Dorsal Pancreas Agenesis in an Organ Donor: To Accept or to Discard for Transplantation?

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INTRODUCTION

Pancreas transplantation (PTx) is an established treatment for end-stage diabetic kidney failure when combined with a kidney transplant or for life-threatening hypoglycemic unawareness. PTx represents a major surgical procedure with its associated risk of surgical complications.1 Therefore, patients with a too high-risk profile for surgery can benefit from intraportal islet transplantation.2 The latter is less invasive although there is a low but actual risk of portal thrombosis.3 The success rate of islet transplantation increased significantly after implementation of the Edmonton protocol, in which an adequate amount of islet equivalents from 2 to 4 donor pancreas are transplanted in combination with a steroid-free immunosuppressive regimen and strict donor/recipient criteria.1-3 However, longer-term outcomes still favor whole-organ pancreas over islet transplantation with 5-y insulin independence rates of 50%–70% versus 25%–50%, respectively.1,4 PTx relies on the availability of pancreatic grafts from deceased donors, as living pancreas donation (with insufficient endocrinological work-up) may cause donor morbidity.

Embryogenesis of the pancreas is a complex process. The procurement surgeon might encounter a variety of pancreas anomalies and be confronted with the decision to accept or discard anatomically abnormal pancreas. We report herein a procurement procedure during which a rare dorsal pancreas agenesis (DPA) was encountered.

CASE DESCRIPTION

A 20-year-old, previously healthy man was admitted with an isolated head trauma secondary to a traffic accident. He developed brain-death 1 d later. After consent of the family, he became a multiorgan donor. He had no medical history of diabetes. He had no history of pancreatitis or abdominal pain. Laboratory tests revealed normal amylase and lipase levels of 27 U/L (normal: 0–150) and 6 U/L (normal: 0–200), respectively. The glucose level was 166 mg/dL (normal: 63–180). Calculated preprocurement pancreas suitability score was 13 (<17 considered for pancreas donation), and the pancreas was allocated for whole-organ transplantation.5 HbA1C and C-peptide were not known. The pancreas graft was procured en-bloc with the spleen (asterisk), the liver (arrow), and the duodenum (arrowheads) (Figure 1). We observed a complete absence of the body and tail of the pancreas, consistent with the diagnosis of DPA. Although the pancreatic head (dotted circle) (Figure 1) had a normal macroscopic appearance with an apparent normal vascular anatomy, the decision was taken to discard this pancreas, based on the suspected insufficient amount of β cells.

DISCUSSION

This case of DPA, a rare embryonic malformation, in an organ donor confronted us with the question on whether or
DPA is invariably associated with a reduced number of β cells and therefore at risk for developing hyperglycemia and diabetes. Schnedl et al found that, out of 53 patients with DPA, 28 (53%) had hyperglycemia. Per analogy, in the case of distal pancreatectomy, the development of diabetes has an incidence varying from 5% to 42%. Resection of a distal pancreas volume exceeding 25% of the whole organ is an independent risk factor for the development of diabetes.

Finally, in the case of living donor PanTx (where the distal pancreas is procured, leaving the donor with the pancreatic head and neck only), there is a 15% risk of developing diabetes.

Of note, some of these patients developed type-2 diabetes due to substantial weight increases over time.

In a transplant setting, characterized by preservation and ischemia–reperfusion injury as well as the risk for rejection, the amount of β cells will further be reduced, compared to a native organ. We are aware of only 2 cases of transplantation of a pancreatic head only. In the first, a pancreas from a DPA donor could be transplanted successfully technically, but the recipient did not achieve full insulin independency (personal experience J. Pirenne, D. Sutherland, 1994). In this case, however, the pancreas had a particularly small volume and was macroscopically slightly fibrotic which per se might have contributed to the inferior outcome. In the second case, a single deceased donor pancreas was split for transplantation into two separate recipients with >70% panel reactive antibodies: one recipient received the pancreatic head only (the transection line was to the left of the portal vein to preserve more tissue for the head), and the other received the more lateral pancreas with the splenic pedicle. Both grafts functioned well posttransplant and both patients became insulin-free.

In addition, 2 successful cases of islet transplantation (1 allotransplantation and 1 autotransplantation) from patients with DPA have been described. One was a type 1 diabetes patient who received islet cells from a single deceased donor with a partial DPA. The total islet mass transplanted was $422 \times 10^3$ islet equivalents with a viability of 85%. Immunocytochemical analysis of islet preparation revealed 53.3% of β cells, 33.3% of α cells, 6.7% of δ cells, and 6.7% of pancreatic polypeptide cells. The islet recipient had a 60% reduction in insulin usage at 1 mo and became insulin-independent at 2 mo. We recently reported a successful case of islet autotransplantation following total pancreatectomy in a patient with DPA who suffered from intractable abdominal pain due to episodes of pancreatitis. Before the procedure, the number of β cells and their functional capacity had been estimated by a hyperglycemic clamp test and were deemed sufficient. The pancreas weighted 66 g (body weight: 48 kg) and a total of $226 \times 10^3$ islet equivalents were isolated, of which $4.7 \times 10^3$ islet equivalents per kilogram were injected intraportally. Insulin therapy could be stopped 19 d posttransplant and the patient remained insulin- and pain-free since then (follow-up: 6 mo). It should be noted that the number of islet cells required for a successful autotransplantation is likely to be inferior to that needed in allotransplantation given the absence of rejection. Besides these DPA cases, we know that complete pancreatectomies (head only) in total pancreatectomy islet auto-transplant patients provide sufficient islet mass to make the patients insulin-independent long-term.

In addition to hyperglycemia, overt diabetes, pancreatitis, and abdominal pain, DPA can be associated with pancreatic malignancies. Adenocarcinoma is the most frequently
reported cancer in DPA. Isolated cases of solid papillary tumors, pseudopapillary tumors, and intraductal pseudopapillary neoplasms have also been described.\textsuperscript{11,22} There is some experimental evidence that retinoic acid and hedgehog signaling pathways may play a role in the pathogenesis of DPA.\textsuperscript{22} These signaling pathways have been implicated in the development of pancreatic ductal adenocarcinoma and nonalcoholic chronic calcific pancreatitis.\textsuperscript{22} This risk of malignant development has also to be taken into account in the decision to use or not a pancreas from a DPA donor.

In conclusion, DPA is a very rare embryonic disorder associated with a reduced amount of β cells and a risk of developing diabetes, pancreatitis, or malignancy. For these reasons, DPA-grafts should not be used routinely for whole-organ PTx, but only in patients in whom it represents, for immunological reasons, a unique chance of transplantation. However, their use for islet allotransplantation should be considered taking into account that the islet cell yield might be inferior. Therefore, HbA1C and C-peptide should be analyzed to estimate the amount of islet cells. Finally, DPA can cause refractory tumor and this can be treated by total pancreatectomy and islet autotransplantation.

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