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Liver Transplantation

by

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There are two basic techniques for liver transplantation. One consists of an orthotopic transplant in which the diseased liver is removed and replaced in-situ with a new organ. The second consists of a heterotopic transplant in which an auxiliary liver is placed in the abdominal cavity leaving the diseased organ in place.

In this presentation we shall deal only with the former, i.e. orthotopic transplantation.

After many years of experimental work the first orthotopic liver transplantation in man was performed by Starzl at the University of Colorado in March of 1963 (Starzl, 1963). The patient did not survive and six further attempts in the succeeding ten months also failed. Finally, in 1967 a successful transplant was performed on an eighteen month girl with an hepatoma. She survived thirteen months before succumbing to a recurrence of her tumor (Starzl, 1968).

From 1963 to the present about 540 transplants have been performed in four medical centers: in Denver and Pittsburgh (USA) 296; University of Cambridge (UK) 137; University of Hannover (W. Germany) 81; University of Groningen (Holland) 26 (Scharschmidt, 1984).

INDICATIONS

The principal indications for liver transplantation according to Scharschmidt (1984) are:

1. Cirrhosis (43.5%). Non-alcoholic cirrhosis (38.9%) represents the majority. Poor results are obtained in alcoholic

cirrhosis (4.6%) because of the patient's poor general condition coupled with enormous technical problems.

2. Hepatic tumors (25.7%). At Hannover and Cambridge this group represents 54.3% and 42.3% respectively while at Pittsburgh only 12.2% of patients had tumors. This large discrepancy confirms the fact that even today it is impossible to define precise indications and definitive results for the procedure. Initially it was felt that tumors were an ideal situation for transplantation but the high incidence of tumor recurrence (Starzl, 1969,1982; Iwatsuki, 1982) diminished the initial enthusiasm. At this moment the only tumor cases that would seem appropriate are small tumors incidentally found in diseased livers or the fibrolamellar hepatomas which are slow growing and late to metastasize (Craig, 1980).

3. Biliary atresia (16.7%). This group has been operated on almost exclusively in Pittsburgh where it represents 26.7% of their cases. The frequent presence of hepatic and extrahepatic congenital anomalies presents a difficult challenge (Starzl, 1982).

4. Congenital metabolic defects. Again the University of Pittsburgh has the largest number of cases, 10.8% in their series. The most frequent condition is that of α1-antitrypsin deficiency, followed by Wilson's disease, tyrosinemia, and Type I glycogenesis. In the latter two enzyme deficiencies a complete correction of the metabolic defects has been noted within hours after the operative procedure (Starzl, 1982; Malatack, 1983).

5. Miscellaneous. Other less frequent indications have been: sclerosing cholangitis (3.5%), Budd-Chiari syndrome (2.6%), and acute hepatic insufficiency (0.4%).

SELECTION OF PATIENTS

There are three basic requirements for liver transplantation:

1. The patient must be afflicted by an irreversible, chronic, progressive liver disease.

2. The illness must be in a stage that is not responsive to any form of conventional therapy.

3. The patient must have no contraindication to transplantation (Van Thiel, 1984).

The contraindications to the procedure are both absolute and relative. Absolute contraindications consist of: age over 55, thrombosis of the portal vein, pulmonary shunting with hypoxemia, extrahepatic sepsis, extra or intrahepatic metastases, alcoholic hepatopathy, advanced cardiopulmonary and renal disease, and posthepatic cirrhosis in patients HBsAg and HBeAg positive in view of likelihood of recurrence.

TISSUE TYPING

Although in uremic patients there is an alternative therapy of dialysis, there is currently no effective artificial support for patients with advanced hepatopathies. For this reason there is always an element of urgency in liver transplanation that has not permitted preoperative tissue cross match as in renal transplants. In some emergency situations it has been necessary to ignore blood ABO incompatibilities (Starzl, 1979) or the presence in the recipient's serum of T-Warm antidonor antibodies, responsible for hyperacute renal rejection (Starzl, 1979; Iwatsuki, 1981). Fortunately the liver seems resistant to this type of humoral rejection.

DONOR SURGERY

To obtain a physiologically suitable liver it is of the utmost importance to perform a careful evaluation of the donor. These should be individuals between the ages of two months and forty-five years, victims of trauma or cerebral hemorrhage, lacking spontaneous cerebral activity, maintained with artificial cardio-respiratory support. There should be no history of hepato-biliary or systemic disease nor traumatic, ischemic, or infectious complications which might involve the liver.

The surgical procedure is basically simple. Incision is made from the pubis to the suprasternal notch, dividing the sternum. The liver is carefully inspected for abnormalities or anomalies. The splenic and left gastric arteries are then divided. The celiac axis with a cuff of aorta will be excised later. The gastroduodenal and right gastric vessels are then sectioned and the common duct divided. The biliary tract is then thoroughly irrigated with saline via the gallbladder.

After sectioning the pancreas the portal vein is isolated to the junction of the splenic and mesenteric veins. The splenic vein is catheterized to perfuse the liver slowly with Ringer's solution cooled to 5°C.

The aorta is then mobilized from the superior mesenteric to the iliac arteries as is the inferior vena cava. After heparinization the aorta and cava are cannulated and the superior mesenteric vessels ligated.

Perfusion through the splenic vein is then increased and, in order to maintain a constant blood volume, venous blood is drained intermittently through the caval catheter.

After perfusion of an adequate amount of Ringer's solution (1500-2000 cc. in an adult) the aorta is clamped above the celiac and a second hepatic perfusion is performed through the aortic catheter using Collin's solution.

After this double perfusion the liver is cooled and free of blood. The celiac axis with an aortic cuff and the suprahepatic with a cuff of diaphragm are divided. Division of the remaining hepatic ligaments permits removal of the organ. It is then placed in a bag containing Ringer's solution and iced in a thermal container where it may be kept for several hours.

RECIPIENT SURGERY

Surgery on the recipient patient consists of two definite stages. The first consists in the removal of the diseased liver, the second of the orthotopic reimplantation of the new or donor liver.

The usual approach is through a bilateral subcostal incision with an upward midline extension. Removal of the xiphoid provides better exposure.

The common hepatic artery, biliary ducts, and portal vein are isolated at the hilus. The falciform, triangular, and right and left coronary ligaments are divided and supra and subhepatic veins are exposed. Before dividing any vessels an external by-pass between portal vein and axillary and femoral veins is established. This shunt while abandoned after its use in the early transplants has been almost routinely utilized by Starzl since 1982. There are two principal reasons for its revival: to avoid intestinal hypertension on the intestine with subsequent third space volume sequestration and renal insufficiency, and the availability of a heparinized catheter-pump

system thus avoiding the risks of systemic heparinization.

At this point the cava is sectioned and the liver is removed.

The donor liver is then seated in place and the reconstructive phase consisting of four vascular and one biliary anastomoses is initiated.

First the end to end anastomosis of the vena cava is performed. Before completing the last anastomosis the liver is irrigated with 500 cc of Ringer's solution through a portal vein catheter. This eliminates excess accumulated potassium and eliminates air bubbles. The portal vein is then reconstructed end to end and the hepatic artery reconstituted by the most suitable technique depending on the local anatomy.

The biliary anastomosis is the last and usually performed end to end with t-tube drainage or by choledochojejunostomy using a Roux-Y loop.

IMMUNOSUPPRESSION AND REJECTION

All the techniques to prevent or delay rejection are based on the experiences with renal transplants.

Of the numerous drugs and therapeutic protocols available (Azothioprene, thoracic duct drainage, anti-lymphocytic globulin, Cyclophosphamide, total lymphatic radiation) none has been satisfactory in preventing rejection. Only one agent, introduced in 1978, Cyclosporin A when coupled with corticosteroids seems to provide real promise. It is currently still being evaluated.

RESULTS

The results of liver transplantation have improved year by

year through improvements in surgical technique, better donor selection, and improved techniques to prevent infections and rejection.

Starzl who has the largest world experience reported a 30% one-year survival through 1979 in patients treated with conventional immunosuppression. In 1984 however he achieved a 70% one-year survival in his series treated with Cyclosporin and corticosteroids.

The most encouraging results have been obtained in patients with biliary atresia and metabolic defects followed by those with non-alcoholic cirrhosis.

The worst results have been in those patients with liver tumors and alcoholic cirrhosis (Scharschmidt, 1984).

In terms of quality of life, in the Pittsburgh series, 80% of patients surviving over one year were able to resume their previous work and activities.

CONCLUSIONS

In the history of medicine feats that were impossible yesterday and difficult today often become routine tomorrow (Starzl, 1982).

Today, twenty years after the first transplant, we can say that this once impossible procedure has emerged from its experimental phase and is becoming a routine procedure.

Despite dramatic improvement in results numerous hurdles remain to improve mortality: earlier interventions, routine use of by-pass, and improving the quality of donor livers. Recently the importance of re-transplantation after initial transplant failure has been emphasized (Starzl, 1982).

The number of patients awaiting transplantation continues to increase and many succumb while waiting. The Pittsburgh experience reveals the mortality of the waiting list is twice that of the transplanted patients (Van Thiel, 1984). A good argument to increase the centers and facilities to perform this procedure.

BIBLIOGRAFIA

I).Craig JR, Peters RL, Edmondson HA, et al. Fibrolamellar carcinoma of the liver: a tumor of adolescents and young adults with distinctive clinico-pathologic features. Cancer I980; 46:372-379.

2).Iwatsuki S, Iwaki I, Kano T, et al.Succesful liver transplantation from cross match positive donors. Transplant Proc. 1981; 13:286-288.

3).Iwatsuki S, Klintmalm GBG, Starzl TE. Total hepatectomy and liver replacement (orthotopic liver transplantation) for primary hepatic malignancy. World j Sur I982; 6:8I-85.

4).Malatack JJ, Finegold DN, Iwatsuki S, et al. Liver transplantation for type I glycogen storage disease. Lancet I983; I4:I073-75.

5).Scharschmidt BF. Human Liver transplantation: analysis of data on 540 patients from four centers.Hepatology I984;4:94-I0I (Suppl.)

6).Starlz TE (with the assistance of Putnam CW).Experience in the hepatic transplantation. Philadelphia: W.B Saunders Co., I969.

7).Starzl TE, Koep LJ, Halgrimson CG,et al. Fifteen years of

clinical liver transplantation. Gastroenterology 1979; 77: 375-388.

8). Starzl TE, Iwatsuki S, Van Thiel DH, et al. Evolution of liver transplantation. Hepatology 1982; 2:614-636.

9). Starzl TE, Iwatsuki S, Shaw BW, Jr., et al. Analysis of liver transplantation 1984; 4:47-49 (Suppl.).

10). Van Thiel DH, Shade RR, Gavaler SJ, et al. Medical aspects of liver transplantation 1984; 4:79-83 (Suppl.).