

# Case Study: HIVAN and IgA Nephropathy as a Cause of Chronic Kidney Disease

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## INTRODUCTION:

Though HIV-associated nephropathy (HIVAN) receives a great deal of attention, causes of chronic kidney disease in HIV-infected patients are varied and multifactorial. We present the case of a man with newly diagnosed renal failure, having features of both HIVAN and IgA nephropathy on renal biopsy.

## HISTORY:

30 y/o Hispanic man presented to our clinic for initial HIV care. He was diagnosed HIV+ two years earlier at a county health department after a disseminated Herpes zoster outbreak. He denied complaints and had not received any healthcare for several years except for a visit to a workman's compensation doctor one month earlier for back pain. He was prescribed celecoxib which he took for two weeks, stopping two weeks prior to entering HIV care. Prior medical records later obtained from the workman's compensation doctor indicated severe normocytic anemia (Hgb 9 gm/dL), elevated sedimentation rate of 138 mm/hr, and urinalysis with nephrotic range proteinuria (300+need units) and granular casts. He was told at this time he should consult a primary care physician for further treatment.

## WORK-UP:

The following labs were received as alert values on the day of initial blood draw: **Hgb.** 7.9 gm/dL, **creatinine** 7.0 mg/dL, **BUN** 47 mg/dL, **CO2** 13 mmol/L. Later results revealed negative serologic testing for Hepatitis B and C.

The patient was called and brought back into clinic the next day still without somatic complaints despite a fever of 102 F. At this time he was sent to the hospital for admission and work up for his renal failure, fever, acidosis, and severe anemia.

The patient was admitted to the hospital for one week with the following diagnostic procedures performed:

- CT of kidneys (negative for hydronephrosis, ureterolithiasis)
- U/S of kidneys (compatible with medical renal disease)
- CXR (negative)
- Lumbar puncture and blood cultures (all negative)

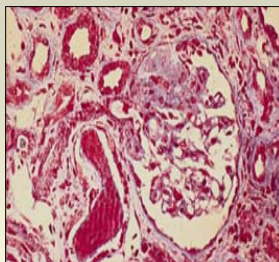
•Microscopic examination (using light microscopy) of left kidney biopsy showed multiple globally sclerotic glomeruli, several other glomeruli with collapsing of capillary tufts with prominent podocyte hypertrophy and hyperplasia. The remaining glomeruli showed mild mesangial hypercellularity with increased mesangial matrix. Many tubules cystically dilated with proteinaceous casts. Immunofluorescence microscopy revealed segmental granular stainings in the mesangial regions for IgG (2+), IgA (2-3+), IgM (1+).

Hospital course included rehydration, red cell transfusion, iron and folate supplementation, and prophylaxis with trimethoprim/sulfamethoxazole and azithromycin.

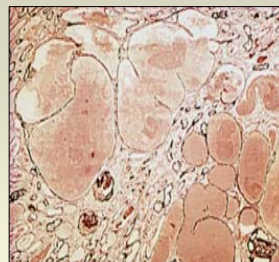
## DIFFERENTIAL DIAGNOSIS:

- HIV nephropathy
- Acute Tubular Necrosis (ATN)
- ATN secondary to recent NSAID or other drug use
- Primary focal segmental glomerulosclerosis (FSGS)
- Immune complex glomerulonephritis (GN)
- Drug-induced interstitial nephritis
- Glomerulonephropathy associated with hepatitis B or C
- Amyloidosis
- IgA nephropathy
- Intravenous Drug Use-associated nephrotoxicity
- Thrombotic microangiopathy
- Chronic glomerulonephritis

**The patient was diagnosed with advanced HIVAN and IgA nephropathy most likely related to HIV disease per pathology.**



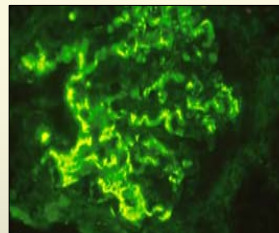
HIV nephropathy. Light microscopy with trichrome staining showing a collapse of the glomerular tuft with segmental glomerular and interstitial sclerosis (bluish staining). The renal tubules are dilated and filled with proteinaceous material.



HIV nephropathy. Light microscopy showing prominent microcystic dilatation of the renal tubules filled with proteinaceous material, which is a finding characteristic of HIV-associated nephropathy but also may be observed in chronic glomerulonephritis.



HIV nephropathy. Electron microscopy showing a segment of the glomerular basement membrane with foot process effacement (black arrow) and prominent tubuloreticular inclusions (red arrow).



IgA nephropathy. Immunofluorescence microscopy demonstrating large mesangial immunoglobulin A (IgA) deposits diagnostic of IgA nephropathy.

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## CONTINUING TREATMENT:

After hospitalization, the patient initiated HAART with boosted atazanavir (300/100mg daily), renal-dose lamivudine (150mg daily), and didanosine (125mg daily). The patient's renal function stabilized and began to gradually improve with immune reconstitution and viral load reduction. He was discharged from nephrology clinic to be followed by his HIV provider.

Date	BUN mg/dL	Creatinine Mg/dL	Hgb. g/dL	Viral load Copies/mL	CD4 /uL
Baseline	47	7.0	7.9	80,952	18
4 Weeks	30	3.0	9.5		
5 Weeks	42	3.1	10.2		
8 Weeks	34	2.5	8.7	436	17
14 Weeks	30	2.4	11.6	1,410	56
18 Weeks	30	2.1		187	113

## DISCUSSION:

HIVAN is the leading cause of chronic kidney disease and ESRD in HIV and the third leading cause of ESRD in African Americans. The vast predominance of cases is seen in African Americans patients (95%). Other risk factors include a low CD4 count and family history of renal disease. Typically, but not always, HIVAN is a late-stage manifestation of HIV with a CD4 <200 (Nuernberger, 2007).

HIV-associated nephropathy (HIVAN), also known as AIDS-associated nephropathy, consists of a pentad of findings, including (1) proteinuria, (2) azotemia, (3) normal-to-large kidneys on ultrasonography, (4) normal pressure, and (5) focal segmental glomerulosclerosis (FSGS) on renal biopsy findings (Salifu, 2007). Renal biopsy is the gold standard for diagnosis. Before the era of HAART, most patients with this diagnosis rapidly went on to develop renal failure and then end stage renal disease. Initiating antiretroviral therapy is the preferred treatment for HIVAN and has improved the prognosis substantially by halting if not reversing renal dysfunction.

IgA nephropathy is characterized by predominant IgA deposition in the glomerular mesangium. Clinical features range from asymptomatic hematuria to rapidly progressive glomerulonephritis (RPGN). The condition can sometimes lead to chronic kidney disease as well. On biopsy, multiple glomerular lesions can be seen, but mesangial proliferation with prominent IgA deposition is almost always observed (Brake, 2007). IgA nephropathy is a noted cause of kidney disease in HIV patients, thought secondary to IgA directed against HIV antigens (Gupta, 2005).

All HIV+ patients should have routine screening for renal disease through urinalysis and chemistry profiles. Many HIV+ patients have multiple co-morbidities that also lead to renal disease such as hypertension, diabetes, and use of potentially nephrotoxic medications. It is important not only to review creatinine and BUN, but also to calculate a glomerular filtration rate via the MDRD equation to detect subtle changes in renal function over time. Noticing these changes may be helpful in determining therapies that are the least nephrotoxic. Providers will also want to pay close attention to the blood pressure of patients with renal decline and consider prescribing agents considered to be renoprotective such as ACE- inhibitors or ARBs.

Renal disease may be multifactorial, especially as drug-toxicities and manifestations of other chronic illnesses play larger roles. It is easy to assume that HIV+ patients in renal failure will have HIVAN, but other etiologies must also be considered as is demonstrated by our case. As this patient presented in renal failure with virtually no medical history and because many of the laboratory test results took several weeks to receive, the list of differential diagnoses was quite extensive. Although the diagnosis was eventually determined to be HIVAN and IgA Nephropathy, recent NSAID use and fever clouded the clinical picture. Another confounding factor was the patient's Hispanic ethnicity which is not typical for patients with HIVAN. Diagnosis of HIVAN ideally should be made by biopsy and not as a default diagnosis.

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