367

Liver Transplantation for Budd-Chiari Syndrome

Charles W. Putnam, MD; Kendrick A. Porter, MD; Richard Weil III, MD; H. A. S. Reid, MRC Path; Thomas E. Starzl, MD, PhD

• Orthotopic liver transplantation was accomplished in a 22-year-old woman dying of the Budd-Chiari syndrome. She is well and has normal liver function 16 months postoperatively. In view of the good early result, it will be appropriate to consider liver replacement for this disease in further well-selected cases.

(*JAMA* 236:1142-1143, 1976)

PATIENTS with many kinds of end-stage liver disease may be candidates for hepatic transplantation.[1,2] We record here the first use of liver replacement for the treatment of the Budd-Chiari syndrome.

Report of a Case

A 22-year-old woman was in good health until one year prior to transplantation, when she noticed fatigue associated with a voluntary weight-reduction diet. In November and December 1974 she received two 5-day courses of medroxyprogesterone acetate (Provera), in an effort to regulate her menstrual cycle. Two months later, while living in Germany, she complained of right upper quadrant pain, nausea, vomiting, and abdominal distention. A needle biopsy of the liver was suggestive of the Budd-Chiari syndrome. The diagnosis was established at Walter Reed Army Hospital in March 1974 by a venacavogram (Fig 1) that showed inferior vena caval narrowing and occlusion of the hepatic veins. Repeat venacavography at Letterman Army Medical Center confirmed the diagnosis.

During the next six months, her liver function deteriorated. There was progressive enlargement of the liver and spleen, and spider angiomata developed. She had increasing ascites and peripheral edema, which eventually could not be controlled by diuretics. Despite a low-protein diet, episodes of hepatic encephalopathy requiring neomycin sulfate became more frequent. She had demonstrable esophageal varices but did not bleed from these. The serum bilirubin concentration increased to about 2.9 mg/100 ml, and the serum albumin concentration remained below 3.0 gm/100 ml, even with intermittent infusions of concentrated albumin. The prothrombin time averaged 18 to 22 seconds while she was receiving vitamin K (Aquamephyton).

Two months prior to transplantation, renal function began to deteriorate. At the time of operation, the blood urea nitrogen was 56 mg/100 ml; serum creatinine, 2.9 mg/100 ml, and urine sodium excretion, less than 1 mEq/liter.

After obtaining informed consent, hepatic transplantation was performed on Nov 28, 1974. The donor was a 21-year-old woman who had suffered a lethal head injury in an automobile accident. The donor and recipient had mismatches of all four antigens of the HLA-A and HLA-B loci. At exploration, the liver was enlarged, weighing 2,035 gm. Large, soft nodules protruded from its surface. The spleen was also enlarged. Dense fibrosis involved the retrohepatic inferior vena cava, as well as the right and left hepatic veins. The latter were nearly occluded by scarring. The donor liver was revascularized orthotopically.[1,2] Biliary drainage was established with a Roux-en-Y cholecystojejunostomy.[1]

Postoperatively, the patient received azathioprine, prednisone, and a three-week course of heterologous antilymphocyte globulin.[1,2] Liver rejection did not occur. Renal function improved rapidly and was entirely normal within three weeks of transplantation. Two episodes of fever associated with elevated liver enzymes were thought to represent cholangitis and were easily controlled with antibiotics. Presently, she has normal liver function and is completely well sixteen months after transplantation.

Histopathologic Changes

The hepatic veins, particularly those of medium and large size, were occluded by organized and recanalized thrombus (Fig 2, left). These changes were associated with loss of hepatocytes from the central and middle zones of the lobules, with only a rim of liver cells surviving at the periphery of the lobules (Fig 2, middle). There was increased reticulin and fibrous tissue in the centers of the lobules, and fibrous septa linked adjacent central zones. Some reticulin strands also extended from the central to the portal areas and were accompanied by regeneration nodules (Fig 2, right). Bile ductules were present in the centrilobular connective tissue. The sinusoids in the central and middle parts of the lobules were dilated, and some had formed large, thin-walled, bypass channels.

Comment

Parker[3] as well as recent[4] reviews have demonstrated the poor outlook with the Budd-Chiari syndrome. In the Royal Free Hospital series of Tavill et al,[4] 17 of their 19 patients died of hepatic failure, with or without gastrointestinal bleeding, from six weeks to 3½ years after the onset of symptoms. However, some patients can recover with supportive therapy[4-6] and others may benefit from portalsystemic shunt operations.[3-7] For this reason, a decision to recommend transplantation could not be justifiably reached by the referring physicians until late in the course of our patient's illness, and only after the

From the Veterans Administration Hospital and the Department of Surgery, University of Colorado Medical Center, Denver (Drs Putnam, Weil, and Starzl); and the Department of Pathology, St Mary's Hospital Medical School, London (Drs Porter and Reid).

Reprint requests to Department of Surgery, University of Colorado Medical Center, 4200 E Ninth Ave, Denver, CO 80220 (Dr Putnam).

Fig 1.—Inferior venacavogram showing tapering and stenosis (larger arrow) of inferior vena cava below site of entry of right and left hepatic veins. Small arrows indicate approximate levels of eventual upper and lower vena caval anastomoses.

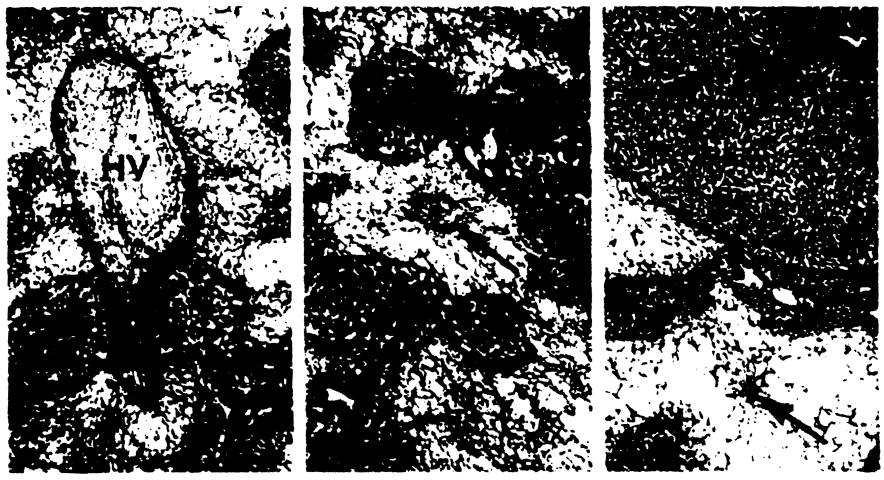

Fig 2.—Features of diseased native liver. Left, Medium-sized hepatic vein (HV) occluded by organized and recanalized thrombus. Middle, Liver lobule with occlusion of central vein (arrow), loss of all hepatocytes except those adjacent to portal tracts, and dilation of sinusoids. Right, Regeneration nodule (RN) adjacent to portal tract; central vein (arrow) is occluded (Silver stain for reticulin counterstained with neutral red, ×20).

grave prognostic signs of encephalopathy and the hepatorenal syndrome had appeared.

Parker[3] and Tavill et al[4] could find no explanation for the hepatic vein thromboses in 70% and 50%, respectively, of their cases. Nor could we in our patient, either at operation or by pathologic analysis of the liver. The removal of the diseased native liver was made difficult by dense fibrosis around the suprahepatic and retrohepatic inferior vena cava, but the hepatectomy was facilitated by a recently described retrograde technique[5] that allowed the dissection of the suprahepatic vena cava to be postponed until just before removal of the specimen. This dissection went well above the constriction seen on the venacavogram (Fig 1), assuring an adequate venous outflow for the homograft.

This work was supported by research projects MRIS 8118-01 and 7227-01 from the Veterans Administration; by grants AM-17260 and AM-07772 from the National Institutes of Health; and by grants RR-00051 and RR-00069 from the General Clinical Research Centers Program of the Division of Research Resources, National Institutes of Health.

LTC George Burdick, MC, USA, MAJ William Peterson, MC, USA; and MAJ Robert L. Myers, MC, USA; Letterman Army Medical Center; and Rudi Schmid, MD, University of California, San Francisco, referred this patient.

Nonproprietary Name and Trademark of Drug

Azathioprine—*Imuran*.

References

1. Starzl TE, Porter KA, Putnam CW, et al: Orthotopic liver transplantation in 93 patients. *Surg Gynecol Obstet* 142:487-505, 1976.

2. Starzl TE, Putnam CW: *Experience in Hepatic Transplantation*. Philadelphia, WB Saunders Co, 1969.

3. Parker RGF: Occlusion of the hepatic veins in man. *Medicine* 38:369-402, 1959.

4. Tavill AS, Wood EJ, Kreel L, et al: The Budd-Chiari syndrome: Correlation between hepatic scintigraphy and the clinical, radiological, and pathological findings in nineteen cases of hepatic venous outflow obstruction. *Gastroenterology* 68:509-518, 1975.

5. Langer B, Stone RM, Colapinto RF, et al: Clinical spectrum of the Budd-Chiari syndrome and its surgical management. *Am J Surg* 129:137-145, 1975.

6. Schramek A, Better OS, Brook JG, et al: New observations in the clinical spectrum of the Budd-Chiari syndrome. *Ann Surg* 180:368-372, 1974.

7. Prandi D, Rueff B, Benhamou JP: Side-to-side portacaval shunt in the treatment of Budd-Chiari syndrome. *Gastroenterology* 68:137-141, 1975.