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Case Report

Acute Gout Precipitated by Total Parenteral Nutrition

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ABSTRACT. Hypouricemia is seen in a variety of clinical situations. Although precipitation of gout is well known following initiation of uricosuric therapy, it has been reported rarely following the institution of total parenteral nutrition (TPN), despite its known uricosuric effect. We describe a patient who developed polyarticular gout on 2 occasions after a sudden decline in serum uric acid after initiation of purine-free TPN. Potential etiologies include increased urate clearance due to the infusion of glycine or amino acids. Monitoring of serum uric acid concentrations in patients with a history of gout may help predict a gout attack. Prophylactic treatment or alternative TPN formulations may be indicated. (J Rheumatol 2003;30:849–50)

Key Indexing Terms:
GOUT PARENTERAL NUTRITION URIC ACID HYPOURICEMIA

Multiple risk factors for the development of hyperuricemia and possible precipitation of acute gouty arthritis are well known[1]. Drugs can lead to a flare of gout by either increasing or decreasing serum urate concentrations acutely[2], and agents that affect urate concentration should not be started or stopped during an acute episode. Hypouricemia is seen commonly after several days of total parenteral nutrition (TPN)[3], although precipitation of gout has been reported rarely[1]. We describe a case of crystal-proven gout occurring several days after institution of TPN. The mechanism for this phenomenon and practical recommendations are discussed.

CASE REPORT

A 61-year-old white man with a history of polymyalgia rheumatica was admitted for a radical esophagogastrectomy for treatment of stage I adenocarcinoma. His history was notable for hypertension, atrial fibrillation, and cardiomyopathy. Medications on admission were quinapril, warfarin, atorvastatin, digoxin, and atenolol. Three days after undergoing successful surgery and starting TPN, he developed generalized stiffness and joint swelling. Examination revealed an uncomfortable appearing white man with a blood pressure of 142/63, pulse 88, and temperature 99°F. Musculoskeletal examination was notable for moderate joint swelling, with flexion contractures of both knees and effusions in both ankles and left wrist. No tophi or other joint deformities were noted. Ten milliliters of hazy yellow fluid were aspirated from his right knee. Culture results were negative; however, the fluid did show moderate white blood cells and numerous intracellular negatively birefringent crystals.

He was treated with intravenous methylprednisolone 40 mg q12h, with marked functional improvement and resolution of joint effusions over the next 24–48 h. Serum uric acid concentration was found to be 4.6 mg/dl at the time of his joint aspiration, decreased from 6.7 mg/dl upon admission. Before discharge, his corticosteroids were successfully tapered and he was prescribed oral colchicine 0.6 mg daily. Due to mild gastrointestinal upset he discontinued the colchicine prematurely after several days.

He was readmitted 2.5 months later due to vomiting, dehydration, and failure to gain weight, but reported no musculoskeletal complaints upon admission. TPN was again instituted, and 4 days later he developed a painful left shoulder and right elbow swelling. Joint aspiration was not repeated due to the anticoagulated state and the patient's wishes. He was again successfully treated with parenteral corticosteroids. Serum uric acid prior to admission was 7.7 mg/dl and decreased to 3.5 mg/dl on his fifth day of parenteral nutrition.

DISCUSSION

TPN associated hypouricemia has been reported by a variety of investigators[3]. Koretz[4] noted in a small retrospective study that the serum uric acid decreased by a mean of 3 mg/dl and postulated a lower rate of uric acid production as a likely mechanism. Al-Jurf, *et al*[3] documented a marked reduction in serum uric acid of 92% of 26 patients during the course of TPN, with the maximum reduction occurring during the first 3 days. Al-Jurf, *et al*[3] described a 3- to 4-fold increase in uric acid clearance. Morichau-Beauchant, *et al*[5] cited similar marked declines in serum uric acid due to increased urate clearance despite substituting fructose for glucose in some patients and switching to purine-free elemental enteral nutrition. In 1987, Derus, *et al*[6] described a case of crystal-proven podagra that developed after 3 days of TPN. Urate reabsorption was felt to be inhibited, either by the infusion of glycine or amino acids. In the references cited above, as in our case, serum uric acid normalized within several days of discontinuation of TPN.

A literature review disclosed a few potential mechanisms of TPN related hypouricemia. The most accepted include increases in urinary urate excretion[3,5,7], likely secondary to decreased tubular reabsorption or decreased production of uric acid due to initiation of a purine-free TPN solution. Protein infusions of 0.1 g/kg/h (2.4 g/kg/day)[3,4] have been noted to be potentially uricosuric, while solutions rich in

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dextrose may increase urate excretion due to an osmotic effect[6]. Other potential causes of uricosuria such as glycine-rich amino acid solutions (17–25 g/day)[3,6,7], high dose ascorbic acid (4 g/day), and elevated blood sugars[6] have been reported as a possible etiology, but not substantiated. Extracellular fluid expansion possibly due to stimulation of antidiuretic hormone has been postulated[5-7].

Evaluation of the TPN formula in this case found the patient was receiving an amino acid infusion of 0.75–1.5 g/kg/day and dextrose infusion rate up to 2.85 mg/kg/min. In each course of TPN, the patient was started at a lower rate and titrated to the maximum rates noted. The glycine content of each day's TPN solution was roughly 0.5 g/day, much lower than the amounts noted to be uricosuric. Unfortunately, we did not measure urinary uric acid clearance or fractional excretion of urate to assess for increased urinary clearance. Standard injectable multivitamins were used daily and contained only 100 mg ascorbic acid.

For patients with or at risk for gout, feeding with TPN becomes a difficult issue. There are no current guidelines for formulating TPN solutions in this population and very few data exist. There is no indication that using lower doses of amino acid or dextrose will prevent hypouricemia. Widhalm, *et al*[8] showed that a lipid emulsion based on soy oil (20%) had no effect on uric acid concentrations, and therefore it may be feasible to use lipid-rich TPN solutions in this population.

Routine daily monitoring of uric acid concentrations in addition to standard biochemical measurements in patients with gout may be helpful to alert clinicians to declining serum levels and potential exacerbations of gout in susceptible patients. It is feasible that this patient's serum uric acid diminished as a result of an acute episode of gout, although no other definite risk factors were temporally identified. The role of prophylactic or therapeutic corticosteroids, colchicine, or nonsteroidal antiinflammatory drugs and of their route of administration is less clear. The potential toxicities of preventive therapy need to be considered carefully.

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