BRIEF COMMUNICATIONS: CLINICAL TRANSPLANTATION

# ADENOCARCINOMA ARISING IN A TRANSPLANTED PANCREAS

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Transplantation: [September 27, 2001 - Volume 72 - Issue 6 - p 1156-1157](https://journals.lww.com/transplantjournal/toc/2001/09270)

Tumor transmission or de novo tumor development in the transplanted organ is a rare event. Appreciation of the organ-specific risk factors for tumor development and careful inspection of the organ at procurement may reduce but not eliminate this complication. We report the first known combined kidney-pancreas recipient who developed adenocarcinoma in the transplanted pancreas. Molecular typing of the tumor by DNA sequencing supports donor derivation of the tumor. Despite cessation of immunosuppression and reconstitution of the recipient’s immune response, the patient died from metastatic pancreatic adenocarcinoma. Comparison is made to the reported outcomes after diagnosis of renal cell carcinoma that appeared early after transplantation.

Expansion of the cadaveric donor pool to include older donors has increased the numbers of transplantable organs. However, there are potential penalties inherent to this approach. Graft outcome and patient survival are lower among recipients of kidneys from older donors (1). These organs may also harbor occult carcinomas that appear in the transplant recipient as reported after renal and cardiac transplantation (2,3). Transmission of pancreatic adenocarcinoma after pancreatic transplantation has not been reported despite the increasing incidence of this tumor. Presumably, careful examination of the pancreas should exclude this lesion. We report the first known case of pancreatic adenocarcinoma arising in the transplanted pancreas.

Multiple organs were procured from a 55-year-old male (HLA-A29,31; B7,61[w6]; Cw2, w7; DR11[52],15; DQ 6,7) with a history of hypertension who died from a spontaneous intracranial bleed. The left kidney was discarded because of an intimal injury. The heart recipient is well 51 months after transplant. The lung recipient died of sepsis and multisystem organ failure 10 days after transplantation. The liver recipient did well for 2 years posttransplant but developed significant depression, discontinued his medications, and died of sepsis complicated by severe rejection.

GF, a 45-year-old male (HLA-A1,3; B8[w6]; Cw7; DR1,17, DR52; DQ2,5) with a 30-year history of insulin-dependent diabetes mellitus, underwent combined kidney-pancreas transplantation with bladder drainage under tacrolimus, mycophenolate mofetil, and prednisone immunosuppression. His early postoperative course was complicated by rejection that was treated with OKT3, by reflux pancreatitis that was treated by enteric conversion, and by cytomegalovirus colitis. He continued to do well until 2 1/2 years posttransplant when he presented with hyperglycemia and increased creatinine, which was believed to be secondary to rejection. An ultrasound demonstrated ectasia of the pancreatic duct. His graft function improved, but 1 year later, the patient presented with abdominal pain, fever, and a transplant peripancreatic fluid collection. At laparotomy, multiple loops of intestine were adherent to the pancreatic transplant and the Roux-en-Y limb of ileum draining the transplant duodenum had perforated. This was resected and intestinal continuity was re-established. Pathology unexpectedly showed a moderately differentiated adenocarcinoma consistent with a pancreatic primary infiltrating the ileal segment.

The patient underwent transplant pancreatectomy. Pathology demonstrated tumor invasion of the entire gland with perineural invasion. To help determine origin of the tumor, a tumor sample was submitted for molecular typing by DNA sequencing following group-specific amplification. HLA-A, -B, DRB1, and DQB loci were sequenced. For HLA-A, only donor A\*2902 and A\*3101 alleles were found. At the B locus, donor alleles B\*0703 and B\*4002 were clearly resolved, although a weak signal consistent with recipient B8 was also found. These data would be consistent with a donor origin for the tumor, whereas the weak signal for recipient B8 may have arisen from polymerase chain reaction (PCR) amplification of recipient alleles in contaminating blood or infiltrating cells. For HLA-DR, typing revealed two donor DRB1 alleles (1101 and 15011) and donor-derived DRB5\*01011. A signal was present for recipient DRB1\*0101 allele. DRB3\*0202 was also found, but it could have been derived from either donor or recipient as a result of linkage disequilibrium. For HLA-DQB1, both donor (0602 and 03011) and recipient (0201 and 0501) alleles were detected.

Immunosuppression was discontinued in an attempt to arrest tumor growth. Normalization of his immune competency occurred as evidenced by progressive loss of renal function. Nonetheless rapid local growth of tumor occurred that resulted in a bowel obstruction. The obstruction was treated with an ileostomy. A large tumor mass was present in the right lower quadrant with extensive mesenteric nodal involvement. Continued growth of the tumor was also suggested by increasing levels of carbohydrate antigen (CA) 19–9. The patient completed two courses of cisplatin, interleukin (IL) 2, and interferon with no effect as determined by clinical examination, repeat computed tomography scanning, and CA 19–9 determination. IL-2 and interferon were added in an attempt to further reconstitute his immune system. There was no apparent tumor resolution, and the patient declined further chemotherapy. He died 11 months after diagnosis and 51 months after transplantation. No autopsy was performed.

Occult tumors may be present in the organ at the time of transplantation. Two types of tumor transmission have been recognized (4). The first and most common type is transplantation of an organ that contains metastatic cells. Less common, but well described, is the transmission of an unrecognized or occult primary tumor in the transplanted organ. These tumors usually appear early after transplantation. Of 17 reported cases after renal transplantation, 10 patients were “fortunate” in requiring a transplant nephrectomy usually within 3 months of transplantation. The tumor was an unexpected finding by pathology. These patients did well. In contrast, the remaining seven patients presented with early and aggressive metastatic disease usually by 1 year after transplantation. Death followed in all cases within months of diagnosis of renal carcinoma.

We report the first known donor-derived pancreatic adenocarcinoma. At procurement nothing unusual was noted in the pancreas. We routinely inspect and palpate all organs, including the pancreas, looking for areas of nodularity. It will never be known whether the tumor was present but undetectable at procurement or whether the tumor developed de novo after transplantation. Despite the absence of any detectable pancreatic abnormality, given the donor’s age, he was at increasing risk for the development of pancreatic carcinoma. The prevalence of pancreatic carcinoma has risen steadily over the past 35 years in the United States with 80% of cases diagnosed in patients 60 to 80 years of age (5).

Donor derivation of the tumor is supported although not absolutely confirmed by HLA typing. Out of eight donor and recipient alleles possible, all eight donor alleles were found to be present in a tumor specimen whereas four and possibly five recipient alleles were detected. Because HLA typing methods depend upon saturated levels PCR amplification, detection of recipient DNA sequences could be attributable to PCR amplification artifacts.

A higher pancreatic graft failure rate and increased patient morbidity and mortality have been reported with older donor grafts (6). In general, procurement of the pancreas from cadaveric donors over the age of 50 years should be individualized based upon donor stability, anticipated cold ischemia time, and a careful examination of the organ at recovery. Only a small percentage of donors more than 50 to 60 years of age are being used as evidenced by two recent reports (6,7). Donor pancreases excluded for whole organ transplantation based only on donor age will likely now be considered for purposes of islet isolation. Will this increase the risk of tumor transmission? This question will mandate careful inspection of the pancreas by the procurement team and the islet team.

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Case Reports

Transplant Proc. . 2017 Dec;49(10):2352-2354. doi: 10.1016/j.transproceed.2017.10.007.

# Case Report: Primary De Novo Sarcoma In Transplant Pancreas Allograft

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* PMID: **29198676**
* DOI: [10.1016/j.transproceed.2017.10.007](https://doi.org/10.1016/j.transproceed.2017.10.007)

## Abstract

**Background:**The majority of malignancies after transplantation appear to be virally mediated and of recipient origin. Donor-derived neoplasms occur early, whereas recipient-origin tumors typically occur many years after transplantation. Sarcomas are a relatively rare form of cancer. The etiology of sarcomas remains largely unknown, although some are linked to viruses, familial cancer syndromes, or therapeutic radiation exposure. Primary sarcomas are extremely rare, accounting for <0.1% of all native pancreatic malignancies. The involvement of the allograft itself in the tumor is rare.

**Case report:**A 53-year-old white woman (body mass index, 20.1 kg/m2) with a history of type 1 diabetes, chronic kidney disease, coronary artery disease, dyslipidemia, and pancreas-alone transplantation in 2007 was admitted with small bowel obstruction secondary to a mass in the head of the pancreas allograft, for which a laparotomy with allograft pancreatectomy was required. Histopathologic exam revealed a stage III high-grade unclassified spindle cell sarcoma positive for polyomavirus. After surgery, the patient was managed with close monitoring for disease recurrence. Her most recent scan was negative for recurrence at postoperative day 489.

**Conclusions:**We report a previously unreported phenomenon of a soft tissue sarcoma arising in a pancreas allograft, likely of recipient origin and polyomavirus related. Standard treatment for sarcoma is wide excision of the tumor and close monitoring for recurrence. Systemic chemotherapy or radiotherapy is usually limited to advanced cases. Sarcomas may occur in a pancreas allograft. Allograft pancreatectomy and monitoring for recurrence is vital for a good outcome.