Frequency of malignant skin tumors in renal transplant recipients in Imam Reza hospital of Mashhad, Iran

Masoud Maleki, MD [1]
Masih Naghibi, MD [2]
Sara Sabouri-Rad, MD [1]
Akram Sardar, MD [1]

1. *Cutaneous Leishmaniasis Research Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
2. *Department of Nephrology, Imam Reza hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*

Corresponding Author:
Sara Sabouri-Rad, MD
Cutaneous Leishmaniasis Research Center, Emam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
Email: dr.sabori@yahoo.com

Conflict of interest: none to declare

Received: 18 November 2013
Accepted: 26 February 2014

Background: The higher frequency of malignant skin tumors is of great significance in renal transplant recipients (RTRs) who should receive immunosuppressive therapy for a long time. This study was designed to determine the frequency of malignant skin tumors in RTRs in Imam Reza Hospital, Mashhad, Iran, in 2001-2002.

Method: This descriptive study was performed on 322 recipients who were examined by a dermatologist for malignant skin tumors in the renal transplant unit. A questionnaire containing a detailed history of age, sex, and site of the lesion, time of transplantation, occupation, and time of cancer development was completed for patients with a biopsy proven skin cancer.

Result: Nine patients (2.8%) had malignant skin tumors. Five patients (55.55%) had Kaposi sarcoma (KS) and 4 patients (44.44%) had non melanoma skin cancer (NMSC). The mean age of the patients was 44.4 ±11.4 years. Eight patients (88.88%) were male. The mean time to development of Kaposi sarcoma and NMSC development was 9.1 months and 5.75 years, respectively. Three patients (60%) with Kaposi sarcoma had lesions on lower extremities and all the NMSCs were located in the head and neck region. Outdoor occupations were seen in at least 50% of NMSCs.

Conclusion: This study again showed the importance of regular dermatologic examination for early diagnosis of skin malignancies, particularly, in high risk groups including renal transplant recipients.

Keywords: basal cell carcinoma, Kaposi sarcoma, malignant skin tumors, renal transplant recipients, squamous cell carcinoma

Iran J Dermatol 2014; 17: 18-21

INTRODUCTION

Immunosuppressive therapy following renal transplantation produces a great inhibitory effect on the immune defense mechanism that might lead to premalignant and malignant tumor formation, most frequently skin cancers [1]. The incidence of cutaneous malignancies among RTRs varies from 8% at 1 year to 44% at 15 years [2,3]. The pathogenesis of skin cancer is multifactorial involving decreased immunity, direct carcinogenic effects of immunosuppressive medications, HPV infection, and UV light exposure. NMSC, primarily squamous cell carcinoma (SCC), is the most frequent skin malignancy as its incidence is 40-250 times more than the normal population. Basal cell carcinoma is also five to ten times more in RTRs [4]. The incidence of iatrogenic KS has been increasing among RTRs receiving traditional immunosuppressive agents such as azathioprine and corticosteroids as well as in individuals receiving cyclosporine therapy. The estimated incidence of post-transplant KS in western countries is less than 1% although it is nearly 4% in the Near East [5]. A survey of

the literature shows that the relative frequency of malignancy after renal transplantation varies widely between different geographical regions [6]. We designed this study to evaluate the frequency of malignant skin tumors in RTRs living in the east of Iran, Mashhad.

PATIENTS AND METHODS

This descriptive study was done on 322 RTRs who were examined by a dermatologist for malignant skin tumors in the renal transplant unit of Imam Reza Hospital, Mashhad, Iran. Patients with suspicious lesions were referred to the dermatology department for a skin biopsy. RTRs with a biopsy proven skin cancer then completed a questionnaire containing a detailed history of their age, sex, occupation, site of the lesion, and time to cancer development. All the RTRs were receiving the same immunosuppressive regimen including cyclosporine, azathioprine, and prednisolone. Chi square and analysis of variance were used for qualitative and quantitative variables, respectively.

RESULTS

A total of 322 consecutive RTRs were examined. Nine patients (2.8%) had malignant skin lesions. Five cases (55.55%) had Kaposi sarcoma, 3 (33.33%) had squamous cell carcinoma, and one (11.11%) had basal cell carcinoma. The mean age of patients was 44.4±11.4 years. The majority of the patients (44.44%) were in the range of 40-49 years. According to Chi-square test, there was no correlation between the type of the tumor and age. Eight patients (88.88%) were male and there was only one female patient suffering from KS. There was also no correlation between the type of the tumor and gender. The shortest mean time to cancer development belonged to KS which was 9.1 months. This figure was 9 years for SCC and 5 years for the only case of BCC. There was a statistically significant correlation between the type of cancer and the mean time to cancer development according to one way variance (p=0.0002). The time to cancer development was shorter for KS in comparison with NMSC. There was no statistically difference between SCC and BCC in this regard.

Outdoor occupations were seen in at least 50% of the patients with non melanoma skin cancers. All the lesions of NMSC were located on the head and neck region. Three patients (60%) with KS had their lesions located on the lower extremities, one patient (11.1%) had the tumor on the upper extremity, and one case (11.1%) had it in his head and neck area. Two KS patient (22.2%) KS had visceral involvement, too. There was no correlation between the site and type of skin cancer. Table 1 presents some detailed data about the patients.

DISCUSSION

Skin cancer is the most common post-transplant malignancy [7]. Because of geographic and ethnic variations and also limited data from developing countries, we evaluated 322 RTRs who were referred to the renal transplant unit of Imam Reza Hospital, Mashhad, during 2001 in order to find the frequency of malignant skin tumors. Nine patients (2.8%) had skin cancer. In another study in 2004 in Mashhad, the incidence of malignancy was 2% and Kaposi sarcoma was the most frequent neoplasm [8].

In our study, KS was the most frequent skin cancer and was detected in 5 patients (55.55% of the patients, 1.55% of RTRs). This tumor develops

Table 1. Data of nine RTRs with malignant skin tumors

	Type of skin cancer	Site of skin cancer	Time to cancer development	Age at the time of diagnosis	Gender
1	KS	Lower extremity, visceral	5 m	45 y	male
2	KS	Lower extremity, palms	2.5 m	57 y	Male
3	KS	Lower extremity, visceral	11 m	42 y	Male
4	KS	Hands	16 m	42 y	Female
5	KS	Right ear	11 m	19 y	Male
6	BCC	Cheek	5 y	58 y	Male
7	SCC	Lower lip	6 y	52 y	Male
8	SCC	Left temporal	8 y	38 y	Male
9	SCC	Scalp	4 y	48 y	Male

M: month Y: year

in 0.4% of western RTRs but has a much higher rate in developing countries [9-12]. The Middle East has been reported as a highly prevalent region for post-transplant KS and reports from Saudi Arabia, Egypt, and Turkey confirm it [13,14]. It accounts for 3.4% of malignancies found in RTRs which is a hundred time higher than the percentage observed in the general population [15,16]. It peaks during the first year after transplantation [17-19]. In this study, 80% of all cases of KS were diagnosed in the first year after renal transplantation. The mean age of KS patients was 40.6 years at the time of receiving renal transplantation. This finding was similar to a study by Penn that reported KS in younger individuals [20]. Previous studies have reported a male preponderance in the incidence of post-transplant KS [21,22]. Similarly, male patients constituted 80% of the KS population in our study.

Transplant recipients are at greatly increased risk of developing skin cancer, particularly squamous cell carcinoma [23,24]. They are at a significant risk as the survival period is now prolonged [23]. In a study by Bordea performed in the south of England, 61% of RTRs developed skin cancer with SCC being the most frequent [24]. The mean age of RTRs with SCC was 46 years while it was 51.2 years in the study by Bordea which is approximately 20 years younger than the normal population. The mean time to first cancer development was 8 years while in our study, this duration was 72 ±19.2 months for SCC and 60 months for BCC. Reversal of the expected ratio of BCC compared with SCC is an important issue in post-transplant skin cancer; the incidence of BCC may be increased by 10 folds and the incidence of SCC is increased by 65 to 250 folds when compared to the normal population. SCC is at least four times more common than BCC in post-transplant patients [1,23]. In our study, 3 patients (33.3%) had SCC and one (11.1%) had BCC. We did not find any multiple premalignant and malignant lesions in our patients but it was found in 25% of RTRs in studies by Bordea and Rubel [24,25].

The risk of tumor is multifactorial and depends on the skin type, cumulative sun exposure history, degree of immunosuppresion, and age at transplantation [4,23]. Genetic factors may also play a part [26]. The risks of SCC and BCC have been found to be strongly associated with the time spent living in a hot climate [27]. All the patients in our study had skin type III or more. All the NMSC were located in the head and neck region and outdoor occupations were seen in at least 50% of the patients with non melanoma skin cancer which emphasized the importance of sun exposure in skin cancer development. Some studies have reported that NMSCs occur more frequently in men with a history of renal transplantation [28]. Merkel cell tumor, appendageal skin cancers, and lymphoma of both B and T cell lineages have also been reported [29-31]. None of our patients had these tumors.

The low frequency of skin malignancy in this research does not seem to be related to the regular use of the sunscreen and hat by our patients but might be due to the shorter follow-up period. Since the course of NMSC in transplant recipients may be highly aggressive and invasive, as it may develop in a very short time and exhibit a stronger tendency to metastasize, and also because of the higher incidence of these malignancies in this population, our study again showed that clinicians should be aware of the importance of careful dermatological monitoring of RTRs for early diagnosis and treatment of malignant skin tumors. It is important to remind RTRs of the harmfulness of the sunlight and the methods of sun protection.

REFERENCES

1. Euvard S, Kanitakis J, Claudy A. Skin cancers after organ transplantation. N Engl J Med 2003; 348: 1681-5.
2. Brown JH, Hutchison T, Kelly AM, McGeown MG. Dermatologic lesions in a transplant population. Transplantation 1988; 46: 530-32.
3. Hoxtell EO, Mandell JS, Murray SS, et al. Incidence of skin carcinomas after renal transplantation. Arch Dermatol 1977; 113:436-8.
4. Berg O, Otley CC. Skin cancer in organ transplant recipients: epidemiology, pathogenesis, and Management. J Am Acad Dermatol 2002; 47:1-17.
5. Weiss SW, Goldblum JR. Enzinger and Weiss`s soft tissue tumors.4th edn.St.louis: Mosby 2001.
6. Morath C, Mueller M, Goldschmidt H, et al. Malignancy in renal transplantation. J Am Soc Nephrol 2004; 15:1582-8.
7. Euvard S, Kanitakis J, Cochat P, Claudy A. Skin cancers following pediatric organ transplantation. Dermatol Surg 2004; 30: 616-21.
8. Nazemian F, Naghibi M. Skin cancer after renal transplantation. Mashad J Med Sci 2004; 47; 224-30.
9. Ghaninejad H, Ehsani A H, Ghiasi M, et al. Benign and malignant skin lesions in renal transplant recipients. Indian J Dermatol 2009; 54:247-50.

10. Moosa MR. Racial and ethnic variations in incidence and pattern of malignancies after kidney transplantation. Medicine 2005; 84: 12-22.
11. Stratta P, Morellini V, Musetti C, et al. Malignancy after kidney transplantation: results of 400 patients from a single center. Clin Transplant 2008; 22:424–7.
12. Einollahi B, Lessan-Pezeshki M, Nourbala MH, et al. Kaposi's sarcoma following living donor kidney transplantation: review of 7,939 recipients. Int Urol Nephrol 2009; 41:679–85.
13. El-Agroudy AE, El-Baz MA, Ismail AM, et al. Clinical features and course of Kaposi's sarcoma in Egyptian kidney transplant recipients. Am J Transplant 2003; 3:1595-9.
14. Moosa MR, Walele AA, Daar AS. Renal transplantation in developing countries. In: Kidney transplantation: principles and practice, 5th edn. Philadelphia, WB Saunders, 2001:659-92.
15. Duman S, Toz H, Aşçi G, et al. Successful treatment of post-transplant Kaposi's sarcoma by reduction of immunosuppression. Nephrol Dial Transplant 2002; 17:892-6.
16. Pedotti P, Cardillo M, Rossini G, et al. Incidence of cancer after kidney transplant: results from the North Italy transplant program. Transplantation 2003; 76: 1448-51.
17. Montagnino G, Lorca E, Tarantino A, et al. Cancer incidence in 854 kidney transplant recipients from a single institution: comparison with normal population and with patients under dialytic treatment. Clin Transplant 1996; 10: 461-9.
18. Mbulaiteye SM, Engels EA. Kaposi's sarcoma risk among transplant recipients in the United States (1993-2003). Int J Cancer 2006; 119: 2685-91.
19. Serraino D, Piselli P, Angeletti C, et al. Risk of Kaposi's sarcoma and of other cancers in Italian renal transplant patients. Br J Cancer 2005; 92: 572-5.
20. Serraino D, Angeletti C, Carrieri MP, et al. Kaposi's sarcoma in transplant and HIV infected patients: an epidemiologic study in Italy and France. Transplantation 2005;80: 1699-704.
21. Penn I. Kaposi's sarcoma in organ transplant recipients: report of 20 cases. Transplantation 1979; 27:8-11.
22. Shepherd FA, Maher E, Cardella C, et al. Treatment of Kaposi's sarcoma after solid organ transplantation. J Clin Oncol 1997; 15:2371-7.
23. Cox NH, Coulson IH. Systemic disease and the skin. In: Rook's textbook of dermatology. Burns T, Breathnach S, Cox N, Griffiths C, eighth edition, 2010. Wiley-Blackwell, Oxford, UK. doi: 10.1002/9781444317633.ch62
24. Bordea C, Wojnarowska F, Millard PR. Skin cancers in renal transplant recipients occurs more frequently than previously recognized in a temperate climate. Transplantation 2004;77:574–9.
25. Rubel JR, Milford EL, Abdi R. Cutaneous neoplasms in renal transplant recipients. Eur J Dermatol 2002; 12: 532-5.
26. Laing ME, Kay E, Conlon P, Murphy GM. Genetic factors associated with skin cancer in renal transplant patients. Photoderm Photoimmunol Photomed 2007;23: 62-7.
27. Ramsay HM, Fryer AA, Hawley CM, et al. Factors associated with non-melanoma skin cancer following renal transplantation in Queensland, Australia. J Am Acad Dermatol 2003; 49: 397-406.
28. Naldi L, Fortina AB, Lovati S, et al. Risk of nonmelanoma skin cancer in Italian organ transplant recipients. A registry-based study. Transplantation 2000; 70: 1479-84.
29. Penn I, First MR. Merkel`s cell carcinoma in organ recipients: report of 41 cases. Transplantation 1999; 68: 1717-21.
30. Harwood CA, McGregor JM, Swale VJ, et al. High frequency and diversity of cutaneous appendageal tumors in organ transplant recipients. J Am Acad Dermatol 2003;48:401-8.
31. Ravat FE, Spittle MF, Russell-Jones R. Primary cutaneous T-cell lymphoma occurring after organ transplantation. J Am Acad Dermatol 2006;54:668-75.