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On the Cover

What Is the Diagnosis?
A 45-year-old woman presented with generalized body ache, fatigue, and significant weight loss. On evaluation, she had anemia (hemoglobin 6 g/dl), hypoalbuminemia (2.3 g/dl), elevated erythrocyte sedimentation rate (90 mm per first hour), and increased serum creatinine (2.9 mg/dl). Bone marrow aspiration/biopsy revealed 32% plasma cells (CD138+; kappa restriction). Biochemical evaluation showed normal serum protein electrophoresis pattern, IgG-kappa monoclonality in serum immunofixation, and elevated free kappa light chain (450 mg/dl) and β2 microglobulin (786 mg/l). Kidney biopsy was performed in view of renal insufficiency.

Image Description:
Kidney biopsy revealed widespread proximal tubulopathy changes in the form of varying sizes and shapes of fuchsinophilic crystals in the proximal tubular cytoplasm. Interstitial plasma cell infiltrates were CD138+ with monoclonal restriction (kappa positive and lambda negative). Glomerular and vascular compartment were unremarkable. Immunofluorescence studies were negative with panel (IgG, IgA, IgM, C3, C1q). Crystals were diffusely kappa light chain restricted and negative for lambda light chain per immunoperoxidase. Ultrastructure study of tubule confirmed crystalline material of variable shapes. Urinalysis for Fanconi syndrome screening did not show elevation of phosphates, potassium, or uric acid.

Teaching Points:
Light chain proximal tubulopathy (LCPT) and infiltration by myeloma cells is a rare phenomenon, occurring in less than 1% of plasma cell dyscrasia. Even though the early reported cases were associated with Fanconi syndrome, the absence of Fanconi syndrome does not exclude the possibility of LCPT (as illustrated by this case). LCPT can morphologically manifest with and without crystal deposition. Proximal tubulopathy with crystals is almost always associated with kappa light chains. These crystals are resistant to proteolysis and serve as a nidus for further accumulation within the lysosomes. Proximal tubulopathy without crystals is predominantly associated with lambda light chains. Our patient was treated with four cycles of a bortezomib/thalidomide/dexamethasone regimen, resulting in complete remission.

(Text and images provided by Mahesh Vankalakunti, Pathology & Laboratory Medicine, Manipal Hospital, Bengaluru, India; Raveendra Madraki, Nephrology, Yashoda Hospital, Vijayapura, India; and Janardhan Kamath, KS Hegde Hospital, Mangalore, India.)