



CASE REPORT

Thrombotic Microangiopathies as Initial Presentation of HIV: Two Case Reports and Literature Review

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Abstract

Thrombotic microangiopathies have been recently a recognizable presentation of patients infected with Human Immunodeficiency Virus (HIV). Most of those who present similarly noted to have poor prognosis as majority have advanced HIV with low CD4 counts. It has postulated by some authors and researches that it should be recognized as an AIDS defining condition.

Here we present two cases of adult males who presented with features of thrombotic microangiopathy and were diagnosed to have HIV for the first time.

Keywords

HIV, AIDS, Thrombosis

the presenting complaint of advanced HIV with clinical features similar to those of idiopathic TMA [2].

Here we present two cases where TMA was the presenting feature of advanced HIV. They were initially admitted under nephrology services to investigate acute kidney injury (AKI) associated with anemia and thrombocytopenia. After thorough evaluation it was recognized as TMA, however, treatment was a challenge.

Case 1

A 51-year-old male post renal transplant for living unrelated donor in July 2021. He was on everolimus 0.5 mg BD, tacrolimus 1 mg BD and prednisone 5 mg OD. The patient was admitted on March 2022 after noticing a drop in hemoglobin from baseline 12-13 g/dl to 5.3 g/dl along with thrombocytopenia of $38 \times 10^9/L$ during routine check-up. His total white cell count was $2 \times 10^9/L$ with absolute neutrophil count of 1, lymphocyte 10.8% and creatinine increase to 161 $\mu\text{mol/L}$ from baseline of 120-130 $\mu\text{mol/L}$. He had lactate dehydrogenase (LDH) level 1238 units/L. Patient denied any history of fever, neurological symptoms, change in urine output, bleeding or anemia symptoms. No history of recent diarrheal episodes, rash or arthropathy and no change in his medications. Ultrasound of grafted kidney was normal.

Upon admission, he was transfused with two packed red blood cells. Investigations showed negative vasculitis screen, positive HIV Ag-Ab test and 6% fragmented red blood cells (RBC) on peripheral blood smear. Absolute CD4 count was 6 and HIV viral load of

Introduction

Thrombotic microangiopathies (TMA) present a challenge to treating physicians. Rapid recognition is essential to initiate proper treatment to improve outcomes. Endothelial injury secondary to various causes predisposes for platelet aggregation and subsequent organ ischemia, is believed to be the basic pathophysiology behind the disease [1]. Patients present with variable combination of neurologic abnormalities, renal impairment, low platelet count and evidence of haemolysis [1]. In the past two decades, due to advancement of treatment with plasma exchange, the fatality rate dropped to 10-20%, however, it's still of significance [1]. Causes of TMA are several including congenital deficiency of ADAMTS-13, drug induced, autoimmune conditions and infections. Human immunodeficiency virus (HIV) is a well-recognized triggering factor [2]. TMA can be

1513561 copies/ml. He denied sexual relations beyond his wife, who tested later on negative, and no history of drug abuse. The patient had negative HIV test few months pre-transplant. The etiology of HIV acquisition is unknown.

Bictegravir 50 mg/ emtricitabine 200 mg/ tenofovir alafenamide 25 mg was started after excluding opportunistic infection by history, examination and investigation. Six sessions of plasma exchange were done via VasCath with approximately of 1.5L exchange done in each session, however, he became oliguric and creatinine gradually increased to 700 $\mu\text{mol/L}$. Subsequently, plasma exchange was stopped and he was scheduled for thrice weekly hemodialysis through his previously created arterio-venous fistula. Immunosuppression was reduced to prednisone 5 mg.

After two months of follow up, his absolute CD4 count increased to 235 and HIV viral load dropped to 982 copies/ml with good health status.

Case 2

A 53 year male not known previously of any chronic medical illness presented to Emergency Trauma Department with complain of shortness of breath, peri-orbital edema and lower limbs swelling for 5 days gradually worsening. He noted few episodes of non-bloody loose motion preceding the symptoms by 2 days. His white cell count was $4.07 \times 10^9/\text{L}$, hemoglobin 9.8 g/dl, platelet $53 \times 10^9/\text{L}$ and serum creatinine was 245 $\mu\text{mol/L}$ with no previous health record. Urine dip stick showed 4+ protein and 24 hour urine protein was 4 grams. Ultrasound kidneys did not show evidence of anatomical or mechanical abnormality.

Peripheral blood smear had 2.51% fragmented red blood cell. Serology and vasculitis screen were done looking for underlying precipitating factor and turned to be of non-significance. HIV Ag-Ab test was positive. Absolute CD4 count was 571 and HIV viral load was 6 million copies/ml. The patient gave history of drug abuse and multiple heterosexual relations.

The impression was acute collapsing glomerulonephritis, due to rapidly increasing creatinine and high protein in the urine, and TMA secondary to HIV. He received 8 sessions of plasma exchange, Bictegravir 50 mg/ emtricitabine 200 mg/ tenofovir alafenamide 25 mg tablet and 60 mg prednisone. His LDH decreased from 571 to 362 units/L, platelets remained stable between $50-68 \times 10^9/\text{L}$ despite the 8 sessions, hemoglobin post multiple blood transfusions increased to 11 g/dl but his creatinine continued increasing to 350 $\mu\text{mol/L}$. Nephrology team was planning to biopsy the kidney, however, patient refused to stay in the hospital and left against medical advice.

Discussion

TMA in HIV patients is found to be raised compared

to the general population [3]. In patients with HIV-TMA, there is male predominance unlike TMA in HIV negative cases where female to male ratio is estimated to be 3:2 [3-5]. de Man AM, et al. noted in their review of 48 cases of HIV-TMA, male majority (73%) [5].

The mechanism of the pathogenesis of TMA-HIV remains hypothetical. Multiple possible mechanisms have been implicated: 1) Direct endothelial cell injury and activation mediated through direct viral invasion by the virus 2) Action of HIV proteins such as gp120 on endothelial cells 3) Indirect effect of secreted cytokines such as tumor necrosis factor alpha and interleukin-1 which are found to be raised in HIV positive patients [6,7]. Other possible factors may be drugs, direct cytopathic effect of infectious agent (e.g. CMV, herpes) or malignancy [6].

The clinical presentation is variable. It can range from mild asymptomatic thrombocytopenia with mild renal impairment to severe illness with neurological deficit and renal failure requiring replacement therapy. A number of patients with HIV-TMA have AIDS defining conditions such as cytomegalovirus retinitis, pneumocystis jiroveci pneumonia or cryptococcal meningitis at the time they present with TMA [8]. Sutor GC, et al. noted on review of 93 cases of HIV-TMA that in 28% of the cases TMA was the first presentation of HIV infection. Majority of cases had symptomatic HIV infection at the time of presentation while one third had mild or no symptoms of HIV. TTP was present in 61 (66%) of the cases and the remainder were HUS. The data supported that TTP patients suffered less severe HIV disease with higher CD4 count compared to HUS (mean absolute CD4 142 vs. 70 respectively). Higher prevalence of HUS patients were classified to have stage III (WHO) disease that those labelled with TTP (76% vs. 58%). This resulted in worse prognosis among those suffered from HUS where 63% died. On the hand, 51% of TTP patients recovered and achieved complete remission [8].

Treatment of HIV-TMA is similar to idiopathic TMA where the mainstay of therapy is plasma exchange. Treating physicians should do daily plasma exchange with aim to exchange 1-1.5 times the plasma volume. Therapy should continue until neurological symptoms improve which tends to recover rapidly, decrease of LDH by at least 50% with stable platelet count which takes usually 3-5 days. For those with renal impairment, renal function is the last to improve [2].

The prognosis and 1 year outcome is poor to HIV-TMA cases and thus, as Sutor GC, et al. recommended to add TMA in HIV patients as AIDS defining illness [8].

Conflict of Interest

None.

Funding Source

Nil.

Ethical Approval Statement

Verbal acceptances were taken from next of kin of case number 1 (his brother) and patient presented in case 2.

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