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Retrospective Analysis of Patients Who Develop Cancer After Renal Transplantation: A 12-Year Experience in a Single Center

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Research Article

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ABSTRACT

Objective: Kidney transplantation is the best treatment option for patients with end-stage renal disease. However, renal transplant recipients have been shown to have a higher risk of cancer than the general population. This has been attributed to malignancies associated with immunosuppression in these patients. In our study, we aimed to investigate the incidence of post-transplant malignancy, duration of development and risk factors in kidney transplant recipients.
Method: 1029 patients who underwent kidney transplantation in our organ transplant clinic between January 2006 and December 2018 were analyzed retrospectively through their demographic data, immunosuppressive protocols, post-transplant cancer types, and cancer onset files.
Results: Cancer developed in a total of 21 recipients (2%). The donor of 89.5% of the cases was alive. There was a history of smoking in 64.3% of the cases, and a family history of cancer in 45.5%. The most common type of cancer was skin cancer (n: 4). Basal cell Ca in 2 cases with skin cancer, Kaposi sarcoma in 1 case, and Merkel Cell Ca in 1 case (Table 2). Two of our patients with lung cancer had a history of smoking. The family history of our 2 cases with gastric cancer was positive. However, no statistically significant difference was found between family history and smoking and cancer incidence (p=0.576)
Conclusions: As transplant recipients continue to live longer with improved outcomes, cancer will increase as a cause of morbidity and mortality in this population. More research is needed to understand whether tumors arising in this population are affected by the patient's immunosuppression.

Keywords: İmmunsupressyon, transplantasyon, malignite.

Böbrek Nakli Sonrası Kanser Gelişen Olguların Retrospektif Analizi: Tek Merkez 12 Yıllık Deneyim

ÖZ

Amaç: Böbrek nakli son dönem böbrek hastaları için en iyi tedavi seçeneğidir. Bununla birlikte, renal transplant alıcılarının genel popülasyondan daha yüksek bir kanser riski olduğu gösterilmiştir. Bu durum bu hastalarda immunsupresyon ile ilişkili malignitelere bağlanmıştır. Bu çalışmamızda transplantasyon sonrası malignite insidansını, gelişim süresini ve böbrek nakli alıcılarındaki risk faktörlerini araştırmayı amaçladık.
Yöntem: Ocak 2006-Aralık 2018 tarihleri arasında organ nakli kliniğimizde böbrek nakli yapılan 1029 olgunun demografik verileri, İS protokolleri, transplantasyon sonrası görülen kanser türleri ve kanserin ortaya çıkma süresi, dosyaları üzerinden retrospektif olarak incelendi.
Bulgular: Toplam 21 alıcıda (%2) kanser gelişti. Olguların%89,5'inin vericisi canlıydı. Olguların %64,3'ünde sigara kullanım öyküsü, %45,5'inde ailede kanser öyküsü mevcuttu. En sık görülen kanser türü cilt kanseriydi (n: 4). Cilt kanserli 2 olgu bazal hücreli kanser, 1 olgu Kaposi Sarkomu, 1 olgu Merkel Hücreli kanser idi (Tablo 2). Akciğer kanseri görülen 2 olgumuzun sigara kullanım öyküsü mevcuttu. Mide kanseri görülen 2 olgumuzun aile öyküsü pozitifti. Ancak aile öyküsü ve sigara kullanımı ile kanser görülme arasında istatistiksel anlamlı fark saptanmadı (p=0,576).
Sonuç: Nakil alıcıları iyileşmiş sonuçlarla daha uzun yaşamaya devam ettikçe, kanser bu popülasyondaki morbidite ve mortalite nedeni olarak artacaktır. Bu popülasyonda ortaya çıkan tümörlerin hastanın İS'dan etkilenip etkilenmediğini anlamak için daha fazla araştırmaya ihtiyaç vardır.

Süreç

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Anahtar sözcükler: İmmunsupresyon, transplantasyon, malignite.

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Introduction

Renal transplantation is the best treatment option for end-stage renal disease [1]. In transplant patients, there is a measurable difference compared to other treatment groups in terms of long-term prognosis and quality of life [2]. On the other hand, it has been reported that kidney transplant recipients face a higher risk of cancer compared to the general population. This has been attributed to immunosuppression-related malignities in such patients [3]. Therefore, it is a significant cause of morbidity and mortality in kidney transplant recipients. Additionally, some medications administered after transplantation may naturally be carcinogenic, thereby promoting tumor growth [4]. Improvements in immunosuppressive (IS) protocols have increased graft life. However, the use of such IS medication requires close follow-up of recipients due to any malignities that may develop in the long term. For this purpose, this study aims to investigate the incidence and duration of development of post-transplant malignancy as well as the risk factors in kidney transplant recipients.

Material and Methods

The files of 1029 patients who underwent kidney transplantation in our organ transplant clinic between January 2006 and December 2018 were analyzed retrospectively in terms of their demographic data, immunosuppressive protocols, post-transplant cancer types and cancer onset periods.

All patients were given a training about their post-transplant lifestyle. Annual routine tests were conducted for all patients who were considered to be in the risky group (smokers and those with a family history). All female patients older than 40 were given annual mammography, gynecological examination and PAP smear tests. Prostate exams and tumor marker tests were annually performed on male patients older than 50. All patients had been administered antiviral drugs (valganciclovir or valacyclovir) for 3-6 months in the post-transplant period.

This study was conducted upon the approval of the Ethics Board of Clinical Studies, Istanbul Prof. Dr. Cemir Taşçıoğlu City Hospital (protocol no. 392, date: November 8, 2021).

For statistical analysis, SPSS 15.0 (SPSS Inc., Chicago, Illinois, USA) for Windows was used. The descriptive statistics of the assessment results were shown as mean, standard deviation, minimum and maximum values for numeric variables and as counts and percentages for categorical variables. The numeric variable differences between the two independent groups were compared by Wilcoxon test since normal distribution conditions were not met. The statistical alpha significance level was taken as $p<0.05$.

Results

A total of 21 recipients (2%) developed cancer. 1 patient dropped out of follow-up. 13 of the recipients who developed cancer were males. In 89.5% of the cases, the donor was alive. 64.3% of the cases had a history of smoking and 45.5% had a family history of cancer. The mean post-transplant diagnosis period was 54.2 (5.2-119.3) months, and the mean follow-up period was 61.6 (11.3-121.9) months (Table 1). 14 cases (70%) died during follow-up. The cause of death was malignancy in 10 cases, sepsis in 2 cases and cardiac-related reasons in 2 cases. Death-censored graft survival was 100%.

Table 1. Demographic data of the patients

Age (Years)	50.2± 10.6
Body mass index (kg/m^2)	26.8± 4.3
Period until diagnosis (months)	54.2± 37.1
Creatinine value at diagnosis (mg/dl)	1.5± 0.7
Final control creatinine value (mg/dl)	1.7±1
Follow-up period (months)	61.6± 36.5

Table 2. Post-transplantation cancer types

	Total	Males	Females
Skin cancer*	4	3	1
Stomach Cancer	3	2	1
Lymphoma	2	2	-
Lung	2	2	-
Cervical cancer*	2	-	2
Colon Cancer	1	1	-
Kidney Cancer	1	1	-
Laryngeal cancer*	1	1	-
LMS	1	-	1
Breast Cancer	1	-	1
Bladder Cancer	1	1	-
MM	1	-	1
Total	20	13	7

As the induction regimen, anti-thymocyte globulin (ATG) (cumulative dose 6-8 mg/kg) was used in 57.9% cases whereas Basiliximab was used in 42.1% cases. As the treatment protocol, Tacrolimus(Tac)+Mycophenolate Mofetil(MMF)+Steroid was administered to 94.7% cases whereas a Cyclosporin +MMF +Steroid protocol was administered to 5.3% cases. The Tac level was adjusted to 8-10 ng/ml.

The most common cancer type was skin cancer (n: 4) among whom 2 cases had basal cell carcinoma, 1 had Kaposi's sarcoma and 1 had Merkel cell carcinoma (Table 2). The two patients with lung cancer had a history of smoking. Family history was positive in 2 cases with gastric cancer. However, no statistically significant difference was found between family history and smoking and cancer incidence (p=0.576)

Discussion

It has been shown that the long-term use of pre-transplant IS and dialysis treatment increases the risk of post-transplant malignancy compared to the general population [5]. Currently, post-transplant graft failure and death risks have gradually decreased with an increase in survival. However, the increase in the survival period has caused an increase in the likelihood of developing a second primary disease [2,6]. It has been reported that post-renal transplant viral infections, IS medication, advanced age, family history and smoking may cause malignancy [6].

A single-center study conducted in South Korea reported a malignancy development risk of 4.3% in the 37-year post-transplant follow-up [2]. Kim et al. also reported the development rate of post-transplant malignancy at 4.2% in 757 patients [7]. In our study, 21 patients (2%) from both sexes developed cancer.

Ramsay et al. showed that at least 50% of renal transplantation patients may have a skin neoplasm within a decade after transplantation [8]. Many studies have determined that age, male sex and IS medication use period are associated with the development of skin neoplasms [9]. In line with the literature, our series also revealed skin cancer as the most common cancer type. The most common skin neoplasm was basal cell carcinoma. Three patients were men. We consider that an emphasis on sun protection in post-transplant trainings will be useful in terms of protection against skin cancer. The family history of 2 cases with gastric cancer was positive. No difference was found between family history and cancer incidence. However, it is known that family transmission may exist in cancer cases, hence we believe that careful screening and more frequent follow-up are necessary for patients with a family history. The risk of lung cancer development is reported as 0.78% in transplant patients [10]. In our series, 2 cases had lung cancer (10%) both of whom were smokers. We attribute such high rate to the smoking habit of our patients.

Our study has revealed a lower frequency of malignancy than other studies [8]. We believe that such lower rate results from the fact that the cumulative IS doses we had used were kept at a minimum. However, it is observed that the cancer rate in our series is higher than the general cancer rate. According to the International Agency for Research on Cancer, the incidence of malignancy in Turkey is 245.5 per 100,000 men and 157.5 per 100,000 women [11].

The results of the current studies prove that kidney recipients show higher mortality rates in comparison to other cancer patients [12]. As transplant recipients continue to live longer with improved outcomes, cancer will increase as a cause of morbidity and mortality in this population. More research is needed to understand whether tumors developing in this population are affected by patients' immunosuppression. In conclusion, further studies are required for determining the most suitable treatment regimen in cancer patients who had been previously subject to transplants.

Conclusion

Kidney recipients have higher rates of malignancy due to the IS therapy administered to them. Keeping cumulative doses at a minimum via lower-dose IS therapy reduces the malignancy rate.

Further research is required in order to understand whether mortality is affected by IS therapy.

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