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CASE REPORT

Successful liver transplantation in a patient with sickle-cell anaemia

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Abstract Liver transplantation in the setting of sickle-cell anaemia poses several new challenges to the transplant team. Hypoxaemia, acidosis and a decrease in body temperature are common occurrences that can cause sickling in the peri-operative period, putting the patient at risk of sickle-cell crises or graft dysfunction. We describe a patient with sickle-cell anaemia who successfully underwent transplantation, and we discuss the rationale of various precautions that had to be taken.

Keywords Liver · Transplantation · Sickle-cell anaemia · Peri-operative management

Case Report

A 23-year-old Caucasian male patient was referred to our department after being admitted and treated elsewhere for bleeding oesophageal varices and hepatic encephalopathy. Five years before he had been diagnosed with secondary haemochromatosis due to sickle-cell anaemia with frequent sickle-cell crises and repeated blood transfusions. For the past 3 years he had been treated with hydroxycarbamide and deferoxamine. At the time of referral, his Child–Pugh score was 10, and it was decided that he should be assessed for liver transplantation. There were no signs of other concomitant liver diseases such as viral hepatitis, auto-immune hepatitis, cholestatic liver disease, or excessive alcohol consumption. Transferrin saturation was 96% with a serum ferritin concentration of 1,018 μg/l. Liver biopsy showed moderate-to-severe fibrosis with extensive iron depositions. Markedly dilated sinusoids were found with prominent aggregation of erythrocytes.

Extensive pre-operative examination revealed no contra-indications for liver transplantation other than major concerns about the risk of his sickle-cell anaemia on the peri-operative and postoperative course. He was listed for liver transplantation in November 1995, and a suitable organ became available in March 1996. An orthotopic liver transplantation with end-to-end cavo-caval anastomosis was performed, with a veno-venous bypass technique being used. A duct-to-duct biliary anastomosis was made. Histological examination of the explanted liver showed the same abnormalities as described in the pre-transplantation biopsy.

Prior to his operation, the patient received an exchange transfusion with 5 units of concentrated erythrocytes, which decreased the HbS concentration from 32% to 19%. During his operation we took meticulous care to maintain optimal oxygenation and hydration and prevent acidosis. To keep the body temperature above 36 °C, we warmed all intravenous fluids prior to infusion. The blood in the extracorporeal circuit was warmed, several heat

exchangers being used. The donor liver was flushed with a 20% albumin solution at room temperature before being placed in the recipient. Extensive blood loss in the hepatectomy phase mandated the transfusion of 44 units of concentrated erythrocytes, 70 units of fresh-frozen plasma, and 60 units of platelets, along with 15 l of scavenged red cells from the cell saver. The precautions taken allowed body core temperature to remain above 36 °C at all times; the oxygen saturation did not drop below 90%, and the Ht levels that were recorded were above 0.26.

The postoperative course was without major complications. After 5 days the patient was discharged from the ICU, and 12 days later he left the hospital. An immunosuppressive regimen combining cyclosporine, azathioprine and prednisone was used. Treatment with hydroxycarbamide and deferoxamine was continued after transplantation. In the immediate postoperative period, no specific efforts were made to lower his HbS level, which was 2.6% at the end of the operation and 4.9% 1 week after. No episodes of rejection were observed. Today, 5.5 years after transplantation, his hepatic function is good. A recent liver biopsy again showed extensive iron depositions and mild lobular inflammation with minimal fibrosis. His sickle-cell anaemia is still complicated by frequent crises.

Discussion

Liver disease in patients with sickle-cell anaemia can be a direct consequence of extensive intra-hepatic sickling, or, more commonly, occurs secondary to transfusion-related causes such as viral hepatitis or iron overload [1]. Four case reports can be found in the literature describing liver transplantation in a patient with sickle-cell anaemia, and one describing a combined liver and kidney transplantation (Table 1) [3, 4, 5, 6, 7]. The major concern in the peri-operative period is the occurrence of sickling, which can be triggered by periods of acidosis, hypoxemia, intra-vascular dehydration or hypothermia, all of which will occur at least locally during every liver transplantation. Peri-operative management is, therefore, aimed at preventing these conditions as well as possible, by keeping the patient warm and well hydrated, giving supplemental oxygen, and by the careful positioning of the patient to prevent stasis.

A pre-operative exchange transfusion is very effective in reducing the HbS concentration. In a randomised trial of partial exchange transfusion (reducing the HbS level to $< 30\%$) vs conservative management prior to a variety of surgical procedures being carried out, no reduction in peri-operative complications was demonstrated [8]. Only one of these operations was categorised as a high-risk surgical procedure, however. In four of the reported cases of liver transplantation in patients with sickle-cell disease, the HbS level was reduced to 9.9%–27% through either pre-operative or peri-operative exchange transfusions. In one report this is not mentioned explicitly, but the patient's HbS level going into the operation was 10.3%. The high transfusion requirement in our patient resulted in an HbS level of 2.6% immediately after surgery. This may have contributed to the uneventful recovery. In three cases the

Table 1 Summary of reported cases of liver transplantation in patients with sickle-cell anaemia (*OLT* orthotopic liver transplantation, *HCV* hepatitis-C virus, *ALF* acute liver failure, *VOD* veno-occlusive disease, *SCIC* sickle-cell intra-hepatic cholestasis)

Authors	Patient	Indication for OLT	Peri-operative management[a]	Outcome
Kindscher et al.	Woman, 47 years	HCV infection	Exchange transfusion, cell saver, HbS < 30% post-OLT	Cerebral haemorrhage
Lang et al.	Boy, 11 years	Secondary biliary cirrhosis	Exchange transfusion, HbS < 20% post-OLT	Alive at 2 years; intact graft function
Lerut et al.	Woman, 42 years	Cryptogenic cirrhosis	Exchange transfusion	Alive at 39 months; liver parenchymal necrosis at 6 months with complete recovery
Emre et al.	Boy, 6 years	ALF	None (HbS at OLT = 10.3%)	Re-transplantation at 3 months because of VOD; died at 6 months after third OLT
Ross et al.	Man, 49 years	SCIC	HbS < 20% post-OLT	Died at 22 months with intact graft function
van den Hazel et al.	Man, 23 years	Secondary haemochromatosis	Exchange transfusion, cell saver	Alive at 5.5 years; intact graft function

[a]Use of pre-operative or peri-operative exchange transfusion, use of cell saver, and use of transfusions after OLT to keep HbS levels below a certain maximum

post-operative HbS level was also kept below 30% for up to 6 months after transplantation, to prevent sickling. Histological examination in one of these cases on post-operative day 39 still showed accumulation of sickled erythrocytes in hepatic sinusoids and was accompanied by mild elevations of bilirubin and transaminases. In the two instances where no effort was made to maintain HbS at low levels after transplantation, both patients experienced sickle-cell-related problems [3, 6]. One patient, 6 months after transplantation, developed extensive parenchymal necrosis in multiple segments of the liver, which was attributed to ischaemia secondary to intra-hepatic sickling. A careful wait-and-see policy led to complete recovery of the laboratory and radiological abnormalities. The other reported patient had to undergo re-transplantation at 3 months for veno-occlusive disease and graft-failure. Histological examination of the explanted graft showed occlusion of the terminal hepatic venules by fibrosis and packed sickled erythrocytes. Although we did not lower HbS levels after transplantation and our patient experienced no problems indicative of intra-hepatic sickling, other reports suggest that it is advisable to keep HbS levels below 20–30% during the initial post-transplantation period.

The use of an extra-corporeal circulation system has both advantages and grave disadvantages. It reduces acidosis and hypoxemia in the lower extremities, lowering the risk of sickling. A veno-venous bypass allows warming of the circulating blood to maintain normal body temperature. On the other hand, the higher average blood loss carries the risk of hypovolaemia and erythrocyte sickling and has been associated with an adverse outcome after transplantation. Reported cases of liver transplantation made use of both extra-corporeal circulation with end-to-end caval anastomosis, as well as end-to-side anastomosis without an extra-corporeal circuit (piggy-back technique). Sickle-cell disease is generally regarded as a contra-indication to the use the cell saver [2]. In principle, the limited number of sickled erythrocytes that remains after an exchange transfusion should be filtered out by the cell saver. This was assessed in one study, where no red cell abnormalities were found in blood recovered from the cell saver [4].

In conclusion, liver transplantation can be performed successfully in patients with sickle-cell anaemia if proper attention is given to optimal prevention of those factors that can provoke erythrocyte sickling. We promote the use of an exchange transfusion prior to operation. It seems, furthermore, advisable to keep HbS levels below 20–30% for the first 6 months post-transplantation to prevent intra-hepatic sickling.

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