NEPHROLOGY GRAND ROUNDS

Henoch-Schönlein Purpura in Adults

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INDEX WORDS: Henoch-Schönlein purpura; rapidly progressive glomerulonephritis; malignancy; vasculitis; immunoglobulin A (IgA).

CASE REPORT

A 65-YEAR-OLD MAN PRESENTED with a 1-week history of abdominal pain and was noted to have acute kidney failure, with a serum creatinine level of 3.9 mg/dL (343 μmol/L). The patient had experienced multiple hospitalizations in the prior 12 months and had demonstrated chronic kidney disease, with a serum creatinine level in the 2.2- to 2.4-mg/dL (194- to 211-μmol/L) range. A recent prior hospitalization had shown unilateral hydronephrosis with stones on the left, and a bladder catheter had been left in place due to urinary retention. The patient presented this time with a 1-week history of nausea and abdominal pain, and was found to have methicillin-resistant *Staphylococcal aureus* in his urine and a positive stool result for *Helicobacter pylori* antigen. He was treated with triple therapy for the *H pylori* (ampicillin, clarithromycin, and a proton pump inhibitor) and vancomycin for his urinary tract infection, with improvement of his abdominal pain. Due to active urinary sediment with the possibility of white blood cell casts, ampicillin and clarithromycin were stopped after 4 days of therapy, but vancomycin therapy was continued for the urinary tract infection. Although urine examination was subsequently negative for eosinophils, due to concern over possible interstitial nephritis, prednisone, 30 mg twice daily, was initiated.

There was no evidence of obstruction on repeat ultrasound, and repeat urinalysis showed 3^+ protein, 60 to 100 red blood cells/high-power field, and 60 to 100 white blood cells/high-power field, with a urine protein-creatinine ratio of 6.2. Platelet count was $132 \times 10^3/\mu L$ (132×10^9/L). Given the active sediment with the high proteinuria, serological workup was performed, and results included normal complement levels, negative anti–glomerular basement membrane antibody, negative antinuclear antibody, antineutrophil cytoplasmic antibody positive at 1:80, but negative myeloperoxidase and proteinase 3 antibodies, negative serologies for hepatitis B and C, and serum and urine protein electrophoreses negative for monoclonal proteins. Despite steroid therapy, the patient's acute kidney failure progressed and subsequently required emergent placement of a tunneled catheter and initiation of dialysis therapy.

The patient's abdominal pain and nausea recurred, and an increased alkaline phosphatase level prompted a computed tomographic scan of the abdomen without radiocontrast due to a history of Crohn disease and concern for sclerosing cholangitis. This showed no abnormalities, but an ultrasound of the liver showed dilated intrahepatic and extrahepatic ducts, with a 1-cm portal vein thrombosis. A questionable mass was seen in the liver on magnetic resonance imaging. Levels of tumor markers, including α-fetoprotein and carcinoembryonic antigen, were normal, but a CA19-9 level was grossly elevated at 12,439 U/mL (normal, $<$55 U/mL). After documentation of the portal vein thrombosis and discovery of an upper-arm deep-venous thrombosis, the patient underwent systemic anticoagulation for presumed Trousseau's syndrome. Fine-needle aspirate of the liver was inconclusive, but a liver biopsy performed prior to anticoagulation subsequently showed mucinous adenocarcinoma. Despite steroid therapy and discontinuation of antibiotic therapy, except for vancomycin, the patient developed purpuric lesions on his legs (Fig 1) and severe ankle arthralgias 2 weeks into his admission. He underwent skin biopsy, which showed leukocytoclastic vasculitis with immunofluorescence demonstrating immunoglobulin A (IgA) diffusely. A presumptive diagnosis of Henoch-Schönlein purpura (HSP) was made based on the clinical scenario of acute kidney failure and skin findings. Kidney biopsy was not performed because of the anticoagulation, the skin biopsy result, the likelihood that the biopsy would not change therapy, and the patient's grim prognosis due to his adenocarcinoma. Chemotherapy with gemcitabine subsequently was started, but the patient died 2 weeks after initiation of chemotherapy.

DISCUSSION

Historical Background

HSP is a leukocytoclastic vasculitis of small vessels with deposition of IgA, commonly resulting in skin, joint, gastrointestinal, and kidney involvement. The first description was attributed to Heberden in 1806, but Schönlein first described the association of arthralgias and purpura, termed "peliosis rheumatica," in 1837. His student, Henoch, described the gastrointestinal manifestations in 1874 and renal involvement in 1899.[1] Commonly called "anaphylactoid purpura" in the distant past, this term has fallen into disuse with the realization that this is not a classic allergic disease.

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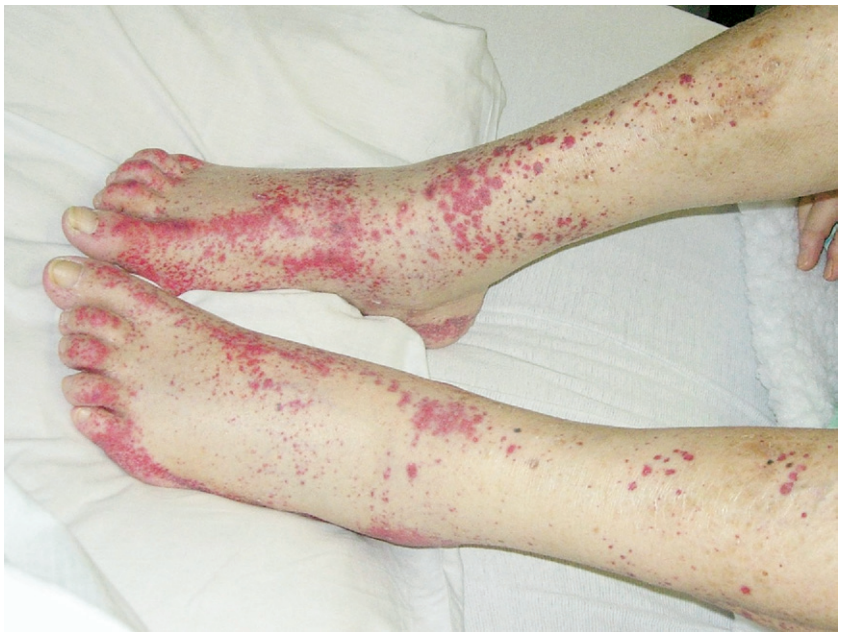

Fig 1. Coalescing purpura over the patient's lower extremities.

Clinical Presentation of HSP in Children

Prior to the last 30 years, this was considered a disease only of children, with an estimated incidence of 20 cases/100,000 children per year. The typical presentation in children includes abdominal pain and a vasculitic purpuric rash, primarily over the lower extremities, sometimes accompanied by hematuria and arthralgias or arthritis. The disease generally is self-limited, often resolving within a month, particularly if no renal involvement is demonstrated. It recurs in approximately one third of children. An upper respiratory infection is the primary precipitating event in children, although approximately two thirds of children with HSP have no precipitating event.[2] Because of the association with respiratory infections and a peak incidence in the fall and winter, a viral etiology has been implied in childhood HSP. Approximately 20% of children have renal manifestations of the disease, with nephritis more likely if the child is older or has gastrointestinal manifestations.[3]

HSP in children often is perceived as a benign disease given that only 2% of children demonstrate residual kidney failure. A recent study reported that in the subgroup of children requiring biopsy because of nephritis or nephrosis, 24% showed kidney dysfunction and 7% went on to dialysis within 5 years.[2] Children with initial kidney disease from HSP followed up for 24 years showed a much higher incidence of chronic kidney disease in adulthood than those without initial kidney disease (35% to 44% versus 7%).[4,5] In addition, long-term follow up of women with a history of childhood HSP demonstrated that 16 of 44 pregnancies were complicated by proteinuria and/or hypertension, even in the absence of active kidney disease.[5] Thus, subgroup analysis and long-term follow-up describe a childhood kidney disease that is not as benign as once thought.

Clinical Presentation of Adult HSP

This disorder is encountered even more rarely by nephrologists caring for adults and accounts for 0.6% to 2% of adult nephropathies. Although an uncommon nephropathy in adults, in a study of biopsy-proven primary cutaneous vasculitides in adults, HSP was the second most common etiology, comprising 32.5% of skin lesions, second only to hypersensitivity vasculitis.[6] Description of the natural history of adult HSP, prognostic studies, as well as any controlled therapeutic trials initially were limited by small numbers of patients. Early studies in the 1970s and 1980s suggested a high percentage with kidney involvement, but they often were small studies with short-term follow-up.[7-10] A small study in the late 1980s described 16 adult patients followed up for more than 7 years and found that 18.7%