A Rare Case of Delirium: Acquired Thrombotic Thrombocytopenic Purpura in an HIV patient

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Introduction :

Thrombotic thrombocytopenic purpura (TTP) is a rare disorder with incidence of one in a million. Manifestations of TTP include fever, thrombocytopenia, thrombotic microangiopathy (TMA) affecting the brain, heart and kidney causing neurological symptoms, and hemolytic anemia.

Less than 10% of patients with acute TTP present with the classic pentad of fever, microangiopathic hemolytic anemia, thrombocytopenia, neurologic symptoms and renal insufficiency.

Deficiency of ADAMTS13 (von Willibrand factor cleaving protease) VWF is linked to TTP and it is predominantly autoimmune in etiology. ADAMTS13 deficiency causes VWF to stick to platelet causing micro-thrombi in small arterioles (Figure 1).

A high index of suspicion is necessary when managing a patient with microangiopathic hemolytic anemia and thrombocytopenia. In recent years, increased incidence of TTP has been reported in patients with coexisting human immunodeficiency virus (HIV) infection, as with the patient we present.

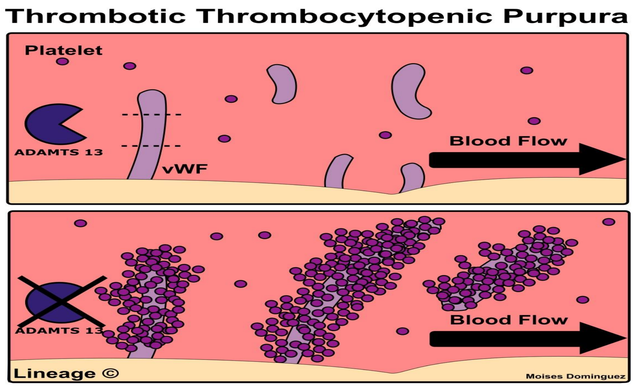

FIGURE 1: Illustrates how deficiency of ADAMTS13 in TTP leads to microangiopathic hemolytic anemia. In TTP, the ultralarge VWF multimers are not cleaved hence combining with the platelets to form aggregates within the microvessels causing hemolytic anemia.

Case Description:

A 55-year-old female presented with confusion after she was found wandering at the airport. She was oriented to self only and gave single phrase answers. Vitals were significant for tachycardia with HR of 125 bmp. Rest of the physical exam was normal. Labs revealed severe anemia (hemoglobin 5.1 g/dL), thrombocytopenia (platelet 6,000/uL), BUN 30 mg/dL, serum creatinine 1.1, and schistocytes on peripheral smear (Figure 2). TTP was the presumptive diagnosis. Without evidence of sepsis, she was treated with intravenous fluids, systemic steroids, blood products and plasmapheresis. She found to be HIV positive with CD4 count of 193 cells/mm3. ADAMTS13 inhibitor was 1.3 (nl <0.4 U) and ADAMTS13 activity level was <3 (nl: 68-163%).

Her mental status improved to baseline and renal failure resolved. Her platelet count returned to normal within 10 days. She was started on antiretroviral therapy and prophylactic antibiotics prior to discharge.

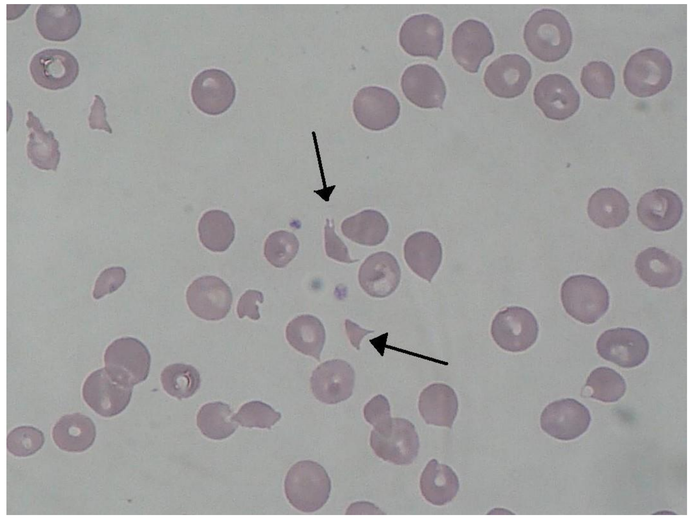

FIGURE 2: Peripheral smear showing schistocytes (arrows).

Discussion:

The exact mechanism for HIV related TTP is unknown, but some proposed ones include the release of large amounts of VWF and downregulation of ADAMTS13 and the production of antibodies against ADAMTS13. ADAMTS13 activity levels below 10% are seen in acquired and hereditary TTP. Acquired TTP with low levels of ADAMTS13 has been increasingly reported in association with HIV infection, such as in this case.

HIV associated TTP is termed as non-idiopathic TTP which represents ~50% of all TTP. It is thought that in non-idiopathic TTP, the clinical syndrome of TTP is a result of the interactions of many factors, in addition to ADAMTS13 enzyme deficiency. These precipitation factors include conditions such as infections, autoimmune disease, HIV, cancer, pregnancy, and drugs.

Historically, TTP and hemolytic uremic syndrome (HUS) were referred to as TMA syndromes. However, now TMA syndrome consists of a wide spectrum of disease which is why it is important to diagnose TTP due to difference in management.

If left untreated, the mortality in TTP can reach up to 90% (it can be reduced to 10-20% with treatment). Treatment is predominantly focused on replacing the ADAMTS13 via plasma exchange. Additional therapies are steroids and Anti-CD20 monoclonal antibodies, rituximab.

References:

1. Joly BS, Coppo P, Veyradier A. Thrombotic thrombocytopenic purpura. Blood. 2017 May 25;129(21):2836-46.
2. Sadler JE. What's new in the diagnosis and pathophysiology of thrombotic thrombocytopenic purpura. Hematology Am Soc Hematol Educ Program. 2015;2015:631-636.
3. Noris M, Remuzzi G. Atypical hemolytic-uremic syndrome. N Engl J Med. 2009;361(17): 1676-1687.