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The HIV-Associated Nephrologist: Advice Straight From the HAART

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EDITORIAL

The HIV-Associated Nephrologist: Advice Straight From the HAART

I saw an HIV-positive patient for proteinuria recently. During the usual history taking, the patient essentially recounted his long sojourn with HIV including an early period of HIV unawareness; ensuing "dark" years when many friends were lost; and hope inspired by long-term survivors, medical progress, and successful drug trials. He was also discouraged by recidivism of unsafe sexual practices that might promote disease dissemination.

Through the patient's recollections came flashbacks of my own *Philadelphia Story.* I remembered my initial patient in 1982, with severe immunocompromise and infection by *Cryptosporidium spp*, before acquired immunodeficiency syndrome (AIDS) had a name including the spread of "the virus" in Philadelphia, New York City, and San Francisco; the grief and despair of families of AIDS victims; and the internecine and often frequently furious debates regarding the feasibility and practicality of treating AIDS patients with renal replacement therapy.

The increasing awareness of HIV through resolute and continual advocacy, safer sex practices, and the respective introductions of antiretroviral agents and drug therapies for infections of immunocompromise altered the course of illness. Indeed, there were some long-term survivors of HIV/AIDS, some from the institution of medical therapy and some for as-yet-undefined reasons (eg, elite nonprogressors). Some patients developed a kidney disorder, AIDS nephropathy, which was later termed HIV-associated nephropathy (HIVAN).

An acquired collapsing glomerulopathy, characterized by a predisposition for African Americans (prevalence: 4%-12% of HIV-infected persons), low CD4+ cell counts, and significant proteinuria, displaced antineutrophil cytoplasmic antibody–associated vasculitis as the du jour glomerulonephritis. Large, hard kidneys with microcystic changes within the tubulointerstitial compartment, tubuloreticular inclusions, and dominating focal, sclerotic lesions became a hallmark of HIVAN, a combined tubulopathy and podocytopathy. With time, HIVAN became just one of the several HIVANs because more histologic patterns of glomerular and tubular disease emerged from this renotropic virion. Notably, by 2020, with the diagnosis of 1,000 or more cases of HIVAN annually, an estimated 10,000 HIV-positive patients will require some form of dialytic treatment (Klotman, *New York Daily News*, July 22, 2009).

During these events, many of us who did not work in cities with high HIV prevalence sat passively on the sidelines until an epiphany took place; long-term HIV/AIDS survivors were now our patients. Suddenly, expertise in HIV/AIDS was required of the contemporary nephrologist, in addition to that which was provided by primary care physicians and infectious disease and HIV specialists. Patients with CKD from HIV are essentially

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unavoidable because of the success of HAART, and those who practice nephrology must have the expertise to assist HIV-positive patients in their quests to maintain function and vitality. Thus, kidney care may be necessary well before the institution of renal replacement therapy. Such care begins with deeper and more broadly based education regarding HIV/AIDS as it pertains to nephrology. Its intersections with multiple other disciplines, in particular, infectious diseases and pharmacology, begs for a timely update.

This issue of *Advances in Chronic Kidney Disease* employs the expertise of its 2 Guest Editors: James Novak and Lynda Szczech. These individuals have assembled a team of authors whose articles provide relevant, up-to-date information regarding how we may best become HIV-aware and -adept nephrologists. So what must we now know?

The genetic predisposition has been mentioned, but now an answer may have been found. The association of the highly penetrant MYH9 gene on chromosome 22 in African Americans with HIVAN is so strong that it cannot be ignored. An abnormality of this gene that encodes a nonskeletal muscle myosin may synergistically augment damage of the HIV-infected kidney and explain in part why acquired collapsing glomerulopathy is a disorder that is nearly seen exclusively in African Americans. However, environmental forces and other host factors (gene-gene interactions) may impart greater risk to susceptible patients and these must be clarified to a greater extent in the future.

If HIVAN occurs and medical therapy is initiated, the nephrologist must be ever vigilant for the metabolic changes that are associated with HAART and the acute and chronic damage that may obtain from them. The nucleoside analog reverse transcription inhibitors zalcitabine (ddC), didanosine (ddI), and stavudine (d4 T) may induce mitochondrial toxicity and lactic acidosis; however, this untoward event may result from other antiviral agents too. Tenofovir may induce a proximal tubular Fanconi syndrome, and ddI and its active form ddA may cause hepatic steatosis. The latter compound is contraindicated in patients infected by hepatitis C virus undergoing treatment with ribavirin because the risk of mitochondrial toxicity increases. In addition, there are other toxicities associated with the treatment of HIV including pancreatitis from didanosine, neuropathy attributable to zalcitabine, and myopathy because of zidovudine.

Despite the myriad complications associated with HIV therapy, emerging data reveal that earlier therapy reduces kidney care by nephrologists, liver, cardiovascular, and tumor-related morbidities. So, HIV-positive patients must be screened for CKD by evaluating estimated glomerular filtration rates and the urine for protein. However, proteinuria is a late biomarker. Hopefully, an earlier one that can complement glomerular filtration rate will soon emerge and provide a monitoring index superior to either alone. Overall, HIV/AIDS patients with CKD, including those requiring renal replacement therapy, are doing better. Greater advances in the prevention and treatment of HIV will be made, but for now, early detection of the HIV-associated nephropathies and their timely treatment by HAART are required.

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Editor