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Case Report

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An Unusual Case of Hemolytic Anemia Reversed with Liver Transplantation

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ABSTRACT

Spur cell anemia is acquired hemolytic anemia seen in patients with advanced liver disease, particularly in the setting of alcoholism, and warrants urgent liver transplant evaluation. We describe the case of a 58-year-old female with alcoholic cirrhosis who presented with worsening liver disease, profound anemia poorly responsive to blood transfusions, and multiple spur cells on the peripheral smear. She underwent a liver transplant, which led to the resolution of hematologic abnormalities and the need for transfusions. Our case highlights the significance of spur cell anemia as a harbinger of poor prognosis in patients with advanced liver disease and its reversibility with liver transplantation.

Keywords: Spur cell anemia; Alcoholic cirrhosis; Liver transplant; Zieve's disease; Plasmapheresis

INTRODUCTION

Anemia in liver disease is often multifactorial with nutrient deficiencies, hypersplenism, alcohol-induced myelosuppression, and chronic gastrointestinal blood loss being the common contributors[1]. Spur cell anemia (SCA) is a rare but well-recognized complication of advanced liver disease characterized by Coombs negative hemolysis and increased acanthocytes on peripheral blood smear[2]. Its presence is associated with poor outcomes and liver transplant evaluation should be carried out urgently in such patients[3]. Here we present a patient with SCA whose anemia resolved after liver transplantation.

Case presentation

A 58-year-old female with alcoholic cirrhosis, hypertension, and depression presented with progressive dyspnea, abdominal discomfort, and bilateral lower extremity swelling. Her last alcoholic beverage was over four months ago, and she reported compliance with medications. Physical exam was remarkable for icterus, diminished bibasilar breath sounds, distended and slightly tender abdomen, and bilateral pedal edema extending up to knees.

Laboratory studies revealed a total bilirubin of 25.2 (0.2-1 mg/dL), indirect bilirubin- 18.3 (0.0-0.8 mg/dL), alkaline phosphatase – 121 (25-105 U/L), aspartate transaminase -51 (8-34 U/L) and alanine transaminase - 51 (3-37 U/L). White blood count was 12.7 (4.1-10.8 k/uL), hemoglobin- 5.6 (11.2-15.7

g/dL), mean corpuscular volume-119 (79.4-94.8 fL) and platelets-51 (140-370k/uL). INR was 2.99, prothrombin time – 33.2 (9.7-13.1s), partial thromboplastin time – 38.3 (24.6-34.4s) and Fibrinogen 106 (230-450 mg/dL). Computed tomography of abdomen showed cirrhotic liver, splenomegaly and ascites. Her MELD-Na score was 32 and she was admitted to the intensive care unit.

She was found to have spontaneous bacterial peritonitis and was treated with antibiotics. Work up for anemia revealed normal folate and B12. Iron profile was consistent with anemia of chronic disease. She received packed red cell transfusions (PRBC), cryoprecipitate, and vitamin K. Interestingly, her repeat hemoglobin after 1 unit of PRBC was 4.8 g/dL and after the second unit, it increased only minimally to 6.1 g/dL. There was no evidence of bleeding, and it raised concerns for hemolysis. Hemolysis labs were remarkable for an elevated lactate dehydrogenase -265 (100-220 U/L), low haptoglobin <15 (35-195 mg/dL), and elevated absolute reticulocyte count -0.125 (0.02-0.10 million/mm3). Direct Coombs test, HIV, and hepatitis panel were negative.

Most of her abnormal labs, including the low haptoglobin, thrombocytopenia, macrocytic anemia, and deranged coagulation profile could be explained by her end-stage liver disease, except for inadequate response to PRBC. Her creatinine remained stable. Peripheral blood smear (PBS) showed anisocytosis, poikilocytosis, occasional schistocytes, and acanthocytes. She was diagnosed with spur cell anemia based on the PBS findings (Figure 1) and the presence of hemolysis in the setting of advanced liver disease. Apolipoprotein A1 level was low at 53 (116-209 mg/dL), consistent with the diagnosis.

She required intermittent transfusion support throughout the admission and was evaluated by the liver transplant team who deemed her a good transplant candidate. She was discharged with a hemoglobin of 8 and was readmitted 2 months later for orthotopic liver transplantation. After transplantation, her hemoglobin ranged from 11-12 g/dL and she did not require any PRBC support. Other laboratory abnormalities were also resolved. PBS 10 days after transplant showed resolution of spur cells.

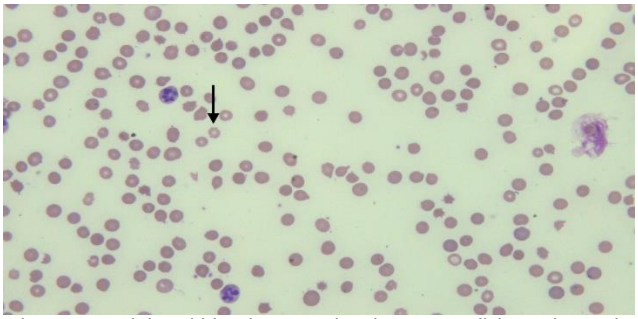

Figure 1: Peripheral blood smear showing spur cell (acanthocyte)

DISCUSSION

Although anemia can be seen in up to two-thirds of cirrhotic patients[3], hemolysis is relatively infrequent. Spur cell anemia (SCA) and Zieve's syndrome (ZS) tend to be the most important considerations in the setting of chronic alcoholism, liver disease, and non-immune mediated hemolysis[4]. Due to drastically different treatment approaches, distinguishing the two is of utmost importance. While ZS is associated with transient hemolytic anemia, which is rapidly reversed with alcohol abstinence, SCA is an indicator of grave prognosis and warrants urgent liver transplant.

The prevalence of SCA in literature is ill-defined[5] and the exact pathophysiology is still unclear; however, abnormal lipoprotein metabolism[6] is thought to play a key role. These patients tend to have decreased serum lipoprotein-a, apo-AI, apo-AII, HDL3, and reduced lecithin cholesterol acyltransferase activity[7]. Their RBCs are less deformable due to excess cholesterol deposition, which in turn leads to splenic sequestration and destruction. Traditionally, alcoholic cirrhosis has been linked to SCA; however, recent reports suggest that it may be present in liver disease regardless of the etiology[8]. It should, however, be noted that the presence of spur cells is not always associated with anemia[3] and the diagnostic criteria established by Sousa et al. requires a hemoglobin < 10 g/dl, the presence of hemolysis, >5% spur cells in the peripheral blood, and the exclusion of other causes of anemia[9]. Our patient fulfilled all the above conditions.

SCA is an independent predictor of mortality in end-stage liver disease with median survival ranging from a few days to less than 6 months[5]. The most effective

treatment is orthotopic liver transplantation. As in our case, SCA resolved promptly after transplantation. Improvement in lipid metabolism, portal hypertension, and possibly resultant hypersplenism[3] are thought to be responsible for this rapid reversion.

Few case reports have explored non-surgical options like plasmapheresis, steroids, and the combination of flunarizine, pentoxifylline, and cholestyramine with varying degrees of success[3,10,11]. Plasma exchange has been shown to improve dyslipidemia and stabilize hematologic parameters with at least transient interruption of anemia progression[10, 12]. Flunarizine and pentoxifylline cause a reduction in the free intracellular calcium concentration, leading to improvement in the spur cell deformability[13,14]. SCA patients tend to have high chenodeoxycholic acid (CDCA) levels which exert a hemolytic effect. Cholestyramine reduces the chenodeoxycholic acid levels, leading to improvement in the lipid composition of the RBC membrane, and lesser hemolysis[11,15]. Steroids may improve RBC stability by increasing the oxygenated cholesterol content in the RBC membrane, or by increasing the intracellular water accumulation[16]. However, more conclusive long-term data for these therapies is lacking.

CONCLUSION

SCA should be considered in patients with worsening advanced liver disease and acquired hemolytic anemia[3]. We propose to assess hematologic parameters and peripheral smear as a part of pre-transplant risk stratification in addition to using the MELD score. Prior studies of SCA in liver disease have excluded patients with hepatocellular carcinoma (HCC), and it may be interesting to study the prevalence of SCA in patients with HCC that develops in the background of cirrhosis.

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