Solutions to Test Your Knowledge: Myeloma and the Kidney

1. C: Myeloma cast nephropathy. In myeloma cast nephropathy, the monoclonal (in this case, κ light chain) protein-containing casts are glassy, refractile, and surrounded by inflammatory cells (histiocytes and giant cells). Acute tubular injury and some degree of interstitial nephritis are almost always present. In granulomatous interstitial nephritis, the giant cells are not within the tubules, but in the interstitium around granulomas. In myoglobinuric acute kidney injury, the casts frequently have a globular bright eosinophilic, sometimes pigmented, appearance without giant cell formation. Changes of diabetic nephropathy were not evident in this biopsy.

2. A: AL (light chain) amyloidosis. Extensive Congo Red–positive amyloid deposition was present in the glomeruli, in the vasculature, and focally in the interstitium. Congo Red positivity was confirmed under polarized light; true Congo Red–positive material shows apple green birefringence. In this biopsy, immunofluorescence showed strong staining for λ light chain in the amyloid material, and electron microscopy revealed deposition of randomly arranged 10 nm fibrils in the glomeruli as well as in extraglomerular structures (amyloid fibrils usually have a diameter of 8-10 nm). Fibrils in fibrillary glomerulonephritis are thicker and Congo Red negative. In κ light chain deposition disease, fibrils are not seen (see question #3). Also, review prior eAJKD quiz on organized deposits.

3. B: Monoclonal immunoglobulin (κ light chain) deposition disease. In monoclonal immunoglobulin deposition disease, the glomerular changes frequently resemble diabetic nephropathy with nodular transformation of the mesangium. This diabetic patient has glomerular nodular mesangial expansion, but immunofluorescence revealed strong κ light chain staining throughout the glomeruli as well as along the tubular basement membranes and vasculature. Ultrastructural findings showed the deposition of finely granular electron dense material along the subendothelial aspect of the glomerular basement membrane (bottom panel). Abundant finely granular electron-dense deposits were also noted in the mesangium and along the interstitial aspect of the tubular basement membranes. The glomerular basement membrane thickness was normal (in fact, segmentally thin), and arterial hyaline deposition (usually severe in diabetic nephropathy) was mild and focal; therefore, the nodular glomerular sclerosis was related to κ light chain deposition disease

rather than diabetic glomerulosclerosis. A Congo Red stain was negative, and fibrillary material was not seen by electron microscopy. In dense deposit disease, the electron dense deposits are homogeneous and within the expanded glomerular basement membrane (not along the subendothelial aspect of it).

4. Proximal tubulopathy secondary to intracytoplasmic monoclonal κ crystal formation. Light chain proximal tubulopathy with crystal formation is a rare but not a very unusual renal complication of myeloma. These crystals are formed by κ light chain. The condition may be missed because these cytoplasmic crystals may not stand out in routine light microscopy sections, and frequently do not stain with routine immunofluorescence methods. Ultrastructural examination of the tubules is diagnostic; the proximal tubular epithelial cells contain elongated angular, sometimes rhomboid, crystals with homogeneous structure or fine paracrystalline substructure. The κ light chain restriction in most cases can be proven by immunoelectron microscopy. Patients with light chain proximal tubulopathy frequently develop Fanconi syndrome. The crystals are easy to distinguish from abnormal mitochondria or other types of tubular epithelial inclusions.