Mod Rheumatol (2004) 14:306–308
DOI 10.1007/s10165-004-0314-5

CASE REPORT

Aliye Kapukıran Tosun · Nadide Torlak Koca
Gülçin Kaymak Karataş

Acute gouty arthritis during pyrazinamide treatment: a case report

Received: January 5, 2004 / Accepted: April 23, 2004

Abstract Gout is a disease caused by an inflammatory response to an aggregation of monosodium urate crystals that develop secondary to hyperuricemia. Throughout its natural history it has four stages: asymptomatic hyperuricemia, acute gouty arthritis, intercritical gout, and chronic tophaceous gout. In this article, we report the case of a patient who had asymptomatic hyperuricemia secondary to pyrazinamide, which was prescribed for pulmonary tuberculosis, and had developed an acute gouty arthritis immediately after the "Feast of Sacrifice" due to a dietary excess of purine.

Key words Diet · Gout · Hyperuricemia · Pyrazinamide · Tuberculosis

Introduction

Gout is a metabolic disease with elevated serum uric acid concentration, recurrent attacks of acute arthritis, and deposition of monosodium urate crystals in and around the tissues. It is classified as primary, secondary, or idiopathic according to the underlying mechanism.[1,2] The most prominent feature of the disease is hyperuricemia, a term defining a serum uric acid level that exceeds 7 mg/dl. An increase in the formation of uric acid and/or a decrease in its excretion can result in hyperuricemia. Although it is a benign condition, asymptomatic hyperuricemia should not be overlooked as it may result not only in gouty arthritis, but also in nephrolithiasis. In this article, we describe a patient who had developed an acute attack of gouty arthritis due to a dietary excess of purine while being treated with antituberculosis drugs, following an asymptomatic hyperuricemic period.

A.K. Tosun (✉) · N.T. Koca · G.K. Karataş
Department of Physical Medicine and Rehabilitation, Gazi University Faculty of Medicine, Senyuva Mah, Meriç Sok, No. 19/C18 Bestepe, Ankara, Turkey
Tel. +90-505-438-329
e-mail: tosunaliye@yahoo.com

Case report

A 48-year-old man was admitted to the emergency room in our hospital with pain, swelling, and erythema of his right wrist and ankle. The articular complaints had begun in his wrist, and after a day his ankle was also involved. As well as a "sharp" articular pain, he also complained of stiffness. He had not had any similar symptoms before. A physical examination revealed signs of inflammation involving his right wrist and ankle. His past medical history showed that he had had a diagnosis of acute pulmonary tuberculosis 2 months previously, and had been treated with pyrazinamide, isoniazid, and rifampin. Twelve days before the start of his complaints, his serum uric acid concentration was found to have increased from 7.1 mg/dl (before initiation of the antituberculous treatment) to 12.4 mg/dl (range 3.5–7.5) during his follow-up in the Pulmonary Medicine Clinic, and allopurinol at 300 mg/day was started. The patient did not complain of fever, sore throat, diarrhea, constipation, dysuria, pollacuria, or oral or genital aphthous lesions. However, it was learned that he had eaten a lot of food containing meat and offal in the "Feast of Sacrifice" during the past week. In his initial laboratory evaluation, which was performed when he came to the emergency room, his hemoglobin was 14.6 g/dl (range 13.5–17.5), hematocrite 43.2% (range 40–53), white blood cell count 16 800/mm^3 (range 4500–11 000), and platelets 400 000/mm^3 (range 130 000–400 000). His erythrocyte sedimentation rate was 114 mm/h (range 0–20) and his C-reactive protein was 48 mg/l (range 0–6). All parameters in his biochemical analysis were normal except for serum uric acid concentration, which was 8.5 mg/dl. Tests for antistreptolysin-O antibodies, rheumatoid factor, brucella agglutination, antinuclear antibodies, and anti-dsDNA antibodies were nega-

tive. An acute attack of gouty arthritis was diagnosed, and the patient was admitted to our Physical Medicine and Rehabilitation Clinic for further examination and treatment, where diclophenac sodium at 150 mg/day and a diet low in purine were started. Pyrazinamide was discontinued after consultation with his physician in the Pulmonary Medicine Clinic. As well as the medical treatment, the application of cold for the inflammation and transcutaneous electrical nerve stimulation to the painful joints for analgesia were prescribed. Within 2 weeks, all his problems disappeared and a physical examination was normal except for a desquamation in the dorsum of his right foot. Except for an erythrocyte sedimentation rate of 71 mm/h, the results of his last laboratory evaluation were normal, including his serum uric acid concentration (4.4 mg/dl). After reducing the dose of allopurinol to 150 mg/day, the patient was discharged.

Discussion

The term "gout" is derived from the Latin "gutta", which means "a drop." In the 13th century, a poisonous drop that had fallen into the joint was said to be the reason for the disease. Gout was also called the "disease of the kings" and the "king of the diseases." The main pathology of the disease is hyperuricemia due to the increased formation and/or decreased excretion of serum uric acid. In illnesses such as lymphoproliferative and myeloproliferative diseases, multiple myeloma, thalassemia, and pernicious anemia, hyperuricemia may develop as a result of increased bone marrow activity.[1] In chronic renal failure, dehydration, hypertension, diabetic ketoacidosis, obesity, hyperparathyroidism, and hypothyroidism, the renal clearance of uric acid decreases, and this may result in hyperuricemia.[1] Some drugs, such as diuretics, ethanol, low-dose salicylates, pyrazinamide, and ethambutol, also decrease the renal clearance of uric acid and may be the reason for hyperuricemia. For that reason, in patients with hyperuricemia and/or acute gouty arthritis, their previous medical history is important in order to check for any related diseases, and to establish the nature of the drugs consumed.

In our patient, a diagnosis of acute gouty arthritis was made according to the American College of Rheumatology Criteria.[3] Taking into consideration the antituberculosis treatment he was on, pyrazinamide was thought to be the cause. Pyrazinamide deaminase, a microsomal enzyme, deaminates pyrazinamide into pyrasionic acid. Pyrasionic acid increases the concentration of serum uric acid via inhibition of its renal tubular excretion.[4–10] Our patient had been treated with pyrazinamide for 2 months when asymptomatic hyperuricemia was detected. Although treatment with allopurinol was started, he developed acute gouty arthritis after 2 weeks. Here, two factors can be considered as possible triggers. Because it has been reported that allopurinol and/or uricosuric drugs can trigger acute gouty arthritis, the first factor could be the alterations in the serum uric acid level as a result of the allopurinol.[10] Considering the timing of the arthritis, which was just after the "Feast of Sacrifice", the second factor could be the dietary excess of purine. During the "Feast of Sacrifice," foods containing meat and offal, such as liver and kidney, are cooked and eaten much more frequently than usual. The patient had stated that because he was given no recommendations about his diet, he had eaten too much meat during this period. Because of the history of a sudden increase in the purine content in his diet, we considered that the second factor might also be a trigger for the acute gouty arthritis, as well as the decrease in serum urate caused by the allopurinol.

The dietary restriction of purines is not the most important factor in controlling hyperuricemia, but it should not be ignored. As well as dietary habits, obesity and alcohol intake should also be controlled.[1,11] Some studies have reported that special dietary regimens had decreased serum uric acid concentrations, and had suggested them as the first step in any treatment.[12,13] Calorie limitation is also suggested, together with a low purine diet.[14] Although we share the opinion that dietary restriction is not the principal treatment, it might be important in some special conditions, as in this case.

In Turkey, the incidence of tuberculosis is higher than in Western populations, and drug combinations involving pyrazinamide are widely used. As a result, the incidence of asymptomatic hyperuricemia is often higher than normal in such patients. Any additional condition affecting the formation and/or excretion of serum uric acid might trigger an acute attack of gout. As a result, we believe that it is very important to warn patients who are taking drugs that might cause hyperuricemia about their eating habits.

References

1. Levinson DJ, Becker MA. Clinical gout and the pathogenesis of hyperuricemia. In: McCarty DJ, Koopman WJ, editors. Arthritis and allied conditions. 12th ed. Philadelphia: Lea and Febiger; 1993. p. 1773–805.
2. Wortmann RL, Kelley WN. Crystal-associated synovitis. In: Ruddy S, Harris ED, Sledge CB, editors. Kelley's textbook of rheumatology. 6th ed. Philadelphia: WB Saunders; 2001. p. 1339–71.
3. Wallace SL, Robinson H, Masi AT, Decker JL, McCarty DJ, Yu TF. Preliminary criteria for the classification of the acute arthritis of primary gout. Arthritis Rheum. 1977;20:895–900.
4. Cohen MG, Prowse MV. Drug-induced rheumatic syndromes: diagnosis, clinical features and management. Med Toxicol Adverse Drug Exp 1989;4:199–218.
5. Inoue T, Ikeda N, Kurasawa T, Sato A, Nakatani K, Ikeda T, et al. Hyperuricemia and arthralgia during pyrazinamide treatment. Nihon Kokyuki Gakkai Zasshi 1999;37:115–8.
6. Kayaalp O. Antitüberküloz ilaçlar. In: Kayaalp O, editor. Rasyonel Tedavi Yönünden Tıbbi Farmakoloji. Ankara: Feryal Matbaacılık; 1991. p. 851–64.
7. Hart FD. Drug-induced arthritis. Curr Med Res Opin 1974;2:505–9.
8. Rao TP, Schmitt JK. Gout secondary to pyrazinamide and ethambutol. Va Med Q 1996;123:271.
9. Higashino K, Moriwaki Y. Pharmacological agents affecting uric acid metabolism. Nippon Rinsho 1996;54:3364–8.
10. Scott JT. Drug-ınduced gout. Baillieres Clin Rheumatol 1991;5:39–60.

11. Loenen HM, Eshuis H, Lowik MR, Schouten EG, Hulshof KF, Odink J, et al. Serum uric acid correlates in elderly men and women with special reference to body composition and dietary intake (Dutch Nutrition Surveillance System). J Clin Epidemiol 1990;43:1297–303.
12. Kullich W, Ulreich A, Klein G. Changes in uric acid and blood lipids in patients with asymptomatic hyperuricemia treated with diet therapy in a rehabilitation procedure. Rehabilitation 1989;28: 134–7.
13. Peixoto MR, Monego ET, Jardim PC, Carvalho MM, Sousa AL, Oliveira JS, et al. Diet and medication in the treatment of hyperuricemia in hypertensive patients. Arg Bras Cardiol 2001;76:463–72.
14. Togashi R, Koike T. Non-drug therapeutics of idiopathic hyperuricemia. Nippon Rinsho 1996;54:3256–60.