Duct-Obliterated Canine Pancreatic Segmental Transplantation

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Summary: In this study 3 various kinds of operation, each with blockade of pancreatic duct by N-octyl-α-cyanoacrylate, were performed in 27 dogs divided into 3 groups: (1) removal of the right two thirds of the pancreas and the left one third left in situ (n = 4), (2) total pancreatectomy and intraperitoneal autotransplantation of the left limb (n = 16), (3) total pancreatectomy and intraperitoneal allotransplantation of the left limb (n = 7). The purpose of injection of cyanoacrylate glue into the pancreatic duct is to suppress the exocrine function of the organ, thereby transforming its dual function of external and internal secretion into purely endocrinous one. After obliteration the animals remained normoglycemic on the first postoperative day, and after autotransplantation the longest observation period was 6 months with normoglycemia. Allografted animals showed an average period for normoglycemia of 19±16 days (5—46 days) and survived for 36.7±17.6 days (13—62 days). Hyperglycemia has been considered as a sign of pancreatic allorejection, but it could be prevented by conventional immunosuppressive therapy.

Key words: duct-obliterated pancreatic segmental transplantation, N-octyl-α-cyanoacrylate

Using whole intact pancreas for transplantation often brings about dangerous early complications caused by the continuous secretion of pancreatic enzymes. Attempts to preserve exocrine function led to a number of methods, whose operative procedures are rather complex.

Our initial approach was to drain the exocrine secretion freely into the peritoneal cavity on the basis that as long as the gut was intact, the pancreatic proenzymes could not come in contact with enterokinase and would remain inactive, and the pancreatic secretions could be reabsorbed from the peritoneum. However, our own and others' experiences showed that intraperitoneal transplantation with open ducts would result in ascites in those recipients with poor capacity for reabsorption.

We hereby report on a method of pancreatic transplantation that involves obstruction of the entire exocrine ductal system by N-octyl-α-cyanoacrylate. This technique has allowed us to obtain a transplantable vascularized pancreatic segment with maintenance of only endocrine function and no escape of pancreatic fluid.
MATERIALS AND METHODS

Adult mongrel dogs of either sex, weighing between 9 and 17 kg, were used. The surgical technique, except the duct obstruction, was the same as previously reported. The pancreatic duct was identified and cannulated and 1.5–2 ml of N-octyl-α-cyanoacrylate (Sian Chemical Industry Institute) were then injected to obliterate the ductal system. Twenty seven dogs were divided into the following three groups: Group 1, removal of the right two thirds of the pancreas and cyanoacrylate injection into the duct of the left one third left in situ (n = 4). Group 2, total pancreatectomy and intraperitoneal autotransplantation of the left limb with cyanoacrylate injection (n = 16). Group 3, total pancreatectomy and intraperitoneal allotransplantation of the left limb with cyanoacrylate injection (n = 7).

Postoperative medication: All animals of group 2 and 3 were treated with 5% dextrose and lactic Ringer's solution 500 ml each to which 100 U/kg of heparin were added daily for 4 days postoperatively. Feedings were supplemented with pancreatin.

Allograft recipients received 5 mg/kg/day of azathioprine tapered to 3 mg/kg/day until rejection was diagnosed, and at the same time 10 mg/kg/day of hydrocortisone were given tapered to 6 mg/kg/day over the same period. Several allograft recipients were administered each a dose of 2 mg/kg of cyclophosphamide on the 3rd or 4th day after grafting. Occasionally, cyclophosphamide administration was repeated for prevention of rejection.

Postoperative study: Plasma glucose and serum amylase determinations were done every day. Pathologic examinations were performed after death or sacrifice of each dog.

RESULTS

Group 1: After partial pancreatectomy, the left limb was left in situ with the duct obstructed. There was no death in the four dogs reported, and in each case the pancreas underwent an aseptic atrophy with preservation of the endocrine elements and no apparent signs of diabetes. There was no peritonitis or fistula formation over 4 months of observation. The plasma glucose was 106.7 ± 20.8 mg% (mean ± SD, the same below) on the first day after surgery, and was maintained at the same level thereafter until the end of follow-up. The serum amylase increased to the highest level, 1864.5 ± 786.3 U/L, on the 2nd day after operation, but thereafter it decreased progressively to normal level in 1 to 2 weeks. The four animals were killed on the 14th, 14th, 37th, and 132nd day respectively after operation for pathological examination. Exploratory laparotomy on the 132nd postoperative day showed the pancreatic remnant to be shrunken and firm, but no other abnormality was observed. Biopsy on the 14th day showed that the islet cells were well preserved, but there was fibrosis with acini atrophy, and the ducts, including the interlobular ones, were filled with cyanoacrylate glue (fig.1). Thus, in the pancreas treated in such a manner exocrine function was abolished but its endocrine secretion was intact, thereby allowing the use of the left segment of the organ as an endocrine transplant.

Group 2: After pancreatic autografting with duct obliteration, six dogs survived

Fig. 1. 14th postoperative day: normal islets (arrow), duct filled with glue (D). HE, 80×.