Curious Case of Thrombocytopenia: Identifying TTP amidst Confounding Factors

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Objectives

- Identify thrombotic thrombocytopenic purpura (TTP) as a cause of thrombocytopenia amidst atypical exam and laboratory findings
- Distinguish TTP from other causes of thrombocytopenia in a patient with concurrent autoimmune processes

Case Presentation

**HISTORY OF PRESENT ILLNESS**

- 51-year-old woman with past medical history of SLE and secondary ITP presents with petechiae and generalized malaise, found with a platelet count of 11 and positive for COVID-19
- Admission vitals within normal limits
- Admission labs: WBC 3.6, Hgb 9.6, Pt 11. Cr: 0.78 (baseline); PT+PTT within normal limits. Labs one month prior with Pt at 117, Hgb at 11.5

**PHYSICAL EXAM**

- RRR, no murmurs, rubs, or gallops
- Lungs clear to auscultation
- Abdomen soft, non-tender; no organomegaly
- AAOx3, normal neurological exam
- Scattered petechiae and bruising on lower and upper extremities

**OTHER LABS**

- Reticulocytes 1.3 (Index: 0.71), LDH: 711; haptoglobin <8
- COVID-19: Positive
- Direct Antiglobulin Test: negative
- ADAMTS13 Activity: <0.03

**ADAMTS13 Activity:** $<0.03$

**Direct Antiglobulin Test:** negative

**COVID-19:** positive

**Hemoglobin:** 9.6

**Platelet Count:** 11

**Discussion**

- Thrombocytopenia in SLE is very prevalent, seen in 20-40% of patients. The most common cause is the development of autoantibodies to platelets, known as SLE-associated ITP, which is managed with steroids and IVIG\(^1\)
- TTP is a disorder characterized by microangiopathic hemolytic anemia, thrombocytopenia, and organ dysfunction. It typically results from a deficiency of ADAMTS13, a protease that cleaves von Willebrand factor multimers. Uncleaved multimers then cause platelet thrombi and shearing of RBC
- There is an association between SLE and TTP: up to 71% of TTP patients possess a positive anti-nuclear antibody and up to 7-11% develop SLE\(^2\)
- Pathogenesis of TTP in SLE is not clear with some low-normal levels of ADAMTS13; one hypothesis is that autoantibodies lead to changed glycosylation and modulation of ADAMTS13, causing its dysfunction\(^1,2\)
- Treatment includes plasmapheresis and glucocorticoids; SLE-specific medications (ex. cyclosporine and azathioprine) may also lead to favorable outcomes\(^3\)
- COVID-19 can also cause coagulopathies, including thrombotic microangiopathies, due to cytokine storm causing inflammation and endothelial damage. This in turn may lead to autoimmune activation and ADAMTS13 inhibitor production\(^5\)

**Clinical Course**

- As patient previously had similar symptoms due to secondary ITP and recently stopped steroids, she was initiated on IVIG and dexamethasone
- Patient's platelets did not improve and nadired to 7 within 2 days
- Due to concern for TTP, plasmapheresis was started with concurrent IVIG and steroids; her platelets showed dramatic improvement within one day
- IVIG was discontinued; patient received a total of 10x plasmapheresis and 1x rituximab. Repeat ADAMTS13 activity level showed mild improvement
- At subsequent outpatient follow-up, patient received additional rituximab, and platelets remained stable $>200s$

**Conclusion**

- Thrombocytopenia is very prevalent in SLE, and patients who develop TTP can have worse mortality
- In thrombocytopenia, it is imperative to consider all diagnoses, even if clinically, the patient may not manifest end-organ damage symptoms associated with TTP
- While assessing for patient's confounding clinical picture, overlapping emergent situations, such as TTP, should always be considered