Kappa light chain nephropathy[1]

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Kappa light chain nephropathy is described in a 45-year-old man who presented with weight loss, anorexia, and unexplained renal failure.

Index terms: Kidneys, diseases • Nephropathy, kappa light chain
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My colleagues and I recently reported the clinical, light microscopic, immunohistochemical, and electron microscopic findings in renal biopsy specimens from 11 patients with light chain nephropathy.[1] Eight patients had kappa and 3 had lambda light chain nephropathy. All but one were men in the fifth to seventh decade of life. Each patient presented with azotemia and features of glomerular rather than tubulointerstitial disease. Osteolytic bone lesions were found in 3 patients. Bone marrow plasmacytosis greater than 30% consistent with plasma cell myeloma was identified in only 4 patients. The light chain deposits were not associated with deposits of other serum proteins such as immunoglobulin heavy chains, complement, transferrin, alpha-2 macroglobulin, and albumin. The light microscopic appearance resembled membranoproliferative glomerulonephritis, amyloidosis, and diabetic nephropathy. Electron microscopy demonstrated distribution and character of the light chain deposits which differed from membranoproliferative glomerulonephritis, amyloidosis, cryoglobulinemia, macroglobulinemia, and benign monoclonal gammopathy.

Case report

A 45-year-old man presented with weight loss, anorexia, and unexplained renal failure that had developed in the previous 18 months. He had been hypertensive for two years. Blood glucose was not elevated, and there was no clinical evidence of diabetes mellitus. Blood pressure was 170/100 mm Hg supine, and 160/100 mm Hg standing. Physical examination was unremarkable. Medications were a thiazide diuretic and alpha-methyldopa. Urine output was normal. The patient did not have the nephrotic syndrome. Proteinuria was not detected by a semiquantitative examination. Two determinations of 24-hour urine protein excretion gave readings of 90 and 200 mg. Urine sediment contained white blood cells and occasional red blood cell casts, but was otherwise unremarkable. Serum creatinine was 6.4 mg/dl, blood urea nitrogen (BUN) was 88 mg/dl, hemoglobin was 8.7 g/dl, and the hematocrit was 25.8%. Platelets were normal at 217,000/mm^3. The white cell count was 7700/mm^3 with a normal differential count. Uncorrected endogenous creatinine clearance was 11.6 ml/min. Serum Ch50, C3, and C4 were normal. ANA and anti-DNA titers were negative. C1q assay for elevated circulating immunocomplexes was negative. A needle biopsy of the kidney was performed to determine the cause of renal failure. Subsequent bone marrow aspiration and biopsy demonstrated an increase in mature plasma cells, not diagnostic of multiple myeloma. Immunoelectrophoresis of the urine demonstrated free kappa light chains. Serum immunoelectrophoresis was not performed.

Pathology

The renal specimen was processed via light microscopy, immunohistochemistry, and electron microscopy as described previously.[1,2] Light microscopic sections demonstrated marked accentuation of the lobules of glomeruli (*Fig. 1*). Mesangial matrix was markedly increased. Nodular structures were present within segments of the glomeruli. Mesangial cellularity was also increased. There was no crescent or necrosis. The glomerular basement membranes did not appear thickened. Crystal violet stain for amyloid was

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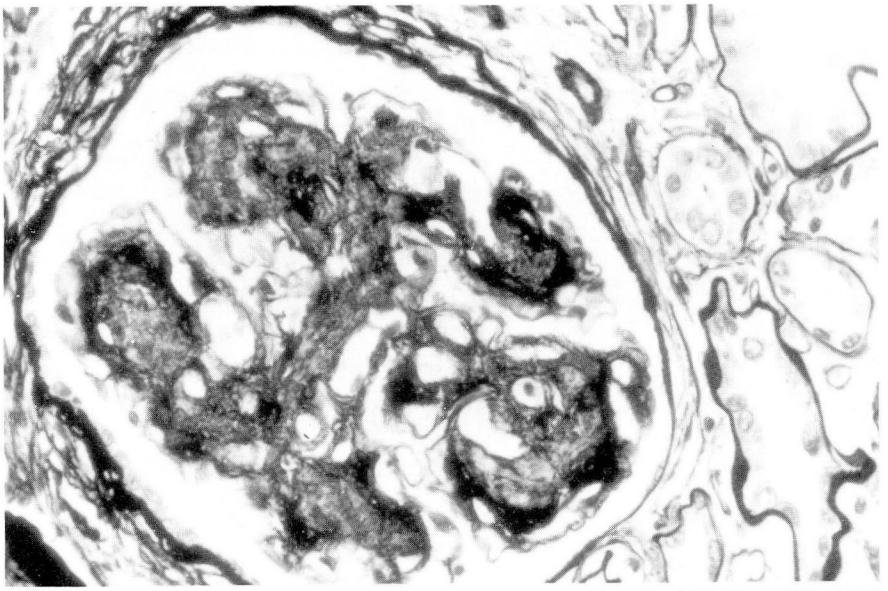

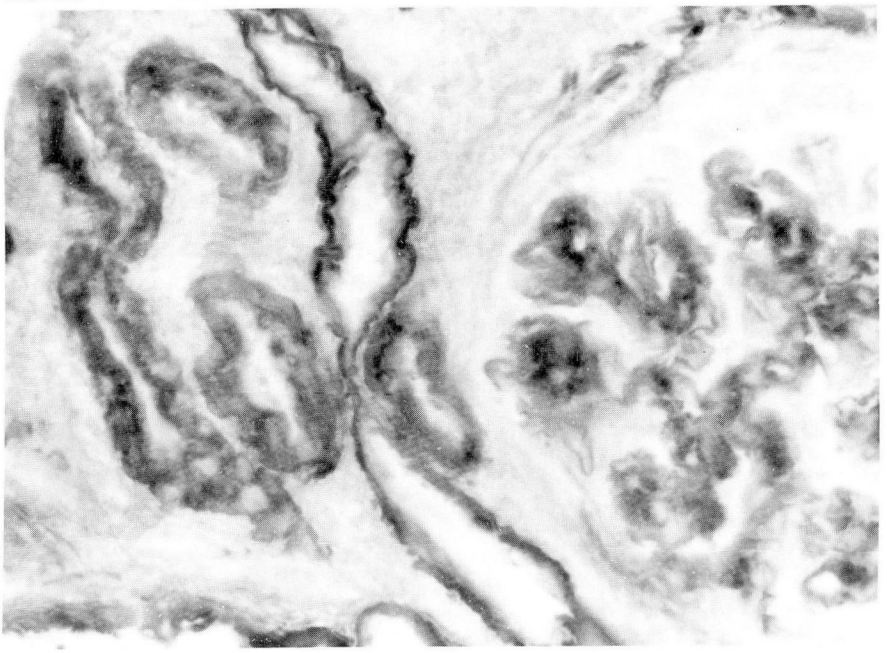

Figure 1. Kappa light chain nephropathy. Note marked lobular accentuation with increased mesangial volume. Capillary loops are patent (Jones' basement membrane stain, ×100).

Figure 2. Kappa light chain nephropathy. Kappa light chain deposits are visible in the tubular basement membranes and in lobules of the glomerulus (direct immunoperoxidase-kappa light chain, ×100).

negative. Interstitial fibrosis and tubular atrophy were noted, as well as a moderate degree of sclerosis of the arterioles and small arteries. Immunohistochemistry demonstrated prominent deposition of kappa light chain in the glomerular basement membrane, mesangium, and tubular basement membrane (*Fig. 2*). No deposit of lambda chain was detected. There was no glomerular, interstitial, or tubular basement membrane deposit of IgG, IgA, IgM, or C3. Granular deposits of C3 were detected in arterioles. Electron microscopy demonstrated finely granular

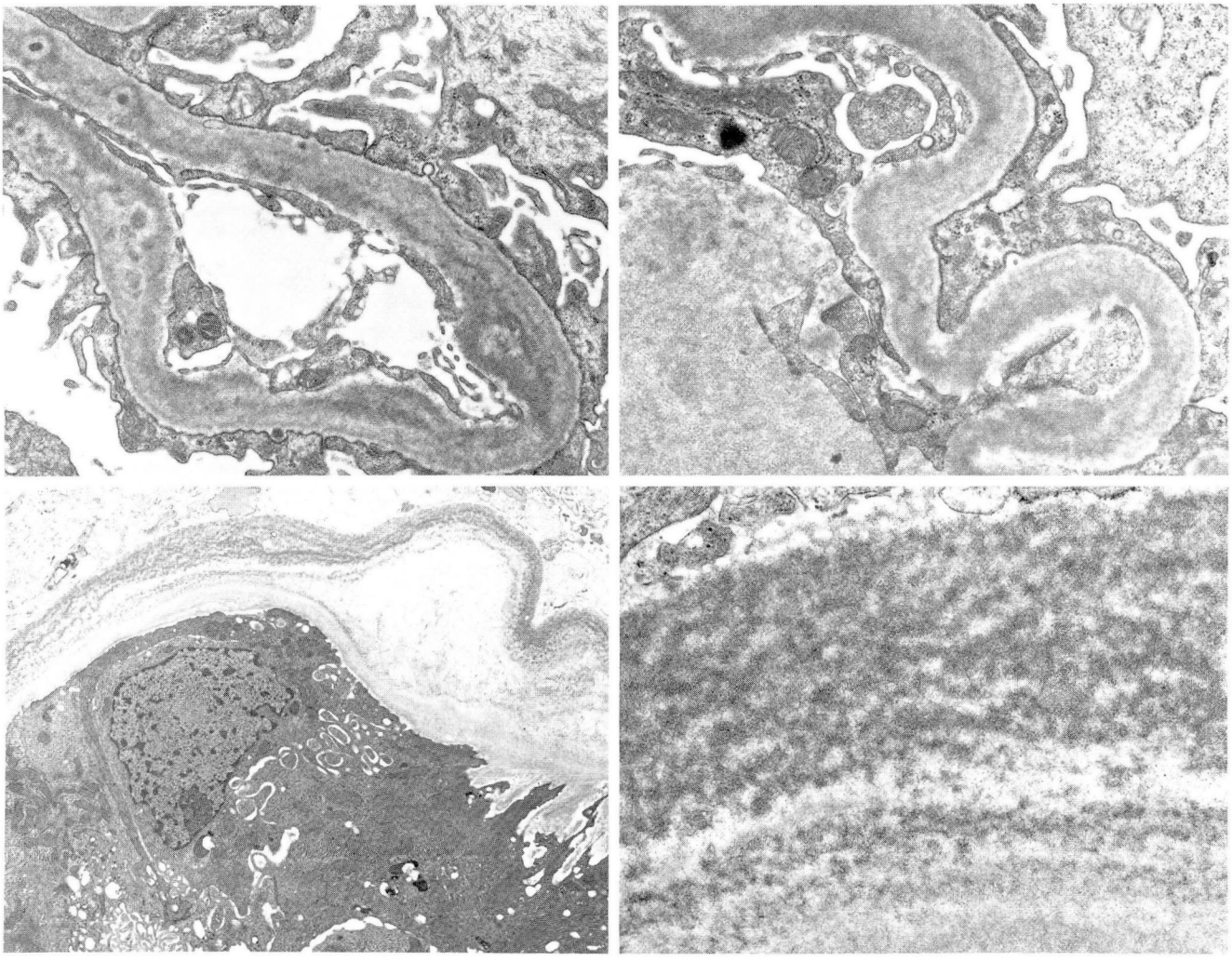

Figure 3. Kappa light chain nephropathy. **A.** Finely granular dense deposits are present in the glomerular basement membrane (×31,200).

B. Diffuse granular dense deposits of the glomerular basement membrane. Granular deposits are also present in the mesangium (lower left corner) (×4800).

C. Granular deposits are visible in the tubular basement membrane (×8640).

D. High-resolution view of granular dense deposits in the tubular basement membrane (×52,800).

deposits characteristic of kappa light chain disease in the glomerular basement membrane, tubular basement membrane, and mesangium (*Fig. 3*). Neither amyloid nor cryoglobulin deposits were detected.

Discussion

Renal biopsy demonstrated features typical of kappa light chain nephropathy, illustrating the importance of performing electron microscopy and immunohistochemistry on renal biopsies.[1,3] The patient's clinical presentation was similar to our recently reported cases, with the exception of absence of proteinuria.[1] The development of renal failure without proteinuria indicates that in some way, the abnormal deposits of light chains in the glomeruli and tubules led to progressive dysfunction without loss of protein. The pathogenetic mechanism of renal failure associated with renal deposition of light chains is unknown. The deposits in the glomerular basement membrane are probably related to the proteinuria observed in most patients.

Free kappa light chains may be present or absent from the urine and serum in kappa light

chain nephropathy.[1] It is difficult to explain the presence of free light chains in patients without myeloma or lymphoma, since the majority do not present with overt clinical features of myeloma or lymphoma; however, some patients eventually develop myeloma or lymphoma. Specific therapy for light chain nephropathy is not available, and some patients progress to renal failure and require chronic dialysis. There is no report of experience with renal transplantation in light chain nephropathy.

References

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