

Thrombotic Thrombocytopenic Purpura Associated with Human Immunodeficiency Virus Infection

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Abstract

Thrombotic thrombocytopenic purpura (TTP) belongs to the group of diseases called Thrombotic microangiopathies (TMA). While several triggering conditions are known, often none is apparent in the individual case.

We report a patient presenting with TTP that was associated with a Human Immunodeficiency Virus (HIV) infection, with its consequent diagnostic, therapeutic and prognostic implications. Further, our case had individual clinical features that were of interest within the TTP-HIV subgroup. ©

INTRODUCTION

Thrombotic Thrombocytopenic Purpura belongs to the spectrum of Thrombotic Microangiopathies (TMA) and is characterized by the classic pentad of fever, anaemia, neurological symptoms, thrombocytopenia, oliguria (renal impairment) and microangiopathy (mnemonic : fantom). Triggers of TMA include infection, drugs, collagen vascular disease, cancer and pregnancy among others.

TMA has also been reported to be rarely associated with Human Immunodeficiency Virus infection. A diagnosis of HIV in the presence of TMA and vice versa, therefore, needs to be considered in the appropriate clinical setting. Further, prognosis of TMA in HIV infection depends on the clinical stage of the latter. In those asymptomatic for HIV infection, it responds as well to adequate therapy as in HIV negative patients. In those with the Acquired Immune Deficiency Syndrome (AIDS), the outcome is often poor.

We report a patient presenting with Thrombotic Thrombocytopenic Purpura who was subsequently detected to be suffering from AIDS, which is an uncommon clinical presentation of the latter disease. Further, our case had individual clinical features that were of interest in the TTP-HIV subgroup.

CASE REPORT

A 39-year-old male engineer, a smoker, presented with paraesthesia of the left side of body and slurring of speech.

Two weeks prior to this, the patient had developed gradual onset of numbness and tingling of the right lower limb progressing to the right half of body including face. He also had slurred speech, swallowing difficulty and occipital headache. He did not complain of dimness or blurring of vision, convulsions or vomiting. Neurological consultation then had revealed an extensor right plantar reflex, finger-nose incoordination and a positive Romberg's sign. Cranial nerves were normal. This episode had resolved spontaneously over a week. The patient had been suffering from irregular fever with cough and perceptible weight loss for some months prior to the present episode.

On initial examination in the hospital, the patient was found to be alert and oriented. Neurological examination was unremarkable barring bilateral horizontal nystagmus. Computed tomography (CT) of the brain on admission showed no abnormality. Five days after admission, the patient had a dizzy spell in the ward followed by a confusional state. Repeat CT and Magnetic Resonance Imaging (MRI) scans of the brain were normal.

Baseline investigations revealed marked anaemia (Hb 6 gm/dl), with hypochromia, anisocytosis and schistocytes visible on the peripheral blood smear. His reticulocyte count was 5%, serum haptoglobin level was decreased (5.83 mg/dl) while lactate dehydrogenase level was significantly elevated (912 U/L). He had unconjugated hyperbilirubinemia. Coombs tests were

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negative. Haemoglobin electrophoresis was normal. There was no evidence of iron, vitamin B12 or folate deficiency. This fitted with a diagnosis of microangiopathic haemolytic anaemia (MAHA). He also had thrombocytopenia. Prothrombin time (PT), Activated partial thromboplastin time (APTT) and fibrin degradation products (FDP) were all normal excluding a diagnosis of DIC. Serological investigations showed absence of Anti Nuclear Factor and antibody to double stranded DNA. Screening for Human Immunodeficiency Virus (HIV) by Enzyme Linked ImmunoSorbent assay was positive further confirmed by a positive Immunoblot test for anti HIV 1 antibody. Flow cytometry showed the absolute CD4 lymphocyte count to be 124/ mm³ (normal: 290 - 2600/mm³) satisfying the criteria for Acquired Immune Deficiency Syndrome. Microbiological investigations were noncontributory.

This guided us to a diagnosis of Thrombotic Micro Angiopathy (TMA), most likely thrombotic thrombocytopenic purpura (TTP) associated with HIV infection. Renal function was however normal.

He was treated with 10 units of fresh frozen plasma infusions daily and transfused with packed red cells. Logistic constraints rendered plasmapheresis infeasible. Highly Active Anti Retroviral Therapy (HAART) as well as prophylaxis against *Pneumocystis carinii* infection was instituted. The patient initially improved, enabling oral feeding and transfer from intensive care to the general ward. After a week, however, his condition precipitously declined over a span of four days, terminated by a fatal cardiac arrest.

DISCUSSION

The causes of cytopenias in HIV Infection or AIDS are listed in Table 1:¹

Thrombotic thrombocytopenic purpura is part of the spectrum of thrombotic microangiopathies (TMA) and is characterized by the classic pentad of microangiopathic hemolytic anemia (MAHA), thrombocytopenia, neurological disorders, noninfectious fever, and renal impairment.² Plasma infusion or plasmapheresis is the recommended treatment modality in TTP, plasmapheresis now showing better outcomes. In idiopathic TMA, plasmapheresis with or without prednisolone decreases the mortality rate from almost 100% to 10%.³ It is therefore suggested that the presence of MAHA and thrombocytopenia alone without another clinically apparent cause may prompt one to initiate plasma exchange.² The triggers of TMA include infections, drugs, collagen vascular disease, cancer and pregnancy among others; often, however, no triggering condition is apparent. TMA is a possible complication of HIV-1 infection.⁴

In 1984, Boccia *et al* first observed a thrombotic microangiopathy, Haemolytic Uraemic Syndrome (HUS), in a man with AIDS being treated with chemotherapy

Table 1 : Causes of cytopenia in HIV infection and AIDS

Anemia	Thrombocytopenia	Leukopenia
Anemia of chronic disease	HIV-associated immune destruction	Lymphopenia (characteristic)
Parvovirus B19 infection	HIV-associated decreased production	Neutropenia due to HIV-related decreased production
Adverse drug reaction	Adverse drug reaction	Adverse drug reaction
Thrombotic thrombocytopenia purpura	Thrombotic thrombocytopenic purpura	Antineutrophil antibodies
Hypersplenism	Hypersplenism	Hypersplenism
Marrow infiltration with tumor or opportunistic infection	Marrow infiltration with tumor or opportunistic infection	Marrow infiltration with tumor or opportunistic infection
Megaloblastic anemia		
Autoimmune hemolytic anemia		
Iron-deficiency or blood loss anemia		
Preexisting or coexisting condition		

for Kaposi's Sarcoma.² Gervasoni *et al* reported a cumulative incidence of 1.4% among patients with AIDS in the pre HAART era but could not identify a single case of TMA in their patients with AIDS since the start of the HAART era.⁴ de Man *et al* observed that TTP usually seems to occur in patients with a CD4 lymphocyte count of less than 250 cells/ mm³ and that plasma exchange is the preferred treatment modality, resulting nevertheless in a mortality of 22%.⁵ Possible triggers of TMA in HIV infection include cytomegalovirus, malignancies and anti neoplastic agents. HIV itself has been implicated following the detection of viral p24 antigen in endothelial cells.⁴

With regard to prognosis, patients with no previous HIV-related symptoms have been reported to respond as well to adequate therapy as HIV negative patients. On the contrary, the outcome in patients with AIDS is often poor, despite administration of treatment and is related to the severity of the underlying disease. In their series, Gervasoni *et al* reported 100% mortality for TTP and 71 % mortality for HUS in patients with advanced HIV infection⁴ echoing our patient's fate.

There were several features of interest in this particular case of TTP associated with HIV. Renal insufficiency to some degree is universal and even necessitates dialysis from the outset in 20% of such cases.⁶ Renal function was normal throughout in this patient. Severe hypertension is present in 50%.⁶ Our patient was normotensive.

To conclude, Thrombotic microangiopathies may be an uncommon presenting feature of HIV infection.

Serological testing for HIV infection may have to be considered in patients presenting with TMA, especially if the patients have associated risk factors and suggestive clinical history. Similarly, a diagnosis of TTP needs to be considered in patients with HIV infection who present with severe anemia and thrombocytopenia.

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