

Title: *Monoclonal Gammopathy of Renal Significance Presenting as Nephrotic Syndrome Secondary to AL Amyloid Nephropathy*

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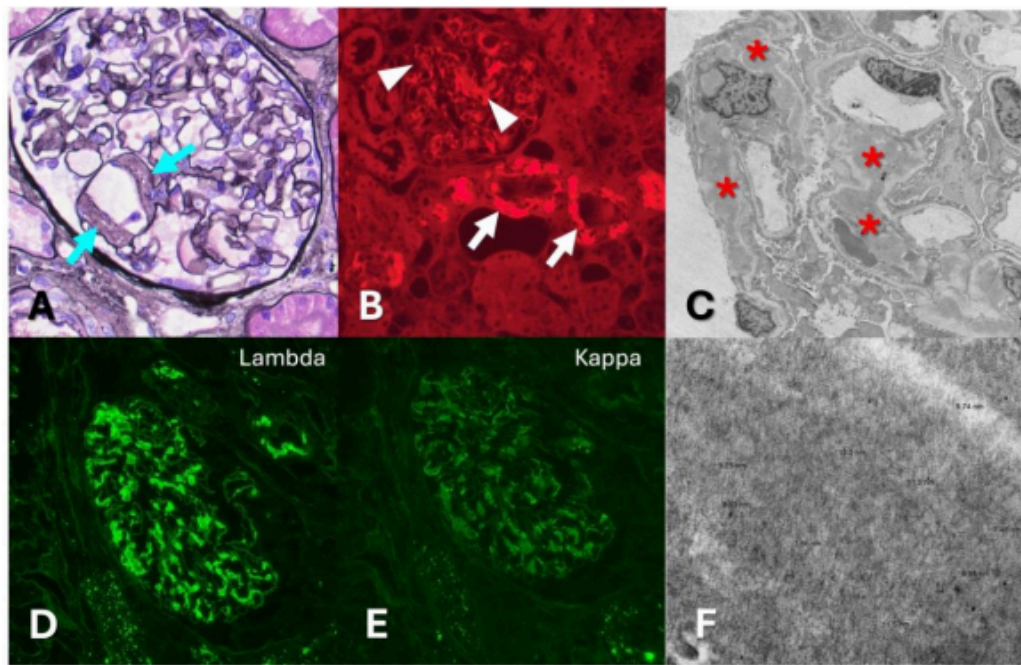
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Introduction: Amyloidosis is a systemic disease characterized by extracellular deposition of amyloid, formed from misfolded precursor proteins which self-assemble into pleated β -sheets, which further aggregate as amyloid fibrils. In North America and Western countries, the most common type is immunoglobulin light chain (AL) amyloidosis, associated with clonal plasma (and rarely B-) cell dyscrasia, resulting in the deposition of insoluble amyloid fibrils that impair the function of vital organs, including the heart and kidneys. Kidney involvement by AL amyloid, specifically with glomerular deposits, typically manifests as nephrotic syndrome.

Case Presentation: An 80-year-old Caucasian man with a history of Bence-Jones proteinuria and monoclonal gammopathy of undetermined significance, atrial fibrillation, CKD stage 3 and low-grade papillary urothelial carcinoma, was referred for persistent nephrotic-range proteinuria and worsening kidney function. A bone marrow biopsy showed no evidence of multiple myeloma or amyloidosis. Laboratory results showed a urine protein-to-creatinine ratio of 6200 mg/g albumin 3.3 g/dL and serum creatinine 1.73 mg/dL, with an eGFR of 57 mL/min/1.73 m². SPEP revealed an M-spike with increased lambda free light chain. Kidney biopsy showed extensive glomerular, arteriolar, and interstitial amyloidosis with lambda light chain-restricted staining, consistent with AL type; there were no other lesions of monoclonal gammopathy of renal significance (MGRS) (Figure 1). Echocardiography demonstrated preserved left ventricular function (ejection fraction 60%) without cardiac amyloid.

Discussion: MGRS encompasses a group of kidney disorders caused by nephrotoxic monoclonal immunoglobulins produced by small B- or plasma cell clones not meeting criteria for overt hematologic malignancy. In patients with monoclonal gammopathy, proteinuria, and declining kidney function, the differential diagnosis of MGRS includes AL amyloidosis, monoclonal immunoglobulin deposition disease (MIDD), proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID), and light-chain proximal tubulopathy. Kidney biopsy is critical in the diagnosis of AL amyloid nephropathy, facilitating timely clone-directed therapy to preserve kidney function and prevent systemic disease progression.

Figure 1. A. Glomerular amyloid deposits as silver negative aggregates in mesangial areas, Jones methenamine silver stain, magnification 600X. B. Glomerular (arrowheads) and arteriolar (arrows) amyloid deposits, stained with Congo Red and visualized by immunofluorescence using a Texas Red filter, magnification 200X. C. Amyloid deposits in glomerular mesangial areas and along glomerular basement membranes visualized by electron microscopy (asterisks), magnification 8000x. D. Immunofluorescence evaluation reveals lambda light chain restricted staining in the glomerular amyloid deposits, magnification 400X. E. Kappa light chain staining is negative in the glomerular deposits, magnification 400X. F. High magnification electron microscopy of the glomerular amyloid deposits reveals characteristic randomly oriented, non-branching fibrils measuring approximately 10 nm in diameter, magnification 40,000X.



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