Distribution of Iron Deposition in Renal Hemosiderosis: Evidence of Multicompartment Involvement

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Abstract

Renal hemosiderosis is an uncommon manifestation of iron overload arising secondary to chronic intravascular hemolysis, including conditions such as prosthetic heart valves, paroxysmal nocturnal hemoglobinuria, and sickle cell disease. In this setting, free hemoglobin binds haptoglobin until binding capacity is exceeded; excess hemoglobin is then filtered by the glomeruli and reabsorbed by proximal tubular epithelial cells. Within these cells, hemoglobin is degraded and iron is stored as hemosiderin in lysosomes. On light microscopy, this appears as coarse granular brown pigment in proximal tubules and is often associated with acute tubular injury, likely due to oxidative damage.

Although classically localized to proximal tubules, the full extent of renal iron deposition is not well defined. In this study, we evaluated iron distribution in renal biopsies using Prussian blue staining by light microscopy and electron microscopy, assessing involvement of glomeruli, tubules, interstitium, and vessels. The cohort consists of 5 patients, 4 with acute kidney injury (1 with thrombotic microangiopathy, 1 with IgA nephropathy and prior valve replacement, 1 with hemorrhagic shock secondary to a large retroperitoneal hematoma, and 1 without identified causes) and 1 with progressive renal decline with hemolytic anemia, and history of mitral valve repair.

Iron deposition ranged from 10–70% of tissue and was present in all cases within tubular epithelial cells. In cases with extensive staining (>60%), iron extended to the parietal epithelial cells of Bowman's capsule, distal tubules, and the loop of Henle. Acute kidney injury cases also showed interstitial involvement, while the chronic case demonstrated iron within podocytes, mesangial cells, and the glomerular basement membrane.

These findings indicate that renal hemosiderosis can extend beyond proximal tubules, particularly in severe or chronic disease, reflecting a more diffuse pattern of renal iron toxicity than previously appreciated.

References

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