Management of Complications

A strategy that balances aggressive immunosuppression against risks of infection. A diagnosis of rejection is dependent on biopsy of either the kidney or pancreas allograft in recipients of SPK transplantation or of the pancreas allograft in pancreas transplantation alone. Because of the double-edged sword of aggressive antirejection treatment, an episode of graft dysfunction should not be treated without biopsy-proven histopathologic evidence of immunologic graft injury. Ruling out infectious and anatomic causes of graft dysfunction with appropriate radiologic studies is equally important. Drachenberg and coworkers [15] and Nakhleh and Sutherland [16] have defined histologic criteria for grading pancreas allograft rejection that are practical from the standpoint of being able to prognosticate outcome and response to therapy. Serial histologic studies of pancreas rejection (as in this case) have shown that lymphocytic infiltrates initially involve the exocrine portion of the gland and that islet cell tissue becomes involved later [12]. As a result, exocrine dysfunction is frequently the first clinical sign of rejection (manifested by either elevated serum amylase or decreased urinary amylase levels). Consequently, early rejections without evidence of islet cell involvement usually can be treated successfully. On the contrary, the success of antirejection treatment is far less successful when initiated after the development of hyperglycemia [17].

**A,** Normal pancreas allograft core biopsy demonstrating an acinar lobule and preserved individual islet of Langerhans without inflammatory infiltrate (magnification × 200). **B,** Needle core biopsy demonstrating glandular architecture with fibrous septae interdigitating between acinar lobules. An infiltrate is present that can be described as mononuclear, predominantly lymphocytic, perivascular, and septal. Endothelialitis is seen in a medium-sized vein at the upper central edge of the biopsy specimen. These features are consistent with mild acute cellular rejection (magnification × 200). **C,** Needle core biopsy demonstrating intense septal inflammation with activated lymphocytes. Early acinar inflammation is present in the right upper lobule. Eosinophils also are present in the dense septal infiltrate. These findings also are consistent with mild acute cellular rejection (magnification × 200). Moderate rejection is characterized by significant acinar inflammation and arteritis. Severe rejection is suggested when, in addition to the features listed above, confluent acinar necrosis with extensive acinar inflammation and ductal epithelial necrosis are present.

Features indicating a poor prognosis include arteritis, confluent acinar necrosis, islet inflammation and necrosis, ductal epithelial necrosis, and fibrosis. Mild acute rejection usually is reversible with bolus corticosteroid therapy. In contrast to renal allograft rejections, however, most mild pancreas allograft rejections are somewhat recalcitrant to bolus steroid immunotherapy. Steroids may worsen potentially compromised glycemic control, thus complicating treatment. Therefore, significant rejection of the pancreas allograft may be best treated with antibody therapy, although a randomized control trial comparing the two treatment options has not been carried out. FK506 is commonly employed as rescue therapy in pancreas transplant episode recipients who are experiencing a significant acute rejection episode while on cyclosporine or Neoral (Sandoz Pharmaceuticals, East Hanover, NJ). Irreversible allograft rejection was a frequent occurrence several years ago. Today, it is unusual, occurring in less than 5% of patients.
Transplantation as Treatment of End-Stage Renal Disease

Indications for enteric conversion

- Hematuria: 19%
- Urethritis: 23%
- Recurrent urinary tract infections: 11%
- Reflux pancreatitis: 3%
- Leak: 42%
- Metabolic acidosis: 2%

Metabolic acidosis postoperatively is present in about 80% of patients after pancreas transplantation with BD and usually is due to excessive urinary loss of bicarbonate-containing exocrine fluids. Because urinary bicarbonate loss is accompanied by an obligate loss of fluid, low serum levels are associated with dehydration. Oral fluid replacement should be instituted to maintain a serum bicarbonate level of at least 20 to 25 mg/dL, and dehydration is treated appropriately. Fortunately, this problem usually stabilizes over time and infrequently requires conversion from bladder to enteric drainage.

Diagnosis is confirmed by cystogram (see Fig. 15-17). Fortunately, this complication is unusual, occurring in 10% to 15% of patients.

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Incidence and procedure in enteric conversion (EC). A, Surgical conversion of pancreatic exocrine secretions from bladder drainage to enteric drainage is necessary in many patients. Whereas half of patients receive EC within the first postoperative year, a significant percentage must undergo EC up to 5 years after transplantation. B, EC involves taking down the duodenocystostomy, repairing the bladder, and performing a simple side-to-side duodenoenterostomy. In our experience of performing 95 ECs over a 14-year period in 480 simultaneous pancreas-kidney (SPK) transplant recipients, only one graft was lost within 3 months of EC [5]. No differences were found in patient, kidney, or pancreas graft survival when comparing SPK transplant recipients who underwent EC with those who did not. The frequency of urologic complications and need for EC have prompted a changing trend toward performing primary enteric drainage; however, neither of these problems appears to impact negatively on graft survival.

Pancreatic enzyme and urinary leaks. A leak of urine, activated pancreatic enzymes, or both, is one of the most devastating and life-threatening infectious complications after pancreas transplantation. Patients exhibit sudden-onset lower abdominal pain, fever, leukocytosis, increased serum amylase levels, and increased serum creatinine levels. Diagnosis is confirmed by cystogram. When no leak is identified, voiding cystourethrography (VCUG) with gastrografin (panel A) or a VCUG using technetium (Tc99m) in normal saline is performed (panels B–E).

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