Ten-Year Experience With Bowel Transplantation at Seoul St. Mary's Hospital

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ABSTRACT

A retrospective review of intestinal transplantation (ITx) at Seoul St. Mary's Hospital was made by collecting clinical data over the past 10 years. Fifteen consecutive cases from 2004 were analyzed. Five children and 10 adults (6 months to 69 years of age) were included. Primary diseases in adults included 4 mesenteric vessel thromboses, 2 strangulations, and 1 each of visceral myopathy, malignant gastrointestinal stromal tumor (GIST), mesenteric lymphangiectasis, and injury. Pediatric cases involved 2 Hirschsprung disease, 2 visceral myopathy, and 1 necrotizing enterocolitis. Three of 7 stomas were closed using a serial transverse enteroplasty procedure before transplantation. The ITx were performed using 3 living-donor Itx, 12 deceased-donor ITx, 14 isolated Itx, and 1 modified multivisceral transplantation. Daclizumab, basiliximab, alemtusumab, or basiliximab with rabbit antithymocyte globulin (rATG) was used for the induction; tacrolimus monotherapy was used as the basic maintenance immunosuppressant; and m-TOR inhibitor was used for renal dysfunction patients. Seven cases of acute cellular rejection were treated with rATG. Three cases of antibody-mediated rejection were treated with rituximab alone or with rituximab and bortezomib combination. There were 4 cases of early mortality within 6 months after Itx. Causes of death were declamping shock, cardiac tamponade with acute cellular rejection, dysmotility, and sepsis. Surgical complications consisted of 1 feeding jejunostomy displacement, and a minor leakage at a colo-colostomy site. One-year survival of the patient and graft was 73.33% (Kaplan–Meier survival curve). Although the total number of ITx is small, its social impact has been remarkable in changing the related laws and reimbursement policy in Korea.

INTESTINAL TRANSPLANTATION (ITX) has become a new and challenging pathway for the care for short-gut syndrome (SGS) and functional bowel failures of absorption or motility. However, it is only within the last 2 decades that remarkable progress has been made to bring this therapeutic modality into clinical reality.

In Korea, ITx, followed by nutritional independence on oral feeding, began with the case of a 56-year-old woman who had received a segment of intestine from her daughter, a living-donor ITx (LDITx), in April of 2004, at Seoul St. Mary's Hospital [1]. Since that time, 15 cases of ITx have been performed with long-term survivors at this single center, Seoul St. Mary's, which has become the domestic tertiary center for ITx and rehabilitation. These progressive accomplishments in ITx and rehabilitation have changed the related laws on organ transplantation and reimbursement policies by government-controlled medical insurance.

This article reports the 10-year experience of ITx at a single center and presents the current status of ITx in Korea.

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0041-1345/16
http://dx.doi.org/10.1016/j.transproceed.2015.12.065

MATERIAL AND METHODS

Fifteen consecutive cases of ITx performed at Seoul St. Mary's Hospital, Seoul, Korea, from April 9, 2004, to January 2015, are included in this report. There were 5 children from 6 months of age, and 10 adults with a median age of 28 years, the most senior being a 69-year-old man. Preoperative status, underlying diseases, type and surgical technique of transplantation, surgical and immunological complications, patient and graft survival, and quality of life after transplantation were analyzed by retrospective review of their medical records.

Immunosuppression

For induction immunosuppression, daclizumab [2] was used in 2 cases (2004–2005), basiliximab [3] in 2 cases (2006–2009), and a combination of basiliximab and rabbit antithymocyte globulin (rATG) [4] in 10 cases afterward. Alemtuzumab [5] was tried in only 1 case in 2011 and was stopped because of disapproval by the medical insurance committee.

For maintenance immunosuppression, tacrolimus monotherapy with early tapering of the steroid has been the standard of care at this institution to date [2,6]. The target trough level of tacrolimus is above 12 ng/dL for 1 month posttransplantation, tapering to 10–12 ng/dL by 3 months, 7–10 ng/dL by 6 months, and approximately 5 ng/dL afterward. However, in cases of progressive renal dysfunction (serum creatinine >1.5 mg/dL or glomerulofiltration rate [GFR] <75 mL/h), use of m-TOR inhibitor alone or combined with low-dose tacrolimus has been used since 2009 [7,8].

Graft surveillance was performed with a fiberoptic endoscope (9 mm Olympus GIF-XQ240 for adults, and 5 mm, Olympus GIF-XP260N for young children) examination and mucosal biopsy through the ileostomy after transplantation at the following intervals: 3 times a week for 2 weeks, 2 times a week for 2 weeks, once a week for 2 weeks, then every 2 weeks twice, once a month, then every 2 months, and finally every 6 months. The gross morphology of the villi under the water submerging view was reviewed. After ileostomy repair, colonoscopy (12 mm, Olympus CF-Q260AI) was performed.

Endoscopic biopsy specimens were taken for histologic surveillance from at least 2 different levels of the graft. Each time there is suspicion of rejection on endoscopy, immunofluorescent histochemical staining for C4d, immunohistochemical staining for cytomegalovirus (CMV), and immunohistochemical staining or in situ hybridization for Epstein-Barr virus were added to the histologic processes.

Statistical data for the graft and patient survivals were analyzed by the Kaplan–Meier survival curves.

RESULTS

Underlying Disease

Primary diseases of intestinal failure (IF) in adults consisted of the following: 4 cases of mesenteric vessel thrombosis (2 in association with colon cancer, 3 during early postoperative periods), 1 case of gastrointestinal pseudo-obstruction, 2 cases of strangulation (1 internal hernia after total gastrectomy for stomach cancer, and 1 midgut volvulus in the early postpartum period), 1 jejunal malignant tumor (GIST), 1 mesenteric lymphangiectasis, and 1 iatrogenic visceral injury. Pediatric cases included 2 cases of extended total aganglionosis, 2 cases of gastrointestinal (GI) pseudo-obstruction, and 1 case of necrotizing enterocolitis (Table 1). In all 3 cases of GI pseudo-obstruction, compatible histologic findings of the visceral myopathy were identified by light and electron microscopy.

Clinical Status at Time of Transplantation

Stoma Status. Seven patients had jejunostomy, whereas 8 did not have any stoma at the time of referral for Tx. Three stomas of 7 stomas were closed with the planned serial transverse enteroplasty (STEP) [9] before transplantation. Three patients had long-term drainage tubes from the GI tract until the time of Tx, and 2 of them were in the early death group (Table 1).

General Status. Case patient 3 had moderate hepatic dysfunction (intestinal failure–related hepatic disease) with a bilirubin level above 10 mg/dL at the time of Tx. Following ITx, this patient's hepatic function completely recovered.

Hospitalization Status at Time of Transplantation. Two case patients (nos. 4 and 5) underwent transplantation while hospitalized; both were included in the early death group. The other 13 cases were called for transplantation from home parenteral nutrition (HPN).

Surgery

Vessel Anastomosis. In LDITx, the connecting vessels to the grafts were selected from 1 of the nominated ones by end-to-end microsurgical anastomosis under an operative microscope at ×10 magnification. The splenic artery and splenic vein in 1 patient (case no. 2), and the inferior mesenteric artery and inferior mesenteric vein in 2 patients (case nos. 1 and 8) were used. In DDITx, the aorta and inferior vena cava were used for end-to-side anastomosis in 12 cases. Arterial bridge grafts were connected between the vessels in all patients, but venous conduits were applied in 10 of 12 patients.

GI Tract Reconstruction. GI tract continuity was restored with end-to-end anastomosis of the proximal end of the graft in all cases. Santuli-type ileostomy was established at 15 to 30 cm proximal to the ileocecal valve or to the distal anastomosis site (when the ileum was the end of the graft) in every case for posttransplantation endoscopic graft surveillance and easy drainage as well. The distal end of the graft was directly connected to the distal native bowel in 11 cases. However, in 4 cases, the distal end was brought out as an end colostomy for delayed colo-anal anastomosis, resulting in double stomas. Tube gastrostomy for drainage was performed in 12 cases, and percutaneous transgastric tube jejunostomy for feeding was done in 14 cases. In 1 case of mesenteric lymphangiectasis (case no.10), direct percutaneous feeding jejunostomy was performed because the abdomen was too rigid and too far from the stomach to adequately accept the transgastric jejunostomy tube.

Transplantation Type. There were 3 LDITx, and all were related; 1 from a daughter-to-mother (case no. 1), 1 from a father-to-daughter (case no. 2), and 1 from a son-to-father (case no. 8). For adult LDITx, 150 cm of the distal ileum was used, and for pediatric recipients 100 cm was