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Renal manifestation in monoclonal gammopathy of renal significance (MGRS)

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Plasma cell disorders (PCDs) are a spectrum of diseases that includes premalignant monoclonal gammopathy of undetermined significance, solitary plasmacytoma, amyloidosis, and both asymptomatic and symptomatic multiple myeloma. The kidney is often affected in the setting of a monoclonal gammopathy. The term 'monoclonal gammopathy of renal significance (MGRS)' was recently introduced to draw attention to renal diseases related to the monoclonal gammopathy.

Renal disease can be caused by deposition of the monoclonal immunoglobulin (MIg) (direct mechanism) or by activation of the alternative pathway of complement by the MIg (indirect mechanism). The deposition of MIg can affect the glomeruli, tubules, and the interstitium and vessels. The glomerular diseases include proliferative glomerulonephritis with MIg deposits, immunotactoid glomerulopathy, and, less commonly, fibrillary glomerulonephritis. Tubular lesions include cast nephropathy and light-chain proximal tubulopathy. Lesions involving the glomeruli, tubules, interstitium or vessels include amyloidosis and MIg deposition diseases (MIDD). Rarely, MIg may also cause C3 glomerulopathy or atypical hemolytic uremic syndrome by interfering with the regulation of the alternative pathway of complement.

The identification of MIg in serum or urine is critical to the diagnosis of PCDs. Protein electrophoresis (PEP) is inexpensive but has relatively poor sensitivity. Immunofixation is more sensitive than PEP but does not quantify the amount of MIg. The newer free light chain (FLC) immunoassay detects kappa and lambda at concentrations less than 2 to 4 mg/L, without confounding from intact Ig. The FLC assay does not directly detect clonality, but suggests it through an increase or decrease in the FLC.

Kidney biopsy should be considered early in the course of kidney disease. In cast nephropathy, the dominant finding is tubular casts in the distal nephron, often with accompanying interstitial nephritis. In MIDD, tubular and glomerular basement membranes are thickened by refractile precipitates that are granular and dense on electron microscopy. Glomerular nodules may be present and cause the nephrotic syndrome. In AL amyloidosis, the tubular basement membranes are typically of normal thickness but the Congo red stain is positive, with characteristic green birefringence under polarizing microscopy. Electron microscopy demonstrates organized deposits of nonbranching amyloid fibril.

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To summarize, the Mlg-associated renal diseases are distinct in their pathogenesis, kidney biopsy findings, clinical presentation, progression, and prognosis. A thorough and complete evaluation needs to be performed to appropriately manage these patients.