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A 54-year-old Man with HIV-Associated Nephropathy

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Abstract: HIV-associated nephropathy (HIVAN) is a renal parenchymal disease that occurs in individuals infected with HIV. HIVAN is commonly found in patients with severe immunocompromise, particularly with CD4 counts <200, although it may also occur during primary HIV infection. HIVAN is rarely reported in Asian countries. In this case, we report a patient with progressively worsening renal function due to HIVAN. A 54-year-old man with a history of HIV presented with fatigue, fever, weight loss, diarrhea, and poor adherence to antiretroviral therapy, leading to a diagnosis of HIVAN. This patient presented with fatigue, fever, weight loss, and diarrhea. Urinalysis showed proteinuria, and renal ultrasonography revealed enlarged, echogenic kidneys. Progressive daily increases in BUN and serum creatinine during hospitalization indicated deteriorating renal function. These findings are consistent with HIVAN. HIVAN is a serious renal disease that may occur in individuals with HIV. It is a known cause of chronic kidney disease and end-stage renal disease (ESRD). Renal function screening in HIV patients is essential to prevent progression to ESRD.

Keywords: HIVAN, ESRD, ARV.

INTRODUCTION

HIV-associated nephropathy (HIVAN) is a renal parenchymal disease occurring in individuals infected with HIV. HIVAN is one of the causes of chronic kidney disease and end-stage renal disease (ESRD), and it is the third most common cause of ESRD among Black individuals aged 20–64 years[1,2]. The clinical spectrum of kidney disease related to HIV infection is broad and may occur at any stage of HIV. HIVAN is thought to be caused by direct injury from HIV infection and HIV gene expression, as well as dysregulation of genes controlling the cell cycle and differentiation of renal epithelial cells. Findings in HIVAN include collapsing focal segmental glomerulosclerosis with hypertrophy and hyperplasia of glomerular epithelial cells; tubulointerstitial changes (tubuloreticular endothelial inclusions and tubular injury with microcystic dilatation); interstitial inflammation; and heavy proteinuria. Focal segmental glomerulosclerosis–type HIVAN is the most common renal manifestation and leads to rapidly progressive renal function decline[3]. HIVAN commonly occurs in patients with severe immunocompromise, particularly with CD4 counts <200, but it may also be seen in primary HIV infection[5,6,7]. Kidney-disease can be detected early by screening renal function at the time of HIV diagnosis, as HIV patients may develop various forms of acute and chronic

kidney disease. Definitive diagnosis of HIVAN requires renal biopsy. Current data demonstrates a direct role of HIV infection in renal cells in the pathogenesis of HIVAN. According to the Infectious Diseases Society of America, early treatment with HAART, ACE inhibitors, and corticosteroids in selected cases can prevent progression to ESRD and reduce premature mortality. Before the ARV era, the incidence of HIVAN was approximately 10%; with earlier and broader use of ARVs, its incidence and the resulting ESRD burden have declined globally[3]. Clinical features of HIVAN include moderate to heavy proteinuria and enlarged, echogenic kidneys on ultrasonography[8,9]. Patients typically have minimal peripheral edema and may have only mild or even normal blood pressure elevations. This may be related to HIVAN-associated salt wasting and reduced oncotic pressure due to increased serum immunoglobulins[10]. Most HIVAN cases are reported in African-American populations; conversely, HIVAN is rarely reported in Asian countries[11]. We presented a case of HIVAN in a 54-year-old man with a history of HIV since 2004 and prior interruption of ARV therapy, who developed progressive renal dysfunction leading to ESRD requiring hemodialysis. The patient had no history of hypertension or diabetes. However, urinalysis revealed proteinuria, raising suspicion for HIVAN.

METHOD

Case Report

A 54-year-old man presented to the Emergency Department with worsening fatigue for two days, accompanied by intermittent fever and night sweats. He had experienced weight loss from 65 kg to 52 kg over the past two months. He reported recurrent diarrhea for three months, decreased appetite, and nausea with vomiting. He had been diagnosed with HIV in 2004, with a CD4+ count of 15 cells/mm^3 at that time. The patient had previously adhered to antiretroviral therapy but had discontinued treatment for six months before resuming ARVs regularly since August 2023. There was no personal or family history of hypertension or kidney disease. Physical examinations showed blood pressure of 110/70 mmhg, pulse 88 beats/minute, respiratory rate 18 times/minute, and axillary temperature of 37.8°C. The left cardiac border was displaced laterally, with the point of maximal impulse palpable at the 6th intercostal space, 2 cm lateral to the midclavicular line. No ballotement was appreciated, and there was no peripheral edema. Chest radiography suggested cardiomegaly, and ECG showed left ventricular hypertrophy. Laboratory tests showed BUN 53.9 mg/dL and serum creatinine 13.73 mg/dL. Urinalysis showed +2 proteinuria. Serial BUN and creatinine levels were as follows: 23rd October 2023 BUN 27.8 mg/dL creatinine 8.21 mg/dL, 26th October 2023 BUN 32.2 mg/dL creatinine 8.74 mg/dL, and 28th October 2023 BUN 53.9 mg/dL creatinine 13.73 mg/dL. The most recent CD4+ count was 113 cells/mm^3. Renal ultrasonography revealed enlarged, echogenic kidneys. The patient was diagnosed with HIV infection, WHO clinical stage IV, with wasting syndrome; acute-on-chronic kidney disease (ACKD) suspected HIVAN; and cardiomegaly under evaluation for possible cardiomyopathy (functional class II). He had a history of ARV use (AZT, 3TC, NVP). During hospitalization, treatment included Abacavir 300 mg orally every 12 hours, Lamivudine 50 mg orally every 24 hours, Lopinavir 200 / Ritonavir 50, two tablets orally every 12 hours, Paracetamol 500 mg orally three times daily, Candesartan 8 mg orally every 24 hours, Omeprazole 40 mg IV every 12 hours, Domperidone 10 mg orally every 8 hours. He also underwent hemodialysis.

RESULT AND DISCUSSION

Kidney disease in patients with HIV may arise from complications of HIV infection, the presence of comorbidities or coinfections, immune dysregulation, as well as HIV therapy and its complications. These factors increase morbidity and mortality among HIV patients with kidney disease, and the risk of renal injury increases with more advanced HIV infection (low

CD4+ count)[3]. HIV infection can be diagnosed through several tests, including HIV antigen–antibody tests and assays that assess immune deficiency[4]. In this case, the 54-year-old patient had been diagnosed with HIV since 2004, with a CD4+ count of 15 cells/mm^3 at that time. The patient did not consistently take ART. Without ART, CD4 counts decline by approximately 70–100 cells/mm^3 per year, placing untreated HIV patients at increased risk for opportunistic infections and direct HIV-related organ damage[12]. Wasting syndrome is characterized by unintentional weight loss of more than 10% of baseline body weight within 30 days, accompanied by loss of muscle and fat mass, and is commonly observed in HIV patients[3,13]. The patient in our case experienced weight loss exceeding 10%, classifying the patient as having WHO clinical stage IV HIV disease.

This patient demonstrated impaired renal function, evidenced by elevated BUN and serum creatinine levels and proteinuria. Chronic kidney disease (CKD) is defined as abnormalities in kidney structure or function lasting at least 3 months with implications for health. CKD is classified based on etiology, GFR category (G1–G5), and albuminuria category (A1–A3)[1]. Proteinuria of +2 in this patient indicated structural renal abnormalities, and the progressively increasing BUN and serum creatinine levels during hospitalization reflected worsening renal function. A limitation in this case is the absence of prior urinalysis, BUN, and serum creatinine data, making it impossible to determine whether renal abnormalities had been present for more than 3 months to classify the patient definitively as having CKD.

Various forms of kidney disease in HIV patients have been described, but HIVAN remains the most frequently reported. HIVAN warrants special attention because of its rapid progression to end-stage renal disease (ESRD)[11]. The diagnosis of HIVAN is based on clinical and histopathological findings in HIV-infected individuals. Clinically, HIVAN typically presents with mild or absent peripheral edema, mild or normal blood pressure, and moderate to heavy proteinuria. These findings may result from HIVAN-related salt wasting and altered oncotic pressure from elevated serum immunoglobulins. Renal ultrasonography generally reveals enlarged echogenic kidneys. Histopathological findings characteristic of HIVAN include focal segmental glomerulosclerosis, glomerular capillary collapse, glomerular epitheliosis (proliferation of podocyte stem cells located in the parietal epithelium), mesangial prominence and hypercellularity, endothelial tubuloreticular inclusions (TRIs), tubular microcysts, interstitial edema, and cellular infiltrates. Collapsing glomerulosclerosis is the most common variant due to hypercellularity of the cells lining Bowman's capsule[15,16]. In this case, the patient exhibited no peripheral edema, maintained normal blood pressure, and demonstrated proteinuria and progressive renal dysfunction. Ultrasonography showed enlarged, echogenic kidneys. These features are consistent with HIVAN; however, renal biopsy was not performed.

HIVAN is believed to result from direct viral cytopathic effects, HIV gene expression, and dysregulation of genes regulating renal epithelial cell cycle and differentiation[3]. HIVAN should be suspected when renal dysfunction occurs without another plausible cause aside from HIV infection. It is most commonly observed in HIV-positive individuals of African descent, with heavy proteinuria and rapidly progressive renal failure. Supporting findings include high HIV viral load, low CD4 count (<350 cells/mm^3), heavy proteinuria, elevated protein–creatinine ratio, and enlarged echogenic kidneys on ultrasonography. The sensitivity and specificity of proteinuria for diagnosing HIVAN are 73% and 61%, respectively[15,16]. In this patient, no other infections were identified, the patient had a very low CD4+ count (15 cells/mm^3), and proteinuria was present. Viral load was not measured. Although no definitive diagnostic criteria for HIVAN exist, these parameters support the diagnostic suspicion.

Management of patients with HIVAN includes initiating or maintaining ART, along with therapeutic modalities such as renin–angiotensin–aldosterone system (RAAS) inhibitors, corticosteroids, and renal replacement therapy (RRT). Combination ART (cART) remains the

primary treatment for HIVAN. A 2012 study by Bigé et al. demonstrated improved median renal survival in HIVAN patients receiving cART. Despite its benefits, HIVAN still carries a poorer prognosis than non–HIV-related kidney diseases[16]. Laboratory evaluations after ART include CD4 counts and renal function monitoring. Renal function testing should be performed annually in stable HIV patients; other studies recommend eGFR assessment every 6 months and urinalysis or urinary protein excretion annually[3]. Other than ARVs, RAAS inhibitors have been shown to slow progression to ESRD. Fosinopril has been associated with stabilization of serum creatinine and protein excretion[16]. In patients with severe renal insufficiency, captopril may improve renal survival[2]. In HIV patients with nephropathy, blood pressure should be controlled below 125/75 mmHg, and ACE inhibitors or angiotensin receptor blockers (ARBs) should be used in those with proteinuria. Calcium channel blockers should be avoided in patients receiving protease inhibitors[17]. Besides ARVs and RAAS inhibitors, corticosteroids may reduce tubulointerstitial inflammation observed on biopsy and may improve protein excretion and serum creatinine while delaying progression to ESRD[16]. In HIVAN patients on ART without evidence of opportunistic infection, prednisone at 1 mg/kg/day (maximum 80 mg/day) for two months followed by a 2–4 month taper may be considered[15]. However, recent studies validating this regimen are lacking, and the potential adverse effects of prolonged steroid therapy must be considered[16]. Patients with HIVAN remain at risk of developing ESRD despite medical therapy. Therefore, renal replacement therapy—including hemodialysis (HD) or peritoneal dialysis (PD)—should be considered for patients who progress to ESRD. Mortality and morbidity rates do not differ significantly between HD and PD in HIV patients[16]. This patient previously received AZT, 3TC, and NVP but demonstrated poor adherence and developed drug resistance; therapy was subsequently switched to abacavir 300 mg every 12 hours, lamivudine 50 mg every 24 hours, and lopinavir/ritonavir two tablets every 12 hours. The regimen of abacavir + lamivudine + lopinavir/ritonavir is considered safe and appropriate for patients with renal failure. Abacavir is not renally eliminated; lamivudine is renally excreted but may be used with dose adjustment; and lopinavir/ritonavir undergoes hepatic rather than renal metabolism, making it safe in renal impairment[18,19]. The patient was also treated with candesartan 8 mg daily and underwent hemodialysis.

CONCLUSION

HIVAN is a serious kidney disease that can occur in HIV-infected individuals and is a known cause of chronic kidney disease and end-stage renal disease (ESRD). In this case, the patient was HIV-positive with poor adherence to ART. The presence of proteinuria indicated structural renal abnormalities, and progressive increases in BUN and serum creatinine reflected declining renal function. Renal impairment in this patient was suspected to be due to HIVAN, consistent with the clinical presentation of absent edema, normal blood pressure, low CD4 count, proteinuria, progressive renal dysfunction without another identifiable cause, and ultrasonographic findings of bilaterally enlarged echogenic kidneys. Definitive diagnosis requires renal biopsy, although this is often not performed. Management included ART, ARB therapy to reduce proteinuria progression, and hemodialysis because the patient had already developed ESRD. Routine renal screening in HIV patients is essential to prevent progression to ESRD.

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