

รายงานผู้ป่วย

การพบร่วมกันของโรคไตอักเสบจากอิมมูโนโกลบูลินเอ และหลอดเลือดอักเสบจากแอนติบอดีต่อไซโทพลาสซึมของเม็ดเลือดขาวชนิดนิวโทรฟิล ในผู้ป่วยติดเชื้อเอชไอวี: รายงานผู้ป่วย

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บทคัดย่อ:

รายงานผู้ป่วยนี้นำเสนอกรณีที่พบได้น้อยและซับซ้อน เกี่ยวกับการพบร่วมกันของโรคไตอักเสบจากอิมมูโนโกลบูลินเอ และหลอดเลือดอักเสบจากแอนติบอดีต่อไซโทพลาสซึมของเม็ดเลือดขาวชนิดนิวโทรฟิล ในผู้ป่วยหญิงอายุ 40 ปี ผู้ป่วยซึ่งมีประวัติติดเชื้อเอชไอวีมา 4 ปี ได้รับยาต้านไวรัสสม่ำเสมอ มี CD4 374 เซลล์ต่อลูกบาศก์เมตร มาด้วยอาการปัสสาวะเป็นเลือดและการทำงานของไตเสื่อมลงอย่างรวดเร็ว การวินิจฉัยยืนยันโดยการตรวจชิ้นเนื้อไตซึ่งพบทั้งการติดของอิมมูโนโกลบูลินเอและลักษณะของหลอดเลือดอักเสบจากแอนติบอดีต่อไซโทพลาสซึมของเม็ดเลือดขาวชนิดนิวโทรฟิล ผู้ป่วยตอบสนองดีต่อการรักษาด้วยการให้ยาคอร์ติโคสเตียรอยด์ขนาดสูงร่วมกับไซโคลฟอสฟาไมด์ ส่งผลให้การทำงานของไตกลับมาดีขึ้น กรณีนี้ชี้ให้เห็นถึงความท้าทายในการจัดการภาวะดังกล่าว โดยเฉพาะในบริบทของผู้ป่วยที่มีภูมิคุ้มกันบกพร่อง รวมถึงชี้ให้เห็นถึงความสำคัญของการวินิจฉัย และการรักษาอย่างรวดเร็ว

คำสำคัญ: ● เอชไอวี ● โรคไตอักเสบจากอิมมูโนโกลบูลินเอ ● โกลเมอรูโลเนฟริตัส

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Case Report

Coexistence of IgA Nephropathy and ANCA-Associated Vasculitis in an HIV Infected Patient: A Case Report

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Abstract:

This case report presents a rare and complex scenario involving the coexistence of HIV infection, immunoglobulin A nephropathy (IgAN), and anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis in a 40-year-old female. The patient, with a 4-year history of HIV, had been on consistent antiretroviral therapy and had a CD4 count of 374 cells per cubic millimeter. She presented with hematuria and rapidly declining renal function. The diagnosis was confirmed through kidney biopsy, revealing both IgA deposition and features of ANCA-associated vasculitis. The patient was successfully treated with a combination of high-dose corticosteroids and cyclophosphamide, leading to the stabilization of her renal function. This case underscores the challenges of managing such conditions, particularly in the context of an immunocompromised state, and highlights the importance of early recognition and timely intervention.

Keyword: ● HIV ● IgA nephropathy ● ANCA ● Glomerulonephritis ● RPGN

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Introduction:

The coexistence of HIV infection, IgA nephropathy (IgAN), and anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis presents a rare and highly challenging clinical scenario. IgAN is the most common form of glomerulonephritis worldwide, characterized by IgA deposits in the glomeruli. ANCA-associated vasculitis, on the other hand, is a systemic autoimmune disorder that can lead to rapidly progressive glomerulonephritis (RPGN) and renal failure. The combination of these conditions in an HIV-positive patient is extremely rare, and their pathogenesis in this context remains unclear.

This case report highlights the complexity of managing a patient with these overlapping conditions. HIV infection is known to be associated with various kidney complications. However, the coexistence of IgAN and ANCA-associated vasculitis adds significant diagnostic and therapeutic challenges. Treatment strategies must therefore be carefully tailored, balancing the need for immunosuppression to control autoimmune activity without further compromising the patient's immune system.

Case Presentation:

A 40-year-old female with a 4-year history of HIV infection presented to the hospital. At her most recent follow-up, her CD4 count was 374 cells/cu.mm, and her HIV viral load was undetectable at less than 20 copies. She had been taking a fixed-dose combination of Tenofovir disoproxil fumarate (300 mg), Efavirenz (600 mg), and Emtricitabine (200 mg), one tablet daily at 8:00 PM. She had never self-medicated, nor had she taken any painkillers or herbal remedies. Her baseline creatinine level, recorded three months earlier, was 0.67 mg/dL.

A week prior to her hospital admission, she noticed fresh blood in her urine, an occurrence she had not experienced before. She denied experiencing dysuria, abdominal pain, orthopnea, and nocturnal dyspnea, but she did complain of fatigue. She had no noticeable edema, cough, hemoptysis, or fever. She was admitted due to abnormal blood results, including a rising serum creatinine, and was subsequently consulted with a nephrologist. Physical examination upon admission revealed the following vital signs: body temperature of 36.5 °C, pulse rate of 82 beats per minute, respiratory rate of 28 breaths per minute, and blood pressure of 150/92 mmHg. The extremities examination noted 1+ pitting edema in both lower limbs.

Laboratory investigations revealed the following results: The complete blood count (CBC) showed a hemoglobin level of 8.0 g/dL, a hematocrit of 23.9%, and a white blood cell count of 4,000 cells/uL with a differential of 75.1% neutrophils, 17.6% lymphocytes, 4.5% monocytes, 2.1% eosinophils, and 0.7% basophils. The platelet count was 241,000 cells/uL, with a mean corpuscular volume (MCV) of 87.9 fL and a red cell distribution width (RDW) of 14.6%. The reticulocyte count was 1.27%. Blood chemistry results indicated a blood urea nitrogen (BUN) level of 55 mg/dL, a creatinine level of 5.58 mg/dL, and an estimated glomerular filtration rate (eGFR) of 8.83 mL/min. Electrolyte levels included sodium at 132 mmol/L, potassium at 3.94 mmol/L, chloride at 105 mmol/L, bicarbonate at 18 mmol/L, and albumin at 3.06 g/dL. Urinalysis results showed proteinuria

with 1+ protein, white blood cells (WBC) ranging from 30-50 per high-power field (HPF), red blood cells (RBC) ranging from 50-100 per HPF and dysmorphic RBCs were observed. There were no RBC casts. Urine protein of 102.2 mg/dL, and urine creatinine of 64.5 mg/dL. Immunological findings included a C3 complement level of 0.5 g/L (reference range: 0.83-1.93 g/L), a C4 complement level of 0.15 g/L (reference range: 0.15-0.57 g/L), and an antinuclear antibody (ANA) titer of 1:1000 with a speckled pattern. Testing for anti-double-stranded DNA (anti-dsDNA) was negative, anti-myeloperoxidase (anti-MPO) IgG was negative, but anti-proteinase 3 (anti-PR3) IgG was positive. Tests for hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (anti-HCV) were both negative. A chest X-ray showed mild interstitial infiltration, consistent with mild pulmonary congestion.

A kidney biopsy was performed, which revealed 10 glomeruli, none of which exhibited global or segmental sclerosis. There was no noticeable increase in mesangial cells or matrix, and no endocapillary hypercellularity was observed. However, one glomerulus had a cellular crescent and fibrinoid necrosis (Figure 1), and another had a fibrocellular crescent. There was no interstitial fibrosis or tubular atrophy, but diffuse acute tubular injury was present. Occasionally, intratubular red blood cells (RBCs) were noted. Immunofluorescence demonstrated IgA (2+) and C3 (3+) coarse granular mesangial staining (Figure 2), with lesser degrees of IgG (1+), IgM (trace-1+), and C1q (trace) staining. Electron microscopy was not performed.

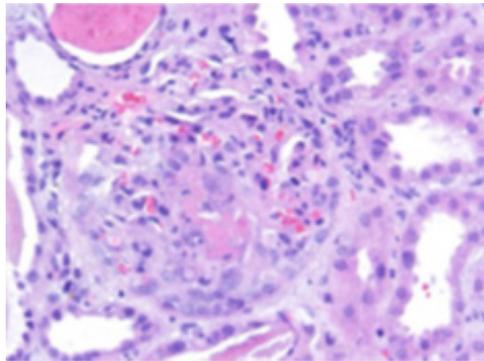


Figure 1 Cellular crescent and fibrinoid necrosis

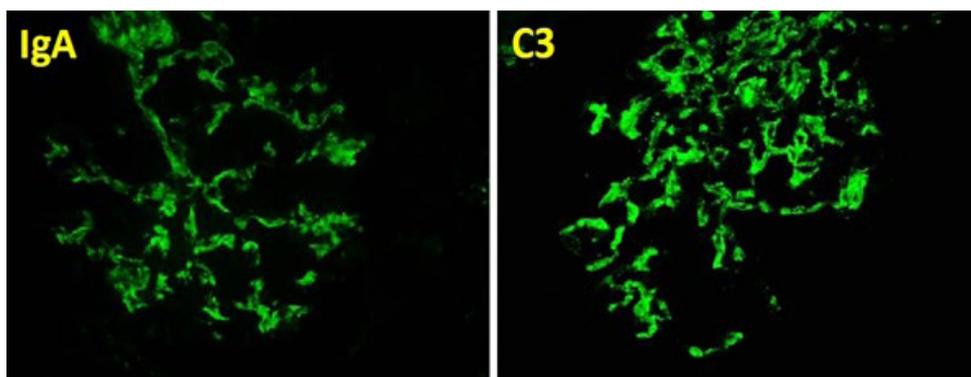


Figure 2 IgA (2+) and C3 (3+) coarse granular mesangial staining

Prior to the initiation of immunosuppressive therapy, the patient was screened for tuberculosis and stool parasites, both of which were negative. She was given furosemide as

supportive treatment. Subsequently, the patient was treated with pulse methylprednisolone at a dosage of 1 g/day for three consecutive days, followed by prednisolone at 0.5 mg/kg/day. One week later, her creatinine level decreased to 4.36 mg/dL and further dropped to 2.61 mg/dL the following week.

Approximately one week after receiving pulse methylprednisolone, she was administered cyclophosphamide 750 mg intravenously, every two weeks for three doses, followed by every three weeks for an additional three doses, for a total of six doses. The patient responded well to the treatment, with her creatinine level eventually decreasing to 1.1 mg/dL. For maintenance therapy, she was placed on azathioprine. Once her creatinine level stabilized, an angiotensin receptor blocker (ARB) was added to her regimen. After a three-year follow-up, her creatinine level remained stable.

Discussion:

This case illustrates the rare and challenging coexistence of HIV infection, IgAN and ANCA-associated vasculitis. IgAN is a common form of glomerulonephritis, characterized by the deposition of IgA in the mesangial region of the kidney. However, the prevalence of IgAN in HIV-infected patients is relatively low and not well documented. In some studies, mesangial IgA deposits were observed in a small percentage, around 7.75%, of HIV-infected individuals during postmortem examinations¹. The pathogenesis of IgAN in the context of HIV is not well understood, but it is hypothesized that HIV-induced immune dysregulation may play a role, potentially leading to B-cell hyperactivation and increased production of immunoglobulins, including IgA. Chronic immune activation and inflammation associated with HIV may further promote the formation of immune complexes and their deposition in the glomeruli².

Even rarer is the coexistence of ANCA-associated vasculitis with HIV infection. Although the relationship between ANCA and HIV is not fully understood, immune dysregulation caused by HIV may contribute to the development of autoantibodies, including ANCA³. The presence of ANCA in HIV-positive patients is associated with an increased risk of vasculitis and RPGN⁴.

In this case, the patient presented with clinical features suggestive of RPGN, including hematuria, proteinuria, and rapidly declining renal function. Before the kidney biopsy results were available, based on the clinical presentation and initial investigations, pauci-immune glomerulonephritis was the most likely diagnosis. However, the observation of low C3 levels raised additional considerations. The differential diagnosis included immune complex glomerulonephritis, specifically HIV-associated immune complex kidney disease (HIVIKD), which can present with a wide range of clinical features. Histopathological findings in such cases can vary, potentially showing patterns like IgAN, lupus-like glomerulonephritis or post-infectious glomerulonephritis^{5,6}. Some of these conditions can occur in non-HIV patients as well. Clinically, determining whether this is a disease caused by HIV requires further data.

The kidney biopsy findings, such as the presence of cellular crescents and fibrinoid necrosis, along with positive ANCA serology, confirmed the diagnosis of ANCA-associated vasculitis. Notably,

the patient also exhibited low serum C3, and immunofluorescence showed IgA and C3 deposition, which raised the possibility of IgA-dominant infection-related glomerulonephritis⁷. However, the light microscopy did not reveal mesangial or endocapillary proliferation, suggesting that ANCA-associated vasculitis was the primary disease, while IgAN was likely an incidental finding. The diffuse tubular injury observed in this case is part of the renal damage commonly seen in glomerulonephritis⁸, including ANCA-associated vasculitis⁹. This injury can result from several mechanisms, such as vascular injury caused by the disease itself or direct damage to renal tubular epithelial cells from cytokines and chemokines produced by the immune response in glomerulonephritis^{10,11}.

The management of this patient is particularly complex, as the immunosuppressive therapy required for ANCA-associated vasculitis may worsen the HIV infection. In this case, treatment was centered on addressing the ANCA-associated vasculitis with high-dose corticosteroids and cyclophosphamide, successfully inducing remission and stabilizing renal function. Cyclophosphamide was selected because the patient presented with severe glomerulonephritis (creatinine >4 mg/dL), despite the presence of factors favoring rituximab, such as being a pre-menopausal woman and having PR3-ANCA disease. According to the KDIGO 2024 Clinical Practice Guideline for the Management of ANCA-Associated Vasculitis, plasmapheresis is recommended for patients with serum creatinine levels greater than 3.4 mg/dL¹². However, plasmapheresis was not performed in this case, as the patient demonstrated a rapid response to immunosuppressive therapy. This swift improvement may be attributed to the timely diagnosis and treatment, as evidenced by the kidney biopsy results, which showed no global sclerosis or other features suggestive of long-standing disease.

Conclusion:

This case underscores the rarity of the coexistence of HIV infection, IgAN, and ANCA-associated vasculitis, and highlights the challenges in managing such complex clinical scenarios. Early recognition and timely initiation of appropriate immunosuppressive therapy are crucial in preserving renal function and preventing complications. The case also emphasizes the importance of careful consideration of treatment risks and benefits in the context of an immunocompromised patient.

References:

1. Beaufils H, Jouanneau C, Katlama C, Sazdovitch V, Hauw JJ. HIV-associated IgA nephropathy--a post-mortem study. *Nephrol Dial Transplant*. 1995;10(1):35-8.
2. Nobakht E, Cohen S, Rosenberg A, Kimmel PL. HIV-associated immune complex kidney disease. *Nat Rev Nephrol*. 2016;12(5):291-300.
3. Klaassen RJ, Goldschmeding R, Dolman KM, Vlekke AB, Weigel HM, Eeftinck Schattenkerk JK, et al. Anti-neutrophil cytoplasmic autoantibodies in patients with symptomatic HIV infection. *Clin Exp Immunol*. 1992;87(1):24-30.
4. Iordache L, Launay O, Bouchaud O, Jeantils V, Goujard C, Boue F, et al. Autoimmune diseases in HIV-infected patients: 52 cases and literature review. *Autoimmun Rev*. 2014;13(8):850-7.

5. Swanepoel CR, Atta MG, D'Agati VD, Estrella MM, Fogo AB, Naicker S, et al. kidney disease in the setting of HIV infection: conclusions from a kidney disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int.* 2018;93(3):545–59.
6. Fogo AB, Lusco MA, Najafian B, Alpers CE. *AJKD Atlas of Renal Pathology: HIV-Associated Immune Complex Kidney Disease (HIVICK).* *Am J Kidney Dis.* 2016;68(2):e9-e10.
7. Paueksakon P, Najafian B, Alpers CE, Fogo AB. *AJKD Atlas of Renal Pathology: IgA-Dominant Infection-Related Glomerulonephritis.* *Am J Kidney Dis.* 2024;83(1): e1-e2.
8. Fenoglio R, Sciascia S, Baldovino S, Roccatello D. Acute kidney injury associated with glomerular diseases. *Curr Opin Crit Care.* 2019;25(6):573-9.
9. Sinico RA, Di Toma L, Radice A. Renal involvement in anti-neutrophil cytoplasmic autoantibody associated vasculitis. *Autoimmun Rev.* 2013;12(4):477-82.
10. Monach PA, Warner RL, Tomasson G, Specks U, Stone JH, Ding L, et al. Serum proteins reflecting inflammation, injury and repair as biomarkers of disease activity in ANCA-associated vasculitis. *Ann Rheum Dis.* 2013;72(8):1342-50.
11. Bulanov N, Chebotareva NV, Novikov PI, Moiseev SV. Role of tubulointerstitial injury in ANCA-associated vasculitis is underestimated. *Ann Rheum Dis.* 2019;78(10):e111.
12. KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis. *Kidney Int.* 2024;106(Suppl 1):s71-s116.

