Some Aspects of the Protein Metabolism in Human Liver Transplant Recipients


In early experimental and clinical studies, the not unexpected finding was reported that most of the electrophoretically measurable protein fractions declined rapidly after the implantation of a poorly functioning hepatic homograft. In contrast, these fractions were well maintained after provision of a well functioning graft. A similar relationship between quality of graft function and protein levels was found also for the liver-based clotting factors. The changes in these latter factors were very rapid and reflected changes in consumption as well as synthesis [2].

Studies of Complement

Recently, the plasma proteins of the complement system were assayed in five recipients of hepatic homografts [3]. All the patients were in terminal liver failure due to cirrhosis, chronic hepatitis or Wilson's disease.

Following replacement of the patients' diseased livers with well functioning homografts, total complement activity as well as the C4 and C3 component activities, rose from distinctly low to normal levels. At the same time, the C5 component increased from low to high normal (Figure 1). In contrast, the C2 and C9 components remained normal throughout, while C1 showed variable changes. Good subsequent

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Fig. 1 Levels of total complement activity (CH 50) and of the components C4, C3 and C5, before and 7-10 days after orthotopic hepatic transplantation. Each line represents an individual patient. Normal range is indicated by a heavy line along the ordinate.
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In several liver transplant recipients, the genetically determined phenotypes of the α-globulins haptoglobin and group specific component have converted to those of the donors. This indicated that the hepatic homograft retained its metabolic specificity in a new host and that liver-based inborn errors of metabolism should be correctable by the provision of a new, normal liver.

There have not yet been any successful liver transplantations for proven inborn errors of hepatic metabolism. However, two teenage boys have undergone liver replacement for Wilson's disease, a disorder that has been speculated to be due to some fundamental hepatic defect. The course of the first patient has been reported earlier [1]. Following transplantation, there was a marked cupriuresis and biopsy specimens have shown no accumulation of copper in the graft as had occurred in the native liver. The patient is presently alive and well three years after transplantation.

The second patient when first seen by us at age 11, had cirrhosis of the liver, a very low level of the copper-containing serum protein ceruloplasmin, a high liver copper, Kayser-Fleischer rings, and the characteristic histopathologic findings in a liver biopsy of Wilson's disease. In spite of treatment with chelating agents, the patient became severely crippled by neurological symptoms. At the age of 14, he underwent orthotopic hepatic transplantation. Except for an early period of graft dysfunction, probably caused by serum hepatitis, liver function has been normal during a follow-up of 15 months (Figure 3). After transplantation, serum ceruloplasmin and total serum copper rose to normal levels and have remained so. An initially elevated urinary excretion of copper has declined toward normal (Figure 3). Biopsy specimens of the homograft have shown no accumulation of copper. The findings are consistent with the hypothesis that the
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- CH50 (units/ml)
- IA50 (reciprocal of titer)
- C1
- C4
- C2
- C3
- C9 (units/ml)
- C1q (mg/ml)
- C4 (mg/ml)
- C3 (mg/ml)
- C5 (mg/ml)
- SGOT (I.U)
- SGPT (I.U)
- Bilirubin (mg/100ml)
- Total Protein
- Albumin
- γ-Globulin
- Azathioprine (mg/day)
- Prednisone (mg/day)

Hepatic Transplantation

0 10 20 30 40 50 60 Time in days
metabolic defect in Wilson's disease is liver-based, although they do not prove it.

Summary

The important relationship between hepatic homograft quality and the maintenance of plasma proteins is reemphasized. The results of serum complement assays in liver transplant recipients are presented. The recovery of the copper-containing protein ceruloplasmin after hepatic transplantation for Wilson's disease along with a cessation of hepatic copper accumulation is described.

References: