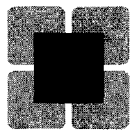

WILLIAM S. WILKE, MD, EDITOR

URIC ACID NEPHROPATHY: MANAGEMENT PEARLS

Normally, the renal clearance of urate approximates 10% of the glomerular filtration rate (GFR) such that the uric acid excretion is less than 600 mg per day. Certain drugs, most notably thiazides, enhance proximal tubule reabsorbtion of uric acid and can lead to its accumulation in the blood. Some endogenous substances also may alter excretion; for example, ketones and lactate inhibit uric acid excretion and can cause profound transient hyperuricemia. Angiotensin also may play a role.

URIC ACID CALCULI: A MEDICAL PROBLEM

Only 5% to 10% of renal calculi are caused by uric acid. Volume depletion, low urinary output, and low urine pH are predisposing factors. Uric acid solubility depends on urine pH, and is markedly reduced if the pH drops to 4 or 5.

Renal calculi caused by uric acid warrant medical therapy, not surgery or lithotripsy. The appropriate treatment is hydration and urinary alkalinization. Raising the urine pH to 7 will increase uric acid solubility tenfold; this, combined with increased hydration, should result in disappearance of the stones—in some cases after as little as 2 weeks. Although oral treatment is usually adequate, in some cases an alkaline solution is dripped directly onto the stone via nephroscopy. Allopurinol therapy is indicated for patients who have high blood or urine levels of uric acid.

ACUTE URIC ACID NEPHROPATHY: PREVENTION IS KEY

Patients who receive chemotherapy for hemopoietic or lymphopoietic malignancy are at risk of acute uric acid nephropathy. The breakdown of tumor cells creates an excessive purine load on the kidney, where the urine pH is already low. Pathologic examination reveals obstructing uric acid casts in the lumen of the interstitial tubule. Linear crystals of monosodium urate monohydrate, similar to gout crystals, may cause a giant-cell–like reaction in the interstitium.

Clinically, the patient has oliguria and urinalysis shows 1+ to 2+ proteinuria, granular casts, and, possibly, uric acid crystals. If the ratio of uric acid to creatinine is greater than 1, then urate nephropathy is a more likely diagnosis than acute renal failure. Acute renal failure lowers uric acid excretion so that serum levels as high as 9 to 12 mg/dL are not unusual. With urate nephropathy, the level may exceed 15.

Although the disease can be treated with forced diuresis and urinary alkalinization, prevention is more relevant and gained importance in the last 15 years with the growing use of chemotherapy. Hydration and moderate to high doses of allopurinol for several days before chemotherapy begins will help.

CHRONIC RENAL DISEASE AND GOUT

"Gouty nephropathy" has become a controversial diagnosis. The term refers to secondary renal disease in a patient who has primary gout. Certain forms of renal disease may set the stage for secondary gout because of abnormal uric acid metabolism.

The most extensive data concerning the relationship between gout, hyperuricemia, and renal disease are from studies by Yu and associates, who reviewed 1,700 cases of primary gout over a 20-year period. In the 253 patients who had varying degrees of renal involvement, the authors found a high prevalence of concomitant conditions that could contribute to renal damage, such as hypertension, cardiovascular disease, urinary tract infection, calculi, and independent intrinsic renal disease.

Yu and colleagues concluded that decreased renal function (proteinuria, azotemia, decreased GFR, and decreased renal plasma flow) generally does not occur in the setting of primary gout unless there is concurrent development of other renal disease. Exceptions to this generalization include younger patients with fulminant gout, patients with deficient hypoxanthine guanine-phosphoribosyltransferase, and aging patients who probably have baseline diminished kidney function. The patient with a long history of gout—more than 15 years—may have some mild deterioration of renal function; but mild to moderate hyperuricemia (uric acid less than 10) by itself has little effect on renal function.

It is generally agreed that gout secondary to chronic

renal disease also is rare. However, certain types of kidney disease are associated with a higher incidence of hyperuricemia and gout, including chronic lead nephropathy, polycystic disease, amyloidosis, analgesic nephropathy, and medullary cystic disease. Hypertension and its therapy are associated with an increased incidence of hyperuricemia and gout.

The management of concurrent marked hyperuricemia and chronic renal disease is directed to preservation of renal function, blood pressure control, and reduction of the serum uric acid. Uric acid homeostasis can be achieved by maintaining urine flow (>2 L/d), restricting dietary purines and excessive alcohol, and, if needed, allopurinol in the lowest dose that can maintain a near-normal serum uric acid. Therapy should start with 50 mg/d and increase in 50-mg increments until the level is under control. Generally, the dosage is 100 mg/d for every 30 cc/min of GFR.

JOSEPH V. NALLY JR, MD
Department of Hypertension and Nephrology

BIBLIOGRAPHY

Batuman V, Maesaka JK, Haddad B, Tepper E, Landy E, Wedeen RP. The role of lead in gout nephropathy. N Engl J Med 1981; **304**:520–523.

Beck LH. Clinical disorders of uric acid metabolism. Med Clin North Am 1981; **65**:401–411.

Emerson BT. Hyperuricemia, gout, and the kidney. [In] Schrier RW, Gottschalk CW. Diseases of the Kidney. Boston: Little, Brown, and Co., 1988, pp 2481–1520.

Yu TAF, Berger L. Renal disease in primary gout: a study of 253 gout patients with proteinuria. Semin Arth Rheum 1975; **4**:293–305.

DIFFERENTIAL DIAGNOSIS OF HYPERSENSITIVITY VASCULITIS

The presentation of palpable purpura that demonstrates small vessel vasculitis and leukocytoclasis on biopsy suggests a hypersensitivity vasculitis disorder. Most often this clinical picture is related to exposure to an antigen, but many patients with clinical and pathologic findings typical of hypersensitivity have no history of drug or toxin exposure. The causes of hypersensitivity vasculitis are diverse, but all of the disorders share the same pathologic mechanism of vascular inflammation mediated by immune complexes.

The diagnosis of true hypersensitivity vasculitis is limited to conditions that can be linked strongly to exposure to an exogenous antigen such as a drug, serum, toxin, or to an infection. Typically, the onset of vasculitis occurs 7 to 10 days after exposure to the antigen. The characteristic rash presents as palpable purpura, although ulcers, nodules, bullae, or urticaria also may develop in some patients.

On biopsy, the lesions display polymorphonuclear leukocytes and associated leukocytoclasis, but the infiltrates may be predominantly mononuclear. Immunofluorescent studies often show deposition of complement and immunoglobulins in vessel walls, and other techniques may show soluble immune complexes and evidence of complement activation; however, these laboratory findings are neither universal nor necessary for the diagnosis.

The clinical course is usually self-limited. Varying degrees of fever, malaise, and weight loss may occur and occasionally, there may be muscle, joint, renal, pulmonary, and central nervous system involvement. The disorder may become chronic or recurrent.

Treatment is directed to removal of the inciting antigen: discontinuation of the responsible drug or treatment of infection, for example. Mild cases may require no treatment, while advanced cases may require therapy with antihistamines, colchicine, corticosteroids, and, in some cases, cytotoxic drugs.

HENOCH-SCHÖNLEIN PURPURA

The lesions of Henoch-Schönlein purpura may be indistinguishable from those of true hypersensitivity vasculitis. To add to the difficulty in differentiating the two conditions, Henoch-Schönlein purpura is frequently reported following upper respiratory infection, and children often have received antibiotics implicated in hypersensitivity vasculitis.

Among the distinguishing features, Henoch-Schönlein purpura occurs most often in the spring, is often associated with gastrointestinal symptoms such as colicky abdominal pain and bleeding, and usually occurs in individuals younger than 18. Henoch-Schönlein purpura is distinguished immunopathologically by the presence of IgA-containing circulating immune complexes and by the deposition of IgA-containing immune complexes within the vasculitic tissues. IgA-associated glomerulonephritis develops in about half of patients and is usually mild and self-limited.

Patients with mild disease require no treatment, but those with life-threatening visceral disease may require high-dose corticosteroids and, possibly, cytotoxic drugs.