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Diffuse Proliferative Exudative Glomerulonephritis in HIV and Syphilis Coinfection: A Case Report

Glomerulonefritis Proliferativa Difusa Exudativa en la Coinfección por VIH y Sífilis: Reporte de un Caso

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RESUMEN

El virus de la inmunodeficiencia humana (VIH) y la sífilis pueden causar compromiso renal de manera independiente; sin embargo, su coexistencia rara vez resulta en glomerulonefritis proliferativa difusa exudativa (GN). El manejo de la GN mediada por complejos inmunes en pacientes infectados por VIH sigue siendo un desafío, particularmente en lo que respecta al uso de terapia inmunosupresora. Se presenta un varón turco de 20 años con coinfección VIH–sífilis que consultó por proteinuria en rango nefrótico (6,5 g/día) e hipoalbuminemia (2,1 g/dL). La biopsia renal reveló hipercelularidad endocapilar difusa con infiltración neutrofílica y depósitos de complejos inmunes de IgG, IgA, C3 y C1q. El paciente fue tratado con penicilina benzatina y terapia antirretroviral, seguido de tacrolimus y prednisona tras la eliminación del citomegalovirus. Bajo un tratamiento combinado antimicrobiano, antirretroviral e inmunosupresor cuidadosamente monitorizado, la proteinuria disminuyó a 1 g/día, la albúmina sérica se normalizó y la función renal se estabilizó. El ARN del VIH se volvió indetectable y el recuento de CD4 aumentó significativamente, lo que sugiere un control viral eficaz sin comprometer la recuperación renal. Este caso resalta la importancia de la biopsia renal en pacientes con VIH que presentan síndrome nefrótico. En casos seleccionados, la inmunosupresión adyuvante puede considerarse una opción terapéutica viable cuando se combina con un control infeccioso eficaz y un seguimiento estrecho.

Palabras Clave: Glomerulonefritis proliferativa difusa exudativa; VIH; Sífilis; Tacrolimus.

ABSTRACT

Human immunodeficiency virus (HIV) and syphilis can independently cause renal involvement; however, their coexistence rarely results in diffuse proliferative exudative glomerulonephritis (GN). The management of immune complex–mediated GN in HIV-infected patients remains challenging, particularly regarding the role of immunosuppressive therapy. We report a 20-year-old Turkish male with HIV–syphilis co-infection who presented with nephrotic-range proteinuria (6.5 g/day) and hypoalbuminemia (2.1 g/dL). Kidney biopsy revealed diffuse endocapillary hypercellularity with neutrophilic infiltration and immune complex

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deposition of IgG, IgA, C3, and C1q. The patient was treated with benzathine penicillin and antiretroviral therapy, followed by tacrolimus and prednisolone after cytomegalovirus clearance. Under combined antimicrobial, antiretroviral, and carefully monitored immunosuppressive therapy, proteinuria decreased to 1 g/day, serum albumin normalized, and renal function stabilized. HIV RNA became undetectable, and CD4 count increased significantly, suggesting effective viral control without compromising renal recovery. This case underscores the importance of kidney biopsy in HIV-infected patients presenting with nephrotic syndrome. In selected cases, adjunct immunosuppression may be considered a viable therapeutic option when combined with effective infection control and close monitoring.

Keywords: Diffuse proliferative exudative glomerulonephritis; HIV; Syphilis; Tacrolimus.

INTRODUCTION

Human immunodeficiency virus (HIV) infection is associated with a wide spectrum of renal manifestations, most commonly focal segmental glomerulosclerosis and HIV-associated nephropathy (HIVAN) [(1)]. Immune complex–mediated lesions, including membranous nephropathy and, less frequently, proliferative glomerulonephritides, have also been described [(1)]. Syphilis, caused by *Treponema pallidum*, is another chronic infection capable of renal involvement, most typically presenting as membranous nephropathy with nephrotic syndrome [(2)]. The coexistence of HIV and syphilis leading to diffuse proliferative exudative glomerulonephritis (GN) is exceedingly uncommon. While membranous patterns have been reported in syphilis, proliferative and exudative lesions are only sporadically documented in HIV-infected patients, and their overlap remains poorly understood [(3)].

Here, we report a case of HIV–syphilis co-infection complicated by nephrotic syndrome, in which kidney biopsy revealed diffuse proliferative exudative GN. The patient responded favorably to combined antiretroviral therapy and immunosuppressive treatment. This case emphasizes the need to consider atypical renal histopathology in HIV–syphilis co-infection and suggests that, under close monitoring, adjunct immunosuppression may be a reasonable option.

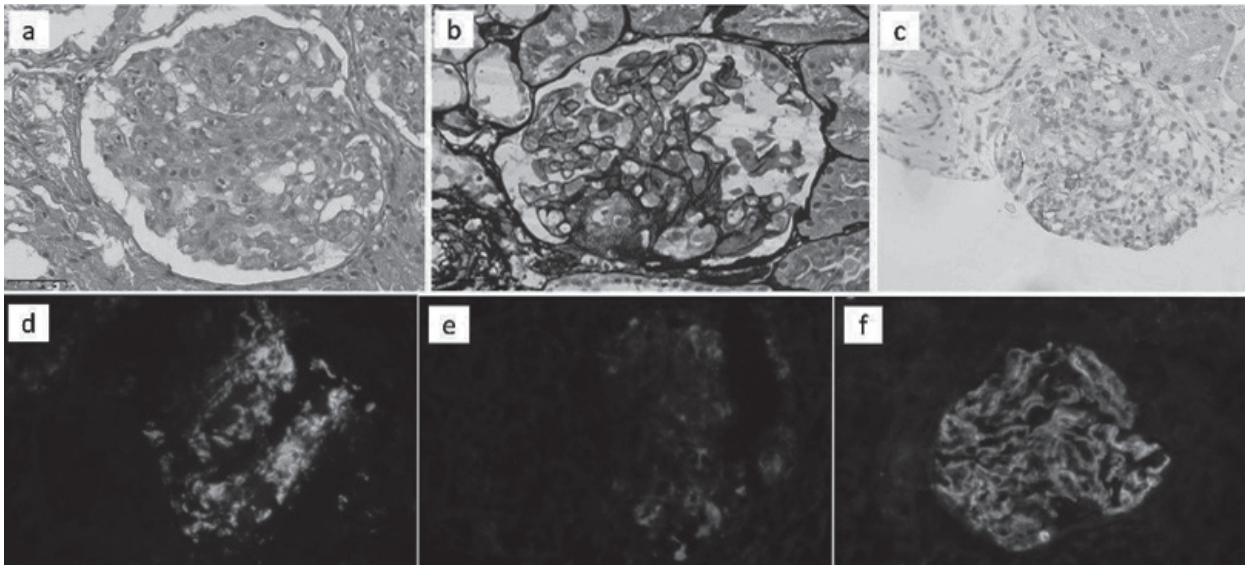
CASE PRESENTATION

A 20-year-old Turkish male hotel worker presented with a 6-month history of recurrent joint pain, nausea, and vomiting, leading to multiple emergency department visits. On October 18, 2024, dermatologic examination revealed widespread, non-scaly, violaceous patches on the extremities, and skin biopsy was consistent with granuloma annulare. On October 26, 2024, he was admitted with repeated vomiting, hematemesis, and abdominal pain. Abdominal computed tomography demonstrated jejunal intussusception and diffuse duodenal wall thickening, suggestive of an infectious or inflammatory process. On October 27, 2024, diagnostic laparotomy revealed serohemorrhagic ascites, microhemorrhagic changes in the colon and small bowel, and multiple intra-abdominal adhesions. Postoperatively, the patient disclosed a history of unprotected sexual contact nine months earlier. Serologic testing confirmed HIV infection (HIV RNA >1,000,000 copies/mL; CD4 count 343/μL) and positive syphilis serology (RPR/VDRL 1:16). He received intramuscular benzathine penicillin. During hospitalization, he developed bilateral upper-extremity thrombophlebitis and deep vein thrombosis, treated with low-molecular-weight heparin and antibiotics.

Three weeks later, on November 21, 2024, nephrology consultation was requested for nephrotic-range proteinuria (6.5 g/day) and hypoalbuminemia (2.1 g/dL). Renal ultrasound performed the same day showed normal-sized kidneys with mildly increased cortical echogenicity and slight urothelial thickening. Kidney biopsy on November 26, 2024 contained 51 glomeruli, none showing global or segmental sclerosis. Light microscopy **(Figure 1)** demonstrated diffuse endocapillary hypercellularity with neutrophilic and mononuclear infiltration, leukocytoclasia, and endothelial proliferation, leading to narrowing or occasional occlusion of capillary lumina. Tubulointerstitial structures were preserved, and Congo red and crystal violet staining excluded

amyloidosis. Immunofluorescence revealed diffuse granular capillary wall staining for IgG, IgA, C3, C1q, κ, and λ light chains, with occasional segmental C4d positivity **(Figure 1c),** consistent with diffuse proliferative exudative glomerulonephritis.

Figure 1: A, B) All glomeruli have a diffuse proliferative pattern with endocapillary polymorphonuclear inflammatory cells in the kidney biopsy (x400, H&E and methenamine silver). C) Focal and segmental staining with C4d (x400). D, E, F) Immunofluorescent for IgA, C1q, and Kappa, respectively (x400)



The patient was discharged on November 27, 2024 on a bictegravir/emtricitabine/tenofovir regimen. During follow-up, he was rehospitalized on the same day for hypervolemia and treated with diuretics. On day 2 of this admission (November 28, 2024), hematochezia and abdominal pain developed; CMV viremia was detected and treated with a one-month course of valganciclovir. Despite therapy, proteinuria increased to 20 g/day and serum albumin dropped to 1.9 g/dL.

After CMV clearance and appropriate vaccination in January 2025, tacrolimus (1 mg AM, 0.5 mg PM) and prednisolone (20 mg/day) were initiated, together with candesartan and furosemide. Tacrolimus trough levels were targeted at 4–7 ng/mL, and therapeutic drug monitoring confirmed that the patient's concentrations remained within this range. Under this regimen, HIV RNA became undetectable, CD4 count rose to 698/µL, and renal function improved markedly: proteinuria decreased to 1 g/day, albumin rose to 4.7 g/dL, and serum creatinine stabilized at 1.0 mg/dL. (see **Table 1** for laboratory parameters at treatment initiation and response).

Table 1: Serial Laboratory and Virological Parameters with Treatment Response

Date	28 october 2024	21 november 2024	27 november 2024	9 january 2025	4 september 2025
BUN (mg/dl)	12	16	15	9	15
Cr (mg/dl)	0,83	0,40	0,56	0,40	1,03
Serum Na (mg/dl)	135	135	141	143	141
Serum K (mg/dl)	4,5	3,9	3,9	3,7	4,5
Serum Albumin (mg/dl)	4,1	2,1	1,9	2,6	4,7
Hemoglobin (g/dl)	14,3	10,1	8,8	13,2	15,2

Date	28 october 2024	21 november 2024	27 november 2024	9 january 2025	4 september 2025
Neutrophil (10^3/μL)	3,3	9,5	8,3	7,5	5,7
Lymphocyte(10^3/μL)	2,1	2,6	3,1	4,3	1,9
IgG (mg/dl)	-	7,25	-	-	-
IgA (mg/dl)	-	3,8	-	-	-
IgM (mg/dl)	-	0,59	-	-	-
C3 (mg/dl)	-	1,02	-	-	-
C4 (mg/dl)	-	0,21	-	-	-
ANA IFA	Negative	-	-	-	-
ANCA IFA	Negative	-	-	-	-
Spot urine Protein-to-Creatinine Ratio (mg/dl)	124	6580	20660	15300	1050
Spot urine Albumin -to-Creatinine Ratio (mg/dl)	25	3660	11140	12700	760
PLA2R (RU/ml)	-	-	<0,6	-	-
HIV RNA (copy/ml)	>1million	-	650	Negative	Negative
RPR-VDRL	1/16 positive	Negative	-	-	-
CMV PCR IU/ml	Negative	Negative	398,1	Negative	Negative
Absolute CD4+ T-lymphocyte count (cells/mm^3)	343	-	757	-	698
Tacrolimus Level ng/mL	-	-	-	4	5

BUN – Blood Urea Nitrogen; Cr – Creatinine; Na – Sodium; K – Potassium; Ig – Immunoglobulin; C3 – Complement component 3; C4 – Complement component 4; ANA – Antinuclear Antibody ; ANCA – Antineutrophil Cytoplasmic Antibody; IFA- Indirect Fluorescent Antibody; PLA2R – Phospholipase A2 Receptor Antibody; HIV RNA – Human Immunodeficiency Virus Ribonucleic Acid; RPR-VDRL– Rapid Plasma Reagin – Venereal Disease Research Laboratory; CMV PCR – Cytomegalovirus Polymerase Chain Reaction.

DISCUSSION

Diffuse proliferative exudative GN represents a distinctive histopathological pattern that is exceedingly rare in patients with HIV infection. Its occurrence in the setting of concurrent syphilis co-infection makes the case even more unusual. Among HIV-positive individuals, the most common renal pathology is HIVAN, typically presenting as collapsing focal segmental glomerulosclerosis. Immune complex–mediated glomerulonephritis, membranous nephropathy, and lupus-like lesions have been reported much less frequently [4]. The occurrence of nephrotic syndrome secondary to diffuse proliferative exudative GN is remarkable, as HIV-associated glomerular diseases have been consistently reported to present with nephrotic syndrome in the literature [5].

Syphilis, known as the "great imitator" because of its wide range of clinical manifestations, only rarely involves the kidney [3]. When renal disease is present, membranous nephropathy is by far the most frequent presentation. Rapidly progressive glomerulonephritis associated with syphilis has been documented but remains extremely uncommon, with only a handful of cases described to date [3].

Our case is remarkable because it highlights an atypical histopathological pattern arising in the context of dual infection. While renal involvement in HIV and syphilis co-infection is usually limited to membranous nephropathy or HIVAN, the finding of diffuse proliferative exudative GN represents a novel pathological convergence rarely reported in the literature. The immunofluorescence pattern, showing diffuse granular deposits of IgG, IgA, C3, and C1q, is compatible with immune complex–mediated disease. However, the florid endocapillary proliferation and neutrophil-rich exudative features suggest a mechanism more closely resembling post-infectious or immune complex–driven glomerulonephritis. Similar immunofluorescence staining patterns have been described in the literature in immune complex–mediated diseases secondary to HIV infection [5].

An important aspect of this case is the treatment approach and the clinical outcome. The patient received highly active antiretroviral

therapy (HAART), benzathine penicillin, and an immunosuppressive regimen with prednisolone and tacrolimus. Following this treatment, HIV RNA levels decreased from more than one million copies/mL to undetectable, CD4 counts increased from 383 to 700/µL, and kidney function improved. Proteinuria declined to 1 g/day, serum albumin returned to normal, and serum creatinine remained stable. This response is in line with reports suggesting that immunosuppressive therapies such as corticosteroids may help preserve kidney function in selected patients with HIV-related kidney disease[6]. In addition, studies in HIV-positive patients with membranous nephropathy have shown that calcineurin inhibitors, including tacrolimus, can reduce proteinuria and stabilize kidney function in some cases[7]. There are also a few case reports describing successful use of tacrolimus and corticosteroids, especially in HIV-associated nephrotic syndrome[8] .These findings suggest that, with close monitoring, immunosuppression can be used safely and effectively in HIV-infected patients with immune complex–mediated glomerulonephritis.

This case underscores the importance of considering atypical renal lesions in the differential diagnosis of nephrotic syndrome in patients with HIV and concurrent infections. Timely kidney biopsy can reveal rare but treatable etiologies and guide effective therapy. Moreover, with the availability of modern HAART—which restores immune function and ensures virological control—the judicious use of additional immunosuppressive agents in selected cases becomes both feasible and beneficial.

As a single case, these findings should be interpreted with caution, and further reports will be necessary to establish the efficacy and safety of this therapeutic strategy. Long-term follow-up data would also be valuable to assess the durability of remission and the risk of relapse. Overall, this report expands the spectrum of HIV- and syphilis-associated renal disease and demonstrates that combined antiviral and immunosuppressive therapy can achieve both virological suppression and renal remission.

CONCLUSIONS

This case illustrates a rare presentation of diffuse proliferative exudative glomerulonephritis in HIV and syphilis co-infection. Kidney biopsy enabled the diagnosis of this unusual immune complex–mediated lesion. The favorable response to antiretroviral therapy, antimicrobial treatment, and monitored immunosuppression highlights the importance of individualized management. While experience remains limited, our findings suggest that adjunctive immunosuppression may support renal recovery in selected patients with controlled HIV infection.

DECLARATIONS

Ethical Approvel

All procedures performed in this case report were in accordance with the ethical standards of the institutional committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent to Participate

Written informed consent was obtained from the patient for publication of this case report.

Competing interests

The authors declare no conflict of interest.

Data availability statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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