Published in final edited form as:

Lancet. 1984 June 23; 1(8391): 1382–1383.

HEART-LIVER TRANSPLANTATION IN A PATIENT WITH FAMILIAL HYPERCHOLESTEROLAEMIA

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Summary

A girl aged 6 years 9 months with severe heart disease secondary to homozygous familial hypercholesterolaemia underwent orthotopic cardiac transplantation and her liver was replaced with the liver of the same donor. In the first 10 weeks after transplantation serum cholesterol fell to 270 mg/dl from preoperative concentrations of more than 1000 mg/dl.

INTRODUCTION

Cardiac transplantation for end-stage heart disease would be futile in a patient with homozygous familial hypercholesterolaemia (FH) unless the metabolic processes responsible for the rapidly progressive atherosclerosis in such patients can be counteracted. We have attempted to meet this objective by orthotopic transplantation of the liver and heart from the same donor into a recipient with severe FH.

CASE REPORT

On September 1, 1983, a girl aged 6 years and 4 months was admitted for metabolic studies to the University of Texas Southwestern Medical School in Dallas. From the age of 3 months progressive xanthomas had developed on the contact areas of her buttocks and extremities. FH had been diagnosed when she was 6 years old. Culture of cutaneous fibroblasts indicated that she had the deficiency of low density lipoprotein (LDL) receptors which is typical of FH.¹ On admission, her plasma cholesterol was 1225 mg/dl and her plasma triglyceride was 154 mg/dl. Liver function tests were normal and she had no cardiac symptoms.

However, angina pectoris quickly developed and she required a double coronary artery bypass. A portacaval shunt was suggested, but liver transplantation was viewed as a better way of reducing serum cholesterol. At this point recurrences of angina led to the performance of a second bypass operation: and when she could not be weaned from the heart-lung bypass because of mitral regurgitation caused by previous papillary muscle necrosis, the mitral valve was replaced.

During late December, 1983, she had recurrent bouts of angina pectoris and heart failure. It was concluded that her heart disease had become too severe to permit liver transplantation, and for this reason concomitant heart replacement was suggested by the transplant team as the

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only realistic option. During late December, 1983, and in early January, 1984, this seemingly drastic proposal was considered and ultimately accepted by a consortium of physicians and surgeons from the Pennsylvania and Texas medical centres. There was approval by the Human Rights Institutional Review Board of the Children's Hospital of Pittsburgh.

The heart and liver replacements were carried out on Feb 14, 1984, during total cardiopulmonary bypass. Although the recipient was aged 6 years and 9 months, she weighed only 19.1 kg. Her blood type was A. The donor was a girl of 4½ of O blood type who weighed 16.2 kg. There was a total donor/recipient mismatch at the HLA A, B, and D_R loci. The technical details of this 16-hour operation will be reported separately (B. W. Shaw, Jr, personal communication). The removed heart had advanced atherosclerotic and valvular disease. The excised liver was normal by gross and microscopic examination.

Good cardiac and hepatic function were achieved from the grafts. Cyclosporin and steroids were used as immunosuppressants.² A persistent increase in serum bilirubin concentration 5 days after surgery suggested rejection but this subsided without an increase in immunosuppression. Standard liver function tests have been normal since the second postoperative week. Immunosuppression with 300 mg/day cyclosporin and 7.5 mg/day prednisone is being continued.

RESULTS

Effects on Circulating Cholesterol and Triglycerides

Serum or plasma cholesterol concentrations were determined in the Dallas and Pittsburgh laboratories with commercial kits that were based on an enzymatic assay principle.³ Differences between the results in the two laboratories in analysing plasma (Dallas) or serum (Pittsburgh) averaged less than 4%. Triglyceride analyses with enzymatic methods⁴ also yielded generally comparable results in the 2 laboratories but with a 15% variation. Plasma cholesterol and triglyceride concentrations of the donor were 120 and 100 mg/dl, respectively, in the Dallas laboratory.

During her stay on the metabolic ward in Dallas in September and October, 1983, the patient was in a lipoprotein turnover study. She was on an isocaloric formula/solid food diet containing 40% of calories as fat and less than 300 mg of cholesterol per day. The patient's average cholesterol concentration (normal <195 mg/dl) was more than 1000 mg/dl and her total plasma triglycerides (normal <150 mg/dl) were less strikingly raised (see figure).

Within a few days of the heart-liver transplantation, serum cholesterol concentrations had fallen to less than a fourth of the pre-existing level, but as the patient recovered from the operation and began to eat, the values rose to above 300 mg/dl and then fell slowly to 268 mg/dl (fig). Triglyceride concentrations were increased in the first month but declined (figure) as the postoperative prednisone doses were decreased from 30 mg/day toward the present level of 7.5 mg/day.

The visible tendinocutaneous xanthomas have undergone a dramatic regression during the 10 weeks of follow-up. The lesions have flattened and have changed from yellow to pink.

DISCUSSION

FH is caused by a defect in the gene for the LDL receptor.¹ Although the abnormality is common to all cells, the liver has a central role in the resulting hypercholesterolaemia,⁵⁻⁷ and the possibility has been raised of treating the disease with liver transplantation.⁸ The paucity of LDL receptors in the hepatocytes of patients with FH has been thought to be the most

important factor in the sluggish catabolism as well as in the heightened total body synthesis of LDL and cholesterol.⁵⁻⁷ If this were true, provision of a normal liver would correct FH because transplanted hepatocytes retain their original metabolic specificity.²

In our patient, the degree of correction has been substantial, at least as judged by serum cholesterol concentrations, but it has not been complete. Serum cholesterol is now about 270 mg/dl. Absorption of cholesterol from rapidly involuting xanthomatous deposits may be contributing to this present level. Repeat metabolic studies in mid-May (to be published in detail elsewhere) will allow quantification of the changes in the synthesis and catabolism of cholesterol and LDL.

ADDENDUM

June 12, 1984: After 6 more weeks of follow-up (total now, 4 months) the patient remains well with normal cardiac and liver function. Plasma cholesterol and triglyceride concentrations remain the same as at the time of the report.

Acknowledgments

This study was supported by research grants from the Veterans Administration; by project grants no AM-29961, HL15949, and HL29252 from the National Institutes of Health and by grant no RR 00084 from the General Clinical Research Centers Program of the Division of Research Resources, National Institutes of Health, Bethesda, Maryland.

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Figure.

Plasma or serum cholesterol and triglyceride levels before and after liver-heart transplantation.