An Interesting Case of Refractory Thrombotic Thrombocytopenic Purpura in an HIV Patient with Relapse: Failure to Triumph!

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Introduction

- Thrombotic thrombocytopenic purpura (TTP) is a rare yet fatal emergency
- Early diagnosis and treatment with first-line modalities such as plasma exchange and steroids are the mainstays of treatment
- Failure to respond to traditional first-line treatment results in a refractory TTP
- We present a unique case of refractory TTP

Case Presentation

- A 50-year-old Hispanic female with HIV (on Biktarvy), dyslipidemia, and major depression was admitted to the hospital for an episode of seizure and unresponsiveness
- MRI of the brain revealed acute infarcts in the right putamen and right parietal cortex. Complete blood count demonstrated platelet count of 18,000/cmm.
- Peripheral blood smear revealed schistocytes. Given microangiopathic hemolytic anemia, fever, altered mentation, acute renal injury, multifocal stroke, and thrombocytopenia, a presumptive diagnosis of TTP was made.
- ADAMTS13 factor was very low (<3) and ADAMTS13 inhibitor level was elevated, confirming the diagnosis of TTP
- The patient was started on plasma exchange therapy (PEX) and systemic steroids. Despite 4 cycles of PEX and steroids, platelet count did not respond, and the patient kept deteriorating
- The patient was then started on immunosuppressive therapy with Rituxan (4 cycles) and anti-VWF agent caplacizumab (daily subcutaneous injections) along with the continuation of steroid and PEX. Platelet count increased along with clinical improvement.
- The patient was discharged on subcutaneous injections of caplacizumab (total duration 1.5 months) and tapering doses of steroids

Case Presentation contd.

- She was followed up in the oncology office with biweekly ADAMTS 13 and inhibitor levels; these levels gradually improved over the next 2 months
- Caplacizumab was discontinued after 1.5 months of treatment when platelets remained normal, with the complete clinical recovery of the TTP. However, approximately 2 months later, she returned with a headache. Her laboratory work revealed a normal platelet count, however there was a sudden drop in ADAMTS13 level, and an increased ADAMTS13 inhibitor level.
- Interestingly, she had the first dose of COVID-19 vaccination 4 days earlier. She was started on steroids and Rituxan with the gradual normalization of lab parameters and improvement of headaches. The patient is currently being closely followed up.

Discussion

- A deficiency of metalloprotease ADAMTS13 cleaves the Von Willebrand factor (VWF) leading to the microthrombi formation from the binding of uncleaved VWF multimers to platelets. The ADAMTS13 deficiency is commonly acquired due to the formation of Anti ADAMTS13 antibodies. Untreated TTP has approximately 90% mortality.
- The first-line treatment of TTP is plasma exchange therapy (PEX) and corticosteroids. Lack of clinical improvement/deterioration and persistence of thrombocytopenia despite the first-line treatment is refractory TTP and seen variably in 10-42% cases. Increasing plasma volume, frequency of PEX, high dose steroids, and Rituxan are found to be effective in managing refractory TTP. Along with those strategies, splenectomy, and immunosuppression with cyclosporine, vincristine, cyclophosphamide is also recommended.
- In a recent stage 3 HERCULES trial, caplacizumab, an FDA-approved humanized immune globulin that inhibits VWF interaction with platelets proved effective for management of refractory TTP. This novel agent helped us to treat refractory TTP in an immunocompromised HIV-positive patient.

Conclusion

- Through this case, we intend to spread awareness regarding the importance of early detection and appropriate management of relapsing and refractory TTP with close post-treatment follow-up in collaboration with hematologists

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