Editorial

PANCREAS TRANSPLANTATION

Type I diabetes occurs due to immune destruction of insulin-producing beta cells of the pancreas. Lack of insulin produces profound hyperglycemia, and exogenous insulin therapy remains the mainstay of treatment. Although extensive research and technological innovations are developing new automated glucose sensing and insulin delivery devices, it is still at a stage where constant euglycemia has not been achieved. Hence, the patients are resigned to manual checking of glucose levels and subcutaneous insulin injections. This results in a wide variation of sugar levels from hour to hour and from day to day. In addition to decrease in insulin secretion, glucagon secretion is reduced in most people who have type I diabetes within the first 2 to 10 years after onset of the disease. Because of this decrease in the counterregulatory hormone, patients can have severe hypoglycemic episodes also in addition to the hyperglycemia.

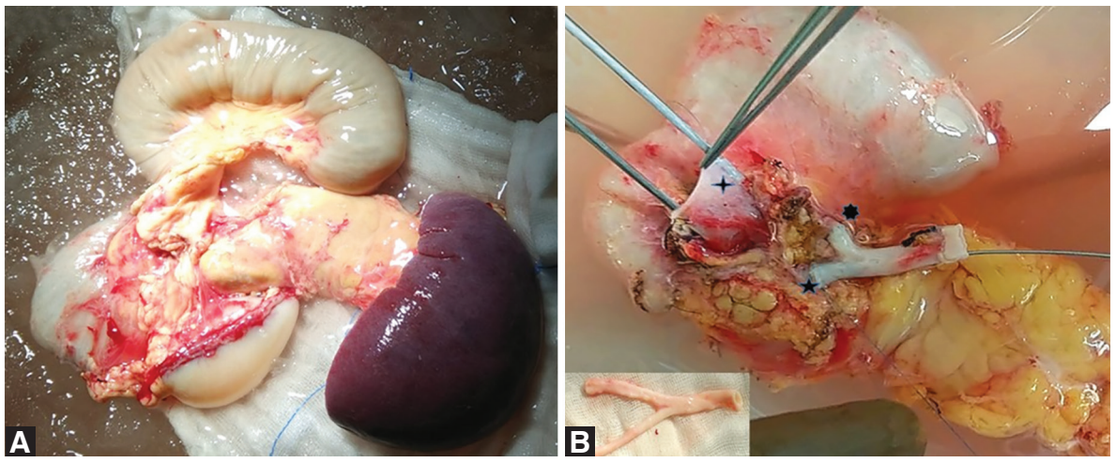
Uncontrolled hyperglycemia remains the most important factor for development and progression of secondary complications of diabetes. Cardiovascular disease (angiopathy), nerve damage (neuropathy), kidney damage (nephropathy), eye damage (retinopathy), and issues with digestion (gastropathy) are few of the common complications along with the many infections which patients with diabetes are prone to. In addition, diabetic foot infections and diabetic ketoacidosis could potentially be life-threatening acute issues. Although exogenous insulin therapy can control the hyperglycemia and to an extent decrease the incidence, it cannot totally prevent the development of these complications. In the Diabetes Control and Complication Trial, even in the intensive treatment arm under the most ideal conditions, 15% of the patients went on to develop secondary complications.[1] Hence, better alternative therapies are the need of the hour, which can not only treat the hyperglycemia but also autoregulate the sugar levels, thus preventing the development or halting the progression of the complications.

A Pancreas Transplant (PanTX) operation is a surgical procedure that places a healthy pancreas from a deceased donor into a person suffering from diabetes. The first reported PanTX was carried out in 1966,[2] and since then, more than 20,000 operations have been carried out worldwide. In India, though the surgery is still evolving, at last count <60 such operations have been carried out. A PanTX has the potential to achieve normal glycemic status without the need for exogenous insulin therapy while also altering the progression of all long-term complications of uncontrolled diabetes. It reverses the diabetic changes in the native kidneys of patients with very early diabetic nephropathy, prevents recurrent diabetic nephropathy in patients undergoing a simultaneous kidney transplantation,[3] reverses peripheral sensory neuropathy, stabilizes advanced diabetic retinopathy,[4] and thus significantly improves patient's quality and quantity of life.[5]

Almost all PanTXs are done to treat type I diabetes, and an ideal PanTX recipient is between the ages of 18 and 40 years, has type I diabetes, and suffers from one or more of its many complications. It is normally performed in one of three settings:

1. A simultaneous kidney and pancreas transplantation: This is the most common surgery performed and is offered for patients suffering from diabetic Kidney failure. The kidney transplant operation treats the renal failure and gets the patient off dialysis while the pancreas transplant treats the diabetes.
2. A pancreas after kidney transplantation: This operation is done in patients who have previously undergone either a living donor or deceased donor kidney transplant operation and now receive a deceased donor pancreas graft.
3. An isolated pancreas transplant alone: This is offered to patients who do not have diabetic renal failure but suffer from other complications of diabetes like frequent hypoglycemic episodes or hypoglycemic unawareness, retinopathy, neuropathy, ketoacidosis, etc.

Once a patient who will potentially benefit from a PanTX operation is identified, he/she undergoes rigorous testing to confirm surgical fitness and is then placed on a waiting list for a suitable deceased donor to become available. Once a donor becomes available, a cross-match test is performed to test the histocompatibility and minimize chances of rejection. The detailed surgical procedure of the transplant is outside the scope of this article. In short, it involves a midline laparotomy and utilization of the iliac vessels for the anastomoses (Fig. 1). The kidney graft is placed in the left iliac fossa and pancreas in the right iliac fossa. The drainage of exocrine



Figs 1A and B: Benching of a pancreas allograft. (A) A freshly procured pancreas allograft from a donor. The spleen and jejunum are still attached to the pancreas. (B) "Benching" of the pancreas includes splenectomy, resecting excess length of intestine leaving behind the C-loop of the duodenum, mobilizing adequate length of the portal vein (✦) and suturing the Y-graft to the stumps of the superior mesenteric artery (★) and splenic artery (✱). Inset: The Y-graft consisting of the common iliac, internal iliac, and external iliac artery procured form the donor A B

secretions of the pancreas is facilitated through a duodeno-jejunostomy. A suitable induction agent is given prior to surgery and antirejection medications are started once the patient can resume oral diet.

The two main complications in the immediate postoperative period include vascular thrombosis and anastomotic/duodenal stump leakage. Vascular thrombosis carries a dismal prognosis and is the major cause of graft loss in the immediate posttransplant period, and so most centers anticoagulate the patients immediate postsurgery. Stump or anastomotic leakage usually necessitates repeat surgery and drainage, but graft function is usually preserved. Other potential complications include graft pancreatitis, ileus, diarrhea, and rejection. Also the side effects of immune suppression, such as increased susceptibility to infections, increased blood pressure, and osteoporosis will need adequate precautions.

The outlook for a successful pancreas transplant patient is quite good, with a more than 95% patient survival rate and >85% graft survival rate (insulin-free rate) at 1 year. At 5 years more than 75% of pancreas and at 10 years about 50% of them are still functional.[6] A retransplant is possible if and when the donor pancreas fails. With refinements in surgical technique and immune suppression, the complication rates continue to decrease and the long-term outcomes continue to improve.

Author's Experience: Dr Suresh Raghavaiah is the Director of the Pancreas Transplant Program at BGS Gleneagles Global Hospitals, Kengeri, Bengaluru, which is the only center to have performed six successful pancreas transplants in 2 years in Karnataka. Dr Raghavaiah trained in multiorgan transplant surgery at Mayo Clinic, USA and has been a part of more than 40 pancreas transplants in his career.

REFERENCES

1. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993 Sep;329(14):977-986.
2. Kelly WD, Lillehei RC, Merkel FK, Idezuki Y, Goetz Fe. Allotransplantation of the pancreas and duodenum along with the kidney in diabetic nephropathy. Surgery 1967 Jun; 61(6):827-837.
3. Fioretto P, Steffes MW, Sutherland DER, Goetz FC, Mauer M. Reversal of lesions of diabetic nephropathy after pancreas transplantation. N Engl J Med 1998 Jul;339(2):69-75.
4. Giannarelli R, Coppelli A, Sartini MS, Del Chiaro M, Vistoli F, Rizzo G, Barsotti M, Del Prato S, Mosca F, Boggi U, et al. Pancreas transplant alone has beneficial effects on retinopathy in type 1 diabetic patients. Diabetologia 2006 Dec;49(12):2977-2982.
5. Morath C, Zeier M, Döhler B, Schmidt J, Nawroth PP, Opelz G. Metabolic control improves long-term renal allograft and patient survival in type 1 diabetes. J Am Soc Nephrol 2008 Aug;19(8):1557-1563.
6. OPTN/SRTR Data as of October 1, 2010. Retrieved from https://srtr.transplant.hrsa.gov/annual_reports/2010/113_surv-new_dh.htm

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