CJASN®
Clinical Journal of the American Society of Nephrology

January 2022 • Vol. 17 • No 1

Patient Voice

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What is the Diagnosis?

A 71-year-old male presented for evaluation of heart failure; the patient had acute on chronic kidney injury (serum creatinine, 2.1 mg/dl) and nephrotic-range proteinuria. Serum immunofixation demonstrated monoclonal IgM lambda (451 mg/dl) and IgM kappa (195 mg/dl), kappa-to-lambda ratio: 0.43; β_2 microglobulin: 7.42 mg/L. Multiple bands with restricted mobility were evident on urine immunofixation.

Image Description:

Kidney biopsy demonstrated diffuse nodular mesangial expansion with Congo red positive birefringent amyloid deposits (top, inset; bar 40 μm) and fibrils on electron microscopy (bottom, inset; bar 40 nm). Immunofluorescence showed 3+ smudgy glomerular IgM (left), 1+ smudgy kappa (middle), and 3+ smudgy lambda (right) staining. IgM and lambda were stronger than kappa. Lambda alone showed interstitial staining (200x).

Teaching Points:

Immunofluorescence staining raised the possibility of AHL amyloid (heavy-and-light-chain amyloid). However, with multiple monoclonal proteins in the serum and urine and a mixed picture on immunofluorescence, mass spectrometry–based confirmation was sought. It revealed only light chain (AL-lambda) amyloid, and not the rare AH (immunoglobulin-heavy-chain amyloid) or AHL amyloid. The IgM heavy chain was not forming amyloid fibrils. Although this may not alter clinical management, prognostic differences have been shown with this rare AH/AHL entity, highlighting the importance for accurate recognition (1). An important clue was the absence of IgM and kappa in the interstitium. Subsequent bone marrow biopsy revealed lymphoplasmacytic lymphoma, the most commonly identified condition associated with IgM-associated AL amyloidosis, with *MYD88*^{L265P} and *CXCR4*$^{WHIM/FS}$ mutations. As therapeutic intervention, the addition of daratumumab to standard therapy—bortezomib, cyclophosphamide, and dexamethasone—was utilized based on the ANDROMEDA trial results (2).

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