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

Fabrizzio Humberto Poma Saavedra, Sergio Bea Granell, Luis Carlos López Romero, Paula Aledón Viñes, Maria Peris Fernández, July Vanesa Osma Capera, Ruxandra Boteanu, Pablo González-Calero Borrás, Andrea Sofía Álvarez Muñoz, Julio Hernández Jaras

Clinical Nephrology Department. Hospital Universitario y Politécnico de La Fe. Valencia

NefroPlus 2020;12(1):66-69

ABSTRACT

We present the clinical case of a patient with HIV coinfected 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 nephrotoxicity[1], HIV-associated nephropathy (HIVAN)[2-5], and immune complex kidney diseases[5-9]. 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].

Corresponding: Fabrizzio Humberto Poma Saavedra
Clinical Nephrology Department.
Hospital Universitario y Politécnico de La Fe.
Avinguda de Fernando Abril Martorell, 106, 46026 Valencia.
fabrizzio48@hotmail.com

Revisión por expertos bajo la responsabilidad de la Sociedad Española de Nefrología.

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.

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 viruses[11-13].

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 syndrome[10]. 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 described[16].

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 glomerulonephritis[17].

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

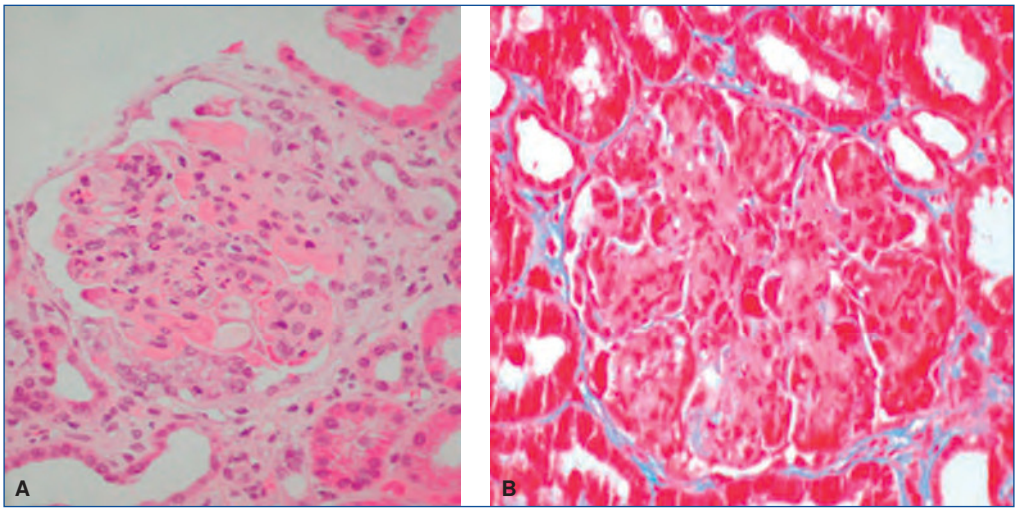

Figure 1. A) Hematoxylin-eosin stain. Glomeruli with mesangial lobulation and increase of mesangial cellularity in a global and intracapillary way. Inflammatory cells and polymorphonuclear neutrophils, with formation of exudative inflammatory foci and fibrinoid necrosis. The capillary lights are occluded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

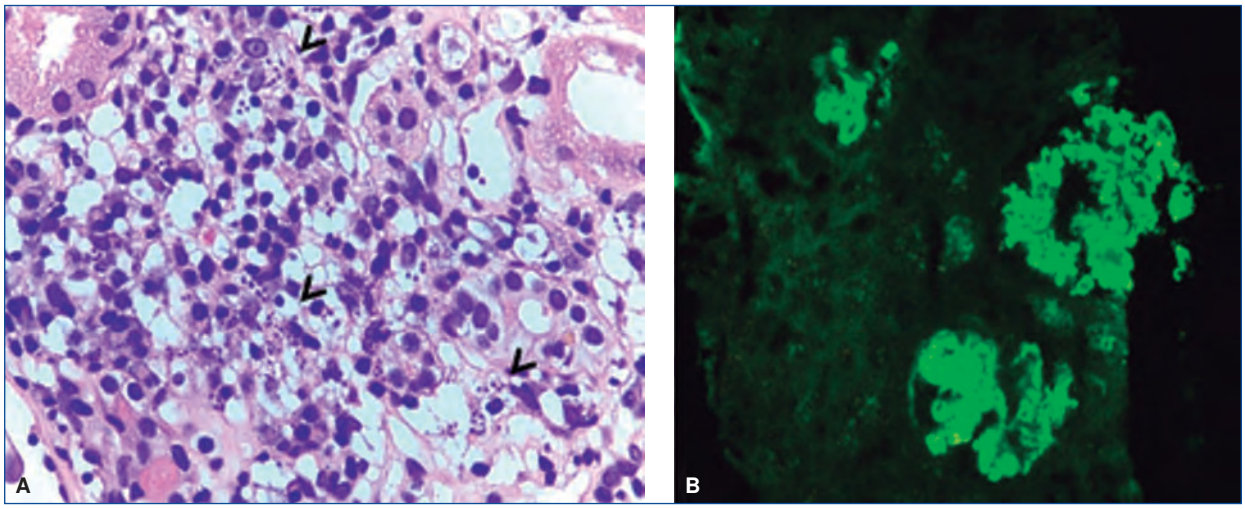

Figure 2. A) Hematoxylin-eosin stain. Leishmania (black arrow) and inflammatory cells. B) Immunofluorescence. Mesangial and capillary deposits of C3+++, C1q+++, C4d+++, IgM++, Kappa++ and Lambda++.

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 patient[10].

Direct injury to the interstitial parenchyma due to Leishmania spp has been reported[20]. Rarely, chronic leishmaniasis may even be associated with renal AA amyloidosis[21]. With respect to glomerulonephritis, 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 leishmaniasis[16]. 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.

REFERENCES

1. Gardenswartz MH, Lerner CW, Seligson GR, Zabetakis PM, Rotterdam H, Tapper ML, et al. Renal disease in patients with AIDS: a clinicopathologic study. Clin Nephrol. 1984;21:197.
2. Pardo V, Aldana M, Colton RM, Fischl MA, Jaffe D, Moskowitz L, et al. Glomerular lesions in the acquired immunodeficiency syndrome. Ann Intern Med. 1984;101:429.
3. Rao TK, Filippone EJ, Nicastri AD, Landesman SH, Frank E, Chen CK, et al. Associated focal and segmental glomerulosclerosis in the acquired immunodeficiency syndrome. N Engl J Med. 1984;310:669.
4. D'Agati V, Appel GB. Renal pathology of human immunodeficiency virus infection. Semin Nephrol. 1998;18:406.
5. Casanova S, Mazzucco G, Barbiano di Belgiojoso G, Motta M, Boldorini R, Genderini A, et al. Pattern of glomerular involvement in human immunodeficiency virus-infected patients: an Italian study. Am J Kidney Dis. 1995;26:446.
6. Kimmel PL, Phillips TM, Ferreira-Centeno A, Farkas-Szallasi T, Abraham AA, Garrett CT. HIV-associated immune-mediated renal disease. Kidney Int. 1993;44:1327.
7. Balow JE. Nephropathy in the context of HIV infection. Kidney Int. 2005;67:1632.
8. Kimmel PL, Phillips TM, Ferreira-Centeno A, Farkas-Szallasi T, Abraham AA, Garrett CT. Brief report: idiotypic IgA nephropathy in patients with human immunodeficiency virus infection. N Engl J Med. 1992;327:702.
9. Lai KN, Li PK, Lui SF, Au TC, Tam JS, Tong KL, et al. Membranous nephropathy related to hepatitis B virus in adults. N Engl J Med. 1991;324:1457.
10. World Health Organization. Report of the Fifth Consultative Meeting on Leishmania/HIV Coinfection. Geneva, Switzerland: World Health Organization Press; 2007.

11. Roccatello D, Fornasieri A, Giachino O, Rossi D, Beltrame A, Banfi G, et al. Multicenter study on hepatitis C virus-related cryoglobulinemic glomerulonephritis. Am J Kidney Dis. 2007;49:69.
12. Lunel F, Musset L, Cacoub P, Frangeul L, Cresta P, Perrin M, et al. Cryoglobulinemia in chronic liver diseases: role of hepatitis C virus and liver damage. Gastroenterology. 1994;106:1291.
13. Dimitrakopoulos AN, Kordossis T, Hatzakis A, Moutsopoulos HM. Mixed cryoglobulinemia in HIV-1 infection: the role of HIV-1. Ann Intern Med. 1999;130:226.
14. Franceschini N, Napravnik S, Eron JJ Jr, Szczech LA, Finn WF. Incidence and etiology of acute renal failure among ambulatory HIV-infected patients. Kidney Int. 2005;67:1526.
15. Roe J, Campbell LJ, Ibrahim F, Hendry BM, Post FA. HIV care and the incidence of acute renal failure. Clin Infect Dis. 2008;47:242.
16. Ortiz M, Mon C, Herrero J, Oliet A, Rodríguez I, Ortega O, et al. Glomerulonephritis and cryoglobulinemia: first manifestation of visceral leishmaniasis. Clin Nephrol. 2015;83:370-7.
17. D'Amico G, Colasanti G, Ferrario F, Sinico RA. Renal involvement in essential mixed cryoglobulinemia. Kidney Int. 1989;35:1004.
18. Pietrogrande M, De Vita S, Zignego AL, Pioltelli P, Sansonno D, Sollima S, et al. Recommendations for the management of mixed cryoglobulinemia syndrome in hepatitis C virus-infected patients. Autoimmun Rev. 2011;10:444.
19. Mukhtyar C, Guillevin L, Cid MC, Dasgupta B, de Groot K, Gross W, et al. EULAR recommendations for the management of primary small and medium vessel vasculitis. Ann Rheum Dis. 2009;68:310.
20. Dettwiler S, McKee T, Hadaya K, Chappuis F, van Delden C, Moll S. Visceral leishmaniasis in a kidney transplant recipient: parasitic interstitial nephritis, a cause of renal dysfunction. Am J Transplant. 2010;10:1486-9.
21. de Vallière S, Mary C, Joneberg JE, Rotman S, Bullani R, Greub G, et al. AA-amyloidosis caused by visceral leishmaniasis in a human immunodeficiency virus-infected patient. Am J Trop Med Hyg. 2009;81:209-12.