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Case Report

A Rare Case of Thrombotic Thrombocytopenic Purpura associated with Cold Agglutinin Hemolytic Anemia in the Setting of HIV Infection.

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Introduction

Autoimmune diseases may present as one or a combination of multiple disorders.

They may be the primary manifestation of a disease or reflect an underlying infection or malignancy.

Thrombotic thrombocytopenic purpura (TTP) is a distinct, rare but potentially life-threatening entity that classically presents with a pentad of fever, hemolytic anemia, thrombocytopenia, neurologic symptoms and kidney injury. Autoantibodies are targeted against ADAMTS13, the von Willebrand factor (VWF) cleaving protease. Rarer hereditary forms of TTP result from mutations in ADAMTS13, causing severe protease deficiency [1].

In rare instances TTP can be concomitant to cold agglutinin hemolytic anemia. Cold agglutinin disease usually develops as a result of the production of a specific immunoglobulin M auto-antibody directed against red blood cell , relatively uncommon, with an estimated incidence of 0.8–3 per 100,000/year, prevalence of 17:100,000, and mortality of 11% in adults [2].

In this case we present a 25 year old female with TTP secondary to HIV infection found to have cold agglutinin on peripheral smear.

Case Presentation

24-year-old female with PMH of perinatally acquired HIV, Asthma, and Thrombotic thrombocytopenic purpura (diagnosed in October 2020) presents to the emergency department with a 3-day history of fatigue, exertional shortness of breath, pressure-like chest pain, and palpitations. Patient also endorsed generalized abdominal pain associated with dark urine and 5 episodes of non-bloody, non-bilious vomiting for 2 days. One week prior to presentation, the patient visited the Dentist for routine dental cleaning and subsequently developed gingival bleeding which is still ongoing.

Upon presentation, the patient was hemodynamically stable and afebrile, saturating 100% on room air. Vital signs were significant for tachycardia with heart rate ranging from 120-130’s and tachypnea with respiratory rate in the 20’s. BP was stable at 121/75. On physical exam, she appeared fatigued, with scleral icterus, pale conjunctiva, and gingival bleeding. She was tachycardic with a normal heart sounds- S1/S2, no S3 or S4 heard. Lungs were clear to auscultation. Abdomen was soft, non-tender, and non-distended with normoactive bowel sounds. There were ecchymoses present on the left shoulder and right arm.

Labs were significant for anemia with hemoglobin of 5.5 g/dL and thrombocytopenia with platelet count of 5,000/uL. There was evidence of hemolysis with elevated retic count of 7.5% (Normal Range 0.5-2.5 %), elevated LDH of 2,709 IU/L (Normal Range 105-333 IU/L), low haptoglobin of <7.75 mg/dL (Normal Range 41-165 mg/dL), and hyperbilirubinemia of 2.4 mg/dL (Normal Range 0.3-1.2 mg/dL) . Fibrinogen level was 401 mg/dL (Normal Range 200-400 mg/dL). Urinalysis was positive for 2+ bilirubin, 3+ blood, and >20 RBC's. Peripheral smear confirmed the presence of schistocytes, helmet and fragment cells. The peripheral smear also showed evidence of cold agglutinin disease with several clumps of RBC's (Figure 1).
Labs were also significant for an initial high-sensitivity troponin of 620 ng/mL (normal Range <0.04 ng/mL) which increased to 830 ng/mL ten hours later.

Of note, the patient has a history of non-compliance with HAART and her last CD4 count was 103 cells/mm3 with a viral load of 327,000 copies/mL of blood. ADAMTS13 activity has been critically low in the past at 4.5% and ADAMTS13 antibody level was elevated at 14. The patient was started on treatment for HIV related TTP with plasmapheresis which was initiated within the first 8 hours of admission. She was also given packed Red Blood Cell transfusion in view of symptomatic subendocardial ischemia. After 2 units pRBC, hemoglobin increased slightly from 5.5 g/dL to 6.8 g/dL. Pt also received 1 unit of platelets and underwent two rounds of plasmapheresis with an increase in platelet count from 5,000/uL to 21,000/uL.

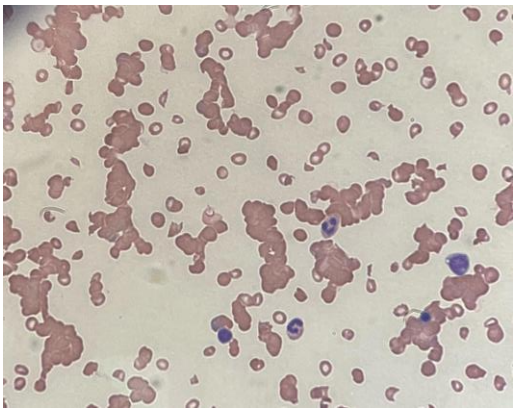

Figure 1 *Cold agglutinin disease with several clumps of Red Blood Cells*

Discussion

Autoimmune haemolytic anemia (AIHA) affects both children and adults with an incidence of 1 per million [4]. The pathophysiology of TTP is the formation of platelet-rich thrombi in affected organs. These thrombi form secondary to large multimers of von Willebrand factor that are not properly broken down within the vasculature [5]. One of the objectives of this case is to emphasize the importance of the adherence to HIV treatment in preventing TTP episodes.

Our patient has elevated troponin, this is common in 50% of cases and is a poor prognostic marker [3]. Serial measurements can be helpful in evaluating disease trajectory. As patients are often young and do not have the classical risk factors of ischaemic heart disease, a high level of suspicion and routine exclusion of myocardial ischaemia in these patients are advised.

Immediate plasma exchange within 4–8 hours is key to management. This reduces the auto-antibody, von Willebrand multimers and replaces ADAMTS13. Immunosuppression with high-dose steroid should be started concomitantly alongside other supportive care measures including red cell transfusion, folic acid to support marrow function, proton pump inhibitors for gastric protection[3].

The association of cold agglutinin and TTP is a presentation that we need to keep in mind although the treatment remains the same, if there is resistance or no response to plasmapheresis, therapies directed at pathogenic process of cold agglutinin such as rituximab, bortezomib, daratumumab, and the anticomplement therapies sutimlimab and pegcetacoplan would be indicated but never as first line.

Conclusion

TTP and cold agglutinin are important differentials in any HIV seropositive patient non compliant with HIV medications. The dramatic clinical presentation of our patient led us to initiate emergency protocol red blood cell and platelet transfusion, however early recognition and immediate management with standard treatment of plasmapheresis are key to ensuring patient survival, which reduce mortality from >90% to 10–20%.[3]

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