Skin cancer after pancreas transplantation

Joshua P. Spanogle, MD,[a] Yogish C. Kudva, MBBS,[b] Ross A. Dierkhising, MS,[c] Walter K. Kremers, PhD,[c] Randall K. Roenigk, MD,[a] Jerry D. Brewer, MD,[a] Mikel Prieto, MD,[d] and Clark C. Otley, MD[a]
Rochester, Minnesota

Background: Skin cancer in patients who have undergone pancreas transplantation (PT) has not been extensively characterized.

Objective: We sought to describe the incidence, tumor burden, and risk factors for skin cancer in PT recipients at Mayo Clinic from 1998 through 2006.

Methods: A retrospective study was performed by analyzing outcomes among a cohort of pancreas allograft recipients at Mayo Clinic between 1998 and 2006.

Results: Among 216 allogeneic PT recipients at 2, 5, and 10 years posttransplantation, the cumulative incidence of any skin cancer was 4.7%, 12.7%, and 19.6%; the cumulative incidence of squamous cell carcinoma was 2.8%, 10.3%, and 16.7%; and the cumulative incidence of basal cell carcinoma was 2.4%, 7.8%, and 17.4%, respectively. The cumulative incidence of a second squamous cell carcinoma developing was 56% at 2 years; the cumulative incidence of a second basal cell carcinoma developing was 36% at 2 years. Of the risk factors examined, only age and having a skin cancer before transplantation were predictive of skin cancer development.

Limitations: This was a retrospective study. Results from a large tertiary center may not be generalizable.

Conclusions: Nonmelanoma skin cancers commonly occur in recipients of PT, and those patients who have a history of nonmelanoma skin cancer have a very high likelihood of further skin cancer development. (J Am Acad Dermatol 2012;67:563-9.)

Key words: basal cell carcinoma; immunosuppression; kidney transplantation; pancreas transplantation; skin cancer; squamous cell carcinoma.

Skin cancers, particularly nonmelanoma skin cancers (NMSCs), are the most common neoplasms in patients with solid-organ transplantation (SOT) and are a major cause of morbidity and death in that population.[1-3] In both the general population and the SOT population, the risk of skin cancer is increased by host factors (older age, fair complexion, male sex, genetic predisposition) and environmental factors (ultraviolet [UV] radiation exposure, smoking).[4-6] However, for SOT recipients, immunosuppressive therapies are additional contributors to the development of skin cancers, and the

Abbreviations used:

ATG:	antithymocyte globulin
BCC:	basal cell carcinoma
HR:	hazard ratio
NMSC:	nonmelanoma skin cancer
PAK:	pancreas after kidney transplantation
PT:	pancreas transplantation
PTA:	pancreas transplantation alone
SCC:	squamous cell carcinoma
SOT:	solid-organ transplantation
SPK:	simultaneous pancreas-kidney transplantation
UV:	ultraviolet

From the Department of Dermatology,[a] Division of Endocrinology, Diabetes, Metabolism, and Nutrition,[b] Division of Biomedical Statistics and Informatics,[c] and Division of Transplantation Surgery,[d] Mayo Clinic.
Funding sources: None.
Conflicts of interest: None declared.
Accepted for publication November 8, 2011.

Reprint requests: Clark C. Otley, MD, Department of Dermatology, Mayo Clinic, 200 First St SW, Rochester, MN 55905. E-mail: otley.clark@mayo.edu.
Published online February 17, 2012.
0190-9622/$36.00

doi:10.1016/j.jaad.2011.11.939

degree of immunosuppression appears to correlate with tumor burden.[7-12] Exactly which immunosuppressive regimen carries the greatest risk for the development of skin cancer is controversial,[7,13,14] although evidence is emerging that sirolimus-based immunosuppression may be protective against the development of skin cancer.[15] Conflicting data exist for HLA antigen mismatching and increased skin cancer in the transplantation population.[16,17]

After SOT, the incidence of skin cancer varies by UV index and type of transplantation: for kidney recipients, the 20-year posttransplantation incidence is 40% to 70%, depending on geographic location[1,18]; for heart recipients, the 10-year incidence is 37.5%[19]; for liver recipients, the incidence was 22.5% during a 9.4-year study period[20,21]; and for lung recipients, the incidence was 1.6% during a 7-year study period.[22] No longitudinal studies have examined the incidence of skin cancer in small-bowel transplant recipients, and only recently has the incidence of skin cancer in recipients of simultaneous pancreas-kidney transplantation (SPK) been characterized and shown to be higher than in recipients of kidney alone.[23]

At Mayo Clinic (Rochester, Minnesota), 216 pancreas transplantations (PT) were performed in the years 1998 through 2006. Of these, 107 were pancreas after kidney transplantations (PAK), 42 were SPKs, and 67 were procedures for PT alone (PTA). We sought to delineate the incidence, tumor burden, and risk factors for basal cell carcinomas (BCCs), squamous cell carcinomas (SCCs), and other types of skin cancer in the 3 cohorts of PT recipients. Furthermore, we hypothesized that there are differences in tumor burden among the 3 cohorts.

CAPSULE SUMMARY

- Although much is known about skin cancer in solid-organ transplant recipients, there are scant data on the incidence and severity of skin cancer in pancreas allograft recipients.
- Skin cancer commonly occurs in pancreas allograft recipients, particularly those with history of skin cancer—in more than half of patients who develop skin cancer, further skin cancer develops within 2 years.
- Pancreas transplant recipients, particularly with history of skin cancer, should receive surveillance for skin cancer.

METHODS

The Mayo Clinic Institutional Review Board approved this study. Patients who received a PT from January 1998 through December 2006 were identified through Mayo Clinic's transplant center database. We identified a total of 216 patients who had given consent to research, and we retrospectively reviewed their medical charts, extracting information on patient characteristics, all skin cancers, risk factors, and death.

Details of immunosuppression have been previously reported.[24] Induction therapy consisted of rabbit antithymocyte globulin (ATG) (Thymoglobulin, Genzyme Transplant, Cambridge, MA) (n = 188); corticosteroids only (n = 6); or muromonab-CD3 (n = 22). SPK recipients received 1.5 mg/kg daily of ATG on days 0, 1, 2, 4, and 6 after transplantation. Recipients of PTA or PAK received 7 doses of ATG at 1.5 mg/kg daily starting on the day of transplantation. SPK recipients received tacrolimus with target trough levels of 10 to 12 ng/dL for the first month, 8 to 10 ng/dL for months 2 and 3, and 6 to 8 ng/dL thereafter. SPK recipients also received mycophenolate mofetil (CellCept, Hoffmann LaRoche Inc, Nutley, NJ) at a dosage of 750 mg orally twice daily. From 1998 to 2003, PAK and PTA recipients received tacrolimus with target trough levels of 15 to 18 ng/dL for the first month, 12 to 15 ng/dL for months 2 and 3, and 10 to 12 ng/dL thereafter. Starting January 1, 2004, PAK and PTA recipients received tacrolimus with lower trough levels (12-15 ng/dL for the first month, 10-12 ng/dL for months 2 and 3, and 8-10 ng/dL thereafter). PAK and PTA recipients also received mycophenolate mofetil (1000 mg orally twice daily). Patients received 500 mg of methylprednisolone intravenously and prednisone tapered to a daily maintenance dose of 20 mg at 1 month and, by 3 months, to 5 mg daily in the SPK group and to 10 mg daily in the PAK and the PTA groups.

Diagnoses of acute rejection of pancreas or kidney (or both) were made by ultrasonographically guided transcutaneous 18-gauge needle biopsy. Biopsies were performed either as a part of the surveillance protocol or for a cause. For PT, *cause* was an unexplained increase in pancreatic enzyme levels; for kidney transplantation, *cause* was an unexpected change in kidney function as indicated by an increase in the serum creatinine level. Antirejection therapy was initiated for rejection of the pancreas allograft that was grade III or greater; therapy consisted of corticosteroid boluses with either muromonab-CD3 or rabbit ATG. Therapy for