Spur Cell Hemolytic Anemia: an uncommon etiology of anemia in liver cirrhosis.

Introduction

A common complication of hepatic cirrhosis is anemia. Anemia in cirrhosis is associated with worse prognosis.[1] It has a broad differential diagnosis and often several etiologies co-exist within a single patient.[2] Causes of anemia in cirrhosis include gastrointestinal hemorrhage (variceal bleeding), hemophilia secondary to thrombocytopenia and coagulation disorders, portal hypertension gastropathy and gastric vascular ectasia, iron deficiency, hemolysis related to splenomegaly, autoimmune disease, and less commonly, spur cell hemolytic anemia, among others.[2]

Spur cell hemolytic anemia is especially associated with poor prognosis in patients with cirrhosis.[3] It was first documented in the literature in 1964 by Smith et. al, which described “curious projections” on erythrocytes found in a patient with alcoholic liver cirrhosis.[4] Although it is commonly linked to alcoholic hepatic cirrhosis, it can occur throughout the spectrum of cirrhosis and has even been found in acute hepatic failure.[5] The erythrocyte deformities are thought to be related to aberrant lipid and protein metabolism leading to defective cell membranes, loss of cellular plasticity, and splenic cellular deformation. Although supportive care has shown some benefit, definitive management is solely achieved through liver transplantation[5].

In this report, we describe the case of a patient with liver cirrhosis admitted to HCA Bayonet Point Hospital who was found to have spur cell hemolytic anemia.

Patient presentation

Chief Complaint

- 54-year-old male with history of alcohol-induced cirrhosis presents with confusion, lethargy, and nausea, consistent with hepatic encephalopathy

Past medical history

- Alcohol-induced cirrhosis. MELD score 29, Child-Pugh 14, class C.
- Prior alcohol abuse (reported abstinence for 8 months)
- COPD - using 3L nasal cannula at home
- History of GI bleed due to esophageal varices

ROS: confusion, nausea, fatigue, blurred vision

- Vitals: afebrile, NSR, normotensive, 3L nasal cannula
- Physical exam: Lethargic, scleral icterus, jaundiced, mild respiratory distress

Labs

- Ammonia 203, total bilirubin 14.9, albumin 2.5g.dL
- Glucose within normal limits, serum ethanol and toxicology negative
- Pancytopenia: WBC 3.2, Plts 20, Hbg 6.1, MCV 130
- Coagulopathy: INR 3.0

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Clinical Course

On admission:

- CT brain: negative. Chest x-ray: mild pulmonary edema
- 2 units pRBCs given, Hbg improved to 7.5
- Lactulose enema and oral lactulose started
- Vitamin K initiated. FOBT negative

Days 2-7

Hepatic encephalopathy

- Mentation improved to baseline with lactulose

Anemia

- GI was consulted, and GI source of bleeding was ruled out.
- Hbg continued to decrease, required 2 additional pRBCs
- Hematology was consulted
- Folate and vitamin B12 were within normal limits.
- Serum ferritin elevated to 1,060 ng/mL, iron 182 ud/dL. Decrease total iron binding-capacity at 231 mcg/dL
- Further labs were suggestive of hemolytic anemia
- Reticulocytes 11.7, LDH of 439, haptoglobin <20.0, fibrinogen 161.
- Peripheral blood smear was consistent with “spur cells”

Coagulopathy

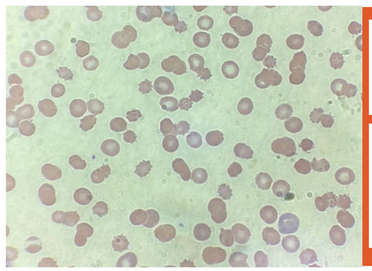
- Vitamin K initiated. INR improved to 2.3.
- 2 units of FFP, 1 unit cryoprecipitate given

Cytopenia: Thrombocytopenia and leukocytopenia monitored and remained stable throughout the hospital course

Day 8: Discharged to home health care

- Instructions for close follow up, repeat labs, and hepatologist referral for potential liver transplant work up.

Follow-up: Patient is currently being evaluated for liver transplant



Peripheral blood smear (May-Giemsa stain, × 1000) showing occasional acanthocytes (spur cells).

Supporting labs

- ↑ reticulocyte, bilirubin, LDH,
- ↑ MCV, RDW
- ↓ haptoglobin

Supporting clinical finding

- Jaundice, splenomegaly

Patient Supporting Labs and Peripheral Blood Smear

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Discussion

Spur cell anemia is a rare but important cause of anemia in patients with hepatic cirrhosis. There are currently no guidelines determining the diagnostic criteria of the disease. Likewise, the prevalence and survival rates of this rare form of anemia are not well documented in the literature. A few studies in the literature have found the prevalence to range from 13-31%.[1] Although previously thought to be a disease associated specifically with alcoholic liver cirrhosis, more recent studies have found it may be equally present in all etiologies of hepatic cirrhosis.[2] There appears to be an association with increased spur cell burden and increasing mortality, with some studies showing spur cell rate >5% portending worse mortality rates. On the contrary, spur cell rates 1-4% with no signs of hemolysis do not appear to be associated with worse mortality as compared to hepatic cirrhosis without spur cell anemia.[3]

The pathogenesis of spur cell anemia is thought to be related to impaired lipid metabolism leading to increased levels of cholesterol within the red blood cell (RBC) membrane.[4] Previous studies have found low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and total cholesterol (TC) levels to be decreased proportionately with worsening hepatic function.[5] More recent studies have found lower levels of apo-lipoprotein A-II and HDL-3 in patients with cirrhosis, but increased levels of HDL-2.[6] These findings suggest fundamental changes in RBC membrane structure and lipid metabolism, specifically HDL.

Definitive treatment of spur cell anemia is achieved with liver transplantation.[7] However, some studies have found varying rates of success with medical management.[8] In our case, the patient was referred for evaluation of liver transplantation.

Conclusion

- Broad differential diagnoses: Anemia is commonly seen with alcohol-induced cirrhosis, with many different etiologies
- Prevalence of spur cell anemia is unclear; it appears to be more prevalent with cirrhosis secondary to alcohol use and with more advanced stages of cirrhosis
- SCA may be underdiagnosed as many patients have multiple etiologies of anemia. Should we be screening for hemolytic anemia in cirrhotic patients?
- Consider hemolytic anemia if no overt evidence of bleeding, labs are useful to determine extra- vs. intra-vascular hemolysis.
- No clear diagnostic criteria for spur cell anemia. Peripheral blood smear is useful, *proposed cutoffs of > 5-20% acanthocytes
- Associated with poor survival: Spur cell anemia is an independent predictor of mortality and survival for cirrhotic
- Liver transplantation is the only curative treatment

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