

CJASN

Clinical Journal of the American Society of Nephrology

August 2013 • Vol. 8 • No. 8

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On the Cover

What's the diagnosis? A 60-year-old man with remote history of lower extremity DVT (on warfarin) presented with diffuse joint pains, and erythematous rash on his right hand and wrist that extended to his forearm. A purpuric rash subsequently developed on his left arm and bilateral thighs. He was initiated on intravenous antibiotics for cellulitis at a community hospital and transferred to Yale-New Haven Hospital. The purpura progressed to hemorrhagic bullae. Biopsy of the rash was consistent with leukocytoclastic vasculitis with negative IgA staining. Abdominal pain and bloody stools developed during hospitalization. The nephrology service was consulted after urinalysis showed 2+ protein and large blood on dipstick and serum creatinine increased from 0.9 mg/dL to 2.0 mg/dL. Nephrologist performed urine microscopy demonstrated 2-5 dysmorphic RBCs/HPF, 1-3 WBCs /HPF and 1-2 RBC casts/LPF (upper left panel). A kidney biopsy was performed revealing a proliferative glomerulus with necrosis on light microscopy (upper right panel). Immunofluorescence staining (lower left panel) revealed dominant IgA staining in the mesangium and capillary loops. Electron microscopy demonstrated electron dense deposits in the mesangium and subendothelium (lower right panel). The clinical presentation and kidney biopsy findings are consistent with Henoch-Schonlein Purpura (HSP) or IGA vasculitis. The patient was treated with intravenous methylprednisolone 1 gram daily for 3 days followed by oral prednisone 60 mg daily. Within a few days, he felt much improved with resolution of arthralgias and abdominal pain, while the rash started to fade over the next week. Kidney function stabilized and improved back to baseline over the next 2 weeks.

HSP, which is more commonly a disease of childhood, is characterized by the tetrad of palpable purpura, arthritis/arthralgias, abdominal pain, and kidney disease. Clinical manifestations, which result from the deposition of IgA-containing immune complexes, typically develop over a period of days, often starting with joint symptoms and purpuric skin rash. Skin biopsy reveals a leukocytoclastic vasculitis with IgA positive staining; however, IgA can be negative in 25%, especially in older lesions. Urinalysis often reveals proteinuria, hematuria, and leukocyturia, while urine microscopy demonstrates an active urine sediment with dysmorphic RBCs and RBC casts (upper left panel). Kidney biopsy reveals a spectrum of glomerular changes ranging from isolated mesangial proliferation, focal and segmental proliferation, to glomerular necrosis with severe crescentic glomerulonephritis. Immunofluorescence reveals prominent IgA staining in the mesangium (lower left panel). IgG, IgM, C3 and fibrinogen may also be present. Electron dense deposits are often found in the mesangial area, which can extend to the peripheral capillary loops (lower right panel). Supportive care is typically sufficient in most cases; however, glucocorticoids enhance the rate of resolution of arthralgias and rash. Intravenous methylprednisolone followed by oral prednisone (for 6 months) are used when glomerular necrosis and crescentic glomerulonephritis are present.

(Images and text provided by Gilbert Moeckel, MD and Mark A. Perazella, MD, Yale University School of Medicine, New Haven, Connecticut)