

A patient with 2 presentations of membranoproliferative glomerulonephritis by HCV and Leishmania infestation

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ABSTRACT

We present the clinical case of a patient with HIV coinfecting with HCV and Leishmania who has 2 glomerular lesions at different times of different presentation. First lesion, cryoglobulinemic glomerulonephritis. The second lesion, proliferative membranous glomerulonephritis due to Leishmania infestation.

HIV infection increases the risk of kidney disease related to opportunistic infections and coinfection with hepatitis B or C virus. Renal damage can have different presentation and in different structures. The etiological treatment is important although immunosuppressive treatment is sometimes necessary when a disproportionate immune response is triggered.

Keywords: Membranoproliferative glomerulonephritis. Cryoglobulinemia. HCV. Leishmania.

Un paciente con 2 presentaciones de glomerulonefritis membranoproliferativa por VHC e infestación por Leishmania

Presentamos el caso clínico de un paciente con VIH coinfectado con VHC y Leishmania que tiene 2 lesiones glomerulares en diferentes momentos de presentación. La primera lesión, glomerulonefritis crioglobulinémica. La segunda lesión, glomerulonefritis membranosa proliferativa a causa de la infestación por Leishmania.

La infección por VIH aumenta el riesgo de enfermedad renal relacionada con infecciones oportunistas y la coinfección con el virus de la hepatitis B o C. La lesión renal puede tener diferente presentación y en diferentes estructuras. El tratamiento etiológico es importante, aunque a veces es necesario un tratamiento inmunosupresor cuando se desencadena una respuesta inmunológica desproporcionada.

Palabras clave: Glomerulonefritis membranoproliferativa. Crioglobulinemia. VHC. Leishmania.

INTRODUCTION

Patients with HIV have increased risk for both acute kidney injury (AKI) and chronic kidney disease (CKD) secondary to medication nephrotoxicity¹, HIV-associated nephropathy (HIVAN)²⁻⁵, and immune complex kidney diseases⁵⁻⁹. In addition, the aging

cohort of HIV-positive patients is at increased risk for kidney disease related to opportunistic infections and hepatitis B (HBV) or C virus co-infection (HCV)^{5,9,10}.

CASE REPORT

We present the case of a 50-year-old patient with antecedents of HIV, HCV and visceral Leishmania. Get treatment for HIV with ritonavir, darunavir and maraviroc; achieving virological suppression but without immunological recovery. He did not receive treatment for HCV. The Leishmania was treated.

He goes to the emergency room for anasarca, polyarthralgia, hypertension, dyspnea, hepatosplenomegaly and foamy urine.

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The complementary tests include proteinuria in the nephrotic range (9.5 g/24 h), glomerular hematuria, consumption of complement factors, hypergammaglobulinemia, and cryoglobulins in 25%. HCV viral load exceeds 5,000,000 copies and undetectable HIV.

Renal biopsy showed cryoglobulinemic glomerulonephritis with exudative focus and diffuse fibrinoid necrosis (fig. 1).

We decided to start treatment for HCV with daclastavir and sofosbuvir associated with rituximab plus prednisone. Three months later he presented proteinuria of 1.73 g/24 h, complement factors in the normal range and viral load of HIV/HCV undetectable.

One year later, in routine controls, he presents with foamy urine and hepatosplenomegaly. The complementary tests showed proteinuria in the nephrotic range (7.31 g/24 h), pancytopenia and hypergammaglobulinemia. Viral load of HIV/HCV was undetectable. Other negative autoimmunity tests, cryoglobulins in 2% and complement factors were in normal range.

The renal biopsy was repeated due to the evident analytical and clinical differences with the previous event. He showed proliferative membranous glomerulonephritis and mesangial deposits of C3+++ , C1q+++ , C4d+++ , IgM++ , Kappa++ and Lambda++ . Infestation by *Leishmania* was observed (fig. 2).

The treatment of visceral leishmaniasis intensified liposomal amphotericin B and miltefosine.

After 6 months of control, he had a sustained impaired glomerular filtration rate and proteinuria of 1.0 g/24 h.

DISCUSSION AND CONCLUSION

Incidence of AKI in HIV-positive patients is higher than in patients without HIV. The etiology of CKD in patients with HIV varies from HIV-independent factors (such as hypertension, diabetes, and incomplete recovery from an episode of AKI) to HIV-related disorders (such as HIVAN and HIV immune complex kidney disease [HIVICK]). In addition, some risk factors are specific to HIV as the increased risk of kidney disease related to opportunistic infections and coinfection with hepatitis B or C viruses¹¹⁻¹³.

Our case is about an HIV patient with double glomerular injury by 2 different entities. The first episode was related to HCV infection and the second episode was related to *Leishmania* infestation. Although both episodes have the same glomerular lesions, the clinical and analytical presentations are quite different. In mixed cryoglobulinemia syndrome, kidney injury occurs in 20 to 60 percent of patients, typically as glomerulonephritis, and is seen more often 2 to 3 years after the first onset of this syndrome¹⁰. Mixed cryoglobulinemia syndrome is etiologically most often related to chronic HCV infection. It is much less frequently associated with hepatitis B virus (HBV), human immunodeficiency virus (HIV), or Epstein-Barr infection^{14,15}. Although it is very unfrequent, mixed cryoglobulinemia syndrome and *Leishmania*-induced MPGN cases have been described¹⁶.

Histological kidney examination reveals membranoproliferative glomerular changes in over 80 percent of patients, with both thickening of basement membrane and cellular proliferation, including a far greater influx of circulating macrophages than in other forms of proliferative glomerulonephritis¹⁷.

The general therapeutic approach in patients with mixed cryoglobulinemia syndrome includes 2 broad principles: initial im-

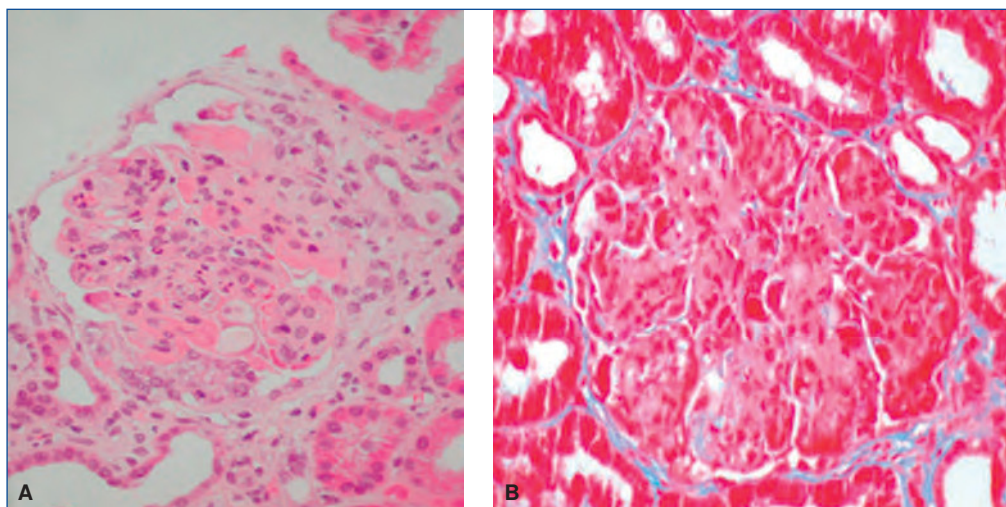


Figure 1. A) Hematoxylin-eosin stain. Glomeruli with mesangial lobulation and increase of mesangial cellularity in a global and intracapillary way. Inflammatory cells and polymorphonuclear neutrophils, with formation of exudative inflammatory foci and fibrinoid necrosis. The capillary lights are occluded by the presence of hyaline thrombi. B) Masson's Trichrome stain. Glomerulus with capillary lights occluded by hyaline thrombi.

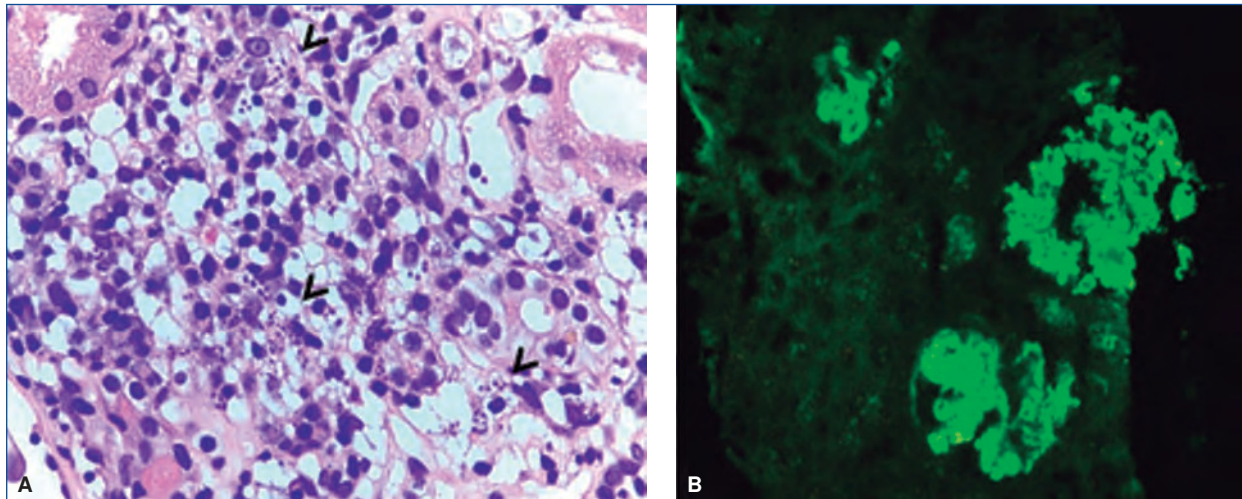


Figure 2. A) Hematoxylin-eosin stain. Leishmania (black arrow) and inflammatory cells. B) Immunofluorescence. Mesangial and capillary deposits of C3⁺⁺⁺, C1q⁺⁺⁺, C4d⁺⁺⁺, IgM⁺⁺, Kappa⁺⁺ and Lambda⁺⁺.

munosuppressive therapy usually combines a short course of glucocorticoids with either rituximab or cyclophosphamide and—in some patients— plasmapheresis and specific therapy of underlying disease^{18,19}.

The second presentation of MPGN, due to infestation by Leishmania, highlights hepatosplenomegaly without anasarca and proteinuria in the nephrotic range, without consumption of serum complement factors. We know that failure of treatment with visceral leishmaniasis or recurrence is common in patients with HIV infection, particularly in patients with CD4 counts below 200 cells/ml, as occurred in our patient¹⁰.

Direct injury to the interstitial parenchyma due to Leishmania spp has been reported²⁰. Rarely, chronic leishmaniasis may even be associated with renal AA amyloidosis²¹. With respect to glo-

merulonephritis, leishmaniasis causes a glomerulonephritis mediated by an immune complex with a pattern of MPGN. Glomerulonephritis mediated by the immune complex of cryoglobulin has also been reported in the context of leishmaniasis¹⁶. There are very few cases reported with direct glomerular damage as our case.

Statement of ethics

The present study adhered to the Declaration of Helsinki and the patient gave his consent for the details of his case to be published.

Disclosure statement

The authors have no conflicts of interest to declare.

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