RENAL COMPLICATIONS IN HIV DISEASE

At the New York course, Paul E. Klotman, MD, presented a case of renal disorder in an individual with HIV disease. Details of the case presentation are summarized, followed by discussion of diagnosis and management.

CASE DESCRIPTION

Presentation

37-year-old black man, former injection drug user diagnosed as HIV-seropositive in 1986 and lost to follow-up, presents to AIDS clinic in 1996

Complaints

Recent cold, took some antibiotics
Malaise
Fatigue
Anorexia
Pruritus

Physical findings

Chronically ill-appearing thin man
Weight, 112 lbs; blood pressure, 120/70 mmHg; pulse, 84 bpm
No edema
Skin: several raised indurated lesions on chest, shoulders, and lower extremities with many excoriations; not typical Kaposi's sarcoma

Laboratory findings

Urinalysis: 2+ proteinuria, no sediment
CD4+ cell count, 30/μL
Creatinine, 3.5 mg%
Calcium, 8.2 mg%; phosphorus, 3.8 mg%
Albumin, 3.0 mg%
Hepatitis B and C negative
Plasma HIV RNA, 1.4×10^4 copies/mL

Diagnosis

In addition to a 24-hour urine test for creatinine clearance and protein excretion, initial workup of this patient included a renal ultrasound to evaluate the possibility of postrenal causes of decreased renal function (eg, urinary obstruction due to urethral stricture from recurrent sexually transmitted diseases). The patient exhibited some physical signs of dehydration, a common finding in patients who are infected with HIV-1. Renal biopsy was considered but postponed until obstruction could be ruled out and kidney size and number could be determined. Ultrasound results showed no evidence of hydronephrosis and 2 kidneys of 11 cm that appeared echogenic, a finding common in patients with HIV-associated nephropathy (HIVAN). Results from the timed urine collection revealed a creatinine clearance of 25 mL/min and 2.5 grams of protein excretion in 24 hours. Biopsy of skin lesions showed leukocytoclastic angiitis with some eosinophils, consistent with a drug reaction.

Based on these initial findings, the most likely diagnosis is HIVAN, so why is a renal biopsy required? This patient has many of the findings typically seen in HIVAN patients with renal disease who are biopsied. He is African American (90% of cases occur in blacks or Hispanics). He has a history of injection drug use (50% of HIVAN diagnoses), a physical exam consistent with volume depletion, significant proteinuria (>1 g), CD4+ cell count <200/μL, and normal to enlarged kidneys that are echogenic by ultrasound. In this case, additional diagnoses were possible although less likely, including heroin nephropathy, interstitial nephritis, lupus nephritis, and membranoprolifitive GN secondary to hepatitis. The rationale for biopsy, however, is that even in patients in which the diagnosis appears likely, only 60% will have HIVAN; 40% have some other renal histopathological diagnosis.

Renal biopsy was then obtained, which revealed FSGS (collapsing variant) with global sclerosis and microcystic dilatation, classic features of HIVAN, as well as mild interstitial infiltration and tubuloreticular arrays (Figure 1). When HIVAN is not found, the other diagnoses include focal and segmental glomerulosclerosis (FSGS) (10-15%), membranoproliferative glomerulonephritis (10%), and tubulointerstitial disease (7%), as well as a variety of other diagnoses.

Management

It may appear to be obvious, but the most reasonable first step in the treatment of HIVAN is the initiation of potent antiretroviral therapy. Patients with HIVAN usually have advanced HIV disease, AIDS, and detectable plasma viral loads. Highly active antiretroviral therapy (HAART) is effective in delaying AIDS progression in patients without renal disease and should be instituted in patients with renal disease as well. The vast majority of published cases of HIVAN have occurred in patients with CD4+ cell counts below 200/μL; in 10 cases at Dr Klotman's institution, CD4+ cell counts have ranged from 0 to 200/μL (mean, 60/μL) and the majority of patients have had high plasma viral loads (mean, 7.4×10^5 HIV RNA copies/mL) despite treatment. Resistance to ongoing treatment

may be common in these patients; very recent findings indicate that the kidney harbors HIV-1, a factor that may contribute to resistance. While there are only anecdotal reports of renal benefits with HAART therapy in HIVAN patients, the possibility of viral replication in the kidney suggests that there is a potentially viable study. A randomized, controlled trial currently is under way to compare effects of different potent antiretroviral regimens on survival and renal function in HIVAN, which may address this point.

From the first description in 1984 to the most recent studies within the past 2 years, HIVAN remains a disease characterized by rapid progression. The time from diagnosis to dialysis or death can be measured in weeks to months. Patients who move to dialysis have a high mortality, usually 50% per year. Several treatment strategies have been employed; the two best studied include the steroids and angiotensin-converting enzyme (ACE) inhibitors. One study of steroid treatment involved 19 patients with biopsy-proven HIVAN, serum creatinine >2 mg%, and 24-hour urinary protein >2 g. These patients received prednisone 60 mg/d for 2 to 11 weeks. Results were encouraging after 2 to 14 weeks with a 20% decrease in serum creatinine in 17 of 19 patients and a decrease in urinary protein in 12 of 13 patients. Unfortunately, only 2 patients survived for greater than 1 year without progressing to ESRD. The use of ACE inhibitors for the treatment of HIVAN has met with greater success. One study compared progression to ESRD in 9 patients receiving captopril (6.25 mg tid increasing to 25 mg tid) and 9 control patients. The mean serum creatinine of both groups was 3.4 mg%, indicative of advanced renal disease. Urinary protein/creatinine ratio exceeded 5, suggesting significant glomerular proteinuria. Time to ESRD progression was 156 ± 71 days in treated patients and 37 ± 5 days in controls. The data demonstrate only modest benefit but suggest that earlier therapy may be appropriate. Another study compared changes in serum creatinine in 12 HIVAN patients receiving fosinopril 10 mg qd for 6 months with those in 8 patients refusing such treatment. This patient population had only mild renal insufficiency, with serum creatinine of 1.5 mg%. At week 24, serum creatinine had increased from 1.5 ± 0.5 to 7.0 ± 3.0 mg% in untreated patients and from 1.5 ± 0.3 to 1.7 ± 0.7 mg% in treated patients. Although impressive, interpretation of these findings is somewhat confounded by the absence of a randomized study design. The bad outcome in the control group may also have reflected differences in antiviral adherence, since these were patients who refused therapy. What is clear from these studies is there remains a need for randomized studies of steroid and ACE treatment in patients with HIVAN.

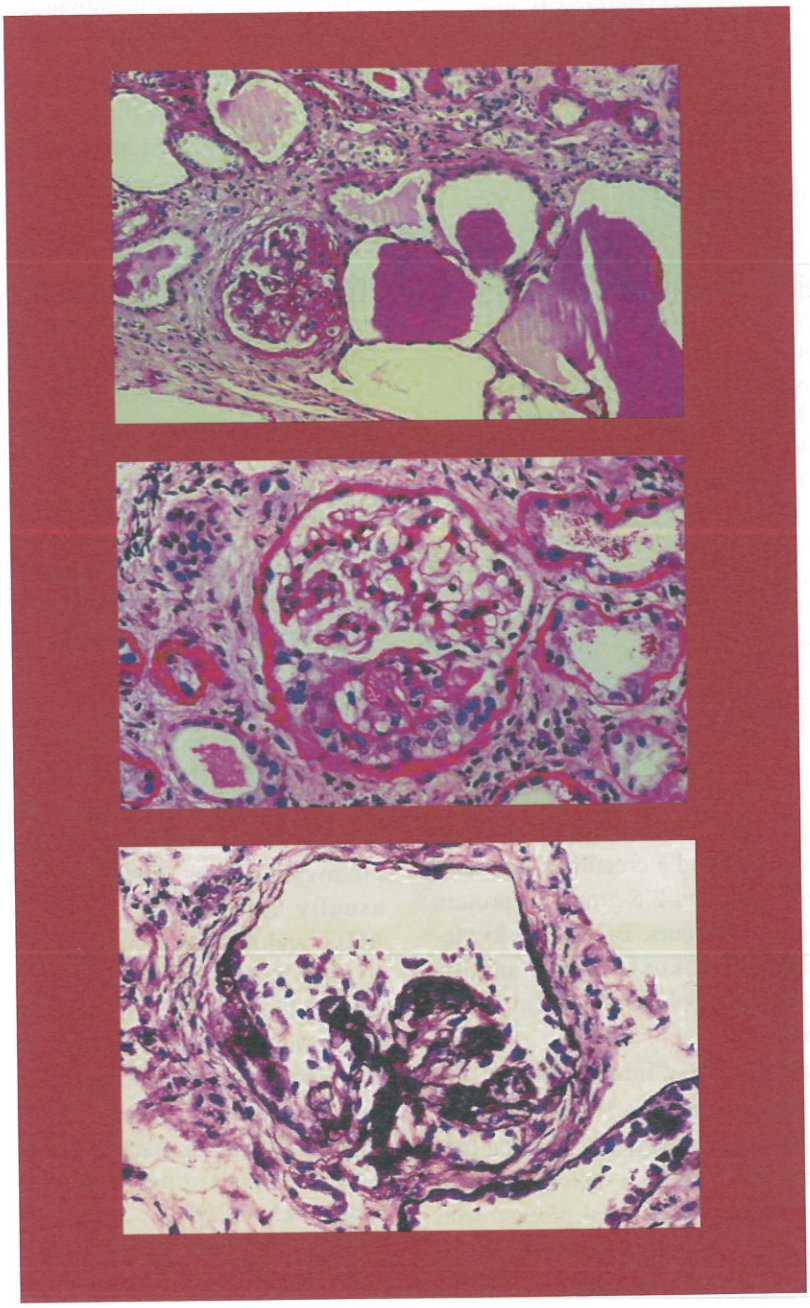

Figure 1. *Biopsy findings in case 1, showing microcystic tubulointerstitial disease* ***top****, focal and segmental glomerulosclerosis* ***middle****, and glomerulonephrosis, collapsing variant* ***bottom****.*

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