Brief report

TRANSPLANT International

Transplant Int (1992) 5: 118–119

Histologic resolution of documented hemosiderosis in a renal transplant recipient

A case report

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Received March 26, 1991/ Received after revision July 23, 1991/ Accepted September 23, 1991

Abstract. A 33-year-old cadaveric renal transplant recipient showed complete histologic resolution of hemosiderosis by liver biopsies obtained pre- and post-transplantation. Although there have been reports in the past of progression of hemosiderosis to hemochromatosis to severe liver failure in the renal transplant population, the correlation has never been clear. This is the first case report of complete resolution of hemosiderosis as documented histologically by liver biopsies in a cadaveric renal transplant recipient.

Key words: Hemosiderosis, in kidney transplantation – Kidney transplantation, hemosiderosis

Hemosiderosis has been described as a relatively infrequently recognized complication in renal transplant recipients that can progress to hemochromatosis and subsequent fulminant liver failure [1, 6–8]. Rao and Anderson showed a 27% incidence of hemosiderosis in a population of 74 renal transplant recipients [7]. Up until the present time, emphasis has generally been placed on the progression of this condition in the post-transplant period. This case report describes the unique resolution of hemosiderosis as documented by liver biopsies pre- and post-transplantation in a renal transplant recipient.

Case report

A 33-year-old male was admitted in October 1983 for pretransplant splenectomy. He had experienced chronic renal failure in 1968, secondary to chronic glomerulonephritis. He had been hemodialyzed since 1982. Prior to this admission, the patient had received a total of six units of packed red blood cells and was given two additional units of packed red blood cells during his 1983 hospitalization.

Preoperative workup, however, revealed abnormal liver function tests: alkaline phosphatase 442 IU/l (normal range 40–130 IU/l), SGOT 68 IU/l (normal range 5–40 IU/l), and direct bilirubin 0.5 mg/dl (normal range 0.1–1.2 mg/dl). Hepatitis B surface antigen and hepatitis B core antibody were negative at that time. An ultrasound of the upper abdomen showed a normal gallbladder and common bile duct without evidence of cholelithiasis. Liver biopsy was not performed at that time due to an abnormal bleeding time, despite transfusion with ten units of cryoprecipitate. In view of the above findings, splenectomy was canceled and kidney transplantation was deferred.

In March 1986 the patient was re-evaluated as a renal transplant candidate. A serum ferritin at that time was elevated at more than 500 ng/ml (normal range 10–200 ng/ml). The patient underwent a percutaneous liver biopsy that showed a moderate degree of hemosiderin deposition within Kupffer cells and hepatocytes without evidence of fibrosis or inflammation (Fig. 1). The procedure was complicated by bleeding at the biopsy site, requiring transfusion with two units of packed red blood cells and subsequent laparotomy for plication of the biopsy site and evacuation of intraperitoneal hematoma.

In November 1987 the patient underwent a cadaveric renal transplant. He was discharged on postoperative day 10 with a serum creatinine of 2.6 mg/dl. Liver function tests during that hospitalization were still mildly elevated: alkaline phosphatase 287 IU/l, SGOT 41 IU/l, and total bilirubin 0.4 mg/dl.

In December 1988 the patient presented with cholecystitis and had cholelithiasis documented by ultrasound. He underwent cholecystectomy with concomitant liver biopsy. Liver function tests at the time of this admission were still mildly elevated: alkaline phosphatase 165 IU/l, SGOT 38 IU/l, and total bilirubin 0.7 mg/dl. The patient's postoperative course was unremarkable and he was discharged on postoperative day 4. The liver biopsy showed complete resolution of the previously documented hemosiderosis with normal hepatic architecture and without evidence of portal inflammation or fibrosis (Fig. 2).

Discussion

Liver disease is a frequent cause of morbidity and mortality in the renal transplant recipient population. It is considered to be the third most frequent cause of death in renal allograft recipients [4]. There are a wide variety of causes for hepatic malfunction in this population of patients, such as bacterial, viral, and fungal infection, in addition to the azathioprine-induced liver dysfunction. The incidence of liver dysfunction in renal transplant recipients depends upon the chemical laboratory criteria used to make the diagnosis and varies between 7% and 67% [3, 4].

Hemosiderosis and hemochromatosis have been described in the renal transplant recipient population as relatively common but not frequently recognized complications post-transplantation. Rao and Anderson studied

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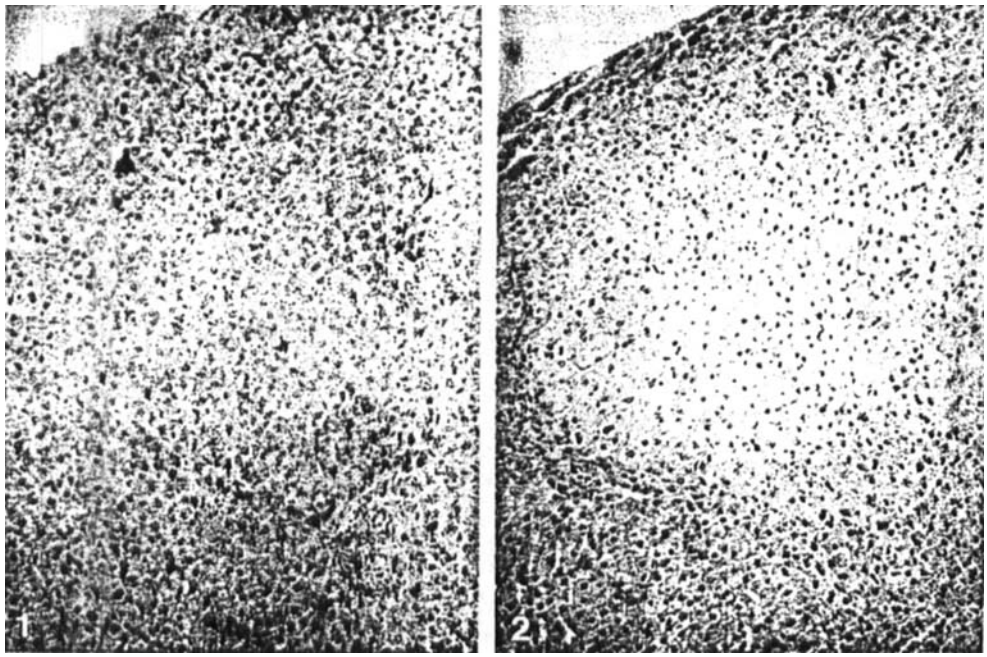

Fig. 1. Liver biopsy prior to renal transplantation showing hemosiderin deposition within Kupffer cells and hepatocytes

Fig. 2. Liver biopsy in the same patient after cadaveric renal transplantation showing complete resolution of previous hemosiderin deposition

liver biopsies of 74 patients, of whom 20 (27%) showed hemosiderosis and 4 (5%) had hemochromatosis [7]. Of the 20 patients with hemosiderosis, 14 died, either from liver failure or concomitant sepsis. They suggested that although the exact mechanism by which hemosiderosis occurs in renal allograft recipients is unknown, there were a number of factors that showed a positive correlation for increased susceptibility to this disorder, such as long-term hemodialysis, a patient's being female, and the number of pretransplant blood transfusions.

In this reported case study, our patient had been on hemodialysis from September 1982 until December 1984 and had also received multiple blood transfusions in the period prior to transplantation. These two factors would have suggested an increased risk for progression of his already documented hemosiderosis. This was not the case, however, and repeat liver biopsy 13 months after transplantation, at the time of cholecystectomy in December 1988, showed complete resolution of his hemosiderosis. The patient had not received any treatment, such as serial phlebotomies or chelation therapy, for this condition.

Hemosiderosis is not a benign condition and can cause considerable liver injury. This is believed to occur through two possible mechanisms. Peters and Seymour observed increased lysosomal enzymes in liver tissue of hemochromatotic patients, suggesting that insoluble iron within hepatocytes causes disruption of lysosomal membranes with the release of acid hydrolase, initiating liver cell injury [5]. Bacon et al. demonstrated hepatic lipid peroxidation in the mitochondria of rats with induced liver iron overload [2]. Thus, there may be peroxidative injury to lipid membranes of cellular organelles or, more particularly, to lysosomal membranes, resulting in their disruption and damage to the hepatic cell.

Hemosiderosis has been reported to have resulted in death from liver failure in a small number of renal transplant recipients who developed progressive hepatic fibrosis and micronodular cirrhosis [7]. Other factors contributing to this progressive process include hepatitis B, cytomegaloviral infection, and alcohol consumption, but presence of the hemosiderosis is felt to be most probably a primary event.

There was no progression of liver disease in our patient, however, and serial liver biopsies showed complete resolution of the pretransplant hemosiderosis. Not all previously reported cases of hemosiderosis or hemochromatosis in renal allograft recipients were followed by serial pre- and post-transplant liver biopsies, thus making it difficult to rule out the possibility that some may have already had significant iron liver deposition prior to transplantation. However, in view of the fact that hemosiderosis has been shown to progress to significant liver disease, we would still recommend careful follow-up, using liver function tests and serum ferritin levels in renal transplant recipients with this diagnosis.

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