

CJASN

Clinical Journal of the American Society of Nephrology

June 2012 • Vol. 7 • No. 6

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On the Cover

What's the diagnosis? Renal biopsy reveals multiple tubules filled with either free red blood cells (RBCs) or RBC casts and associated acute tubular injury. A little-known complication of warfarin is AKI from severe glomerular bleeding and obstructing red blood cell casts, which has been coined "warfarin nephropathy." However, in actuality, this form of AKI can occur with any type of excessive anticoagulation in at-risk patients. It has been described predominantly in patients with an underlying glomerulopathy who are excessively anticoagulated with warfarin, but has also occurred in patients with other forms of CKD. Glomerular hemorrhage with subsequent obstruction of tubules with RBC casts is thought to be the initial event. AKI appears to result from tubular obstruction and/or heme-related tubular injury from lysosomal overload and oxidative damage. Hemoglobin may enter cells via megalin-cubulin receptor-mediated endocytosis, with cell free hemoglobin promoting lipid peroxidation and heme/iron generating reactive oxygen species, mitochondrial damage, and apoptosis. Treatment consists of reversal of anticoagulation initially, followed by more closely monitored anticoagulation in those who truly require it. Unfortunately, many patients do not recover from AKI and are left with CKD, sometimes requiring chronic renal replacement therapy. (Image and text provided by Ursula Brewster, Gilbert Moeckel, and Mark A. Perazella. Yale University School of Medicine)