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Acute polyarticular gout

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SUMMARY We report here on 41 male patients with acute polyarticular gout seen in 3 years. Acute polyarticular gout continues to masquerade as other commoner rheumatological disorders such as septic arthritis, rheumatoid arthritis, degenerative joint disease, and even hemiparesis. Almost all of these patients had clues to the diagnosis of acute gout in their medical history. These clues included a past history of intermittent acute gout, prior attacks of polyarticular arthritis, previous hyperuricaemia, and/or obvious tophi. The patients all responded promptly to nonsteroidal anti-inflammatory drugs. We observed serious toxic drug reactions in 8 patients.

Forty-five years have elapsed since Hench comprehensively detailed the stages of gouty arthritis and admonished 'it is the suspicion of gout, unfortunately, not the disease which has disappeared'.[1] The clinical presentation of acute monoarticular gout and extensive, deforming chronic tophaceous gout are well described[1-3] and readily recognised. However, acute polyarticular gout may be confusing clinically because the features are less familiar.[4-7] Effective hypouricaemic therapy became available first with probenecid in 1950[8] and then with allopurinol in 1963.[9] Therefore acute polyarticular gout, indicative of more severe or uncontrolled gout,[6] should now be a medical curiosity rarely seen by a consulting rheumatologist. Nevertheless in a 3-year period we saw 41 cases of acute polyarticular gout at the Minneapolis VA Medical Center. Nearly half of these patients were not diagnosed initially as gouty arthritis. The purpose of this study is to characterise the masquerade of acute polyarticular gout in order to increase suspicion for this entity. During the treatment and follow-up of these patients we also encountered several important problems which are discussed.

Materials and methods

Between November 1976 and December 1979 41 patients with acute polyarticular gout were seen by the Rheumatology Consult Service at the Minneapolis VA Medical Center. The diagnosis of acute polyarticular gout was made if acute arthritis was present in 2 or more joints and if urate crystals were seen in synovial fluid by polarising microscopy[10] in one or more joints. These 41 cases represented 2·8% of all rheumatology consultations and 28% of patients with gout seen during that period. All patients were examined by one of the authors. We carefully reinterviewed all patients and obtained information from relatives or the primary physician or both to augment data recorded in the hospital chart. Serum uric acid determinations were performed in the Clinical Chemistry Laboratory with an AutoAnalyzer which employed the phosphotungstate method of Folin.[11] The normal mean ± SD for this laboratory was 0·15 to 0·47 mmol/l (2·5 to 8·0 mg/dl).

Results

PATIENTS

Forty-one male Caucasian patients were diagnosed as having acute polyarticular gout (Table 1). Their mean age was 59 years with a range of 25–85 years. As a whole this group had very complex medical histories and frequently had one or more serious medical illnesses (Table 2). A patient was identified

Table 1 *Acute polyarticular gout 1976—9*

Acute arthritis in 2 or more joints
Urate crystals in synovial fluid
41 caucasian males
Mean age 59 years, range 25 to 85

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Table 2 *Medical conditions in patients with acute polyarticular gout*

Medical condition	*No. of patients*	%
Hypertension	23	56
Obesity	19	46
Chronic alcoholism	13	32
Cardiac disease	10	24
Chronic renal disease	10	24
Malignancy	6	15
Diabetes	5	12
Hypothyroidism	2	5
No disease	2	5

Table 3 *Chronic renal disease in patients with acute polyarticular gout*

Renal disease	*No. of patients*
Diabetic nephropathy	1
Obstructive uropathy	2
Hypertensive nephropathy	3
Idiopathic glomerulonephritis	2
Proteinuria and azotaemia with heart failure	1
Gouty nephropathy	1
Total	10

Table 4 *Clinical characteristics of acute polyarticular gout*

	No. of patients	%
Simultaneous onset	23	56
Additive onset	18	44
First attack polyarticular	5	12
Fever >100°F (37·8°C)	18	44

as hypertensive if the blood pressure was greater than 160/90 mmHg or if they were diagnosed previously and taking antihypertensive drugs at the time of admission. Twenty-three patients had hypertension, 18 were on drug therapy, and 5 were untreated. Obesity was defined as greater than 10% above average weight as recorded in the Build Study 1979.[12] The obese patients weighed more than 180 lb (82 kg). Diuretic therapy was noted frequently (26 patients) and had been administered for hypertension in 18, peripheral oedema in one, and congestive heart failure in 7 patients. In all but one patient the duration of the diuretic therapy was longer than 2 weeks. Chronic renal disease (Table 3) included nephropathy associated with diabetes mellitus, obstructive uropathy (one fungus ball and one carcinoma of the prostate), hypertensive nephropathy, idiopathic glomerulonephritis, and proteinuria and mild azotaemia with congestive heart failure. In only one case was gouty nephropathy confirmed by the finding of microcrystalline tophaceous deposits on post-mortem sectioning of the kidney.

CLINICAL CHARACTERISTICS (Table 4)

The symptoms of joint pain and swelling were present for several hours to as long as 2 weeks before the diagnosis of acute gout was made. In 23 patients the onset of acute polyarthritis was simultaneous; that is 2 joints became acutely inflamed within 24 hours. The remaining 18 patients had an additive onset of acute polyarthritis. The initial acute inflammation in one joint was followed by additional involvement of more joints within 3–7 days.

Fever, defined as an oral temperature in excess of 100° F (37·8°C), was present in 18 of the patients. In 4 patients the body temperature was above 102°F (38·9°C). Constitutional symptoms such as malaise, lassitude, and anorexia were noted frequently.

PRECIPITATING OR ANTECEDENT EVENTS

Precipitating factors described previously were common in our patients with acute gout.[1–3] Severe medical illness was present in 9 patients (see Table 5). Five patients developed acute polyarticular gout 2–4 days postoperatively. Changes in medication within 2 weeks of the attack were noted in 11 patients. The medication changes included: institution of diuretics in one case, institution or cessation of hypouricaemic drugs in 4 cases, and cessation of anti-inflammatory drugs in 6 cases. Overall 25 of the patients had one or more of these antecedent events prior to the attack of polyarticular gout.

ARTICULAR INVOLVEMENT

The total number of joints involved was 159, with a mean of 3·9 joints per patient (Table 6). The majority of patients (71%) had acute inflammation in 3 or more joints. Joint inflammation was limited to the lower extremities in 56% of the patients, to the upper extremities in 7%, and involved both upper and lower extremities in 37%. The most common joint involved was the first metatarsal phalangeal joint,

Table 5 *Antecedent events in acute polyarticular gout*

Antecedent events	*No. of patients*
Severe medical illnesses	9
pneumonia	
peritonitis	
urinary tract infection	
gastrointestinal haemorrhage	
Postoperative (2–4 days)	5
Alcohol withdrawal	1
Severe dehydration	1
Trauma	1
Rapid weight loss	1
Medication changes	11

Table 6 *Articular involvement*

No. of joints	*No. of patients*	%
2 joints	12	29
3–5 joints	24	59
5 joints	5	12
Mean joints per patients = 3·9		
Joint distribution		
Lower extremity only	23	56
Upper and lower extremity	15	37
Upper extremity only	3	7
Asymmetrical in 34 (86%) patients		

Table 7 *Individual joints involved in acute polyarticular gout*

Upper extremity	*No. of joints*	*Lower extremity*	*No. of joints*
Shoulder	None	Hip	None
Acromioclavicular	2	Knee	23
Elbow	13	Ankle	31
Wrist	14	Mid-foot	10
MCP	5	MTP 2–5	10
PIP	10	IP	2
DIP	3	First MTP	36

Note: MCP = metacarpophalangeal; PIP = proximal interphalangeal; DIP = distal interphalangeal; MTP = metatarsophalangeal; IP = interphalangeal.

Table 8 *Laboratory abnormalities*

Serum uric acid: 0·50 mmol/l mean (8·4 mg/dl); range 0·24 to 0·88 mmol/l (4·2 to 15·6 mg/dl); 17/37 were normouricaemic
Peripheral leucocytes: 17 700/mm³ mean (4800 to 63 000); 16/35 with leucocytes >10 000/mm³
Synovial fluid leucocytes: 29 800/mm³ mean (700 to 105 000)

SI conversion: leucocytes/l = leucocytes/mm³ × 10^6.

followed by the ankle and knee (Table 7). Foot or ankle joint inflammation was present in 88% of the patients.

LABORATORY ABNORMALITIES

Serum uric acid measured in 37 patients at the time of the acute attack (Table 8) was 0·5 mmol/l mean (8·4 mg/dl), with a range of 0·24–0·88 mmol/l (4·1 to 15 mg/dl). Serum uric acid was elevated in 20 patients, with a mean of 0·61 mmol/l (10·3 mg/dl) and a range of 0·48 to 0·92 mmol/l (8·2 to 15·6 mg/dl). It is important to emphasise that 17 patients (46%) were normouricaemic at the time of the acute attack. Determinations of serum uric acid before or after the attack were available for all of these normouricaemic patients. Hyperuricaemia was noted at some time in 16 of these 17 patients. The peripheral white blood cell count was elevated more than 10 × 10^9/l in 16 out of 35 patients and ranged from 4·8 to 63 (mean 17·7) × 10^9/l. In 5 patients with leucocytosis, a concomitant infectious focus was identified (see associated medical conditions). Synovial fluid contained negatively birefringent crystals in all 41 cases. All but 2 of the synovial fluids appeared inflammatory or tophaceous. Sufficient fluid was available for leucocyte determination in 16 cases and ranged from 0·7 to 105 (mean 29·8) × 10^9/l. When septic arthritis was considered possible, synovial fluid was cultured and was negative. Other laboratory abnormalities were primarily related to the additional medical illnesses and included mild abnormalities in liver function tests in 5 patients and abnormal renal function in 7 patients, with the serum creatinine ranging from 2·0 to 3·8 mg/dl (177–336 μmol/l).

INITIAL DIAGNOSIS IN PATIENTS WITH ACUTE POLYARTICULAR GOUT

Rheumatological consultation was requested by the primary physician because of either diagnostic or therapeutic uncertainty. The diagnosis of gout was made by the primary physician in 22 patients. However, in 19 cases the initial diagnoses included septic arthritis, rheumatoid arthritis, degenerative joint disease, trauma, and acute hemiparesis.

CLUES TO DIAGNOSIS OF ACUTE POLYARTICULAR GOUT

We carefully reviewed available historical and physical data for clues to the diagnosis of gout in these patients (Table 9) and the importance of a 'good history' was reaffirmed. Most patients (85%) had a previous history of intermittent acute arthritis. The attacks were polyarticular in almost two-thirds. Prior hyperuricaemia was documented in 56% and tophi were present in 39%. One patient had nephrolithiasis due to a calcium oxalate stone. Overall, in 39 out of 41 patients, there was an undoubted or very suggestive history of gouty arthritis, hyperuricaemia, or tophi.

TREATMENT

Three patients were treated initially with oral colchicine and 37 received nonsteroidal anti-inflammatory agents. Drugs used included phenylbutazone 400–600 mg/24 hours in 2 patients,

Table 9 *Clues to the diagnosis of acute polyarticular gout*

Clue	*No. of patients*	%
History of 'gouty arthritis'	34	85
History of acute polyarthritis	27	66
History of hyperuricaemia	23	56
Tophi present	16	39
History of nephrolithiasis*	1	2

*Identified as a calcium oxalate stone.

indomethacin 100–200 mg/24 hours in 33 patients, ibuprofen—2400 mg/24 hours in 1 patient, and tolmetin sodium 1200 mg/24 hours in 1 patient. Intra-articular steroids were given to one patient who had 9 joints involved 2 days after a gastrectomy complicated by pneumonia and sepsis. Fever decreased in all patients within 4–6 hours of drug therapy. There was a striking decrease in joint pain, tenderness, swelling, and/or erythema in all patients within 48 hours and in most (85%) in less than 24 hours. The time required for complete clinical recovery or return to baseline status was variable and ranged from 1 to 7 days in 88% of the patients. Hypouricaemic therapy was begun in 28 out of 33 patients (see below) with either allopurinol (24 patients) or probenecid (4 patients) after the acute polyarticular attack subsided. The dose of nonsteroidal anti-inflammatory drugs was gradually tapered after the attack subsided but was often continued at a lower dose as prophylaxis against acute flares or for symptoms of chronic gout.

FOLLOW-UP

We obtained follow-up information on 33 patients after the acute polyarticular attack. Five patients died before follow-up and 3 did not return. The period of follow-up ranged from 1 to 43 months (mean 14 months). Acute gout recurred during the follow-up period in 20 out of 33 patients (61%). Recurrences were seen in 13 patients within 3 months and in 7 patients between 3 and 13 months. Acute gout recurred after changes in anti-inflammatory drug therapy in 12 patients or after institution of hypouricaemic therapy in 4 patients. In 4 patients the recurrence could not be explained by an associated drug change.

Nine instances of serious drug toxicity occurred in 8 patients being treated with nonsteroidal anti-inflammatory drugs (Table 10). Three patients had severe gastrointestinal haemorrhage which required admission to hospital and resulted in 2 deaths. Another patient died following perforation of a duodenal ulcer. Renal toxicity occurred in 3 patients with transient elevations of blood urea nitrogen (BUN) up to 88 mg/dl (14·6 mmol/l). An 82-year-old man with acute gout in the wrists, ankles, knees, elbows, and 3 interphalangeal joints was treated initially with 125 mg/day of indomethacin. Within 24 hours he became confused, disorientated, ataxic, and developed slurred speech with generalised weakness. The symptoms disappeared within 12 hours of stopping the drug. Ibuprofen was substituted at 3200 mg/day and the exact symptoms recurred within 24 hours. Thereafter his gout was controlled with colchicine 1·2 mg/day.

Table 10 *Toxic drug reactions*

Toxic effect	*No. of patients*
Gastrointestinal haemorrhage	3 (2*)
perforation	1*
Renal insufficiency	3 (transient)
Central nervous system	1 (2 episodes)

*Resulted in death.

Discussion

The clinical characteristics and course of these patients with acute polyarticular gout are similar to those in previous reports,[4 5] but the proportion of all cases of gout of the polyarticular cases (28%) is higher.[7] Associated medical conditions and precipitating factors have not changed appreciably in the past few decades.[13] However, many of these patients presented diagnostic difficulties for the primary physician because of confusion with other causes of acute polyarthritis. In nearly half the patients acute polyarticular gout masqueraded as another rheumatological disorder. An initial diagnosis of septic arthritis was made in 11 patients because of fever, leucocytosis, and a generally toxic appearance in the presence of multiple acutely inflamed joints. Five patients were thought to have rheumatoid arthritis because of the polyarticular distribution in both upper and lower extremities, isolated upper extremity joint involvement, or because tophi were mistaken for rheumatoid nodules. In two patients a diagnosis of degenerative joint disease was based on either involvement of weight bearing joints of the lower extremity or antecedent trauma. One patient had a strikingly asymmetrical multiple joint involvement which incapacitated him to such a degree that acute hemiparesis was diagnosed.

Ours and 2 previous studies of polyarticular gout were retrospective and conducted by rheumatologists.[4 5] This may have introduced a bias toward selection of patients with more severe disease or atypical features which could cause difficulties in early diagnosis. Many of our patients had concomitant serious medical illnesses which contributed to diagnostic uncertainty. However, it is important to emphasise that with careful scrutiny of the medical history we found clues to suggest the diagnosis of gout. Acute polyarticular gout was the initial attack of gout in only 12% of these patients, which is lower than the 27 to 44% previously reported.[2 4 5] There was a history of intermittent acute arthritis highly suggestive of gout in 85%, prior polyarticular attacks in 66%, and documented hyperuricaemia in 56%. Tophi were present in 39%. All 19 cases not initially recognised as gout had one or more of these clues in the medical history to suggest the diagnosis.

Fever, leucocytosis, and normouricaemia were present in nearly half of the patients. However, there was no correlation between these factors and the observed diagnostic confusion.

We noted 2 different modes of onset in this group of patients. The arthritis was more fulminant in the 'simultaneous onset' patients than in the 'additive onset' group, but there were no differences in degree of hyperuricaemia, fever, leucocytosis, incidence of tophi, or therapeutic outcome. The mode of onset did not appear to influence the recognition of acute polyarticular gout.

As has been previously noted, the distribution of joint involvement was asymmetrical in most cases.[1-6] In contrast to previous reports of proved polyarticular gout[4] the foot and ankle joints were spared in only 12% of our patients.

These patients responded promptly to anti-inflammatory therapy. Fever decreased within 4 to 6 hours in all patients. Initial improvement in joint symptoms was always prompt, but complete recovery of normal joint function was variable. Five patients took longer than one week to return to baseline and 4 of these had tophi. The quality of therapeutic response did not correlate with the duration of symptoms prior to diagnosis.

There have been no previous reports on extended follow-up of patients after an episode of acute polyarticular gout. Two-thirds of the patients had a prior history of recurrent attacks of acute arthritis and a large percentage had tophi requiring chronic hypouricaemic therapy. Recommendations for prescribing anti-inflammatory drug therapy with uric acid lowering agents vary[14-18]; therefore we were interested in characterising the subsequent clinical course. The majority of the patients received anti-inflammatory drugs for at least 3 months after beginning hypouricaemic agents. It is of interest that more than half of the patients (20 out of 33) had recurrences of acute gout during follow-up. Most of the recurrences were related to discontinuing anti-inflammatory drugs because of gastrointestinal side effects or to rapid tapering of the dose after the acute gouty attack subsided. Eight patients with recurrences had underlying tophi. This high recurrence rate is consistent with the concept that acute polyarticular gout reflects a more severe gouty diathesis[6] and may suggest a need for long-term anti-inflammatory drug therapy in these patients.

The serious drug toxicity we observed in these patients is cause for concern. These toxic effects led to fatal complications in 3 patients and prompted or prolonged hospitalisation in the remainder. Of the 4 patients with gastrointestinal ulceration only one had a remote history of ulcer disease, but all complained of nausea, vomiting, or abdominal pain within one week of the catastrophic event. Transient renal insufficiency has been noted with nonsteroidal anti-inflammatory drugs.[19-21] Elevated BUN and creatinine occurred in 3 of our patients taking indomethacin 150 to 200 mg/day. The drugs were stopped and renal function returned to baseline within 4 to 5 days. Central nervous system side effects are well known with indomethacin[22] but have occurred with ibuprofen as well.[23 24]

The appearance of acute polyarticular gout was described over 4 decades ago.[1] The clinical features are no longer unfamiliar.[4-6] The key to the diagnosis is a lower threshold of suspicion for gout in patients with acute polyarthritis.[25] This will lead to a more aggressive search for the historical clues which were present in almost all of our patients. The diagnosis can be readily confirmed by synovial fluid analysis.[10] Although these patients responded promptly to drug therapy, the risk of serious drug toxicity requires careful continued monitoring.[26]

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Notes