Liver Transplantation for Polycystic Liver Disease

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• **Four female patients with severe complications of polycystic liver disease were treated with liver replacement; two patients were also given kidneys from their liver donors. All four of the patients were suffering from extreme fatigue. Three of the recipients have survived for 8, 11, and 60 months with normal liver function and present good health. The fourth patient recovered from a liver-kidney transplantation, but 5 months later, fulminant hepatic failure developed in this patient due to hepatitis B virus, and she died despite emergency hepatic retransplantation.**
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Most patients with polycystic liver disease bear a heavy but nonlethal burden. Hepatic failure is unusual.[1,2] Between half[1] and two thirds[2] of patients with the adult autosomal dominant disorder also have polycystic disease of the kidney. Before the availability of dialysis and kidney transplantation, renal failure was a common cause of death. Now that renal disease can be treated effectively, more patients can be expected to survive long enough to experience hepatic complications.[2]

The nature and seriousness of the hepatic complications, which are largely caused by mass effects, have been emphasized increasingly in recent reports.[3-5] Although many palliative procedures have been proposed,[4] these operations are of questionable value and are excessively dangerous unless there are "dominant" or regional cysts.[3,4] We report here the first use, to our knowledge, of total hepatectomy and liver transplantation for the treatment of polycystic liver disease in four patients who also had polycystic kidney disease. Concomitant renal transplantation was performed in two of the four liver recipients.

PATIENTS AND METHODS

Case Material

The four female recipients were aged 37 to 57 years (Table). Jaundice, hypoalbuminemia, clotting disorders, and other laboratory evidence of hepatic dysfunction were not present. However, one patient had esophageal varices, and two patients had ascites. Three of the four patients had pain from the huge liver masses (Figure), and two patients were addicted to narcotics (Table).

Significant symptoms had been present for 3 to 13 years (Table). All four patients complained of shortness of breath and/or extreme fatigue. The exhaustion was so profound that the four patients had stopped professional or domestic work and were confined to bed most of the time. Patient 4 (Table) whose main complaint was that she was dying of exhaustion had respiratory insufficiency, and she eventually required ventilatory support until a liver could be found. This same patient had undergone a left transverse colostomy and cecostomy 1 year previously because of colonic obstruction and toxic megacolon.

Liver volume was estimated with computed tomographic scans[6] in two patients to be 7120 and 12 790 mL (Table). It was too inconvenient and uncomfortable to attempt these measurements in the other two patients.

Patient 3 (Table) had undergone a right hepatic lobectomy and cyst fenestration in 1980, with a consequent reduction in the hepatomegaly and symptomatic relief. However, the liver slowly enlarged back to and beyond its original size (Figure, at right). The cysts were present throughout the liver (Figure) in all of the patients.

All four of the patients had polycystic renal disease. Two of the four patients had slightly elevated serum creatinine concentrations and subnormal creatinine clearances of 0.50 to 0.58 mL/s (Table).

Surgical Procedures

The orthotopic liver transplantations were performed by using standard techniques,[7] with an estimated blood loss of 4 to 45 L. The most serious bleeding was in patient 3 (Table) who had undergone a right hepatic lobectomy plus cyst fenestration 8 years previously. The liver graft did not function well, necessitating retransplantation 11 days later.

In patient 4 (Table), the previously placed colostomy and cecostomy were closed at the time of transplantation. Numerous ulcerations of the stretched and necrotic anterior abdominal wall in this patient were eliminated by excising a wide strip of skin and subcutaneous tissue from the xiphoid process to the pubis.

Patients 1 and 4 (Table) were given a kidney from their liver donor. The degree of renal failure (Table) would not have justified kidney transplantation under normal circumstances. However, it was feared that the subnormal renal function would preclude giving a full therapeutic dose of cyclosporine because of this drug's nephrotoxicity. The liver was transplanted first in both patients, followed by the kidney transplantations only after the conditions of the patients were stable.

Aftercare

The four patients required ventilatory support postoperatively for 9, 2, 15, and 13 days. Baseline immunosuppression was with cyclosporine and steroids. Two patients also had supplemental therapy with OKT3 and/or azathioprine.

RESULTS

Liver Size

The excised livers weighed 4000 to 12 900 g (Table). This weight range was a gross underestimate of the actual weights since a large amount of fluid was lost when the cysts were ruptured during the hepatectomies or when the specimen was cut afterward. The heaviest surgical pathology specimen (from patient 1, Table) weighed 12 900 g. The histopathologic

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Clinical Findings in Four Patients With Polycystic Liver Disease*

	Patient			
	1	2	3	4
Date of transplantation	7/23/84	8/6/88	10/31/88, 11/11/88	11/21/88
Age, y	40	37	57	42
Race	White	Black	White	White
Sex	F	F	F	F
Weight, kg	75	84	62	60
Symptoms and signs				
Pain	X	–	X	X
Addiction	X	–	–	X
Mass	X	X	X	X
Exhaustion	X	X	X	X
Dyspnea	X	X	X	X
Jaundice	–	–	–	–
Ascites	–	X	–	X
Anorexia	–	X	–	X
Varices	X	–	–	–
Duration of symptoms, y	5	3	12	13
Previous operations	–	–	Cyst drainage (1960), cyst drainage (1974), RHL and F (1980)	Cyst aspiration colostomy and cecostomy
Estimated liver volume, mL	...	7120	...	12790
Weight of excised liver, g	12900	4000	4100	7350
Kidney transplant	X	–	–	X
Preoperative serum creatinine level, μmol/L	221.2	53.4	61	144.9
Creatinine clearance, mL/s				
Preoperative	0.50	3.00	1.50	0.58
Postoperative	1.33	1.86	0.56	0.83

*X indicates yes; minus sign, no; RHL, right hepatic lobectomy; and F, fenestration.

At left, Computed tomographic scan in patient 4 (Table) whose liver had not previously been instrumented surgically. At right, Computed tomographic scan, taken in January 1987, in patient 3 (Table) who had undergone a right hepatic lobectomy and cyst fenestration in 1980.

findings in the specimens were typical of polycystic liver disease.[8]

Survival

Three of the four recipients have been well from 8 months to 5 years postoperatively. Patient 4 (Table) recovered completely from a liver-kidney transplantation, but 5 months later, she experienced fulminant hepatic failure caused by hepatitis B virus. She died 2 days after emergency liver retransplantation. The transplant hospitalization was for 35, 54, 71, and 99 days. The longest hospitalizations were required because of pneumonitis (patient 3, Table) and a postoperative psychosis (patient 1, Table).

Function of Grafts

The liver function has been normal in the surviving recipients and was normal for 5 months in patient 4 (Table) until the onset of acute hepatitis. The subnormal renal function in patients 1 and 4 was improved with the renal grafts (Table). The previously normal renal function was decreased in patients 2 and 3 (Table) who were given a liver only; their loss of renal function was ascribed to cyclosporine nephrotoxicity.[9]

COMMENT

Surgical complications of polycystic liver disease and ways of treating these have been reported from clinics with special expertise in hepatic disease.[3,4,10-12] Such complications were thought to be rare until recently. The study by Grunfeld et al[2] provided a more realistic assessment of the hepatic risks to these patients now that death from renal failure could be forestalled so effectively. In patients with renal polycystic disease who were undergoing dialysis at the Hôpital Necker, Paris, France, a hepatic origin was the leading cause of death.[2] Findings from subsequent reports from other centers[3,4] have confirmed that there is a small subset of high-risk patients.

Initially, it was difficult for us to recommend such a drastic solution as liver transplantation for patients with polycystic liver disease who typically have normal liver function. Liver transplantation was not even considered until 1984, when another patient with polycystic disease was brought in desperate condition to the operating room for a combined liver and kidney transplantation, only to die of a fatal pulmonary embolus before either organ could be transplanted. Instead, we have tried in past years to reduce the hepatic mass in such patients with a partial hepatectomy and with the fenestration procedure, as originally described by Lin and colleagues.[13] Although these operations can relieve symptoms temporarily, usually there is little reduction in the hepatomegaly.[3] A right hepatic lobectomy and fenestration operation in our patient 3 (Table) left so many adhesions that liver replacement nearly 8 years later was extraordinarily difficult.

An exceptionally conservative attitude is still warranted about liver transplantation or, for that matter, any other operation for polycystic liver disease. The most common reason to go forward could be a syndrome of lethal exhaustion. The diagnosis of this condition may depend more on common sense and longitudinal clinical observations than on sophisticated tests. All four of our patients had reached an end to their functional lives because they could no longer carry the weight of their slowly enlarging livers. Three of them had intractable pain, and two patients were narcotic addicts. Fatigue had closed off almost all activity, except that required to breath and carry out other basic bodily functions. Peltokallio[14] may have seen patients with this kind of disability, and one patient in Grünfeld and colleagues'[2] series died of cachexia. The complaints in our four patients were eliminated with the removal of the mass and transplantation of a normal-sized organ. Weaning from ventilator support was possible in 2 to 15 days. The two recipients who had become narcotic addicts never again asked for pain medications, even during the first postoperative days. The patients all regained a vigorous life-style, and all remained well, except for the liver-kidney recipient who experienced fulminant hepatic failure from hepatitis B virus after 5 months and died despite emergency liver retransplantation.

Whether to provide a kidney at the same time as liver replacement in patients with polycystic disease of both organs is a matter of judgment. Because the nephrotoxicity of cyclosporine is the limiting factor in the dose of this drug,[9] subnormal function of native kidneys that still may be life supporting could make it impossible to give enough cyclosporine to protect the new liver. It was this consideration that prompted the decision in two of our four patients to transplant a kidney from the donor who also provided the liver. Under normal circumstances, it would have been too early in the course of the renal failure to have warranted kidney grafting.

If a decision is taken to transplant a kidney, there are good reasons to obtain the kidney from the liver donor, especially if the patient's serum contains the wide-ranging cytotoxic antibodies that can promptly destroy renal homografts. The liver is peculiarly resistant to this kind of antibody attack,[15] and once the hepatic graft is in place, it can remove or neutralize the donor-specific antibodies, thereby allowing a kidney from the same donor to survive in the immunologically hostile environment.[16] For a patient who is highly sensitized, this may be the only opportunity to transplant a kidney with a reasonable expectation of success.

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