TWO CASE HISTORIES OF PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION ASSOCIATED WITH GLOMERULOSCLEROSIS

41-year-old black Jamaican woman

October 1985:
- Viral syndrome. 125 lbs; proteinuria, 1+; serum creatinine, 0.5 mg/dL; blood pressure, 130/70 mm Hg

December 1986:
- Fever, fatigue, cough. 120 lbs; proteinuria, 1+; interstitial pneumonia; serum creatinine, 1.5 mg/dL; ex-husband used intravenous drugs; 11-cm, echogenic kidneys

February 1987:
- 3+ edema. 116 lbs; proteinuria, 12.7 g/24 h; serum creatinine, 11.4 mg/dL; albumin, 2.5 g/dL; blood pressure, 150/86; renal biopsy showed focal segmental glomerulosclerosis

May 1987:
- 100 lbs; patient died after 3 months of hemodialysis from sepsis and cryptococcal meningitis

28-year-old black Haitian man

A dockworker until 3 months before admission, when fevers began to occur. No identifiable risk factor. He presented with a blood pressure of 110/80 mm Hg, periorbital and trace ankle edema, interstitial pneumonitis, and diffuse adenopathies. Serum creatinine increased from 5.3 to 9 mg/dL in 6 days; albumin, 1.6 g/dL; proteinuria, 6.9 g/24 h; 15-cm, echogenic kidneys. Renal biopsy showed focal segmental glomerulosclerosis. Lymph node biopsy showed Mycobacterium gordonae. This patient returned to Haiti after six hemodialyses.

FIGURE 7-24
These two patients illustrate typical presenting features of HIV-associated glomerulosclerosis, i.e., proteinuria, usually in the nephrotic range; normal-sized or large echogenic kidney; and renal insufficiency rapidly progressing to end-stage renal disease (ESRD). The onset of the nephropathy is often abrupt, with uremia and massive nonselective proteinuria (sometimes in excess of 20 g/24 h). These fulminant lesions may present as acute renal failure in patients who were well only a few weeks or months before hospitalization. In other patients, minimal proteinuria and azotemia at presentation increase insidiously over a period of several months until a nephrotic syndrome becomes evident, with rapid evolution thereafter to uremia and ESRD. Hypertension and peripheral edema may be absent even in the context of advanced renal insufficiency or severe nephrotic syndrome. The status of the patient’s HIV infection rather than the presence of renal disease per se has the greatest impact on survival.

FIGURE 7-25
Ultrasonography of a hyperechogenic 15-cm kidney in a patient with HIV-associated glomerulosclerosis, nephrotic syndrome, and renal failure.

PATHOLOGIC FEATURES OF GLOMERULOSCLEROSIS ASSOCIATED WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

- Collapsed glomerular capillaries
- Visceral glomerular epitheliosis
- Microcystic tubules with variegated casts
- Focal tubular simplification
- Interstitial lymphocytic infiltration
- Endothelial reticular inclusions

FIGURE 7-26
Pathologic features of glomerulosclerosis. None of the features listed is pathognomonic. The concomitant presence of glomerular and tubular lesions with tubuloreticular inclusions in the glomerular and peritubular capillary endothelial cells, however, is highly suggestive of glomerulosclerosis associated with human immunodeficiency virus infection [134,166–171].
Renal Disease in Patients Infected with Hepatitis and Human Immunodeficiency Virus

**FIGURE 7-27**
Glomerulosclerosis. Micrograph of segmental glomerulosclerosis with hyperplastic visceral epithelial cells (arrows).

**FIGURE 7-28**
More advanced glomerulosclerosis. Micrograph of a more advanced stage of glomerulosclerosis with large hyperplastic visceral epithelial cells loaded with hyaline protein droplets, interstitial infiltrate, and tubules filled with proteinaceous material.

**FIGURE 7-29**
Collapsing glomerulosclerosis. Micrograph of global collapsing glomerulosclerosis. No patent capillary lumina are present. In the same patient, normal glomeruli, glomeruli with segmental sclerosis, and glomeruli with global sclerosis may be found [172].

**FIGURE 7-30**
Dilated microcystic tubules. Micrograph of massively dilated microcystic tubules filled with variegated protein casts adjacent to normal-sized glomeruli. These casts contain all plasma proteins. The tubular epithelium is flattened. The tubulointerstitial changes likely play an important role in the pathogenesis of the renal insufficiency and offer one explanation for the rapid decrease in renal function.
FIGURE 7-31
Diffuse mesangial hyperplasia and nephrotic syndrome. Micrograph of diffuse mesangial hyperplasia in a child with perinatal AIDS and nephrotic syndrome. Both diffuse and global mesangial hyperplasia are identified in 25% of children with perinatal AIDS and proteinuria. The characteristic microcystic tubular dilations and the kidney enlargement of glomerulosclerosis associated with human immunodeficiency virus infection are absent in patients with diffuse mesangial hyperplasia.

FIGURE 7-32
Tubuloreticular cytoplasmic inclusions. Micrograph of tubuloreticular cytoplasmic inclusions in glomerular endothelial cell. The latter are virtually diagnostic of nephropathy associated with HIV infection, provided systemic lupus erythematosus has been excluded. On immunofluorescent examination, findings in the glomeruli are nonspecific and similar in HIV-associated glomerulosclerosis and idiopathic focal segmental glomerulosclerosis. These findings consist largely of immunoglobulin M and complement C3 deposited in a segmental granular pattern in the mesangium and capillaries. The same deposits also occur in 30% of patients with AIDS without renal disease [134,163,167].

FIGURE 7-33
Possible pathogenic mechanisms of glomerulosclerosis associated with HIV infection. HIV-associated glomerulosclerosis is not the result of opportunistic infections. Indeed, the nephropathy may be the first manifestation of HIV infection and often occurs in patients before opportunistic infections develop. HIV-associated glomerulosclerosis also is not an immune-complex-mediated glomerulopathy because immune deposits are generally absent. Three mechanisms have been proposed: direct injury of renal epithelial cells by infective HIV, although direct renal cell infection has not been demonstrated conclusively and systematically; injury by HIV gene products; or injury by cytokines and growth factors released by infected lymphocytes and monocytes systemically or intrarenally or released by renal cells after uptake of viral gene products. The variable susceptibility to glomerulosclerosis also suggests that unique viral-host interactions may be necessary for expression of the nephropathy [132,156,166,173–175].