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On the Cover
What’s the diagnosis? A middle-aged previously healthy patient was referred to the nephrology service for evaluation of acute kidney injury (AKI) and proteinuria. Serum free light chain test revealed an elevated kappa/lambda ratio while urine immunoelectrophoresis revealed elevated monoclonal kappa light chains. The patient underwent kidney biopsy, which demonstrated both cast nephropathy and light chain deposition disease (LCDD). Bone marrow biopsy revealed 15% abnormal plasma cells, consistent with a diagnosis of multiple myeloma. In the upper left panel, fractured casts with associated mononuclear cell and giant cell reaction are noted in two tubular lumens. This is consistent with myeloma cast nephropathy—the “myeloma casts” are comprised of kappa light chains bound to Tamm Horsfall proteins (uromodulin). The patient also had findings compatible with LCDD. In the upper right panel, a glomerulus with nodular mesangial expansion is present. Deposition of monoclonal light chains within the mesangium and glomerular basement membranes result in this glomerulopathy. LCDD does not show positive Congo red stain, while Amyloidosis, which may also cause nodular mesangial expansion, is usually Congo red positive. In the lower left panel an immunofluorescence stain demonstrates linear staining for kappa light chains along glomerular and tubular basement membranes (lambda light chain stain is negative). In the lower right panel, electron microscopy reveals granular, powdery electron dense light chain deposits along the glomerular basement membrane. This pattern of light chain deposition was also noted along tubular basement membranes and in mesangial nodules. In contrast to this granular pattern seen with LCDD, amyloidosis would show haphazardly arranged fibrillary substructure in the deposits. (Images and text provided by Gilbert Moeckel and Mark A. Perazella, Yale University, New Haven, Connecticut)