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THOMAS E. STARZL, PH.D., M.D.
BARBARA I. BROWN, PH.D.
HERVE BLANCHARD, M.D.
LAWRENCE BRETTSCHNEIDER, M.D.
Denver, Colo.
and
St. Louis, Mo.

From the Department of Surgery, University of Colorado School of Medicine and the Denver Veterans Administration Hospital, and the Department of Biological Chemistry, Washington University School of Medicine

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On October 15, 1963, an 8½-year-old girl with glycogen storage disease was treated at the University of Colorado by performance of a portacaval transposition.[8] The objectives of the operation were to make dietary glucose more readily available to the peripheral tissues by means of the portal diversion, to deglycogenate the swollen liver, and to spare the patient the possible hazards of Eck fistula by restoring a portal inflow with systemic blood from the suprarenal inferior vena cava. The physiologic basis for the undertaking had been laid by extensive investigations in dogs.[7, 8] The original report of this case speculated that the same result might have been obtained with a simple portacaval shunt, omitting the potentially hazardous anastomosis of the inferior vena cava to the central portal vein.

The enzyme deficiency in the first patient was of hepatic amylo-1,6-glucosidase, thereby classifying the glycogen storage disorder as Type IIIB.[3] One and a half years later, a 7-year-old boy underwent the same operation, performed by Riddell, Davies, and Clark[6] in Bristol, England, this time for the indication of an hepatic glucose-6-phosphatase deficiency (Type I). Their patient had a stormy postoperative course, with profound metabolic acidosis and acute ascites formation, but he ultimately, recovered. The same amelioration of symptoms, as well as rapid body growth, that was seen in the original patient was observed in this one. The child was in good condition when last seen in December, 1967, just before his family's immigration to Canada terminated the possibility of further examinations at the Bristol clinic.[5]

A third attempt at portal diversion for the treatment of glycogen storage disease has been reported from the Cleveland Clinic by Hermann and Mercer,[1] again with encouraging results. However, there was an important deviation from the technique used in the earlier cases inasmuch as no attempt was made to restore portal venous inflow. The patient has not suffered any apparent adverse long-term effects from the Eck fistula.

The foregoing experience has suggested that cautious further exploration of portal diversion for the treatment of glycogen storage disease can be justified. This possibility will be supported in the present report by a 5 year follow-up of the first patient so treated. In addition, a more recent attempt at portacaval transposition which led to death will be described. In the last case, inability of the glycogen-laden liver to transmit an augmented portal venous inflow from the inferior vena cava was the cause of fail-

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ure. As a consequence, it may be wise in future trials to consider performing only a portacaval shunt, as was done by Hermann and Mercer.[1]

CASE REPORTS

Case No. 1. The portacaval transposition was performed almost exactly 5 years ago and was reported with a 15 month follow-up.[8] At operation the child had been found to have extensive venous collaterals in the abdominal wall, indicating the presence of portal hypertension. The procedure was well tolerated, and she was discharged from the hospital 9 days later. A venocavagram 3 months postoperatively showed the portacaval anastomosis to be patent, although a large amount of the vena caval blood passed through paravertebral collaterals.

The child weighed 65 pounds prior to transposition and was 49 inches tall. Eleven months later she had gained 10 pounds in weight and 4½ inches in height. On the Harvard growth chart, the jump in height represented a change from the tenth to the fiftieth percentile. By June, 1967, 4 months posttransposition, her height had increased to 61 inches, and she weighed 116½ pounds. At present she is 63⅛ inches tall and weighs 122 pounds. Her height and weight positions on the growth chart are now at the 55 and 80 percentile levels.

Biopsies were obtained of the child's liver a few weeks before and 9 and 43 months after portacaval transposition; the opportunity for the last open biopsy was provided by the need to perform splenectomy for the treatment of hypersplenism. The tissues were analyzed for glycogen and enzyme concentrations at Washington University, St. Louis. The results are shown in Table I. Except for a progressive fall in phosphorylase activity, there were no significant changes in any of the measures in the several years between study of the first and last tissue specimens.

Table I. *Enzymatic activities of homogenates prepared from liver biopsies of the first patient treated with portacaval transposition*

	*Data of biopsy**		
Enzyme	*October, 1963*	*July, 1964*	*June, 1967*
Glucose-6-phosphatase	1.9	2.1	2.2 (2.0-5.3)†
Amyol-1, 6-glucosidase	0	0	0 (0.04-0.18)
Phosphorylase	17.4	10.3	7.5 (16-33)
Glycogen content	10.1%	9.7%	9.5%

*Activities in micromoles substrate utilized per minute per gram tissue.

†The figures in parentheses are the normal range.

It should be emphasized that these biochemical determinations were of concentration rather than content, a distinction of special importance in discussing total hepatic glycogen. The accelerated growth postoperatively has already been described. Serial hepatic scans during this time showed that the liver remained of fixed size. Thus, it might be said that after operation the child grew up around the enlarged organ to the extent that its relative, although not its absolute, size was decreased.

Case No. 2. A portacaval transposition was performed on a 7-year-old boy on June 26, 1968. The preoperative diagnosis was glycogen storage disease, Type I. This impression was confirmed by the demonstration of absent glucose-6-phosphatase deficiency in the liver biopsy and a glycogen concentration of 9.4 percent; phosphorylase activity was essentially normal. The child had had 3 siblings of whom only one was normal. The other 2 had died, one a few days after birth and the other after almost 4 years.

The patient was exceedingly small in stature, with a height of 36 inches and a weight of 32.3 pounds; both values were at less than the 3 percentile level on the Harvard growth chart. The bone age, judged with a skeletal x-ray survey, was less than 3 years. There was massive hepatomegaly.

Despite the small size of the patient and the marked liver enlargement, the portacaval transposition with the use of the previously described technique[8] was quite easy. There was no evidence whatever of increased venous collaterals. The portal pressure was not measured, but it was not thought to be elevated. The operating time was 3 hours, and the blood loss was 100 ml. The only disquieting note during the procedure was the observation that the liver consistency became perceptively firmer after the vena caval flow had been released into the liver.

Within a few hours postopertively it became evident that a serious complication was evolving. Hypotension developed, as well as a metabolic acidosis more profound and refractory to treatment than any other ever seen by the pediatricians in our institution; a total of about 1,000 mEq. of bicarbonate was given in the ensuing 24 hours.

Concomitantly, the liver became increasingly firm by palpation. It was concluded that the cause of the problem was an overperfusion of the liver's portal system, and re-exploration was decided upon. On opening the abdomen, the anastomoses of the portacaval transposition were found to be patent. However, the inferior vena cava had a greatly increased presure, so high that there had

been diffuse hemorrhage in the adjacent retroperitoneal space. An attempt was made to reduce the portal venous inflow. Initially, it was hoped to perform a splenorenal shunt. However, the splenic vein was too small for this purpose, and the spleen was removed. Finally, a caval mesenteric shunt was performed. There was no apparent benefit from this secondary intervention, and the child died 24 hours later. Permission for autopsy was denied.

DISCUSSION

There have now been 4 known attempts at portal venous diversion for the treatment of glycogen storage disease. Two of these patients are still alive, 1 and 5 years postoperatively, and the third is assumed to be surviving after 3½ years. All 3 appeared to have been protected from acute metabolic derangements, such as those of hypoglycemia and acidosis. In addition, the most striking feature in the 2 cases with the longest follow-up was the rapid growth rate which followed operation. There is reason to doubt that the procedure caused any change in the glycogen concentration of the liver and that its benefits must be explained on other grounds.

The principle involved in these cases was to make ingested glucose more readily available to the peripheral tissues. This was accomplished by the portacaval anastomosis. The second part of the procedure in the 3 patients subjected to portacaval transposition represented an attempt to prevent the development of a portal-prival syndrome, such as that which is observed in dogs after Eck fistula or in man with normal livers who are subjected to the same procedure.[2, 4]

Hermann and Mercer's[1] experience has suggested that such attempts at restoration of portal flow may not be necessary in patients with glycogen storage disease. The outcome of our own second case has shown that attempts to meet this objective may be dangerous. In our patient death followed operation within 2 days, apparently because of the inability of the glycogen-laden liver to transmit an augmented portal venous inflow.

SUMMARY

Two children with glycogen storage disease were treated with portacaval transposition. The first is alive and in good health more than 5 years later. She underwent a rapid increase in growth after the operation, while the liver remained the same size. The second patient died within 2 days after the transposition, apparently because the portal system of the swollen liver was unable to transmit the vena caval inflow.

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