Title

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CLINICAL VIGNETTE

A Cryptic Case of Acute Pancreatitis

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Case Presentation

A 24-year-old woman with systemic lupus erythematosus (SLE), antiphospholipid syndrome, prior pulmonary embolism on warfarin, and chronic pain presented with three days of crampy abdominal and back pain with emesis. She also described headaches with photophobia, intermittent double and yellow vision, and hematuria. She had no fevers, chills, diarrhea, joint pains, or rashes. She reported near complete compliance with mycophenolate, hydroxychloroquine, and methylprednisolone.

Her exam was notable for normal vital signs. She had diffuse abdominal tenderness without peritoneal signs but with intermittent writhing. Labs revealed a normal white blood cell count, hemoglobin of 8.4 g/dL, platelets of 12,000 and creatinine of 0.85 mg/dL (baseline 0.5 mg/dL). Urinalysis was remarkable for 3+ blood and 3+ protein. Chemistries were notable for total bilirubin 3.4 mg/dL, direct bilirubin 2.0 mg/dL, and lipase 947 U/L. International Normalized Ratio was 1.7, haptoglobin undetectable, lactate dehydrogenase 1139 U/L, and fibrinogen and lactate were normal. Complement levels were low.

She was initially treated for pancreatitis. Ultrasound revealed a mildly dilated common bile duct without stones. Magnetic resonance cholangiopancreatography showed pancreatic edema, consistent with acute pancreatitis. Her severe thrombocytopenia, hemolytic anemia, acute kidney injury, and neurologic symptoms were concerning for thrombotic thrombocytopenic purpura (TTP). Peripheral smear had mild schistocytes and spherocytes (Figure 1). High dose intravenous methylprednisolone and plasma exchange were urgently started. Her ADAMTS13 activity resulted at <5% (normal >67%), confirming the diagnosis of TTP. Her platelets normalized, anemia stabilized, and abdominal pain resolved with these interventions (Figure 2). Steroids were tapered, and she was stabilized on rituximab.

Discussion

TTP is a life-threatening thrombotic microangiopathy classically characterized by thrombocytopenia, microangiopathic hemolytic anemia, neurologic symptoms, renal injury, and fever.[1] Presence of all symptoms is rare, especially at its onset. Our patient had subtle acute renal insufficiency with new hematuria and worsening proteinuria in the absence of fevers. Deficiency in ADAMTS13, a protease that cleaves von Willebrand factor, leads to large von Willebrand multimers that incite platelet aggregation and formation of microthrombi. These microthrombi cause organ ischemia and red cell breakdown. There have been some reports of TTP presenting as pancreatitis, likely due to microthrombi in the pancreas, which was the likely culprit in our patient.[2] Other reports suggest that pancreatitis may trigger TTP.

Clinicians may miss the diagnosis of TTP in patients with SLE or antiphospholipid syndrome due to overlapping features. Our patient had findings of an SLE flare—hemolytic anemia, thrombocytopenia, and low complement levels. Timely review of her blood smear revealed schistocytes, raising suspicion for TTP. The pathogenesis of TTP in SLE patients is not fully understood but likely relates to heightened immune responses.[3] One study showed decreased levels of ADAMTS13 in patients who had active SLE.[4] Awareness of the different presentations of TTP is essential to clinch the diagnosis. Mortality without early treatment is high, even greater in patients with SLE.

The cornerstone of management of TTP is plasmapheresis. It is typically performed daily until organ dysfunction resolved and platelet count stabilized. Complete response to therapy is defined as a platelet count of 150,000 for two consecutive days.[5] High dose steroids are often added concurrently. There is evidence that very high dose methylprednisolone (10mg/kg/day) is more effective induction therapy than lower doses. With prompt initiation, the survival rate for the first episode of TTP is 80-90%. The use of rituximab is variable. Some include it in first-line therapy, while others recommend it for those who do not respond to initial treatment with plasmapheresis and steroids. It can induce sustained remission in most patients who did not adequately respond to steroids and plasmapheresis.

Caplacizumab is a monoclonal antibody that binds to von Willebrand factor and prevents binding to platelet glycoprotein IIb/IIIa, which can block microthrombi. Although, it stops the formation of microthrombi, it does not suppress autoantibody production. Therefore, it should be used in combination with other immunosuppression. Experts recommend adding it for high-risk presentations such as severe neurologic symptoms or high troponin levels. The HERCULES trial randomized 145 patients with TTP to caplacizumab or placebo and found that there were fewer deaths, faster normalization of platelets, and fewer exacerbations in the 30 days after stopping plasmapheresis.[6] The estimated cost of therapy for an episode of TTP

is $270,000, which underscores the need to use this medication judiciously.

There is little evidence for next-line treatments, but therapies that have been tested include cyclophosphamide, vincristine, bortezomib, and splenectomy. Further research is underway to determine the optimal treatment for this often aggressive systemic disease.

Conclusion

TTP can be a life-threatening condition that requires a high index of suspicion given its variable presentation. Pancreatitis is a rare but potential complication of TTP. The backbone of treatment is prompt initiation of plasmapheresis and steroids. Rituximab and caplacizumab are promising treatments for this under-recognized systemic condition.

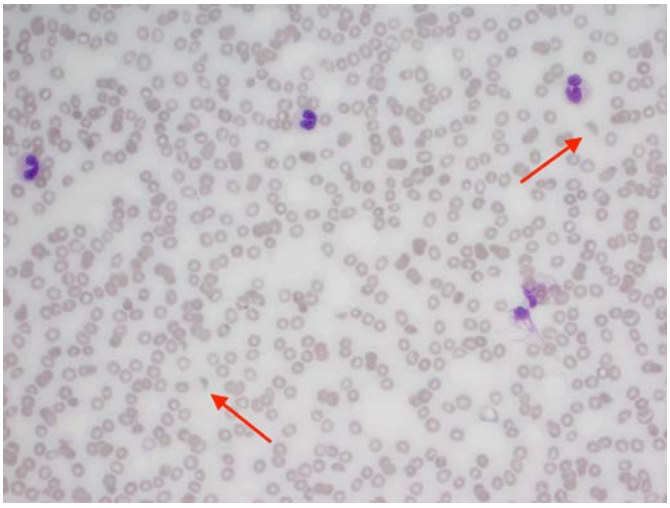

Figure 1.

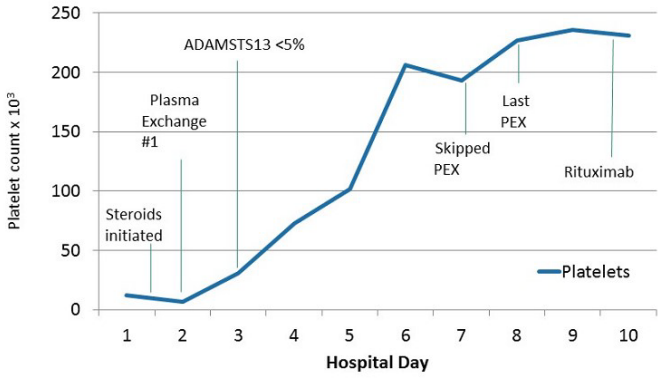

Figure 2. Hospital course by platelet count and treatments received.

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