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## Enteric-Drained Pancreas Transplants Monitored by Fine-Needle Aspiration Biopsy

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As we previously reported<sup>1,2</sup> documentation of pancreas rejection remains problematic because of the lack of specific and sensitive markers. Since most pancreas transplants are performed simultaneous with a kidney, clinical dysfunction from rejection, documented by an increase in serum creatinine and renal-core biopsy, automatically leads to the treatment of both grafts. Rejections of pancreatic grafts are in some way preemptively treated by the initiation of kidney-transplant treatment. Nevertheless, in combined kidney-pancreas transplantation, an incidence of isolated pancreas rejection has been documented.<sup>3,4</sup> We report herein our experience in documenting rejection episodes with fine-needle aspiration biopsy (FNAB) in pancreas transplant patients.

The FNAB rationale resides in the fact that the immunoinactivation phenomenon begins in the graft, where infiltrating mononuclear cells endure a transformation process into "blasts." Acute cellular rejection is defined by an accumulation of immature cells (lymphoblasts, plasmablasts, monoblasts) that can be quantified according to established cytologic criteria. Vascular rejection is generally assigned to humoral immunity with the proliferation of mononuclear phagocytes and tissue macrophages. However, on several occasions the cellular and humoral component of rejection can be simultaneously detected.

### MATERIALS AND METHODS

Between July 1994 and July 1996, a total of 72 pancreas transplants were performed at the University of Pittsburgh in type I diabetic patients. Sixty-two patients received a simultaneous kidney transplant (SPK), five patients received a sequential pancreas (PAK), and five patients received a solitary pancreas (PTA).

Immunosuppression consisted of tacrolimus (0.05 mg/kg IV for 3 to 6 days followed by 0.15 mg/kg p.o. bid), azathioprine (5 mg/kg IV followed by 1.5 to 2.0 mg/kg p.o.), or mycophenolate mofetil (1 g p.o. bid, if tolerated) and steroids. No antilymphocyte antibody infusion (induction therapy) was employed. Rejection episodes were treated with methylprednisolone boluses. OKT3 monoclonal antibodies were used only in four patients and ATGAM in two others.

CMV prophylaxis was not used except in the sero-positive to sero-negative donor-recipient combinations (15 patients) or during anti-T cell treatment.

To avoid the high complication rate related to bladder drainage,<sup>5</sup> enteric drainage was performed in most (54) of the patients.<sup>6</sup>

FNABs of both grafts were performed as previously described<sup>1,7</sup> according to an established protocol and when clinically indicated.

### RESULTS

In this series of patients there was no mortality. The kidney and pancreas survival was 95% and 86%, respectively.

In the SPK group, 40 patients presented one or more rejection episodes. In the majority of cases, they were documented with FNAB. In 25 cases, FNAB evidenced rejection in both grafts, whereas in five cases, FNAB showed isolated rejection of the pancreas. One patient lost both organs from antibody-mediated rejection and another one rejected both grafts following discontinuation of immunosuppression because of severe systemic candida infection.

Two PTA patients lost the graft (one patient because of persistent active rejection despite OKT3 treatment and one other because of reflux pancreatitis).

No grafts were lost in the PAK group despite every patient-presented rejection episode, detected by FNAB without other clinical symptoms of pancreatic dysfunction.

### CONCLUSIONS

FNAB of the pancreas transplant has been proven to be a reliable technique for monitoring rejection episodes that otherwise could have been overlooked with the usual biochemical markers. No complications (bleeding, fistula, infections) have been reported in our series of patients who underwent repeated FNABs.

The enteric-drained patient group had significantly lower rates of surgical complications in comparison with the bladder-drained group. The fact that we could easily perform FNAB in enteric-drained pancreata has permitted a timely diagnosis of rejection and might have optimized the amount of immunosuppression, thus avoiding infections and further complications.

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