ELSEVIER

Kidney Transplantation and Diabetes: Posttransplantation Malignancy

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THE DEVELOPMENT of de novo malignancies in kidney transplant recipients represents a major problem. The reported prevalence is between 1% and 16% in Western countries and 1% to 3% in Asian countries.[1–3] In our Center, the overall prevalence of 7.13% was reported in 1997 by Arnaldo et al.[4] The most prevalent cancers are squamous cell carcinomas and basal cell carcinomas of the skin with an increasing cumulative incidence with longer survival of the patient.[5,6] Epidemiological data show several risk factors, including pigmentary characteristics, solar irradiation, viral warts, type and doses of long-term immunosuppressants, presence of an oncogenic virus (Epstein-Barr), with age, with time of dialysis, genetic factors and diabetes among other considerations. The posttransplantation lymphoproliferative diseases, lymphoma, and Kaposi's sarcoma are associated with the immunosuppressive therapy and oncogenic viruses.[7–9] Type 2 diabetes mellitus (DM2) has been related to the risk for colon, endometrial, pancreatic, and hepatic cancers as well as an increased risk of non-Hodgkin's lymphoma. Until now there are no reports of similar correlations with type 1 diabetes mellitus (DM1).[10–12] Posttransplantation diabetes mellitus is in some ways similar to DM2, including insulin resistance and the presence of an overweight or obesity situation, but there are no reports on the prevalence of malignancy in this group of patients. The aim of this study was to determine the prevalence of malignancy during follow-up of all patients with diabetes bearing a kidney transplant in our Center.

PATIENTS AND METHODS

Between 1992 and 2001, 1070 patients underwent transplantation with a kidney including, 55 (5.6%) diabetics: 33 with DM1, 22 with DM2, and 109 (10.4%) with posttransplantation diabetes (PTDM). We reviewed the files of these patients and performed statistical analyses using mean and SD values with the chi-square test.

RESULTS

We observed nine cases of malignancies (5.6%), namely six men and three women. Two patients had DM1 (6.1%), one patient had DM2 (4.5%), and six patients had PTDM (5.7%). The types of cancer, included single cases of multiple myeloma, non-Hodgkin's lymphoma, melanoma, skin basal cell cancer, breast cancer, laryngeal cancer, and lung small-cells cancer as well as two cases of skin squamous cell cancer (Table 1). The mean age at diagnosis was 49.2 years (range: 28 to 63 years), the mean duration of the kidney transplant was 58.7 months (range: 27 to 108 months), although in seven cases it occurred at more than 36 months. The mean creatininemia at diagnosis was 1.1 mg/dL (range: 0.8 to 2 mg/dL). The immunosuppressive therapy was a triple-regimen in 66.6% of patients using azathioprine or mycophenolate together with oral methylprednisolone and cyclosporine. In 33.3% of patients it was double-therapy with methylprednisolone and cyclosporine. The follow-up revealed four deaths. Among the five living patients, two have returned to dialysis and three have functioning grafts.

DISCUSSION

The causes of cancer are multifactorial. Several risk factors have been reported, including type and cumulative dose of immunosuppressive agents, age, sex, duration of dialysis, smoking, obesity, sunlight exposure, oncogenic virus (EBNA, cytomegalovirus), diabetes, world region and genetic factors. The prevalence in our patients was 5.6%, a rate similar to other reports. The risk increased after 36 months posttransplantation. Reduction in immunosuppression was performed in all patients; some returned to dialysis. This posttransplantation complication shows a high mortality rate and poses problems with immunosuppression.[7] Tumors diagnosed before 100 days after transplantation may be viewed as previously existent or possibly donor-transmitted malignancies, a particular problem with older cadaveric donors. We must be alert for the potential risk of donor-transmited malignancies, which are associated with a high incidence of disseminated disease and mortality in recipients.[13] The outcome of a malignancy depends on several factors: the type of cancer, the time of diagnosis and the delay to therapy. Early diagnosis and treatment are

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Table 1. Patients with Diabetes Who Underwent Kidney Transplantation and Malignancies

Cases	Sex	Age (y)	Type of Diabetes	Malignancy	Treatment	Outcome
1	F	48	PTDM	Lung small cell	Chemotherapy	Dead after 6 mo with functioning TX
2	F	50	PTDM	Multiple myeloma	Chemotherapy	Dead in 3 mo with functioning TX
3	M	61	PTDM	Non-Hodgkin's lymphoma	Radiotherapy	Dead after 48 mo with functioning TX
4	M	63	PTDM	Skin squamous cell	Surgery radiotherapy	Alive with nonfunctioning TX
5	M	59	PTDM	Skin squamous cell	Surgery	Alive with functioning TX
6	M	38	PTDM	Skin basal cell	Surgery	Alive with nonfunctioning TX
7	F	28	DM1	Breast	Surgery	Alive with functioning TX
8	M	43	DM1	Laryngeal	Surgery radiotherapy	Alive with functioning TX
9	M	53	DM2	Melanoma	Surgery	Dead after 11 mo with functioning TX

Abbreviations: F, female; M, male.

essential for a satisfactory outcome, so a regular screening examination is recommended for all patients bearing a kidney transplant.[14]

REFERENCES

1. Min SK, Huh S, Ahn MS, et al: Transplant Proc 32:1980, 2000
2. Park JH, Bok HJ, Kim BS, et al: Transplant Proc 32:1979, 2000
3. Min SK, Huh S, Ahn MS, et al: Transplant Proc 32:1980, 2000
4. Arnaldo et al: Presented at the Congresso Português de Transplantação, December 18–20, 1997
5. Naldi L, Fortina AB, Lovati S, et al: Transplantation 70:1479, 2000
6. Harden PN, Fryer AA, Reece S, et al: Transplant Proc 33:1302, 2001
7. Chisholm MA: Pharm D 2(2), 2001. 2001 Medscape Portals Inc. Available from: URL http:www.medscape.com/viewarticle/408586
8. Canfield CW, Hudnall SD, Collona JO, et al: Clin Transplant 6:1, 1992
9. Mattila PS, Aalto SM, Heikkila L, et al: Clin Transplant 15:337, 2001
10. Hjalgrim H, Frish M, Ekbom A, et al: J Intern Med 241:471, 1997
11. Howard D, Strikler MPH, Judith W-R, et al: Diabetes Technol Therap 3,2:263, 2001
12. Kath R, Schiel R, Muller UA, et al: J Cancer Res Clin Oncol 126:412, 2000
13. Robert J, Stratta MD: Medscape Transplant 2001. Available from: URL http:www.medscape.com/medscape/transplantation/journal/2001/v02.n05/mtl016.stra
14. Ishikawa N, Tanabe K, Tokumoto T, et al: Transplant Proc 32:1907, 2000