Sickle Cell Hepatopathy: A Rare Complication of Sickle Cell Anemia

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Introduction

- Sickle cell hepatopathy (SCH) describes the spectrum of hepatobiliary complications seen in sickle cell disease (SS).
  - The hepatobiliary system is most commonly affected within the GI system in sickle cell anemia [1]
  - Chronic manifestations include viral hepatitis, iron overload, cholelithiasis, ischemic cholangiopathy[1]
- The etiology is multifaceted - repeated sickling of RBCs causes liver vaso-occlusion and sinusoidal obstruction, contributing to ischemic hepatic damage.
- Treatment is largely supportive:
  - supplemental oxygen
  - intravenous fluids
  - exchange transfusions in severe cases
- We present the diagnosis and management of a rare case of sickle cell hepatopathy.

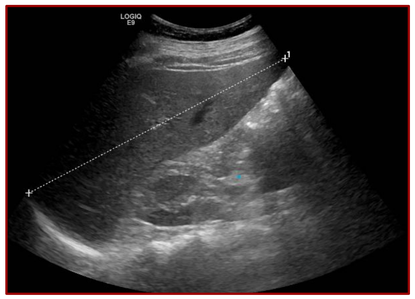
Patient Presentation

- 30 year old male with SS anemia (complicated by avascular necrosis of the shoulder), infrequent pain crises, and a history of cholecystectomy presented to hospital with jaundice
- Prior to the hospitalization, patient was experiencing:
  - Subjective fevers
  - Generalized abdominal pain
  - Acholic stools
  - Dark urine
  - Jaundice
- Outpatient labs showed elevated liver enzyme studies
- Vitals upon presentation:
  - Temperature 98.7 (later spiked to 100.4)
  - Heart Rate 64
  - Blood Pressure 112/57
  - Oxygen Saturation (SPO2) 96% on room air
- Physical exam:
  - General appearance: no acute distress, A&Ox3, jaundiced
  - HEENT: NCAT, PERRL, +scleral icterus, moist mucous membranes
  - CV: regular rate and rhythm, no murmurs
  - Pulm: lungs clear to auscultation bilaterally, no crackles or wheezes
  - GI: bowel sounds normal, soft, mild diffuse tenderness to deep palpation most notably in right upper quadrant, no palpable hepatosplenomegaly
  - Extremities: normal pulses, no lower extremity edema
- Initial labs: Alkaline Phosphatase 189, ALT 104, AST 145, total bilirubin 46.5 (direct >30)

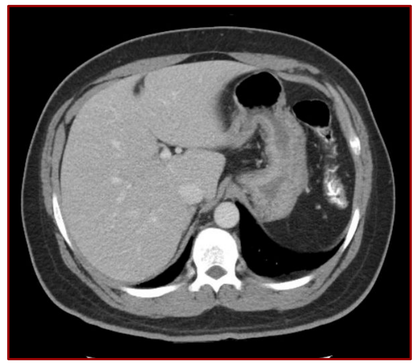
Clinical Course

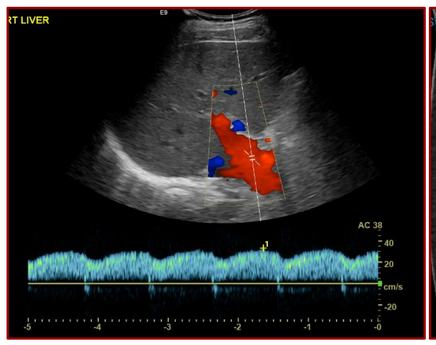
- Recurrent fevers prompted an infectious workup:
  - Acute viral hepatitis studies were unremarkable
  - Blood cultures, chest x-ray, urinalysis unrevealing
- Autoimmune processes were ruled out with a normal ANA, ASMA, and immunoglobulins
- Pt was treated supportively with IV fluids and PRN pain medications
  - Home hydroxyurea was held (thought to be contributing factor to hepatitis)
    - Resumed as an outpatient
- Fevers eventually subsided with supportive care, however his abdominal pain and jaundice persisted
  - Total bilirubin increased, peaked at 51 with a direct bili >30.0
  - Remained without infectious signs
  - Renal function remained stable
  - INR remained stable, suggesting stable synthetic function
- Given persistent cholestasis, there were concerns from the hepatology team for intrahepatic cholestasis
  - We considered exchange transfusion and liver transplant, but our patient had many antibodies in his blood
    - Exchange transfusion benefits DID NOT outweigh the risks of a transfusion reaction
  - Liver biopsy deferred due to known increased risk of bleeding in SS patients and for lack of change in management if biopsy results were to confirm intrahepatic cholestasis
- Our patient was continued on supportive care, and his liver function gradually improved

Imaging

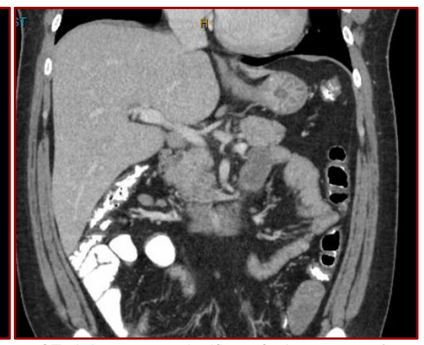


Liver ultrasound: hepatomegaly, up to 19cm without focal lesions





Patent vasculature with hepatopetal flow in the main portal vein, up to 0.3m/s



CT abdomen was significant for hepatomegaly without focal lesions or biliary ductal dilation, atrophic spleen, changes of sickle cell disease

Discussion

- Acute sickle cell hepatopathy has various degrees of severity:
  - Intra-hepatic sickle cell crisis
  - Acute liver sequestration
  - Intrahepatic cholestasis
  - All present with fever, RUQ pain, and jaundice, with varying degrees of lab abnormalities and end organ complications with acute liver failure, renal failure, and coagulopathies [1]
- There are limited treatments available, consisting of supportive care and exchange transfusions as needed to reduce sickling
  - Exchange transfusions for elevated INR or other signs of hepatic dysfunction, fresh frozen plasma for coagulopathies[2]
  - Severe cases may require a liver transplant
    - The best candidates for liver transplant do not have evidence of failure of other organ systems[2]
- Our patient's presentation with severe hyperbilirubinemia was concerning for acute intrahepatic cholestasis:
  - No persistent fevers
  - No evidence of worsening sickling on peripheral smear
  - No evidence of multi-organ failure; he remained hemodynamically stable, with stable renal function, and did not have signs of failure of hepatic synthetic function
- We would consider exchange transfusion or liver transplant if he did not improve with supportive care

Conclusion

- Sickle cell anemia is a condition that can lead to serious complications, one of which includes SS Hepatopathy
- Our patient eventually recovered with only supportive care
  - However pursuing exchange transfusion or liver biopsy were both high risk given his risk of developing a transfusion reaction and bleeding from an invasive procedure
- Liver transplant appears to be the only definite treatment for severe cases of sickle cell hepatopathy
  - This may not be a feasible option for all patients, especially those in resource poor areas
- Further areas of research could be advanced treatment modalities for sickle cell anemia, including:
  - Gene therapy
  - Stem cell transplantation[2]
  - Pharmacologic methods to reduce the risk of progression to complications

References

1. Shah, R., Taborda, C., & Chawla, S. (2017). Acute and chronic hepatobiliary manifestations of sickle cell disease: A review. World journal of gastrointestinal pathophysiology, 8(3), 108–116. https://doi.org/10.4291/wjgp.v8.i3.108
2. Samuel SS, Jain N. Sickle Cell Hepatopathy. [Updated 2021 Oct 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK574502/