IgA Kappa-Associated Non-Crystallizing Light Chain Proximal Tubulopathy in the Monoclonal gammopathy of renal significance (MGRS) spectrum: A Rare Presentation with Diagnostic and Prognostic Implications

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Abstract

Background: Monoclonal gammopathy of renal significance (MGRS) is a rare renal disorder caused by monoclonal immunoglobulin light chains without meeting criteria for hematological malignancy. Although the underlying clone is often small and difficult to detect, it can cause significant acute kidney injury with poor outcomes. Most MGRS lesions involve glomeruli, while proximal tubulopathies appear to be less common; IgA kappa-associated non-crystallizing light chain proximal tubulopathy (LCPT) is extremely rare. MGRS is often underdiagnosed, renal biopsy is essential for diagnosis and guiding therapy. Early recognition and timely clone-directed therapy can preserve renal function.

Case presentation: A 77-year-old male with hypertension, obesity and CKD developed progressive renal dysfunction (serum creatinine 4.0 mg/dL, eGFR 14 mL/min/1.73 m²) with significant proteinuria (UACR >300 mg/g; UPCR 2.1 g/g). Workup revealed IgA kappa monoclonal protein (M spike 0.2 g/dL, FLC ratio 3.27) with a corresponding urine kappa band without evidence of clonal plasma cells on bone marrow or PET-CT. Renal biopsy showed interstitial fibrosis, tubular atrophy, basement membrane thickening, focal thyroidization, and hyaline tubular casts, along with multifocal mononuclear inflammatory infiltrates, tubulitis, and tubular injury. Immunofluorescence showed focal granular Kappa restricted staining in proximal tubular cell cytoplasm, and electron microscopy demonstrated tubular injury with prominent lysosomes, with some enlarged and atypical forms. The patient received Dara-VCD, achieving hematologic response with undetectable M spike, normalized FLC ratio, and stabilized renal function.

Conclusion: This case illustrates IgA kappa-associated, non-crystallizing, LCPT, an uncommon MGRS subtype. While MGRS is uncommon, it is a clinically important cause of progressive CKD. This case also exemplifies the diagnostic complexities typical of non-crystallizing proximal tubulopathy, as even small clones can cause severe tubular injury, making early recognition essential in patients with unexplained proteinuria or renal dysfunction. On the other hand, prompt intervention allows for tubular regeneration and renal function stabilization or recovery. Renal biopsy, integrating light microscopy, immunofluorescence, and electron microscopy, is crucial for diagnosis, and timely clone-directed therapy can improve outcomes and prevent irreversible renal failure.

Keywords: Light Chain Proximal Tubulopathy (LCPT); Non-crystallizing; IgA Kappa; Monoclonal Gammopathy of Renal Significance (MGRS); Renal Biopsy; Chronic Kidney Disease (CKD); Clone-Directed Therapy.