OBSERVATIONS

Liver Transplantation: A Potential Cure for Hepatogenous Diabetes?

Hepatogenous diabetes is a common complication of liver cirrhosis (1). It develops gradually as a result of profound insulin resistance and increased endogenous glucose production that unmask or lead to pancreatic β-cell dysfunction. Since the liver plays a major role in maintaining glucose homeostasis, it is important to investigate whether liver transplantation (LT) could prevent or cure hepatogenous diabetes in patients with liver cirrhosis. We report a case of 2-year diabetes remission in a 49-year-old Chinese female LT recipient treated with tacrolimus who had previously been on intensive insulin therapy for 5 years.

The patient was diagnosed with diabetes in July 2006 at the age of 43 years, when she presented to the clinic because of severe ascites and peripheral edema. Subsequent investigations revealed the presence of hepatitis B with secondary liver cirrhosis, complicated by portal hypertension and esophageal varices. Her initial HbA_{1c} was 12.8% (116 mmol/mol), and the patient already had bilateral nonproliferative diabetic retinopathy. Intensive insulin therapy was initiated (36 IU/day).

At the 3-month follow-up, the patient's overall glycemic control improved, as reflected by an HbA_{1c} of 6.6% (49 mmol/mol) that further decreased and remained stable at >6% (42 mmol/mol) while on a basal-bolus regimen. Since January 2009, the diabetes control had deteriorated, with an HbA_{1c} of 7.6 (60 mmol/mol) to 8.4% (68 mmol/mol), along with a progression of diabetic retinopathy with proliferative changes. Concurrently, the patient was under regular review by hepatologists. Additional medications included propranolol, spironolactone, and tenofovir.

In March 2011, the patient successfully underwent LT and was subsequently treated with steroids, tacrolimus, and mycophenolate mofetil. Her glycemic control improved after prednisolone was discontinued. In July 2011, the HbA_{1c} was 5.0% (31 mmol/mol). Because of recurring nighttime hypoglycemia, the doses of basal insulin were gradually decreased, and the overall insulin therapy was further adjusted.

Since January 2012, the patient has been completely off insulin/any antidiabetic medication while continuing her antiviral (telaprevir) and combined immunosuppressive therapy (tacrolimus plus mycophenolate). The HbA_{1c} level continued to remain good at 5.2 (33 mmol/mol) to 6.3% (45 mmol/mol). Since LT, the patient's kidney function has been stable, and her BMI had decreased from 27 to 24 kg/m^2 after regression of ascites and peripheral edema.

The cause of diabetes resolution in this case remains less well-understood. Although current evidence suggests that immunosuppressive agents generally increase risk of diabetes after organ transplantations (2), our observations strengthen previous findings (3,4) of hepatogenous diabetes resolution after LT in some of the cyclosporine-treated patients with post–hepatitis B or C cirrhosis. It is important to point out that tacrolimus rather than cyclosporine is associated with hyperglycemia, one of the main side effects ascribed to reduced insulin secretion (5). Surprisingly, and as shown in our case, successful LT with subsequent tacrolimus therapy led to a complete diabetes remission in an insulin-treated cirrhotic patient. The findings suggest that normalized glucose production and insulin sensitivity after LT may reverse β-cell dysfunction and thus cure hepatogenous diabetes in patients with preserved β-cell function. Further prospective studies should be conducted to test this hypothesis.

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