Multivisceral Allotransplantation in Pigs

1952

Y. Zhu, H. Furukawa, K. Nakamura, T.E. Starzl, and S. Todo

MULTIVISCERAL transplantation was first applied clinically for the treatment of short bowel syndrome complicated by liver failure from long-term hyperalimentation. The first experimental work in dogs was reported by Starzl et al in the early 1960s.[1] Recently, several experiments using large animals showed that multivisceral transplantation is a technically complicated procedure with high mortality.[2-4] In this report, we describe the operative technique, postoperative graft function, and immunological aspects of multivisceral transplantation in pigs.

MATERIALS AND METHODS

Twenty-six white female pigs, weighing 15 to 25 kg, were used. The multivisceral grafts consisted of the liver, pancreas, stomach, small intestine, and colon. No immunosuppressive agents were given to any animals.

Donor Operation

The abdomen was entered through a midline incision. The abdominal aorta was dissected from the diaphragm to the common iliac arterial bifurcation. All of the abdominal organs, except for the kidney, were freed from the retroperitoneum in continuity with the abdominal aorta. After completing the dissection, a cannula was inserted into the lower abdominal aorta for perfusion. After systemic heparinization, the abdominal organs were flushed with 4 L of cold lactated Ringer's solution. The abdominal viscera were removed en bloc.

Recipient Operation

The dissection and removal of native abdominal organs was similar to the donor operation, except for retaining the aorta in situ. After removing the native organs, the multivisceral graft was implanted by end-to-end anastomoses of the suprahepatic vena cava and the infrahepatic vena cava, and end-to-side anastomosis of the proximal donor aorta to the recipient aorta at the origin of the celiac axis. Gastrointestinal continuity was restored by end-to-side gastrogastrostomy and end-to-end anastomosis of graft descending colon to recipient's sigmoid colon. Veno-venous bypass was not used.

Postoperative Management

One gram of cephalosporin was given intravenously during surgery and intramuscularly for 5 days after transplantation. Animals were allowed to eat and drink from the morning after surgery.

Postoperative Studies

Serum glutamic-oxaloacetic transaminase, glutamate pyruvate transaminase (SGPT), bilirubin, glucose, and amylase were measured on postoperative days 1, 3, 5, 7, and 10 and twice weekly until the animal died. Tissues were collected at autopsy and assessed histopathologically.

RESULTS

Animals were grouped according to how long they survived. Group A (n = 6, 23%) animals died within 1 day after operation from respiratory failure (n = 3), cardiac arrest (n = 2), and intra-abdominal bleeding (n = 1). Group B (n = 11, 42%) animals died 2 to 5 days after surgery from respiratory failure (n = 5), peritonitis (n = 4), graft-versus-host disease (GVHD, n = 1), and technical failure (n = 1). Group C (n = 9, 35%) animals survived more than 5 days after surgery. Group C animals died from intestinal necrosis (n = 4), biliary tract infection (n = 2), GVHD (n = 2), and intestinal obstruction (n = 1). The longest surviving group C animal survived for 15 days. Except for two pigs with biliary tract infection, all group B and group C animals had almost normal liver function at the time of death, with SGPT less than 100 U/L and total bilirubin levels less than 2.0 mg/dL. Histologic examination of the grafts showed a higher incidence of moderate to severe rejection in the small intestine than in the other abdominal organs. Cutaneous lesions (GVHD) were found in 3 of 20 animals in groups B and C (Table 1).

Table 1. Histologic Findings of the Multivisceral Grafts

Group	Skin lesions (GVHD) (n)	Liver (n)	Rejection	
			Pancreas (n)	Small bowel (n)
B (n = 11)	1	1	3	4
C (n = 9)	2	4	3	6*

Abbreviation: GVHD, graft-versus-host disease.
*Two of six were severe rejection comparing with none in the liver and the pancreas in group C.

CONCLUSION

Multivisceral transplantation in pigs is complex and technically difficult. Animals that survive the procedure are faced with life-threatening respiratory failure, infection, GVHD, and rejection.

REFERENCES

1. Starzl TE, Kaupp HA Jr, Brock DR, et al: Am J Surg 103:219, 1962
2. Mitsuoka S, Tanaka N, Orita K: Transplant Proc 26:2450, 1994
3. Starzl TE, Rowe MI, Todo S, et al: JAMA 261:1449, 1989
4. Rossi G, Gridelli B, Colledan M, et al: Transplant Proc 24:1214, 1992

From the Pittsburgh Transplantation Institute, University of Pittsburgh, Pittsburgh, Pennsylvania.
Address reprint requests to Yue Zhu, MD, 4C Falk Clinic, 3601 Fifth Avenue, Pittsburgh, PA 15213.

0041-1345/96/$3.00/+0