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

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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.

ESSENTIAL CRYOGLOBULINEMIA

Patients with essential cryoglobulinemia have the clinical and pathologic features of hypersensitivity vasculitis, and have high concentrations of cryoprecipitable proteins in their blood with no identifiable cause such as chronic infection or connective tissue disease. Many patients have secondary causes of cryoglobulinemia (ie, subacute bacterial endocarditis, hepatitis B, or connective tissue disease) and these must be sought. The term "essential" should be reserved for patients who have no identifiable cause.

The cutaneous manifestations of essential cryoglobulinemia do not differ from other hypersensitivity vasculitis disorders, but the course is usually chronic. Significant renal disease, which develops in half of patients, is a major cause of morbidity and mortality.

The prognosis for these patients is good, depending on the degree of visceral target organ involvement—particularly the kidneys. Patients with mild disease need little treatment other than nonsteroidal anti-inflammatory drugs, antihistamines, and low-dose corticosteroids. Although colchicine has been reported to be effective, our experience has shown it to be of limited value. Plasmapheresis may benefit patients with serious disease, but the procedure is costly and may be required indefinitely. Patients with significant renal disease may require combination therapy with high doses of corticosteroids and immunosuppressive drugs.

VASCULITIS ASSOCIATED WITH CONNECTIVE TISSUE DISEASE

Patients with rheumatoid arthritis, systemic lupus erythematosus, and Sjögren's syndrome occasionally have cutaneous vasculitis involvement such as palpable purpura, but large-vessel disease resembling systemic necrotizing vasculitis also may be associated. Connective tissue disorders are readily apparent causes for hypersensitivity vasculitis. Treatment is directed to the underlying disease.

HYPERSENSITIVITY VASCULITIS AND MALIGNANCY

Vasculitis is occasionally a manifestation of an underlying malignancy. Lympho- or myeloproliferative disorders are the conditions most frequently associated. In most cases, the vasculitis precedes the diagnosis of malignancy by many months.

The most common manifestations are palpable purpura, petechial lesions, maculopapular rashes, and ulcers. Vasculitis associated with malignancy generally responds poorly to treatment, but may remit with treatment of the underlying condition.

URTICARIAL VASCULITIS

Palpable purpura is the classic cutaneous manifestation of small-vessel vasculitis, but other cutaneous findings are possible. Urticarial or hypocomplementemic vasculitis presents with urticaria which, upon biopsy, reveals leukocytoclastic vasculitis. Complement levels may be normal in some cases and, in others, hypocomplementemia may be observed without urticaria.

Patients present with attacks of urticaria that last for 24 hours or more. Arthralgias and low-grade fever are common features. Angioneurotic edema of the face and bowel may be encountered. Renal disease is not common, although glomerulonephritis has been reported. Although the urticarial vasculitis may have many features of systemic lupus erythematosus, it does not meet American College of Rheumatology diagnostic criteria.

The presence of urticaria and immune complexes is not specific for urticarial vasculitis; the diagnosis depends on exclusion of a variety of other conditions and appropriate documentation by biopsy. Treatment involves antihistamines, colchicine, and corticosteroids.

HYPERSENSITIVITY VASCULITIS AND SYSTEMIC DISEASES

Most hypersensitivity vasculitis disorders are caused by exposure to drugs or toxins, infection, Henoch-Schönlein purpura, and connective tissue diseases. A variety of systemic diseases have been associated with the onset of small-vessel vasculitis and prominent skin involvement, and warrant consideration in the differential diagnosis. Among these are certain infections, including subacute bacterial endocarditis, hepatitis B, cytomegalovirus, HIV, and Epstein Barr virus.

LEONARD H. CALABRESE, DO
Department of Rheumatology and Immunology

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