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• CLINICAL RESEARCH •

Combined small bowel and reduced auxiliary liver transplantation: case report

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Abstract

AIM: To present a case of combined small bowel and reduced auxiliary liver transplantation.

METHODS: A 55-year-old patient with short bowel syndrome and TPN-related liver dysfunction received small bowel transplantation combined with a reduced auxiliary liver graft. A liver was added to restore the patient's liver function and to protect the intestinal allograft from rejection. His own liver was not removed.

RESULTS: Without donor pretreatment and by conventional immunosuppresive therapy following transplantation, the patient experienced had only one episode of mild intestinal rejection, which was easily reversed by treatment with Methylprednisolone. No liver rejection occurred. Unfortunately, the patient died of heart and lung failure 30d after transplantation, despite successful graft replacement. Histopathologic examination of specimens after death demonstrated normal structure in both intestinal and liver grafts.

CONCLUSION: The auxiliary liver graft might play a role in preventing intestinal allograft rejection. However, the observation period in this case is short. Further study is needed to determine the risks, effect on the protecting the small-bowel from rejection, and feasibility of general application of this procedure.

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INTRODUCTION

Small bowel transplantation is a possible choice of treatment for patients with irreversible failure of the intestine[1-8]. Compared with the success in other solid organ allografts, attempts at small bowel transplantation in human have got poor results in terms of patient and graft survival[9-17]. Rejection, immunosuppression-related infections and graft-versus-host reaction (GVHR) are the main obstacles to clinical application[18-30].

In 1990, Grant *et al*[31] first reported a case of successful small-bowel transplantation combined with a liver graft. This patient had only one episode of mild intestinal rejection, which was easily reversed by treatment with OKT_3. She had maintained normal nutrition for more than 2 years after surgery. The authors considered that the lack of serious intestinal rejection in this case may be due to immunological protection provided by the liver graft. Subsequently, some investigators demonstrated the same observations[32-38], others reported that combined liver-bowel transplantation has no immunologic advantage over bowel transplantation alone[39-41]. Furthermore, it has been shown that auxiliary liver transplantation had a slight protective effect on simultaneously transplanted small bowel, and it was not as strong as has been observed with orthotopic liver transplantation[42].

We report a case of short-bowel syndrome and secondary TPN-related hepatic dysfunction who received small-bowel transplantation combined with a reduced auxiliary liver graft in our institute. After operation, only one episode of mild intestinal rejection occurred without liver rejection.

CASE REPORT

Case history

A 55 year old patient has had the short-bowel syndrome since February 1999 after the resection of whole small bowel and right colon because of thrombosis of the superior mesenteric artery. He was then alive on total parenteral nutrition (TPN), but was not discharged from hospital due to uncontrollable diarrhea. Besides, the TPN-related liver impairment developed. After extensive discussion with the patient and his family, small-bowel transplantation was performed on April 15, 1999. An auxilliary liver was simultaneously transplanted for the purpose of both restoring his liver function and protecting the intestinal graft from rejection. We did not remove his own liver.

Transplantation procedures

The donor is a brain death adult. Both donor and recipient were blood group O. The donor's HLA phenotype was A11,-; B75, -; DR12, 15 and DQ6 (1),-. The recipient's HLA phenotype was A2,23;B44,62;DR7,- and DQ2,5. The lymphocytotoxic crossmatch was negative. No pretreatment was given to alter the graft immunogenicity with antilymphocyte or other modalities.

To reduce the volume of donor liver, left lateral lobectomy and right frontal lobectomy were performed. The reduced liver and small bowel including the duodenum, jejunum and partial ileum were grafted into the abdominal cavity of the recipient. The donor's abdominal aorta duct containing the origins of the superior mesenteric artery and coeliac artery was anastomosed end-to-side to the recipient's infrarenal aorta. The donor's infrahepatic vena cava was anastomosed end-to-side to the recipient's infrarenal vena cava. The end of the donor

jejunum was anastomosed to recipient' s duodemum; intestinal continuity was restored with an end-to-side ileocolic anastmosis. The end of the donor' s ileum was exteriorized as an ileostomy (Figure 1).

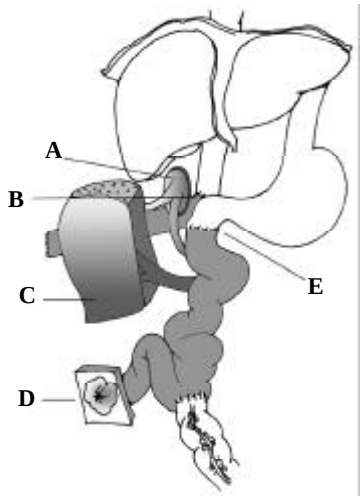

Figure 1 Small-bowel and auxiliary liver allograft. A. Carrel patch containing the origin of the superior mesenteric artery and the coeliac artery is anastomosed to the recipient's aorta; B. Anastomosis of end of the donor infrahepatic vena cava to the side of recipient's vena cava; C. The reduced liver; D. Ilesotomy; E. Anastomosis of donor jejunum to the recipient's duodenum

Immunosuppression management

Methylprednisolone was given intravenously 30 min before graft revascularization (first dose of 500mg bolus) and rapidly tapered to 20 mg· d^{-1} over the next 10 days. Cyclosporin A by continuous intravenous infusion was begun intraoperatively (3mg· kg· d^{-1}) to maintain the whole blood concentration of 350-450 μg· L^{-1} by monoclonal radioimmunoassay. Cyclophosphamide 100 mg was also given intravenously daily for the first 3 days. Prostaglandin E_1 (600 μg· d^{-1}) was began intraoperatively and continued for 20 days.

Postoperative course

Detection of graft rejection was based primarily on clinical observations and mucosal biopsies. During his postoperative course, the bowel graft developed only one histologic evidence of rejection. Mucosal biopsy on the seventh postoperative day showed lymphocyte infiltration in epithelium, slight fattening of the villi, decreased numbers of goblet cellls, but the mucosal destruction and necrosis were not observed (Figure 2). The rejection was successfully reversed by a 3 day course of methylprednisolone bolus (15mg· kg· d^{-1} per day in tapering doses).

There was no clinical or histological evidence of liver rejection. The liver function including ALT, AST, Tbil, cholesterol, triglyceride returned to the normal range 5 days after surgery. On the 9th and 23rd postoperative day, laparotomy was performed because of surgical complications. During the operation, the liver was biopsied, and a normal histological appearance was found (Figure 3).

The patient did not receive any specific treatment for preventing graft-versus-host disease (GVHD) other than the immunosuppression therapy previously described. No sign of GVHD developed. Unfortunately, some severe complications occurred including intestinal fistula, stress ulcer and bleeding, ARDS, pulmonary and abdominal infection. The patient died of heart and lungs failure 30 days after transplantation despite successful graft replacement. The histopathologic examination of specimens after death demonstrated normal structure in both intestinal and liver grafts.

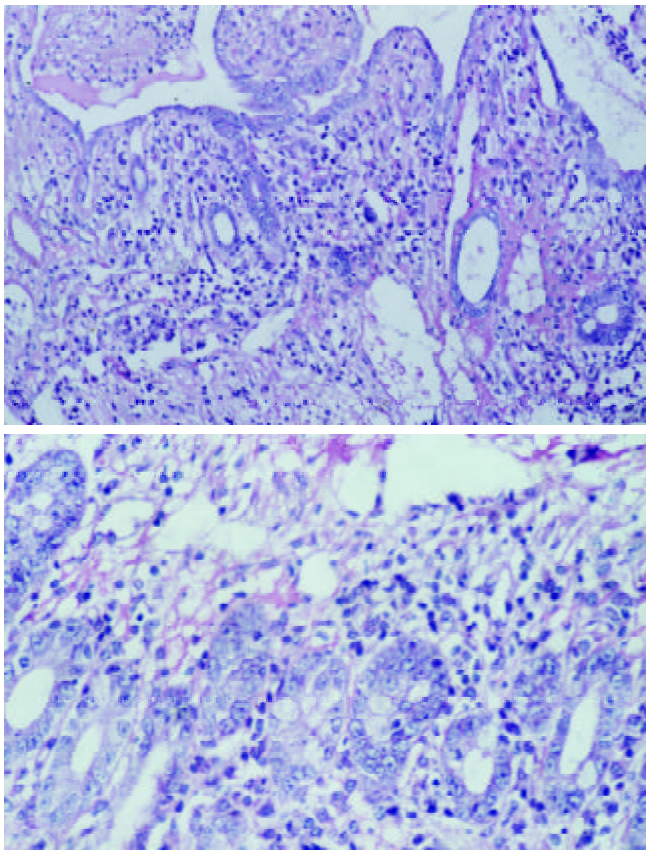

Figure 2 Photomicrographs showing acute rejection with lymphocytic crytitis on the 7 th postoperative day, the mucosal destruction and necrosis were not observed (H&E, A, ×200; B. ×400).

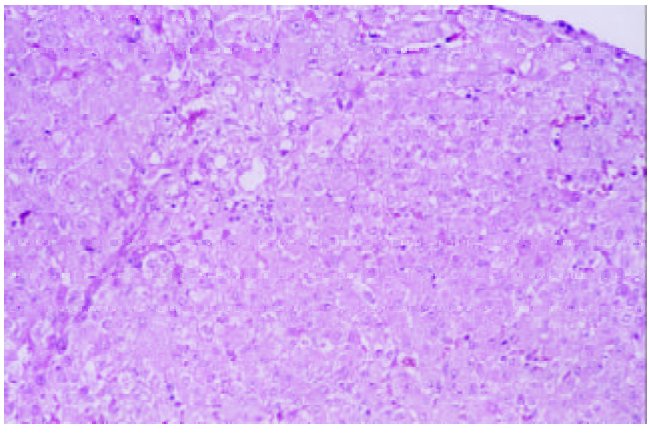

Figure 3 Liver biopsy specimens on the 9th postoperative day showed normal appearance of the allograft (×200), no inflammatory infiltrate in the portal tract.

DISCUSSION

Liver dysfunction is a well-recognized complication of intestinal failure. Advances in TPN have allowed the patient

suffering from short bowel syndrome to survive. However, in many instances total parenteral nutrition causes severe liver damage leading to cirrhosis. Thus, combined liver and small bowel transplantation becomes an established life-saving therapy for the treatment of liver disease and intestinal failure[43-46]. In the general, an orthotopic liver and small bowel are transplanted. To our knowledge, this case is the first report of transplantation of combined auxiliary reduced liver and small bowel in human. We tried to restore the patient' s liver function and to protect the intestinal allograft from rejection. For these reasons, an auxiliary liver was simultaneously transplanted. The auxiliary reduced liver-small bowel transplantation model represents a new, less aggressive possibility for multiorgan transplantation[31,47,48]. It offers some advantages over multivisceral transplants, including simplicity and less mortality than the combined orthotopic liver-intestinal transplantation. This procedure is useful for the patients with reversible hepatopathy associated with intestinal insufficiency because it can offer temporal or definitive hepatic support.

Without donor pretreatment and under conventional immunosuppresive therapy, this patient had only one episode of mild intestinal rejection, which was easily reversed by treatment with Methylprednisolone. These data indicate a possible role of the auxiliary liver graft in preventing intestinal allograft rejection. In fact, the immunoprotecting effect of the liver was first described by Calne in 1969 in a porcine model[49]. The animal can reject skin, kidney and hearts rapidly. However, orthotopic and accessory heterotopic liver allografts can protect preferentially from rejection grafts of donor specific skin, kidney and heart. Injected soluble liver antigen may also protect donor specific tissue from rejection. It suggested that allogeneic liver can induce immunological tolerance in immunologically mature pigs[49]. Subsequent studies demonstrate that specific tolerance can be achieved in combined liver/small bowel transplantation after a transient rejection crisis[32-38].

The mechanism of immunological protection of the liver is not very clearly until now[50-52]. Apoptosis of T lymphocytes may be involved in graft rejection and tolerance induction[50]. Apoptosis is a mechanism for eliminating autoreactive cells during T cell maturation in the thymus. T cells themselves use apoptosis to eliminate alloantigen-expressing donor cells during rejection responses. Apoptosis of parenchymal cells in the grafted livers correlated directly with interleukin-2 receptor expression of the infiltrating T cells. In the late phase of rejection, a peak of apoptosis in the lymphocyte infiltrate was demonstrated, characterized as predominantly apoptotic $CD8^+$ T lymphocytes. T cell inactivation seems to result in apoptosis of cytotoxic T cell and tolerance[50]. In addition, microchimerism is associated with long-term graft acceptance in combined liver/small bowel transplantation[51,52]. Donor specific leucocytes could be detected immunhistochemically in the combined liver/small bowel group and isolated liver group in spleen, host Peyer patches, and mesenteric lymph nodes. Particularly in the liver sinusoids investigators[52] found a great number of persisting donor leukocytes in all long-term survivors in combined liver/small bowel rats. The persisting leucocytes obviously originate from the initially transplanted white cell population of the liver. The liver as constant source of antigen plus a persisting and obviously active leukocyte popuolation may provide the basis for a long-term survival of the liver graft and any cotransplanted organ.

However, the observation period in this case was short and it is difficult to extrapolate that the complex immune responses between the donor and recipient are affirmatively associated with adding a liver graft. Moreover, other studies found that liver grafting failed to prevent intestinal rejection in human and large animal model[39-41]. Further studies are needed to determine the risks, effect on the protecting the small bowel from rejection, and feasibility of general application of this procedure.

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