Light chain tubulopathy without Fanconi syndrome

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A 59-year-old white male was found to have mild proteinuria and renal insufficiency during a life insurance test in 2003. His serum creatinine has been stable at 1.6 mg/dl since then. His 24 h urine protein was 720 mg in 2003 and 861 mg in 2006. Urinalysis showed 1+ protein with inactive sediment. His ANA, hepatitis B surface antigen, hepatitis C antibody and serum cryoglobulin were all negative. He had normal serum complement and anti-streptolysin O (ASLO) titer. In December 2005, he was found to have IgG-κ paraprotein on serum protein immunofixation and κ-Bence Jonce protein on urine protein immunofixation. He subsequently underwent a bone marrow biopsy which revealed 20% plasmacytosis with κ restriction and was diagnosed with ‘smoldering’ multiple myeloma. The patient underwent a renal biopsy to determine the cause of his renal insufficiency and mild proteinuria.

With normal glomeruli, many proximal tubules contained numerous intracytoplasmic needle-shaped crystals that stained hypereosinophilic on haematoxylin and eosin, periodic acid-Schiff stain-negative and trichrome-red. The proximal tubules displayed intact brush borders without degenerative changes or atrophy. On electron microscopy, the intracellular crystals appeared as rhomboid and rod-shaped electron dense inclusions. (Figure 1A). The crystals were present predominantly free within the cytoplasm (not membrane-bound). The crystals stained strongly for κ-light chain (with negativity for lambda, IgG, IgM and IgA) by immunofluorescence performed on pronase-digested paraffin sections (Figure 1B).

Despite the abundant light chain inclusions in proximal tubular cells, extensive laboratory investigations failed to reveal the cause of these unusual intracytoplasmic crystals.

Fig. 1. (A) The proximal tubular cells are engorged with abundant electron-dense intracytoplasmic crystalline inclusions. The tubular brush borders are intact (arrow) (original magnification 2500×). (B). On immunofluorescence performed on pronase-digested paraffin sections, the intracellular crystals stained strongly for κ-light chain with negativity for λ (data not shown) (original magnification 400×).
evaluation revealed no evidence of proximal tubular dysfunction (Fanconi syndrome) or type II renal tubular acidosis.

Light chain tubulopathy is the rarest histological pattern of renal disease associated with dysproteinemia, with <80 reported cases in the English literature. In contrast to the case presented herein, the vast majority of the reported cases were associated with full-blown or incomplete Fanconi syndrome clinically, and with significant tubular atrophy and interstitial fibrosis or tubular degenerative changes histologically [1]. When features of Fanconi syndrome are present clinically, the entity is called light chain Fanconi syndrome. Light chain Fanconi syndrome is almost always caused by κ-light chains of the Vk1 subgroup, which are resistant to lysosomal proteolysis [2]. Many patients have pre-myeloma or ‘smoldering’ myeloma at the time of diagnosis, but may subsequently develop full-blown myeloma.

Conflict of interest statement. None declared.

References


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