Sickle Cell Crisis Or Thrombotic Thrombocytopenic Purpura: A Diagnostic Dilemma

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Clinical Presentation

A 19-year-old African-American man with a history of sickle cell disease (hemoglobin SS) presented with increasing back and bilateral leg pain, with associated fever, chest pain, and shortness of breath. Vital signs were notable for fever of 38.9 C, oxygen saturation of 95% on room air, and tachycardia to 140 with otherwise normal hemodynamics. Heart and lung exam were unremarkable. Pt appeared lethargic, with flat affect and mild confusion but otherwise showed no focal neurological deficits. There were no notable skin findings.

Clinical Data

Work up was significant for decrease in hemoglobin from 8 to 6.8 g/dL with hyperbilirubinemia, elevated lactate dehydrogenase, reticulocytosis, and low haptoglobin. Peripheral blood smear showed many sickled cells but no schistocytes. Platelets trended from 256 to nadir of 45 K/uL within 48 hours. No splenomegaly was noted on abdominal ultrasound and HIT antibody returned negative. Kidney function tests were normal. Chest X-ray was clear. ADAMSTS13 activity level was not immediately available for evaluation.

LDH *(IU/L)*	671	6180	
Troponins *(ng/ml)*	1.93	1.48	1.32
Platelets *(K/uL)*	154	86	45
HB *(g/dL)*	8	8	6.8
WBC *(k/uL)*	20.1	24.4	20.2
Bands *(%)*	6	16	15

Overview of Sickle Cell Vaso-Occlusive Crisis (VOC)

- Sickle cell disease is an autosomal recessive genetic disorder with numerous genotypes and a wide range of clinical severity.
- The most common clinical presentation of sickle cell disease is the painful vaso-occlusive crisis. This is the result of intravascular sickling in the capillaries and small vessels that produce not only pain but tissue ischemia, hemolysis, and thrombocytopenia.
- Thrombocytopenia in the setting of a vaso-occlusive crisis is believed to be secondary to platelet consumption and sequestration in multiple organs or disseminated intravascular coagulation due to infections or fat embolism.
- The management of sickle cell crisis may include analgesics, adequate hydration, rest, incentive spirometry, and oxygenation

Overview of Thrombotic Thrombocytopenic Purpura (TTP)

- TTP is a micro vascular occlusive disorder characterized by systemic or intrarenal aggregation of platelets, thrombocytopenia, and mechanical injury to erythrocytes.
- It is associated with a pentad of signs and symptoms:
  - Thrombocytopenia
  - Microangiopathic hemolytic anemia with schistocytes on peripheral blood smear
  - Neurological abnormalities
  - Renal failure
  - Fever
- In practice, thrombocytopenia, microangiopathic hemolytic anemia, and elevated lactate dehydrogenase levels are often sufficient for the diagnosis
- The first-line treatment for TTP is plasmapheresis with fresh frozen plasma, with adjunctive immunosuppression in cases of acquired inhibitors to ADAMTS13

Discussion

An atypical presentation of sickle-cell vaso-occlusive crisis can show significant overlap with TTP, as evidenced by our patient who presented with thrombocytopenia, hemolysis, neurological abnormalities, and fever, thus raising the suspicion for TTP. The peripheral blood smear did not show schistocytes, but this can sometimes be difficult to evaluate in the setting of numerous sickled cells. While there are cases in the literature of patients with SCD developing TTP, it is interesting to note that the majority are in patients with hemoglobin SC disease who typically retain functional splenic activity, putting them at risk for sequestration crisis and thrombocytopenia.

It is important to note that at the time of presentation, results of the ADAMTS13 activity level were not available, which is an important piece in making the distinction between VOC and TTP.

Our patient was ultimately diagnosed with VOC associated with severe sepsis and treated accordingly. He had a rapid recovery and was discharged home without complications.

Take home points

- ✓ An atypical presentation of sickle-cell vaso-occlusive crisis can show significant overlap with TTP, and making the distinction requires a nuanced understanding of their clinicopathologic presentation.
- ✓ The treatment protocols for VOC and TTP are fundamentally different, and in the case of TTP, the prompt treatment can be lifesaving, highlighting the importance of making an accurate and timely diagnosis.

References

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