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Patient Voice

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On the Cover

What is the diagnosis?

A 45-year-old male developed fever, weight loss, and persistent cough of 3 months' duration. His sputum was positive for *Mycobacterium tuberculosis*, and he was started on antitubercular treatment with four drugs: isoniazid, rifampicin, ethambutol, and pyrazinamide. His baseline kidney and liver function tests, before initiating antituberculosis therapy, were normal. Two weeks later, he presented with edema, breathlessness, oliguria with kidney failure requiring dialysis, and serum creatinine of 7.2 mg/dl. His laboratory tests were significant for hemoglobin with a level of 8.3 g/dl, bilirubin of 3.2 mg/dl with mild transaminitis, and serum lactate dehydrogenase of 750 U/L. Antitubercular treatment was withheld, and kidney biopsy was performed.

Image Description:

The biopsy demonstrated histological features of acute tubular injury including loss of brush borders, flattening (simplification) of the tubular epithelial cells, and cell drop-off, and dissolution of the cytoplasm and in many of the tubular epithelial cells. Brightly eosinophilic granular-to-globular pigmented tubular casts were seen in some of the tubules. These casts were different from red cell casts as there was no identifiable residual red cell morphology (red cell ghosts) within them. There was mild interstitial edema, but no inflammatory cells were observed in the interstitium. No interstitial fibrosis or tubular atrophy was seen. Glomeruli and blood vessels appeared normal with no evidence of microangiopathy. The casts did not show light chain restriction on immunofluorescence test. They were negative for myoglobin immunohistochemical stain but strongly positive for hemoglobin immunohistochemical stain, thus establishing the diagnosis of hemoglobin cast nephropathy.

Teaching Points:

Rifampicin is routinely used in multidrug treatment regimens for tuberculosis, nontuberculous mycobacterial infections, and leprosy. AKI is not a common complication of this drug. The most frequent biopsy findings in rifampicin-associated AKI are acute interstitial nephritis and acute tubular injury. Rifampicin-associated AKI develops as a result of type II or III hypersensitivity reaction. Anti-rifampicin antibodies are known to develop. These may cross-react with blood group I antigen on red blood cells leading to complement-mediated hemolysis. Heme pigment is toxic to the tubular epithelial cells. It can precipitate with Tamm–Horsfall protein to form pigmented tubular casts. Hemoglobin cast nephropathy should be suspected if a patient on rifampicin therapy develops AKI. The accurate diagnosis requires a kidney biopsy with immunostain for hemoglobin.

After five sessions of hemodialysis, urine output improved and reached nadir creatinine of 1.4 mg/dl after 6 weeks. Antitubercular treatment was restarted sequentially without rifampicin, and the patient tolerated it well.

(Text and images provided by Anila Abraham Kurien, Department of Pathology, Renopath Center for Renal and Urological Pathology, Chennai, India; Myvizhiselvi Murugan, Department of Nephrology, Madras Medical College, Chennai, India; and Gopalakrishnan Natarajan, Department of Nephrology, Madras Medical College, Chennai, India.)