Glomerular Lesions in HIV-Infected Patients

A Yale University Department of Medicine Residency Peer-Teaching Conference

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(Received April 12, 1997)

HIV-associated nephropathy (HIVAN) is a clinicopathologic entity characterized by heavy proteinuria, absence of edema and an irreversible decline in renal function. Findings on renal biopsy include: collapsed glomerular capillaries; visceral glomerular epitheliosis; microcystic tubules; mesangial prominence; and endothelial tubuloreticular inclusions. Early in the AIDS epidemic, HIVAN was the predominant glomerular lesion observed in HIV-infected patients. It is being increasingly recognized, especially in Caucasian populations, that a variety of immune complex-mediated lesions such as membranoproliferative glomerulonephritis, proliferative glomerulonephritis and IgA nephropathy are associated with HIV infection.

In this review we present two cases: one patient whose first presentation of AIDS was end-stage renal disease, who on biopsy was found to have HIVAN, and the second, who was infected with HIV, and on biopsy was found to have hepatitis C-related hepatitis C related membranoproliferative glomerulonephritis. We also review the current literature on HIVAN and HIV-associated immune complex diseases (HIVICDs). Each case illustrates an important clinical point. The first that renal disease can be the first manifestation of HIV infection and the second that HIV-infected patients may develop immune complex related renal diseases, some of which may be potentially treatable.

INTRODUCTION

The association of HIV infection and renal disease first emerged in the mid-1980s with the initial description of HIV-associated nephropathy (HIVAN) [1]. After a brief debate on whether this syndrome was related to heroin nephropathy, clinical experience subsequently revealed that HIVAN was indeed a distinct clinicopathologic entity. HIVAN affects predominantly young black males, including those with risk factors for HIV infection other than intravenous drug abuse, and is characterized by heavy proteinuria and a rapid, irreversible decline in renal function. Pathologic findings include: collapsed glomerular capillaries; visceral glomerular epitheliosis; microcystic tubules containing proteinaceous casts; mesangial prominence; and endothelial tubuloreticular inclusions.

Biopsy series have subsequently expanded the spectrum of glomerular lesions in HIV-infected patients to include immune complex disorders such as membranoproliferative glomerulonephritis [2], proliferative glomerulonephritis [3] and IgA nephropathy [4]

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b Abbreviations: AIDS, acquired immunodeficiency syndrome; CAPD, continuous ambulatory peritoneal dialysis; EEG, electroencephalogram; ESRD, end stage renal disease; FSGS, focal segmental glomerulosclerosis; HIV, human immunodeficiency virus; HIVAN, human immunodeficiency virus-associated nephropathy; HIVICD, human immunodeficiency virus-associated immune complex diseases; TGF, transforming growth factor.
for which HIV likely plays an important pathogenetic role. HIV-associated immune complex diseases (HIVICDs) share common clinical manifestations with their counterparts in non-HIV-infected patients. However, as clinical syndromes related to HIV infection they have not been as widely characterized or speculated to have the same epidemiological impact as HIVAN.

This article will present two cases that demonstrate the importance of a diagnostic renal biopsy in HIV-associated renal disease and review the clinical presentation, pathology, pathogenesis and potential therapies of HIVAN, as well as emerging concepts regarding the recently recognized HIVICDs.

CASES

Case 1: A 35 year old black male with a history of chronic alcohol abuse, whose last stated drink was three weeks prior to admission, presented to the emergency department after two generalized tonic-clonic seizures. He had noted increased urination, occasional pruritus and a 9 kg weight loss over the previous year. There was no significant past medical history, and he was on no medication. He denied intravenous drug use, but admitted to having multiple heterosexual partners.

On physical examination, he was alert, in no distress and afebrile. Blood pressure was 150/90 mm Hg, and the pulse was 108. Examination of the head and neck was unremarkable. No thrush was noted. Cardiac, chest, and abdominal exam were normal. There was no peripheral edema. Neurological exam was unremarkable.

Laboratory data: BUN, 116 mg/dl, creatinine, 8.6 mg/dl, electrolytes within normal limits, Hct, 25.6 percent and creatine kinase, 527 U/l. Urinalysis revealed 3+ protein and an inactive sediment. Renal ultrasound examination showed no hydronephrosis, and the kidneys were 11 cm bilaterally with increased echogenicity. Computerized tomography of the head, a lumbar puncture, and EEG were unremarkable. A renal biopsy was performed.

Figure 1. Light micrograph demonstrating several characteristics of HIVAN including: diffuse tubular dilatation with microcysts; glomerular collapse and sclerosis; and a pseudocrescent (shown at the arrowhead). (Magnification: 75X).

Figure 2. Light micrograph demonstrating interstitial nephritis and scarring. (Magnification: 75X).
A light microscopic section of the renal cortex is shown in Figure 1. There is diffuse tubular dilatation with microcystic tubules containing large proteinaceous casts. The interstitium is widened, and a patchy cellular infiltrate can be seen. The glomerulus at the bottom of the figure is collapsed, and a second glomerulus shows evidence of sclerosis and capillary loop collapse, as well as a pallisading of visceral epithelial cells that form a pseudocrescent (shown at the arrowhead). A prominent area of interstitial scarring and focal interstitial nephritis is visualized in Figure 2. Widespread effacement of visceral epithelial foot processes was seen on electron microscopy (arrowhead Figure 3). This constellation of findings was strongly suggestive of HIVAN, and HIV serology subsequently returned positive.

**Case 2:** A 45 year old black male, known to be HIV positive since 1985, was admitted to the hospital with increasing abdominal girth and leg edema. The patient had a known history of intravenous drug abuse and was continuing to use three bags of heroin daily. He had no previous history of opportunistic infection. Past medical history was significant for hypertension, endocarditis, aseptic meningitis and microscopic hematuria. He was on no medication. In 1992, a 24-hour urine showed 1.4 grams of protein.

On physical examination he was in no distress and appeared chronically ill. The temperature was normal, with a blood pressure of 200/100 mmHg, and a pulse of 80. The remainder of the physical examination was remarkable only for ascites and peripheral edema to the mid-thigh.

Laboratory data: BUN, 32 mg/dl, creatinine, 1.6 mg/dl, albumin, 1.5 g/dl, total protein, 8.1 g/dl. Urinalysis revealed 3+ protein, large blood, 2-5 WBC/HPF and 11-20 RBC/HPF. Twenty-four-hr urine studies revealed a creatinine clearance of 34.7 ml/min, and 2.34 g protein. Renal ultrasound examination revealed moderate ascites and enlarged echogenic kidneys. A renal biopsy was performed.

A light microscopic section of the kidney cortex is shown in Figure 4. Two glomeruli are seen, and each shows evidence of hypercellularity and lobular accentuation. The interstitium is also widened with a marked increase in cellularity. Electron microscopy
Figure 4. Light micrograph showing a hypercellular glomerulus with evidence of lobular accentuation. (Magnification-180X)

Figure 5. Electron micrograph showing diffuse subendothelial deposits (shown at the arrowhead). (Magnification 7,950X).
revealed both diffuse subendothelial deposits (arrowhead in Figure 5), as well as numerous large subepithelial deposits (arrowhead in Figure 6). There was prominent mesangialization of the glomerular basement membrane seen in additional sections, along with focal glomerular intracapillary deposits suggestive of cryoglobulins (not shown). These findings were felt to be most compatible with membranoproliferative glomerulonephritis secondary to hepatitis C. A test for hepatitis C antibody was positive.

Each of the above cases illustrates an important point regarding HIV-associated glomerular disease. The first case shows that renal involvement may be the first manifestation of HIV infection, and the second case demonstrates that patients infected with HIV can develop potentially treatable renal diseases that are not unique to HIV infection.

Consistent with the classic clinical picture of HIVAN, the first patient presented with azotemia, proteinuria, the absence of edema and hypertension, and enlarged echogenic
kidneys. However, the second patient had an indolent course of moderate renal insufficiency, proteinuria, edema, and hypertension, inconsistent with the usual presentation of HIVAN. Renal biopsy established the diagnosis of membranoproliferative glomerulonephritis secondary to hepatitis C and the patient was subsequently treated with α-interferon.

In this manuscript, we will review the spectrum of glomerular lesions that have been associated with HIV infection. These disorders will be divided into two major categories: HIV-associated nephropathy (HIVAN) and HIV-associated immune complex diseases (HIVICDs). With respect to HIVAN we will discuss its epidemiology and history, clinical presentation, pathologic features and emerging concepts regarding its pathogenesis and treatment. We will also describe several recent studies that suggest that glomerular disorders classically associated with immune-complex deposition may be associated with HIV infection (HIVICDs) and close by discussing what is known about hepatitis C-related renal disease in HIV-positive patients.

HIVAN

Epidemiology and history

Early biopsy series from New York City [1, 2] and Miami [5] showed that focal segmental glomerulosclerosis (FSGS) was the principal pathologic lesion in patients with AIDS and nephrotic range proteinuria. Rao et al. [6] reported that among a series of 750 patients treated with AIDS at two New York City hospitals, 55 had azotemia and proteinuria (43 of these developed irreversible uremia). Of this group 30 had either a renal biopsy or autopsy. Pathologic examination showed FSGS in 27 patients and mesangial changes in three. Risk factors for HIV infection included: intravenous drug use, 55 percent; homosexual contact, 9 percent; and unknown, 11 percent. Five patients had a history of both intravenous drug use and homosexual contact. All 55 patients were black, and only six were women.

This finding remained controversial in view of the fact that early studies from San Francisco and Washington, D.C. failed to demonstrate a clinical syndrome of AIDS-associated nephropathy [7, 8]. The controversy centered on the premise that since FSGS was characteristic of heroin nephropathy, and that intravenous drug use is a common risk factor for AIDS, that the nephropathy seen in AIDS patients might be related more to intravenous drug use than to HIV infection. In retrospect, this lack of early geographic concordance was probably due to differences in the racial makeup of patient populations, in that the San Francisco and Washington, D.C. series were made up primarily of white homosexuals [9]. Subsequently, as the AIDS epidemic progressed it was evident that HIVAN was indeed a distinct clinicopathologic entity.

Current evidence supports race as a significant co-factor in the development of HIVAN as it is for many renal disorders [10]. In the United States, 90 percent of all patients with HIVAN are black [11], and the gender breakdown is similar to that of HIV infection. At the University of Miami/Jackson Medical Center, 88 percent of patients with HIVAN are black, while the ratio of white to black patients at this center is 2:1 [12]. A European series involving 203 patients, all of whom were white, failed to identify any biopsy documented cases of HIVAN [13]. The classic clinical and pathologic presentation of HIVAN has been confirmed in patients with every known risk factor for HIV transmission [14]. Overall in this country, 30-50 percent of cases have intravenous drug use as a risk factor.
Clinical presentation

Patients generally present with varying degrees of proteinuria and/or renal insufficiency. More than half are at an early stage of HIV infection. It is not uncommon for patients previously undiagnosed with HIV to present with end-stage renal failure secondary to HIV-associated glomerulosclerosis as seen in our first case [15]. Typically, the serum creatinine is 2 mg/dl or higher, and the serum albumin is low. Ten to 20 percent may have normal renal function. The progression to nephrotic-range proteinuria occurs over several weeks to months, although some patients have a more indolent time course [16].

Despite nephrotic-range proteinuria and hypoalbuminemia, edema is conspicuously absent. Several potential explanations have been offered including: intravascular volume depletion due to chronic diarrhea and malnutrition/malabsorption; that the excess globulins due to the polyclonal gammopathy of HIV infection may offset the loss of oncotic pressure from hypoalbuminemia; and salt wasting.

After the onset of nephrotic-range proteinuria, the progression to end-stage renal disease (ESRD) is characteristically rapid [16, 17]. Patients often remain normotensive throughout unless underlying essential hypertension is present, in which case the progression to ESRD is even more rapid. Langs et al. reported 15 patients with HIVAN without edema or hypertension (except one that previously had essential hypertension) [17]. Thirteen progressed to ESRD: eight within four months; four within four-10 months; and one within 27 months. Other larger series have shown similar results. Ultrasound studies in HIVAN reveal enlarged echogenic kidneys that remain large despite the progression to ESRD [18].

Pathology

Grossly the kidneys are enlarged bilaterally. Occasional cysts are visible, which represent massively dilated tubules. On light microscopy there are abnormalities involving the glomeruli, tubules and interstitium [19]. These include: collapse of the glomerular capillary; mesangial prominence; visceral epithelial cell swelling and vacuolization; interstitial fibrosis and edema; cystic tubular degeneration and necrosis with the tubular lumen filled with eosinophilic proteinaceous material (microcysts) [20]. Immunofluorescence analysis shows deposition of immunoglobulins, chiefly IgM and complement, in areas of glomerular sclerosis. Tubular casts contain immunoglobulins, complement, light chains, albumin, and fibrin but not Tamm-Horsfall protein, which is frequently found in adjacent nondilated tubules [19]. Electron microscopy reveals widespread effacement of visceral epithelial foot processes. Characteristic tubuloreticular inclusion bodies are found in tubular, interstitial, endothelial and glomerular epithelial cells, as well as in interstitial leukocytes [21]. Other ultrastructural abnormalities include: granular degeneration of the nuclear chromatin; and increased numbers of nuclear bodies [20, 21].

Pathogenesis

Early investigations centered around an attempt to identify an infectious agent, and at various points, cytomegalovirus and Mycoplasma fermentans were invoked and subsequently dismissed [22]. Renal ischemia has been suggested as an explanation for the tubular cell necrosis and glomerular collapse; however, this would not explain the proteinuria nor the structural abnormalities in glomerular visceral epithelial cells [17]. The strikingly dilated tubules occluded with proteinaceous material has led to tubular obstruction being postulated as another possible mechanism in the rapid progression of the nephropathy [17].

The presence of HIV genome in renal cells has been demonstrated in two studies. Cohen et al. employed immunohistochemistry using an antibody to p24 and in situ hybridization to show the presence of HIV genome in many glomerular and tubular
epithelial cells in patients with both HIVAN and HIVICDs [23]. Kimmel et al. evaluated 22 biopsy specimens from HIV-positive patients with renal disease using the polymerase chain reaction of microdissected tissue with primers and probes to the gag gene [24]. HIV genome was demonstrated in glomeruli, tubules, interstitial cells and infiltrating inflammatory cells, but not interstitial cells. HIV DNA was detected in 21 of 22 specimens. Control specimens from HIV-infected patients without clinical evidence of renal disease were positive as well. This study included patients with both HIVAN and HIVICDs. These data suggest that the presence of HIV genomic material may be necessary, but not sufficient to produce clinically evident disease. To date, HIV RNAs or cDNAs have not been identified in kidney.

Cytokines and growth factors are important agents in the pathogenesis of many renal diseases [25]. Several studies involving animal models have suggested that TGF-β plays a role in the pathogenesis of glomerulosclerosis [26]. HIV-infected human mesangial cells increase expression of HIV genes in response to exposure to TGF-β in vitro [27]. AIDS patients are known to have increased circulating levels of this growth factor, and patients with HIVAN have increased expression of TGF-β in biopsy specimens [27]. It has been suggested that TGF-β might induce increased matrix production by either mesangial or other cells, and that this could then result in decreased renal function.

Mice transgenic for a noninfectious HIV provirus gene develop renal disease characterized by FSGS, proteinuria, interstitial nephritis and tubular cysts [28]. These mice express HIV-specific transcripts in several tissues including the kidney, suggesting that certain viral gene products, but not the virus itself, may exert a pathologic effect. Further studies employing this model have shown a potential pathogenetic role for cytokines including TGF-β and basic fibroblast growth factor [29].

Treatment

There is no proven effective treatment for HIVAN. In a small study involving four patients with biopsy-proven HIVAN and advanced renal insufficiency corticosteroids were administered for two-six weeks (1 mg/kg/day) [30]. Although mean plasma creatinine fell from 9.1 to 3.3 mg/dl, there was no change in urinary protein excretion. Two patients suffered serious adverse effects (Mycobacterium avium-complex infection and steroid-induced psychosis). The improvement in renal function without a change in proteinuria may be more indicative of a reversal of an interstitial nephritis than a glomerular lesion.

Experience with cyclosporine is limited to three pediatric patients with HIVAN and nephrotic syndrome treated for very short periods of time (three, six and 12 months) [31]. The nephrotic syndrome resolved in all three cases.

Three recent studies have suggested that there may be a role for zidovudine in the treatment of patients with HIVAN. In a retrospective study six patients with biopsy-proven HIVAN were administered 300 to 800 mg/day of zidovudine [32]. In two patients with advanced renal disease, there was no benefit. In four patients with less advanced disease (serum creatinines ranging from 1.2 to 5.2 mg/dl), there was a delay in the need for chronic dialysis for up to 33 months. In the second study, 23 patients with a mean serum creatinine of 1.2 mg/dl were treated prospectively with 400 to 800 mg/day of zidovudine [33]. Of the eight patients who stopped taking zidovudine, all progressed to ESRD within a mean of eight weeks. In the 15 patients who were zidovudine compliant, none developed ESRD or a progression of azotemia. However, only five members of the study group had undergone renal biopsy (all had HIVAN), and only 14 of the 23 had proteinuria. In the third study, 43 of 54 patients with 2+ or greater proteinuria were given zidovudine and 11 were not [34]. Six patients who were already azotemic before zidovudine administration went on to develop ESRD. Of the nonazotemic patients, 40 percent that did not receive
zidovudine progressed to mild azotemia (four of 10), while only five of 37 receiving the
drug progressed during a two-year period.

Captopril was recently shown to increase renal survival in small groups of patients
with biopsy proven HIVAN in two studies. In the first nine patients were treated with cap-
topril, and an additional nine patients served as controls [35]. Subjects in each group were
matched for age, race, gender and level of serum creatinine. At the onset of treatment, the
mean serum creatinine was 3.4 ± 0.7 in the captopril group and 3.7 ± 0.5 in the control
group. Renal survival was defined as the time from renal biopsy to the time of onset of
treatment for ESRD. Mean renal survival was 156 ± 71 days in the captopril group vs. 37
± 5 days in the control group (p < .002). In the second study, three patients with biopsy-
proven HIVAN were treated with fosinopril (10 mg/day), and compared to four controls
matched for age, sex, race, baseline creatinine and 24-hr urinary protein excretion [36].
After six months, the treated patients had a lower serum creatinine (1.5 mg/dl ± 0.09 vs.
5.4 mg/dl ± 0.14) and lower 24-hr protein excretion (1.5 ± 0.14 g vs. 8.5 ± 0.72 g) com-
pared to the control group.

It was noted early in the epidemic that patients maintained on hemodialysis experi-
cenced a wasting syndrome leading to death after about six months [37]. Although survival
is generally short once ESRD develops, it may exceed one to two years in those at an early
stage of illness [38]. In a recent report of 61 patients treated at Wayne State, the overall
survival at one, two and three years was 50 percent, 30 percent and 10 percent, respec-
tively. Mortality was related to infectious complications and the number of AIDS-related
organ involvement [39]. There appears to be no difference in mortality between contin-
uous ambulatory peritoneal dialysis (CAPD) and hemodialysis, and the peritonitis rate of
HIV-infected patients was similar to that of non-HIV infected patients on CAPD in one
study [40]. Another study showed that the peritonitis rate in HIV-infected patients was 2.6
times higher than in non-HIV infected patients [41]. However, peritonitis related compli-
cations rarely resulted in the discontinuation of CAPD.

Most centers will not transplant HIV-positive patients. However, before systematic
screening of recipients and donors began in 1985, whole organ transplants were inadver-
tently carried out on HIV carriers. In one study, 25 HIV-positive patients received whole-
organ transplants, five of whom were kidney transplants [42]. Mean follow-up in these
patients was 3.4 years, and two patients have survived for more than five years. HIV-pos-
itive whole-organ transplant recipients appear to have a shorter time to the onset of AIDS
than control patients who have acquired the virus from the transfusion of blood products.
However, in this study, AIDS-defining opportunistic infections were assumed to be the
result of HIV infection rather than secondary to transplant-related immunosuppression.

**HIV-ASSOCIATED IMMUNE COMPLEX DISEASES (HIVICDS)**

*Background*

Several biopsy series now support the contention that HIVAN is not the only glomeru-
lar lesion seen in HIV-infected patients. The histopathology in 40 patients with HIV infec-
tion and clinical evidence of renal disease undergoing kidney biopsy at the George
Washington University Medical Center in Washington, D.C. since 1986 is shown below in
Table 1.

Further studies were carried out on four of the above patients with proliferative
glomerulonephritis [43]. All were black, and had renal insufficiency and proteinuria.
Circulating immune complexes and HIV-reactive antibodies were found in the sera of all
four patients. Eluted samples from biopsy specimens were analyzed and demonstrated com-
plexes of antibody with various HIV antigens, uncomplexed HIV antigens and complement.
IgA nephropathy is reported, however, Table [46].

In addition, eluted antibodies were shown to react with HIV antigens from the isolated circulating immune complexes.

In Europe, among whites infected with HIV, a variety of glomerular lesions have been reported, however, HIVAN is rare. In Italy, Casanova et al. reviewed 26 renal biopsy specimens from HIV-infected patients with suspected glomerular involvement [44]. All patients were Italian, and 19 of the 26 were intravenous drug abusers. Glomerular pathology included: minimal change disease (two patients); mesangial proliferative glomerulonephritis (four patients); post-infectious glomerulonephritis (six patients); membranoproliferative glomerulonephritis (one patient); membranous glomerulonephritis (three patients); IgA nephropathy (four patients); mixed membranous and proliferative glomerulonephritis (three patients); diffuse proliferative glomerulonephritis with subendothelial deposits and intraluminal thrombi (two patients); proliferative glomerulonephritis with subepithelial and subendothelial deposits (one patient). Tubuloreticular inclusions were seen in all patients. There were no cases of HIVAN. Nochy et al. studied 60 patients from Paris area hospitals; 29 patients were black and 31 were white [45]. Only three of the 31 white patients were found to have HIVAN (the majority had glomerulonephritis), while 23 of 29 black patients had HIVAN, and only 21 percent of black patients had glomerulonephritis.

**IgA nephropathy**

While HIV-infected patients may develop diseases unrelated and coincidental to HIV infection, evidence is accumulating for a unique form of IgA nephropathy stemming from an HIV-related immunologic process. Other possibly HIV-related immune complex diseases such as membranous glomerulonephritis, membranoproliferative glomerulonephritis and acute proliferative glomerulonephritis have been described. However, the role of HIV infection in their pathogenesis has yet to be determined.

Several mechanisms have been proposed as possible explanations for an increased susceptibility of HIV-infected patients to IgA nephropathy. HIV-infected patients commonly have increased levels of circulating IgA (primarily directed at the HIV envelope glycoproteins gp160, gp120 and gp41), as well as circulating immune complexes containing IgA and IgA rheumatoid factors, suggestive of abnormalities of IgA regulation [46]. Race and genetic factors have also been invoked since all of the HIV-infected patients with IgA nephropathy reported to date have been white.

Katz et al. studied four white HIV-positive patients with IgA nephropathy on biopsy [47]. Elevated serum levels of IgA, as well as IgA immune complexes and rheumatoid factors were found. IgA antibodies to multiple HIV antigens were detected by Western blot in serum. However, the authors were unable to demonstrate HIV antigens in the biopsy specimens using either monoclonal antibodies or in situ hybridization.

Kimmel et al. studied two HIV-positive patients with IgA nephropathy [48]. Circulating immune complexes were isolated (composed of IgA and IgG in one patient,
and IgA and IgM in the other) as well as IgA idiotypic antibodies (antibodies that inhibited the binding of HIV antigen to anti-HIV antibodies). Identical material was recovered from the renal tissues of one of the patients by elution.

A proposed mechanism for the development of immune complex-mediated renal disease in HIV-infected patients is the deposition of circulating immune complexes or polyclonal B-cell activation against an HIV-related antigen in renal tissue. HIV DNA has been demonstrated in renal tissue, and HIV p24 antigen has been shown in biopsy specimens suggesting that there may be cellular incorporation of HIV genome products and the subsequent deposition of antibody or circulating immune complexes. Interstitial inflammatory infiltrates are present in both HIVICDs and HIVAN. These cells are perhaps important in the pathogenesis of both entities due to their elaboration of various cytokines. Bodi et al. characterized the interstitial cell population in HIVAN and HIVICDs and in HIV-negative FSGS control patients [49]. He found that in HIVAN a greater proportion of the cells were macrophages and a lesser proportion B-cells as compared to HIVICDs.

**HEPATITIS C, MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS AND HIV INFECTION**

As in case 2, HIV-positive patients are susceptible to other renal diseases including those that respond to specific treatment, making kidney biopsy a potentially important diagnostic tool. Hepatitis C virus infection has been associated with immunologically-mediated renal disease. Johnson et al. reported eight patients with chronic hepatitis C infection and membranoproliferative glomerulonephritis [50]. Four of these patients were treated with α-interferon for periods of 2–12 months with a decrease in proteinuria. Two small series consisting of eight and 12 HIV-positive patients, respectively, have reported using α-interferon for three-six months for the treatment of chronic hepatitis with no differences noted in the response to, or tolerance of, therapy when compared to patients without evidence of HIV infection [51, 52]. Taken together, these studies suggest that α-interferon may be useful for the treatment of membranoproliferative glomerulonephritis in the HIV-positive population. However, it should be noted that long-term, high-dose α-interferon therapy has been associated with the development of membranoproliferative glomerulonephritis in at least one HIV-positive patient [53]. In this case report antigen-antibody complexes containing α-interferon were isolated from both the circulation and renal tissue.

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