Light Chain Deposition Disease After Kidney Transplantation With Long Graft Survival: Case Report

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ABSTRACT

Light Chain Deposition Disease (LCDD) is a monoclonal immunoglobulin deposition disease that commonly affects kidneys among other organs. It leads to end-stage renal disease and has a high disease recurrence rate after kidney transplantation. This has led some authors to advise against transplantation in view of the poor long-term graft and patient outcomes. Recent literature has shown improvement/stabilization of native kidney disease following the use of bortezomib. We present 2 cases of LCDD after transplantation with graft dysfunction. They were both treated with different therapeutic agents to induce remission. Because sustained remission was not achieved they received bortezomib following which they have experienced a prolonged period of stable renal function with no clinically detectable disease. These unique cases highlight the possibility to achieve long-term stable graft function and disease remission after renal transplantation for LCDD.

LIGHT CHAIN DEPOSITION DISEASE (LCDD) is characterized by the deposition of monoclonal light chains in organs that include the kidney, heart, liver, or peripheral nerves. The kidney is most commonly affected, leading to irreversible damage. The median survival of patients with LCDD and end-stage renal disease (ESRD) on dialysis is 4 years [1]. Renal transplantation for LCDD carries a high risk of disease recurrence and allograft failure due to which it was considered as an option for few selected patients [2]. Recently, the use of bortezomib has been reported to lead to rapid hematologic response and preservation/improvement of renal function in patients with native kidney LCDD [3,4]. We would like to report 2 cases of LCDD that recurred after kidney transplantation where treatment included bortezomib and the patients had functioning grafts more than 10 years after their transplantation. With the newer proteasome inhibitors it may be time to readdress the recommendations regarding renal transplantation for LCDD.

CASE REPORTS

Case 1

A 30-year-old man was diagnosed with chronic kidney disease (CKD) from kappa (κ) LCDD after a kidney biopsy in September 1999 (Fig 1, parts 1–3). At that time his serum immunofixation electrophoresis (SIFE) showed no monoclonal immunoglobulins and urine immunofixation electrophoresis (UIFE) showed several diffuse κ bands consistent with degradation of aggregations of polyclonal κ chains. No monoclonal immunoglobulins were detected in the urine. His serum kappa light chains (κ) measured 449 mg/L, lambda light chains (λ) 176 mg/L with a κ/λ light chain ratio (LCR) of 2.55 (normal, 0.26–1.65). A bone marrow (BM) biopsy showed 5% plasma cells. Immunocytochemistry on the BM sample showed strong staining for κ light chains with only rare lambda staining cells. He was treated with Vincristine, doxorubicin, and Dexamethasone following which his BM plasma cells decreased to 1%. Despite the decrease in κ positive plasma cells, renal function did not improve. He initiated hemodialysis in May 2000 and 3 months later received a living donor kidney transplant from his sister. At the time of his transplantation he had no detectable κ light chains in his urine. After transplantation he attained a serum creatinine (SCr) level of 1.5 mg/dL. He was maintained on tacrolimus, mycophenolate mofetil, and prednisone. In 2007 he had an increase in his creatinine to 2.0 mg/dL and a kidney biopsy showed recurrence of κ LCDD (Fig 1, part 4). The κ/λ LCR was 13.14 (κ 345.7 mg/L; λ 26.3 mg/L) and he started treatment with lenalidomide and dexamethasone. A week later he developed interstitial pneumonitis that led to discontinuation of lenalidomide. He was maintained on dexamethasone and his κ/λ LCR decreased to 1.25

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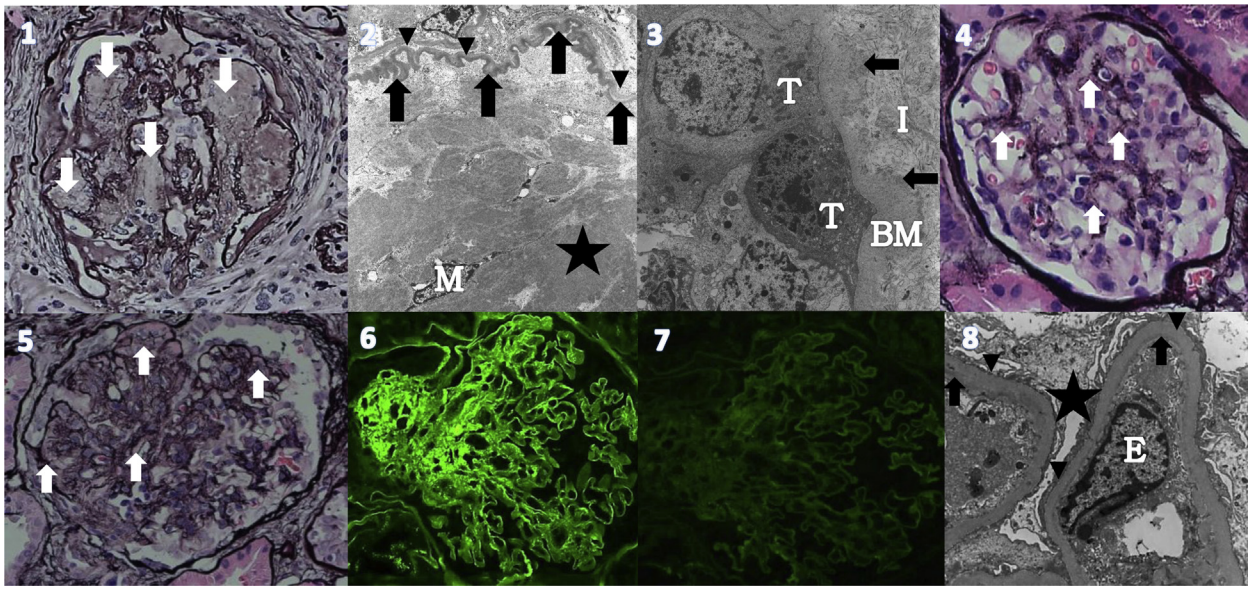

Fig 1. Case 1. (1, 2, and 3) Biopsy of native kidney (1999): κ LCDD. (1) Light microcopy section (silver stain): glomerulus with its mesangial-capillary architecture nearly totally replaced by deposition of amorphous material (silver negative) in a nodular configuration (arrows). Immunofluorescence studies (not depicted) showed positive glomerular staining with κ light chain and negative lambda light chain staining. (2 and 3) Electron microscopy images. (2) Glomerulus: aligned confluent dark punctate (light chain type) electron-dense depositions along the endothelial side of the glomerular basement membranes (arrows). The also electron-dense, but lighter, glomerular basement membranes are facing the visceral epithelium and urinary space (arrowheads). Massive granular light chain type electron dense depositions were also observed replacing the mesangium (star). Note a residual mesangial cell (M) "compressed" by the massive deposits. (3) Tubulointerstitium: light chain type punctate dark electron-dense depositions (arrows) were also identified along the tubular basement membranes (BM). To the left, the tubular epithelial cells (T) line the tubular basement membrane, and, to the right, is the interstitium (I) with its elongated bundles of collagen-type fibers. (4) Biopsy of renal allograft (2007): recurrent κ light chain deposition disease. Light microscopy section (silver stain): glomerulus shows segmental nearly incipient basement membrane light pink amorphous material depositions (arrows), giving the glomerular basement membranes a "split" appearance. Immunofluorescence and electron microscopy studies (not depicted) confirmed recurrence of the κ light chain deposition. Brightly positive κ light chain and negative lambda light chain staining were noted by immunofluorescence, and confluent glomerular and tubular basement membrane electron-dense deposits were seen on electron microscopy. (5, 6, 7, and 8) Biopsy of renal allograft (2012): persistent κ light chain deposition disease. (5) Light microscopy section (silver stain): progression of deposition of the pink amorphous (silver negative) material in the glomerular basement membranes (arrows). The depositions are increased in comparison to the allograft biopsy from 2007, but not as prominent as seen in the native renal biopsy from 1999. (6 and 7) Immunofluorescence studies. (6) Glomerulus and tubular basement membranes: positive bright staining with κ light chain in capillary loops, mesangial areas, around the Bowman's capsule and tubular basement membranes. (7) Glomerulus and tubular basement membranes: negative lambda light chain staining. (8) Electron microscopy image (glomerulus): aligned confluent dark punctate (light chain type) electron-dense depositions along the endothelial side of the glomerular basement membranes (arrows). The also electron-dense, but lighter, glomerular basement membranes are shown facing the visceral epithelium and urinary space (arrowheads). The deposits are less than those seen in the electron microscopy images of the native kidney biopsy from 1999. The endothelial side of the glomerular basement membrane is lined by the endothelial cell (E), and its urinary side is lined by the visceral epithelial cells (V) with its foot processes, which are partially effaced (star). A Congo red stain for amyloid was negative in all 3 renal biopsies.

(κ 3.41 mg/L; λ 2.73) over the next 5 years. His SCr levels ranged between 1.8 and 2.0 mg/dL. In 2012 another kidney biopsy was performed for a random urine protein creatinine ratio (UPCR) of 3.6 (0.3, 2 years prior). This showed persistence of κ light chain disease (Fig 1, parts 5–8). His free κ/λ LCR had abruptly increased to 1.90 (κ 4.83 mg/L; λ 2.54 mg/L). BM biopsy showed no amyloid and only 1% plasma cells. In view of the persistence of κ LCDD on renal biopsy and increasing free κ/λ LCR he received 2 cycles of bortezomib (4 doses each) with dexamethasone and losartan for proteinuria. His κ/λ ratio normalized, but due to development of peripheral neuropathy further cycles of bortezomib were discontinued. Since then he has been monitored regularly for his plasma cell disorder. He is now 15 years from his transplantation with a SCr level of 2.0 mg/dL, a normal κ/λ LCR of 1.44 (κ 42.20 mg/L; λ 29.30 mg/L), and a UPCR of 0.15.

Case 2

A 51-year-old male presented with asymptomatic CKD in 2002. His had a creatinine clearance of 14 mL/min, 24-hour urine protein excretion of 897 mg/d, and normal-sized kidneys without hydronephrosis. He tested negative for antineutrophil cytoplasmic antibody and had normal serum protein electrophoresis and complements. His renal disease progressed and he underwent a