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On the Cover
What is the diagnosis?
A 43-year-old woman, with diffuse cutaneous systemic sclerosis on oral steroids for past 6 months, presented with acute onset breathlessness and newly detected accelerated hypertension. On examination, there was skin tightening involving her neck, chest, and upper and lower limbs with hypopigmented lesions over her limbs and oral mucosa. Her BP was 170/100 mmHg with bilateral papilledema. Laboratory evaluation revealed microcytic hypochromic anemia (hemoglobin, 7.7 g/dl). Urinalysis showed 2+ proteinuria with occasional white blood cells, and her spot urine protein-creatinine ratio was 0.9. Serum creatinine was 9.7 mg/dl, sodium and potassium were 141 and 2.8 mmol/L, respectively, and lactate dehydrogenase was 489 IU/L. Her antinuclear antibodies, anti–U1 ribonucleoprotein autoantibodies, anti–Scl-70 (also called anti–topoisomerase I) antibodies, and anti-Ro52 antibodies were positive. Radiologic evaluation showed normal-sized kidneys with preserved corticomedullary differentiation, and the renal blood flow (as detected by renal Doppler study) was normal. She was initiated on hemodialysis, and a kidney biopsy was performed. The patient was treated with angiotensin-converting enzyme inhibitors (20 mg of enalapril per day, which was slowly tapered to 5 mg/day) and thrice weekly hemodialysis. A month later, she developed flash pulmonary edema and passed away.

Image Description:
Left: The biopsy specimen showed severe concentric, myxoid intimal proliferation, giving an “onion-skin” appearance, with almost total obliteration of the vascular lumen. Hematoxylin and eosin stain. Original magnification, ×200. Right: Shown is the prominent juxtaglomerular apparatus and ischemic wrinkling of the glomerular capillaries. Jones methenamine silver stain. Original magnification, ×400. These biopsy specimen findings are consistent with scleroderma renal crisis.

Teaching Points:
Scleroderma renal crisis occurs in about 5%–10% of patients with diffuse cutaneous systemic sclerosis. It has an abrupt onset with moderate to severe hypertension, AKI, and relatively bland urine sediment with minimal proteinuria. Risk factors include rapidly progressive diffuse cutaneous disease within 5 years of diagnosis, palpable tendon friction rubs, pericardial effusion, and thrombocytopenia. Anti–Scl-70 and anti–RNA polymerase 3 positivity increases the risk. High-dose corticosteroid treatment is also known to increase the risk of scleroderma renal crisis. The histologic picture of scleroderma renal crisis is that of a thrombotic microangiopathy process with myxoid intimal changes, thrombi, onion-skin lesions, and fibrointimal and adventitial sclerosis involving mainly the small vessels. Kidney biopsy helps in confirming the clinical diagnosis and also in excluding superimposed diseases that might lead to AKI. Nearly half of the patients progress to kidney failure. Renin-angiotensin-aldosterone system activation plays a critical role in the pathogenesis of scleroderma renal crisis, and use of angiotensin-converting enzyme inhibitors, along with kidney replacement therapy, helps reduce the mortality rate.

(Images and text provided by Anila Abraham Kurien, Department of Pathology, Renopath, Center for Renal and Urological Pathology, Chennai, India; and Badri Kannan and Gopalakrishnan Natarajan, Department of Nephrology, Madras Medical College, Chennai, India.)