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Case Report

Dual Glomerular Lesion in HIV Patient

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Abstract

HIV-associated nephropathy (HIVAN), the classic kidney disease associated with HIV infection, was first described in 1984 as a complication of AIDS although HIVAN may also occur in patients with less advanced HIV infection or following acute seroconversion Histologically, HIVAN is a collapsing form of focal segmental glomerulosclerosis (FSGS) accompanied by microcystic tubular dilatation and interstitial inflammation. HIV-immune complex kidney disease (HIVICK). Other immune complex diseases may also occur in HIV-infected patients, including IgA nephropathy and postinfectious glomerulonephritis, and are best diagnosed as those specific entities

The pathophysiological mechanism of HIVAN injury is mediated by direct infection of renal epithelial cells by HIV, expression of intrarenal viral genes, and dysregulation of host genes by modulating cell differentiation and the cell cycle. In contrast, kidney disease by HIV immune complexes (HIVICK) involves a different immune mechanism with antibody deposits within glomerular structures. Both entities progressively present different degrees of proteinuria and progressive decrease in the glomerular filtration rate, depending on the commitment or histology suffered by the patient.

In this case reports patient with clinical picture of 3 months of evolution of temporo-spatial disorientation and alteration of the state of consciousness associated with hyperthermia. We perform neuroimaging without alterations, a lumbar punctures performed with evidence of an infectious process by coconuts + in the GRAM of the cerebrospinal fluid , normochromic normocytic anemia and renal failure , sub nephrotic proteinuria, glomerular hematuria, HIV positive, recount of normal CD4, renal biopsy with diagnosis of immune-mediated glomerulonephritis (IgG and C3), in the immunofluorescence (HIVICK) and with membrano pattern proliferative and in two glomeruli focal segmental sclerosis collapsing variant (HIVAN)is observed.

Keywords: Covid-19; acute kidney injury; nephrology

Introduction

Kidney disease is among the leading causes of morbidity and mortality in patients with human immunodeficiency (HIV) [1]. Groups of glomerular diseases that are related to HIV: podocytopathies and those mediated by immune complexes [2].

HIV-associated nephropathy (HIVAN) IS the most frequent podocytopathy and is the most important cause of end- stage renal disease is this population [3], mediated by direct infection of renal epithelial cells by HIV, expression of intrarenal viral genes, and dysregulation of host genes that govern cell differentiation and cell cycle [4].

HIV-immune complex kidney disease (HIVICK) involves a different immune mechanism with antibody deposits within glomerular structures. Both entities lead to proteinuria and progressive decrease in the glomerular filtration rate, although HIV not only has glomerular involvement but also vascular, interstitial involvement, we will focus on glomerular involvemen [5], (SEE TABLE 1)

GLOMERULAR-DOMINANT[a]
A. Podocytopathies (all characterized by extensive foot process effacement)[b] • Classic HIVAN • FSGS (NOS) in the setting of HIV • Minimal change disease in the setting of HIV • Diffuse mesangial hypercellularity in the setting of HIV • Other podocytopathy in the setting of HIV
B. Immune complex-mediated glomerular disease • IgA nephropathy in the setting of HIV • Lupus-like glomerulonephritis in the setting of HIV • Lupus nephritis in the setting of HIV • Membranous nephropathy in the setting of HIV - Indicate whether HBV positive, HCV positive, PLA2R positive (should not preclude workup for other secondary causes) • Membranoproliferative pattern glomerulonephritis in the setting of HIV - Indicate whether HCV positive (should not preclude workup for other secondary causes) • Endocapillary proliferative and exudative glomerulonephritis in the setting of HIV - Post-streptococcal, staphylococcal-associated, other • Fibrillary or immunotactoid glomerulonephritis in the setting of HIV • Other immune complex disease in the setting of HIV
a) Indicates likelihood of HIV casuality **b) Indicates association with APOL1 risk allele genotype.**

Tabla 1: Pathologic classification of HIV-related kidney diseases. Adapte from KDIGO

In this paper we report a case of a Latino patient with HIV had immune-complex mediated glomerular disease (HIVICK) plus a collapsing glomerulopathy (HIVAN) with normal CD4 cell count.

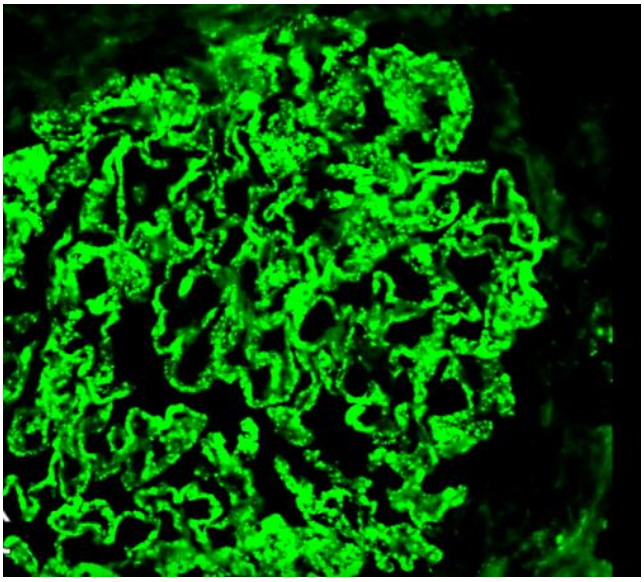

Figure 1: *Global IgG immunofluorescence in capillary Walls and discontinues mesangial*

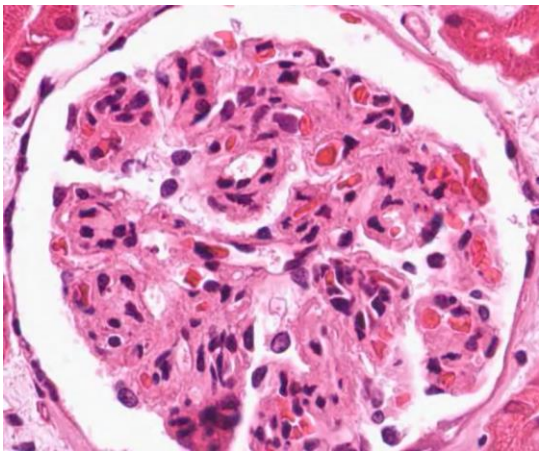

Figure 2: *PAS staining: Mesangial and endothelial hypercellularity. Mesangial expansión and mesangial nodule*

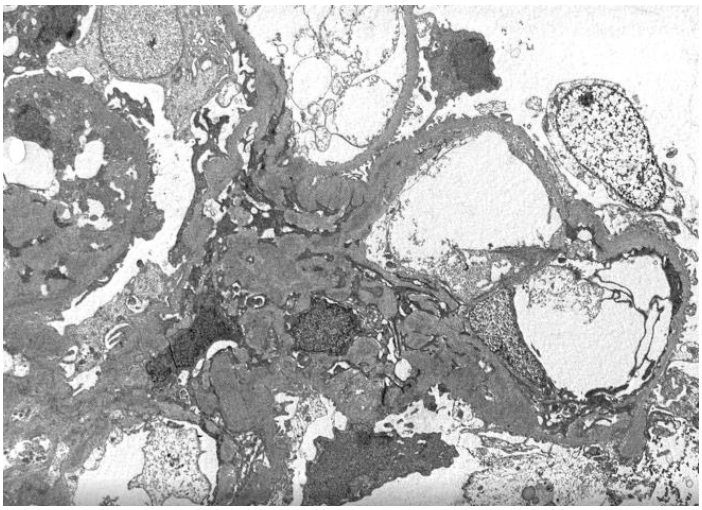

Figure 3: *Electron microscopy (Ultrastructure) permeable capillary lights, thickening of the peripheric capillary walls, mesangial expansion with electrodense accumulations compatible with immune deposits are observed.*

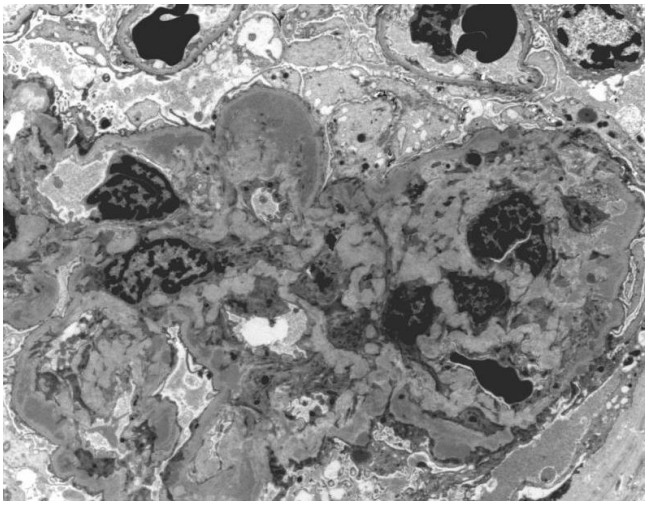

Figure 4: *Electron microscopy that shows collapse of capillary loops, podocyte damage, and swelling of cytoplasmic, loss of podocyte extensions*

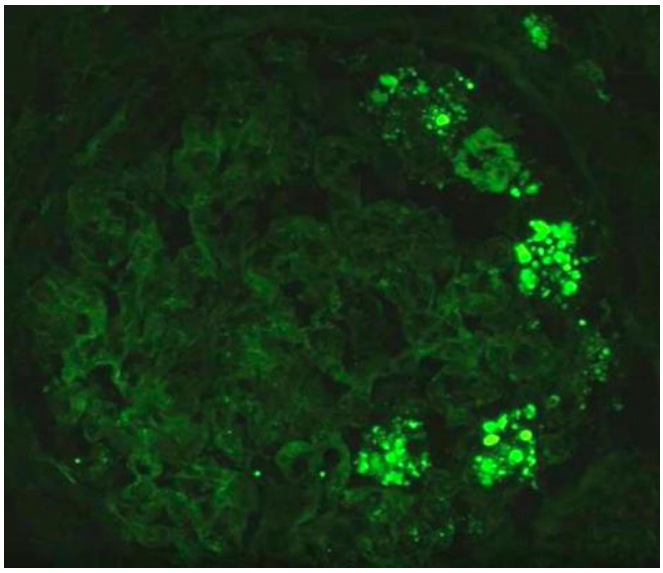

Figure 5: *Immunofluorescence with evidence of protein resorption granules in epithelial cells.*

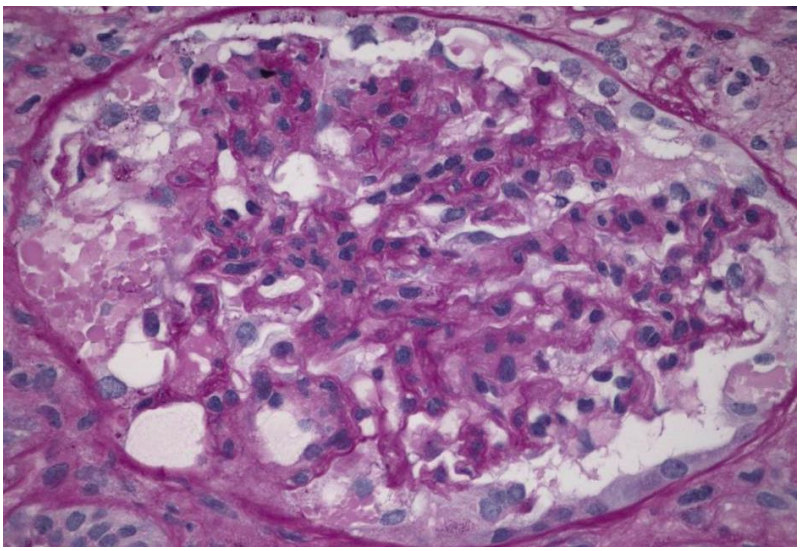

Figure 6: *PAS Technique: segmental collapse of capillary loops, hypertrophy of epithelial cells, vacuolization and granules of protein reabsorption.*

Case Presentation

It presents in the emergency department male of 72 years with behavioral alterations of 3 months of evolution, associated with hyperthermia in the last week. On physical examination he with PA 150/100 mmHg, neurologically responds to simple commands, and has disorientation in time and space. In the laboratory with Hematocrit 27%, Hemoglobin 8.7 mg/dl, white blood cells 6370 cel/ul (CD4 795 cel/ul), platelets 222000 cel /ul, ureic nitrogen 57 mg /dl, creatinine 2.03 md /dl. A simple brain CT scan is performed without alterations and lumbar puncture with normal opening pressure, cerebrospinal fluid with 120 cells/ul (70% monocities'), glucose 48 mg/dl, (glycemia 124 mg/dl) , proteins 40 mg/dl, gram with coconuts (+) , HIV rapid test (+), viral load 69,780 copies 8log 4.8), urinary sediment with density 1012mOsm/L, Ph 5, proteinuria 4+, 30-40 dysmorphic red blood cells (> 5%acontocytes). He was admitted to the ICU with septic shock due to meningeal and respiratory focus. Initiates dialysis and antimicrobial coverage with ceftriaxone, vancomycin, acyclovir and TMS/SMX. Proteinuria of 24 hrs. of 2.7 gr, albuminemia 3,03 gr/ml, HCV (-), HBV (-), VDRL (-), igG toxoplasmosis (+), Chagas IFI/HAI (-), C3 52 mg/dl, C4 16 mg/dl, abdominal ultrasound and fundus without pathological findings. Renal biopsy puncture with diagnosis of active GN mediated by antibodies with IgG, IgM and C3 in immunofluorescence and membranoproliferative pattern. Two glomeruli with focal and segmental sclerosis with collapsing features and microcysts at the tubular level (2/11). Acute, moderate interstitial nephritis.

An infrequent case of two histopathological patterns of glomerulopathies in relation to HIV simultaneously is presented in the context of a patient with a recent diagnosis of retrovirus infection and normal CD4 count. In the world literature there are few reported cases of both histopathological findings together and with the characteristics of infect-immunological profile presented in our case.

Human immunodeficiency virus HIV infection is associated with acute kidney injury AKI and chronic kidney disease CKD. HIV-associated nephropathy HIVAN [6], is the classic kidney disease associated with HIV infection, was first described in 1984 as a complication of AIDS , although HIVAN can also in acute seroconversion.

Histologically, HIVAN is a clinical form of the collapsing variant of focal and segmental glomerulosclerosis FSGS, accompanied by microcytic tubular dilation and interstitial inflammation. Antiretroviral treatments ART have transformed the spectrum of HIV-related kidney disease. Disease different or related to the chronicity of the patient such as arterial hypertension, diabetic nephropathy and various glomerulonephritis mediated by immunocomplexes. Patients with HIVAN typically present with severe nephrotic syndrome associated or not with renal failure. Marked hypoalbuminemia, peripheral edema and hypertension are often marked, and very rapid progression to end –stage renal disease (CKD.) Most patients are characterized by reduced renal function

Associated with proteinuria in the nephrotic range > 1 gr /m2 / d y or > 40 mg / m2/ hour[7].

The spectrum of renal pathology in HIV- positive individuals ranges from lesions directly related to intrarenal HIV gene expression to lesions related to their comorbidities, drug effects, immune dysregulation and confections, which is why renal biopsy discriminates between these lesions.

Hivan Clasico

HIV-1-associated nephropathy (HIVAN) is clinical disease similar to focal and segmentary glomerulopathy with variant collapsing and concomitant tubule-interstitial disease. In 2004 [8-9-10], Columbia classification of FSGS revised the histological definition of collapsing glomerulopathy. The new definition required the collapse of at least one capillary loop, with obliteration of light, into a glomerulus, in addition to hypertrophic or hyperplastic podocytes lining collapsed capillaries , regardless of the presence of other variants of FSGS or tubule – interstitial lesions, including the formation of tubular microcysts, interstitial inflammation, and tubular injury. Glomerular "collapsing" is defined as at least one glomerulus with collapse of the glomerular, basement membranes accompanied by hypertrophy and hyperplasia of the ad recumbent glomerular epithelial cells. These hyperplastic cells occupy space and produce kidney damage [11]

Electronic microscope, shows edema with diffuse swelling (effacement) of pedicels and endothelial tubule reticular inclusions are classic features. the immunofluorescence, with staining for IgM, C3 and C1q in collapsed segments and mesangial areas. Protein reabsorption droplets can stain in the presence of albumin and immunoglobulins. In the later stages, the sclerotic areas retract into a solid and compact sphere, covered by a monolayer of epithelium; This has been described as resembling a "fetal glomerulus [12]". Phenotypic studies suggest that the monolayer of glomerular epithelial cells is composed of parietal epithelial cells. In some cases, sequential biopsy and post-mortem studies have shown an evolution from collapsing glomerulopathy to FSGS (NOS).

Tubule- interstitial disease is invariable component of HIVAN and often appears out of proportion to glomerular disease causing kidney enlargement and hyperechoic appearance by ultrasound. Tubular "microcysts are dilated tubules (at least 3 times larger than normal) they contain glassy protein cylinders and are lined by simplified epithelium. Tubular microcysts are easily distinguished from tubular "Thyroidization "based on their larger diameter, irregular size and absence of tubular atrophy or colloid-type cylinders [13]. Microcysts can affect all tubular segments and intracellular viral trans critical expression has been demonstrated [14]. Prominent interstitial inflammation and degenerative and regenerative tubular changes may also occur. Interstitial edema in the acute phase is followed by fibrosis and tubular atrophy. Finally, the discovery of two coding variants of the APOL-1 gene, called G1 and G2, may increase the risk of untreated HIV- infected people developing HIVAN by about 50% [15-16]

Hivan Treatment

Treatment of HIVAN includes anti-retroviral therapy (ARTV), inhibitors of the renin system-angiotensin-aldosterone, angiotensin receptor antagonist (ACE inhibitors and ARBs 2) and corticosteroids.

Patients with HIVAN who are not receiving ART recommended to start ART, in accordance with the guidelines and recommendations of the United States Health and Human Services [17].

Proteinuria and/or hypertensive patients with HIVAN, treatment with ACE inhibitors and/or ARBs 2 is recommended [18].

Inpatients with HIVAN the use of corticosteroids is not of routine use, however, some experts use corticosteroid therapy in rapidly progressive kidney disease despite management with ARTV and inhibitors of the renin system-angiotensin-aldosterone, interpreting that the pathophysiological compromise has the same substrate, regardless of whether the patient is HIV positive or not [19].

Evaluation of other treatment strategies for kidney disease in the context of HIV has been limited to small, unicentric, short-term studies, and most often focusing on HIVAN. No rigorous studies have evaluated the efficacy of blood pressure control, diabetes treatment, or renin-angiotensin-aldosterone system inhibitors in slowing the progression of CKD in people with HIV. However, it is reasonable to extrapolate from the strong evidence supporting the efficacy of these interventions in the general population [20].

Treatment of HBV, HCV and tuberculosis co-infections should be considered on the basis of existing treatment guidelines for each infection presented [21-22].

Kidney replacement therapy (RRT) in HIV-positive people

With ARTV, the survival of HIV-positive people receiving RRT is comparable to that of their HIV-negative counterparts. Therefore, HIV serological status should not influence the candidacy for initiation of RRT. Observational studies demonstrate similar results between hemodialysis (HD) and peritoneal dialysis (PD) among patients treated with ARTV. The selection of the individual by the RRT modality depends on patient preference and regional resources [23-24]. Arteriovenous fistulae are the preferred vascular access, as arteriovenous grafts and catheters are associated with an increased risk of infection and thrombosis [25]. In patients in hemodialysis units, the reuse of the dialyzer for the same patient is practiced in resource-limited settings as a cost-saving alternative, except in those with hepatitis B virus infection.

Kidney transplant in HIV-positive people

Kidney transplantation in HIV-positive recipients is associated with excellent 1- and 3- year recipient and allograft survival rates, rates intermediate to those seen in the general kidney transplant population in the U.S. As well as a subgroup of higher-risk recipients over the age of 65 [26]. Data from the registry also suggest good outcomes at 5 and 10 years, with an improvement in survival compared to patients who remain on the waiting list. Studies in other settings have confirmed the safety of kidney transplantation in people with well-controlled HIV. Eligible patients with advanced CKD and well-controlled HIV infection should be referred for kidney transplant evaluation.

Immunosuppression protocols for the general population can be applied to HIV-positive people. In view of the increased immune risk, some centers prefer induction therapy with an interleukin-2 receptor antagonist, polyclonal ant thymocyte globulin, or alemtuzumab. Tacrolimus is the calcineurin inhibitor of choice for maintenance immunosuppression.

Existing guidelines for prophylaxis against opportunistic infections and management of hepatitis co-infection should be followed. Recipients co-infected with HCV have worse outcomes compared to recipient's whit HIV or HCV infection, but are still superior to those who remain in the waiting list. Clinicians should be aware of the significant drug interaction between immunosuppressive agents, ARTV, and antiviral drugs for HCV co-infection. To minimize drug interactions and achieve steady-state drug levels, integrase inhibitors and nucleoside analog reverse transcriptase inhibitors are the preferred antiretroviral agents, while protease inhibitors and the pharmacological enhancers ritonavir and cobicistat are avoided. Given the complexity of the problems, a multidisciplinary team, it is essential to have experts in transplant nephrology, infectious diseases and clinical pharmacology [27].

Conclusion

HIVAN/HIVICK are the most frequent forms of kidney disease directly related to HIV infection, HIVAN usually occurs in patients with advanced disease with low CD4 count, with massive proteinuria and progressive renal failure, and HIVICK are several the spectrum of diseases associated with immune complexes such as membranous nephropathy , glomerulus nephritis with proliferative membrane pattern, in this patient had coexistence of dual glomerular lesion, it is an infrequent case of two histopathological patterns of glomerulopathies in relation to HIV simultaneously in the context of a patient with recent diagnosis of retrovirus infection and normal CD4 count. In the world literature there are few reported cases of both histopathological findings together and with the characteristics of infect-immunological profile presented in our case

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