CLINICAL VIGNETTE

New Diagnosis of TTP after a Spontaneous Abortion

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Case

A 41-year-old G2P1A1 female with no reported past medical history presents to the community emergency department with a new onset right sided headache, dizziness, blurry vision, nausea with non-bilious, non-bloody vomiting and weakness for 3 days. Her review of systems was otherwise negative for any fevers, chills, chest pain, dyspnea, new rashes, easy bleeding or bruising.

She was hemodynamically stable on arrival. A non-contrast head CT was unremarkable. The patient was found to have to have a hemoglobin of 8 g/dL, normal WBC, and platelets of 7,000/uL, down from 245,000/uL from 6 months prior to presentation. She was also found to have elevated AST 163, ALT 156, tBili 2.1, dBili 0.5 with negative hepatitis serologies, and RUQ ultrasound showing hepatosteatosis. Her basic metabolic panel was otherwise normal and pregnancy screening was negative. The patient was originally admitted under the working diagnosis of ITP, before schistocytes were seen on blood smear and return of additional tests showing signs of hemolysis, LDH 2447 U/L, haptoglobin <8 g/L, corrected reticulocyte % 7.09). Hematology was consulted and confirmed TTP through serially low levels of ADAMTS13 < 3. An IJ Quinton catheter was placed and the patient was initiated on plasmapheresis (PEX) therapy and pulse dose steroids.

A limited secondary workup included a pan-CT scan showing fibroids but no evidence of underlying malignancy, a negative HIV test, and an ANA titer of 1:80. Further rheumatologic tests including antiphospholipid antibody syndrome (APLS) labs returned negative. Upon further investigation, the patient mentioned that 1 month prior she had a spontaneous abortion of a 4 month old fetus.

With treatment, the patient experienced a brief interval improvement with resolution of her neurologic symptoms and platelets increased to 195,000/uL. However this was short lived and with PEX holidays, and her platelet level dipped to a nadir of 11,000/uL. Since her condition was refractory to first line therapy, a referral was requested for transfer to a higher level of care center for rituximab infusions. In the meantime, the patient received up to 15 sessions of PLEX as a temporizing measure prior to transfer.

Discussion

Thrombotic thrombocytopenic purpura (TTP) is a rare, life-threatening disorder with a reported annual incidence of 4-11 cases per million people, affecting mostly young women in their 4^{th} to 5^{th} decade.[1] Predominant in the literature is the association between TTP and pregnancy,[2] with the greatest risk near term and during the postpartum period. This risk of TTP is compounded as pregnancy is already a prothrombotic state with IVC compression leading to stasis, along with an increase in fibrinogen, factor VIII, vWF (1.5-3.0 fold), and loss of endothelial cell thrombomodulin.[3] Other associations include infections, occult malignancy, concomitant autoimmune conditions (present in up to 55% in the Milan registry[1]), and up to 50% of patients will have a positive ANA.[4]

Both congenital and acquired forms of the disorder are characterized by a deficiency in ADAMTS13, a protease that normally cleaves von Willebrand factor (vWF). The deficiency of this enzyme leads to circulation of large vWF multimers that ultimately disseminate to form thrombi in the microvasculature, with resultant depletion of platelets, fibrin particles, and the shear force within capillary beds causing hemolytic anemia. The “classic pentad” of TTP involves fever, thrombocytopenia, microangiopathic hemolytic anemia, renal dysfunction and neurologic symptoms is neither sensitive nor specific, and there is a remarkable diversity in presentation. The absence of symptoms and a normal exam do not exclude the diagnosis of TTP. For example, reports described sudden death of patients during acute presentation even when they did not seem to be critically ill.[3] Suggestive laboratory results include elevated markers of hemolysis, while a low/undetectable ADAMTS13 clinches the diagnosis.

The standard of treatment for decades has been PEX with pulse dose steroids, methylprednisolone 1g x3 days. As prior to PEX treatment patient mortality exceeded 80%.[5] However, relapses can be as high as 55%. The B-cell depleting agent rituximab is usually reserved as salvage therapy for refractory cases. Recent evidence has shown that the early use of rituximab in the acute phase of illness, in tandem with PEX and steroids can shorten the time to response, decrease hospital stay, quicken laboratory normalization of ADAMTS13 activity, reduce relapse rates (10% vs. 50% in the historical gold standard) and increase the time to relapse.[6]

Conclusion

Our patient was admitted and diagnosed with TTP, with a recent terminated pregnancy being the likely trigger. Her positive ANA was not felt to have clinical significance. Because her laboratory indices suggested that she had TTP refractory to PEX with pulse dose steroids, she was transferred to a higher level of care center for rituximab infusions. In the future, we may see more instances where targeted immunotherapy can improve patient trajectories on initial presentation.

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