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On the Cover

What is the diagnosis? A 54-year old man presented with shortness of breath, fatigue and rash on his arms and legs. The patient was an active cocaine user, and last used four days prior to presentation. The patient's rash was an angulated purpuric rash with erythematous rims that were tender to touch (left image). Serum creatinine was 2.1 mg/dL (baseline 0.9 mg/dL). Urinalysis demonstrated 3+ blood, trace leukocyte esterase, and 2+ protein with protein/creatinine ratio of 0.76. Urine sediment revealed dysmorphic red blood cells (middle image) and mixed cellular casts. Other labs include positive anti-MPO, positive IgM antiphospholipid antibodies, elevated rheumatoid factor, negative ANA, and normal complement levels. Kidney biopsy (right image) revealed fibrinoid necrosis of the glomerulus. Immunofluorescence and electron microscopy were negative, consistent with levamisole-induced vasculitis. The patient improved with supportive care and did not require renal replacement therapy.

Cocaine-induced vasculitis is caused by the adulterant, levamisole, which is found in 60-80% of cocaine sold in the United States. In the past, levamisole was employed as an adjuvant treatment for colon cancer and an immunomodulator for various conditions. However, the drug was removed from the market due to agranulocytosis. It is now used in veterinary practices as an anthelminthic agent. The most common clinical manifestations of levamisole-induced vasculitis are arthralgias and skin lesions. Other manifestations include fever, night sweats, myalgias, weight loss, or other constitutional symptoms. Urinalysis positive for protein, blood and cellular casts suggests kidney involvement. MPO-ANCA is positive in all patients and 50% may also have positive PR3-ANCA, which is a tip off to levamisole-associated vasculitis. While urine toxicology can confirm cocaine use within the preceding 2-3 days, testing for levamisole in serum or urine is of limited utility due to the drug's short half-life (approximately 5 hours). Treatment hinges on discontinuation of levamisole and supportive care. Data on treatment are limited but steroids have been used for skin lesions and severe nephropathy with variable results. It is imperative the avoid levamisole re-exposure as there is a greater than 25% risk of recurrence. (*Images and text provided by Bryan Tucker, DO and Mark A. Perazella, MD, Yale University School of Medicine, New Haven, Connecticut*)