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What's the diagnosis?

Case description: A 63-year-old Caucasian man in the southeastern USA developed a flu-like illness with fever and myalgia. He developed unilateral tingling in his toes and tea-colored urine. No rash, hemoptysis or epistaxis were noted. He went to his primary care physician who performed a urinalysis that revealed 3+ hematuria and 2+ proteinuria. He was referred to a nephrologist. Physical examination identified fever, mid hypertension, loss of sensation in several toes, and slight motor weakness in one foot. Laboratory results included hematuria with RBC casts, urine P/C ratio 3.2, creatinine 4.1 mg/dl, positive P-ANCA/MPO-ANCA, normal C3 and C4, and no elevation in rheumatoid factor, C-ANCA/PR3-ANCA, ANA, or anti-GBM.

Description of Images: Renal biopsy demonstrated segmental cellular crescents in 35% of glomeruli, adjacent to segments with necrosis, sclerosis or both. The remaining glomeruli were unremarkable. Three different small interlobular arteries had arteritis with segmental fibrinoid necrosis and adjacent inflammation. The cover photographs demonstrate Masson trichrome stains of a glomerulus with segmental red fibrinoid necrosis and an adjacent small cellular crescent in one panel, and a small interlobular artery in the other panel with segmental transmural fibrinoid necrosis with adjacent interstitial inflammation with slight leukocytoclasia. Immunofluorescence microscopy demonstrated low level segmental granular mesangial staining for IgG (1+), IgA (1+), C3 (2+), and kappa and lambda light chains (1+). 20% of glomeruli had segmental staining for fibrin consistent with necrosis/crescents. There was no glomerular staining for IgM or C1q. One interlobular artery had segmental staining for fibrin indicative of fibrinoid necrosis. Electron microscopy of a glomerulus with segmental necrosis revealed segmental GBM breaks, a cellular crescent with fibrin tactoids, focal foot process effacement, and small scattered mesangial and rare subendothelial immune complex type electron dense deposits. The pathologic diagnosis was MPO-ANCA pauci-immune focal nerotizing and sclerosing glomerulonephritis with 35% crescents and necrotizing arteritis (Berden focal class), consistent with microscopic polyangiitis (MPA). Treatment was begun with methylprednisolone and cyclophosphamide.

Major Teaching Points: Prior to biopsy, the evidence for severe glomerulonephritis in an older adult predicted a likelihood of ANCA glomerulonephritis of >50%, because ANCA disease is the most common cause for new-onset glomerulonephritis in patients >50 years old in North America. The added evidence for peripheral neuropathy increased the likelihood to >75%, and the positive ANCA serology pushed the likelihood to >90%. The biopsy confirmed the diagnosis of ANCA glomerulonephritis, and the focal distribution of lesions (i.e. affecting <50% of glomeruli) provide confidence that high level immunosuppressive therapy was not only justified but very likely to result in complete remission of active disease with very low risk for progression to ESKD. The fact that the patient was MPO-ANCA positive rather than PR3-ANCA positive, was MPA rather than GPA, and had no evidence for respiratory tract disease, indicated a lower risk for relapse after induction of remission. In conclusion, with prompt diagnosis and appropriate treatment, this patient with a potentially life threating disease had an excellent prognosis for full recovery.

(*Images and text provided by J. Charles Jennette and Patrick Henry Nachman, University of North Carolina, Chapel Hill, North Carolina*)