LETTER TO THE EDITOR

Is there a role of exchange transfusions in patients with sickle cell anemia and major liver surgery?

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Clinical manifestations of sickle cell (SC) disease include viral hepatitis, cirrhosis, cholelithiasis and intrahepatic cholestasis [1,2]. A rare but potentially fatal complication of SCA is SC intrahepatic cholestasis (SCIC) presenting with hyperbilirubinemia, coagulopathy and liver failure. A common pathophysiologic explanation confirmed by histology is ischemic necrosis caused by impaired intrahepatic circulation due to intravascular sickling and sinusoid congestion [3]. Unlike splenic sickling, hepatic sickling has been described as a frequent but benign, self-limited process leaving no permanent sequelae [3]. 'Hepatic crisis' occurs in 10% of patients and are associated with few signs and symptoms. Even though the liver is protected by its dual blood supply, sinusoidal obstruction by enlarged Kuppfer cells and clumps of sickle red cells causing degenerative liver lesions have been reported [3]. Hepatic focal necrosis, portal fibrosis, regenerative nodules and cirrhosis is a wide range of pathologic events described in an autopsy series of SC patients from Johns Hopkin's [4]. Few studies also proved that SCA or SCD patients undergoing elective surgery often experience significant complications in the peri- and post-operative period [2].

A limited experience of intrahepatic cholestasis is documented following liver transplantation. There are only three reported cases of liver transplantation in patients with SCA [1,5]. The prognosis of the liver allograft is difficult to estimate, but higher rates of vascular complications have been described [1]. However, other studies in patients with SCA end-stage kidney disease demonstrate a survival after kidney transplantation similar to that of transplanted patients without SCA but a higher prevalence of SC crisis after surgery [5].

We add our experience of a 19 year old Caucasian female with SCA underwent a liver transplant due to hepatitis B cirrhosis. One month later, the patient developed central biliary strictures required multiple dilatations with percutaneous biliary stent placement although the inflow vessels (hepatic artery and portal vein) were patent by Doppler ultrasound.

Seventeen months post-transplant the patient was readmitted with elevation of liver enzymes (bilirubin: 2.7 mg/dl, AST: 322 μg/l, ALT: 236 μg/l, ALP: 380 mg/dl and GGT: 152 mg/dl). Liver biopsy revealed hepatocellular cholestasis with sinusoidal congestion and sickling of erythrocytes. Prominent plasmacytic infiltrates in the portal tracts were also identified. The patient was started on solumedrol and a cholangiogram through the stents was performed which revealed no signs of obstruction. The hematocrit was 28.5% with HbS: 33.8% and HbD: 32.8% at the time of the admission. Although treatment of acute rejection was instituted the liver enzymes remained elevated. Subsequently, exchange transfusion was performed of approximately 4 units of packed red blood cells. The HbS titer was decreased to 7.8% and the liver function tests declined slowly towards normal in a few days. In our case although no definite proof exist, we assume that biliary stenosis and intrahepatic cholestasis might be due to SC disease supported further by the clinical evidence that applied exchange transfusions reduce HbS levels and led to relieve of cholestasis secondary to SC sequestration.

Liver transplantation is a complex procedure and intraoperative events such as ischemia, reperfusion injury, hypothermia and acidosis, can induce sickling. Avoiding factors that promote this vicious cycle can lower the risk of complications postoperatively [5]. Transfusions can also suppress erythropoiesis of HbS-containing erythrocytes and consider an alternative approach to reverse liver damage [6].

More recently we published a case of intrahepatic cholestasis after major hepatectomy for colorectal liver metastases in a 43-year-old white female with SCA [7]. Due to the persistent high liver enzymes for >4 days postoperatively combined with sinusoid congestion in the specimen an intrahepatic cholestatic pattern was suspected. Therefore, an exchange transfusion of 3 units packed red blood cells was administered to reduce the HbS level from 35% to 7.3%. A decline of the liver function tests (LFTs) and bilirubin levels towards normal were noted the following day and remains until discharge. Although no definite proof exist, the IHC was assumed to be due to sickling of erythrocytes with subsequent sinusoid congestion caused by venous stasis. However, there is strong clinical evidence that the applied exchange transfusions my be one

key step in the treatment of intrahepatic cholestasis due to cell sickling in SCD.

Apparently, the high HbS level along with the surgical stress promotes sickling and sinusoid congestion due to venous stasis. In our case, poor microvascular circulation due to SC sequestration is suspected as the cause for IHC. This inclination urged our team to perform a trial exchange transfusion in hope of reducing the HbS level. The decline of liver enzymes and bilirubin the following day of transfusion as well as the pathology report from the specimen, support the concept of a reversible IHC pattern.

In conclusion, we believe that SC crisis needs to be in the differential diagnosis of increased liver enzyme post-major hepatic surgery including liver transplantation in patients with SCA. Exchange transfusion is a reasonable treatment providing success.

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