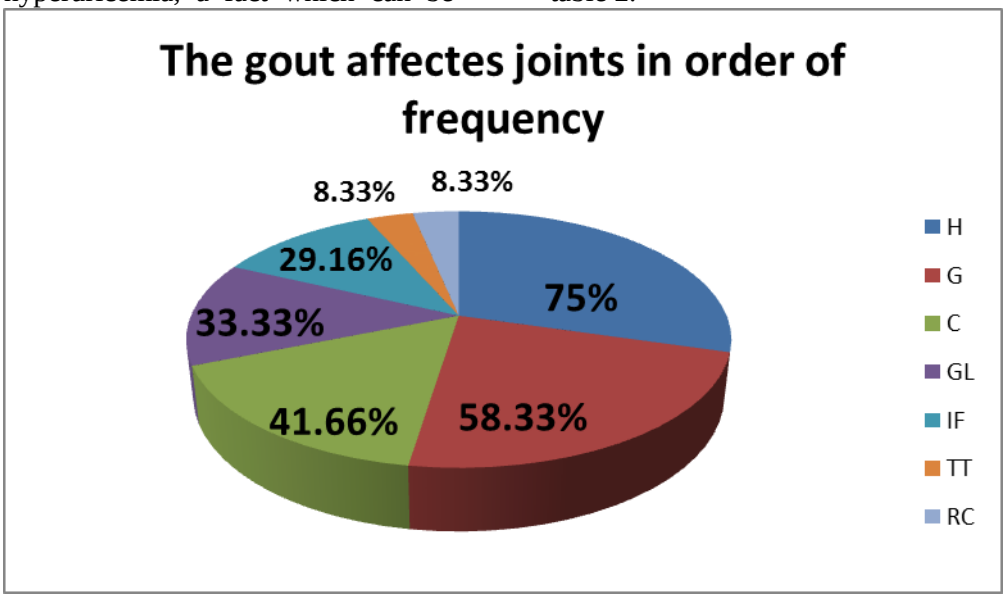

Fig.1. The affected joints in order of frequency

Table 2. Results of the laboratory explorations

TEST	AVERAGE	SD	MINIMUM	MAXIMUM
Weigth (kg)	78.81	10.27	60	98
Height (m)	1.72	0.07	1.6	1.85
Hb (g/dL)	12.45	1.31	10.05	14.89
WBC (/mm^3)	8187.5	2205.4	6000	15600
Platelets (/mm^3)	212500	42544	150000	300000
Urea (mg/dL)	63.75	78.82	20	300
Creatinine (mg/dL)	1.38	1.75	0.56	6.88
Uric acid (mg/dL)	5.55	2.88	2.74	12.6
Glucose (g/dL)	0.92	0.16	0.66	1.2
Cholesterol (mg/dL)	255.62	73.88	129	350
Triglycerides (mg/dL)	200	71.2	120	280
Fibrinogen (mg/dL)	434.68	145.34	220	690
ESR 1h (mm)	61.18	36.7	6	130
ESR 2h (mm)	89.62	41.38	13	148
Proteins (g/dL)	7.45	0.79	6.2	8.6
albumin (g/dL)	4.43	0.7	3.22	5.4
α_1 globulin (g/dL)	0.41	0.4	0.12	1.42
α_2 globulin (g/dL)	0.9	0.17	0.35	1.27
β globulin (g/dL)	0.57	0.1	0.48	0.86
γ globulin (g/dL)	1.3	0.2	0.65	1.6

We observed significant increased values over the normal values of urea (P<0.05), creatinine (P<0.01), uric acid (P<0.05), fibrinogen (P<0.05) and ESR at 1h and 2h (P<0.01). Only 32 patients (66.66%) had values of uric acid over the upper limit in men (> 7.0 mg/dL).

We found positive correlations between urea and creatinine (r=0.9), urea and uric acid (r= 0.7), creatinine and uric acid (r = 0.56), fibrinogen and ESR 1 (r = 0.51), fibrinogen and ESR2 (r = 0.63), ESR1 and ESR2 (r = 0.96), fibrinogen and α_2 globulin (r = 0.62), α_2 globulin and ESR1 (r = 0.71), α_2 globulin and ESR2 (r = 0.65). C-reactive protein was found in 24 patients (50%). Positive correlations were also found between weigth and uric acid (r = 0.55) and between height and uric acid (r = 0.64).

Cases distribution between the three clinical stages was approximately equal: 37.5% with gout arthritis, 29.16% found during the intercritical period and 33.33% with chronic tophaceous gout (figure 2). A large number of patients, almost half (45.83%) had gout nephropathy and in 16 patients (33.33%) renal lithiasis was observed using ultrasound.

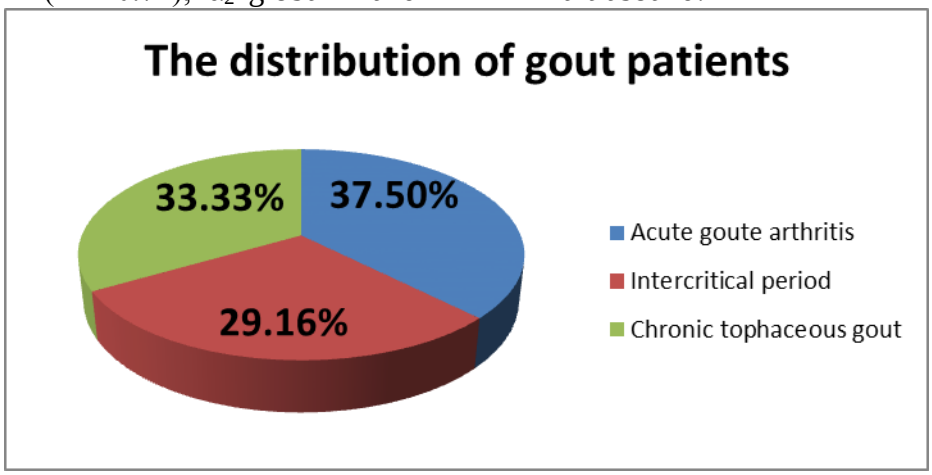

Fig.2. The distribution of gout patients

- The patients with acute gout arthritis (18 patients, 37.5%) had frequently a single joint affectation (14 patients, 77.77%), the majority at the level of the hallux metatarsophalangeal joint and the knee. We found systemic signs of the inflammation as leukocytosis (average 10235.43 ± 2654.4, with limits between 8500 and 15600 / mm^3), increases of the fibrinogen level (average534.23 ± 35.91, with the limits between 410 and 690 mg/dL), increases of the ESR at 1h (average 82.34 ± 23.56, with the limits between 75 and 130 mm), at 2h (average 112.64 ± 47.86, with the limits between 89 and 148 mm), C-reactive protein found to all 18 patients, increase of α_2 globulins (average 1.15 ± 0.26, with the limits between 0.7 and 1.27 g/dL). The values of uric acid were increased (average 8.5 ± 2.6, with the limits between 6.3 and 12.6 mg/dL) in 14 out of the 18 patients with acute gout arthritis.
- Between the acute gout arthritis attacks, we recorded complete remission of the symptoms (the intercritical period), during which the diagnosis of gout is difficult but can be clarified through the puncture of metatarsophalangeal or knee joint, which reveals extracellular uric acid crystals. Fourteen patients (29.16%) were found in this stage, with normal values of the inflammation systemic tests. A large number of patients found on this stage had normal values of the uric acid (8 patients).
- A number of 16 patients (33.33%) had chronic tophaceous gout, 14 patients had tophi, 10 of them periarticular and 4 at the ear pavilion level. The joint radiographs have indicated changes, cortical erosions in 10 patients and cartilaginous lesions in 8 patients.
- Almost half of the patients (45.83%) had kidney injuries (gout nephropathy). Urate nephropathy appears after the deposit

of sodium urate crystals in the kidney interstice which will lead to the appearance of giant cell type inflammatory reaction (the defining histological characteristic of the gouty kidney) [15-18]. The observed laboratory changes were the creatinine increase (average 3.25 ± 0.8, with the limits between 1.3 and 6.88 mg/dL), urea increase (average 75.2 ± 30.9, with the limits between 48 and 300 mg/dL). The urine test showed decreased values of the spontaneous urine density (average 1016.5± 4.74, with limits between 1007 and 1024 kg/m^3), acid pH in 18 cases, uric acid or amorphous urate in 10 cases, calcium oxalate in 4 cases, albuminuria in 8 cases. Arterial hypertension was found in 4 patients and the renal insufficiency in 8 patients. Renal calculi were found in 16 patients (33.33%) through ultrasound. The renal injury represented, in fact, the most important complication of the studied patients and which darken the prognosis of this patients together with the chronic renal insufficiency installation. [12-14]

The main objectives in all evolutive stages are control of pain and inflammation, preventing or limiting redor, prevent or limiting loss of articular mobility and maintaining or enhancing muscular force [19-25].

In the acute phase, control of the pain and inflammation can be achieved through antalgic electrotherapy (galvanic baths, diadynamic currents, Trabert, TENS or interferral currents); hydrotherapy (cold applications) or through anti-inflammatory or antalgic medication. Joints are kept immobile through a splint, gypsum bandages or simple rest in an antalgic position. Brushing or ice massaging can be used [25-28].

In the chronic-active phase, medical treatment may be applied as well as antalgic electrotherapy, as previously described. Ortheses are used to maintain physiological postures. Sedative and de-contracting massages may be used. Kinetotherapy for maintaining articular mobility involves either passive, passive-active or active exercises on maximum amplitudes [28-33].

Conlusions

1.The restrospective study performed on 24 patients showed a maximal prevalence of the gout in the age interval 40-60 year with dominant poliarticular damage.

2.Based on the family history, personal pathological history and working and living conditions, as well as based on the laboratory findings, can't be established the exact type of gout (primary or secondary) and the type of metabolic defect (the increase of uric acid production or the decrease of uric acid urinary excretion).

3.The affected joints were in order of frequency: hallux (36 patients, 75%), knee (28 patients, 58.33%), elbow (20 patients, 41.66%), ankle (16 patients, 33,33%), interphalangeal (14 patients, 29.16%), tarsotarsal (4 patients, 8.33%) and radiocarpal (4 patientis, 8.33%).

4.We found positive correlations between some of the physiological variables and the uric acid: weigth and uric acid (r = 0.55), height and uric acid (r = 0.64), urea and uric acid (r = 0.7), creatinine and uric acid (r = 0.56). Also correlations between systemic inflammation tests were found: fibrinogen and ESR 1 (r = 0.51), fibrinogen and ESR2 (r = 0.63), ESR1 and ESR2 (r = 0.96), fibrinogen and α_2 globulins (r = 0.62), α_2 globulins and ESR1 (r = 0.71), α_2 globulins and ESR2 (r = 0.65). C-reactive protein was found in 24 patients (50%).

5.The distribution of patients in the three clinical stages, was approximately equal: 37.5% with gout arthritis, 29.16% found during the intercritical period and 33.33% with chronic tophaceous gout. A large number of patients, almost half (45.83%) had gout nephropathy and in 16 patients (33.33%) renal lithiasis was observed using ultrasound.

6.The association of mixed dyslipidemia (with a high risk of atherogenesis) and gout nephropathy (with the evolution to chronic renal disease) represented the main causes which determined a reserved prognosis for this patients.

7.Antalgic electrotherapy, anti-inflammatory or antalgic drugs as well as immobilization represent viable methods for controlling the pain during acute phases of gout.

8.During the chronic-active phase, kinetotherapy is essential for maintaining the mobility of articulations, ortheses being used to maintain physiological postures. Medical treatment is also viable.

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