Skin Diseases in Kidney Transplant Recipients

Abbas Zamanian, Hossein Mahjub, Azame Mehralian

Introduction: The aim of this study was to evaluate the frequency of skin diseases in kidney transplant recipients.

Materials and Methods: This cross-sectional study was performed on 233 kidney transplant recipients in Ekbatan Hospital of Hamedan in 2004. The patients were examined by a dermatologist and diagnosis was made on the basis of clinical observations. Biopsies and scraping of the lesions were taken whenever necessary.

Results: Of the patients, 226 (97%) suffered from one or more skin lesions. The most common lesions were drug related, including hypertrichosis, gingival hyperplasia, acne, and cushingoid feature which were detected in 86.7% of the patients. Also, infectious and premalignant or malignant lesions (actinic keratosis, squamous cell carcinoma, and basal cell carcinoma) were seen in 48.9% and 14.2% of the patients. The mean duration of immunosuppressive therapy was significantly higher in patients with infectious skin diseases ($P < .001$).

Conclusion: Skin lesions are a significant problem in kidney transplant recipients. A careful monitoring of these patients is recommended in order to detect these lesions in early stages and treat them.

Keywords: kidney transplantation, skin diseases, skin neoplasms, infections, immunosuppressive therapy

Urol J (Tehran). 2006;4:230-3.
www.uj.unrc.ir

INTRODUCTION

Intensive immunosuppressive therapy is generally warranted to prevent the rejection of a kidney allograft and provide a long-term graft survival. Immunosuppressive therapy, as presently available, generally suppresses all immune responses including those to bacteria, fungi, and even tumors. The frequency of internal organs malignancies common in the general population is not increased in transplanted patients; however, a variety of uncommon cancers are more frequent.[1,2] Kidney transplant recipients are at the risk of a broad spectrum of skin diseases. The most important lesions are skin and lip cancers, carcinoma in situ of the cervix, and non-Hodgkin lymphomas.[3] Also, actinic keratosis, squamous cell carcinoma (SCC), basal cell carcinoma (BCC), and malignant melanoma have been reported to be more common in these patients.[4-10] Immunosuppressive therapy may predispose these patients to various skin infections caused by herpes simplex, herpes zoster, pityriasis versicolor, fungi, etc.[11] Drug-related lesions including hypretrichosis, gingival hyperplasia, acne, cushingoid features, and striae frequently occur as a result of the immunosuppressive administration. Additionally, there are miscellaneous skin disorders that may be detected in kidney allograft recipients. Kidney transplantation has been performed in Iran since years ago, but skin diseases have not been assessed adequately in the transplantation recipients. This

Department of Dermatology, Sina Hospital, Hamedan University of Medical Sciences, Hamedan, Iran

Corresponding Author:
Abbas Zamanian, MD
Department of Dermatology
Sina Hospital
Hamedan, Iran
PO Box: 379
Tel: +98 918 111 1704
E-mail: zamanian@umsha.ac.ir

Received September 2005
Accepted September 2006

study was designed to evaluate the spectrum of the dermatological diseases in kidney transplant recipients.

MATERIALS AND METHODS

In 2004, this cross-sectional study was performed on a total of 233 patients who had undergone kidney transplantation at Ekbatan Hospital, in Hamedan. They were visited by a nephrologist and a dermatologist during their monthly follow-ups. A thorough physical examination for skin lesions was done (except for genitalia). Skin biopsies and scrapings were taken whenever necessary. Diagnosis of the skin diseases was made on the clinical basis and pathological studies. Statistical analysis was performed by chi-square test and *t* test to compare dichotomous and continuous variables, respectively. A *P* value less than .05 was considered significant.

RESULTS

Of 233 patients, 118 (50.6%) were men and 115 (49.4%) were women. The mean age of them was 38.6 years (range, 13 to 65 years; 95% confidence interval [CI] = 36.9 to 40.3) at transplantation. Mean time of immunosuppressive therapy after the transplantation (follow-up) was 43.7 months (range, 1 to 145 months; 95% CI = 39.0 to 48.5). Immunosuppressive regimen consisted of cyclosporine, prednisolone, and azathioprine in 148 (63.5%) patients; cyclosporine, prednisolone, and mycophenolate mofetil in 83 (35.6%); and cyclosporine and prednisolone in 2 (0.9%).

Skin lesions were observed in 226 (97%) patients. Drug-related, infectious, and premalignant/malignant lesions were seen in 202 (86.7%), 114 (48.9%), and 33 (14.2%) patients, respectively. No relation was found between the age and the skin lesions ($P = .84$). Frequency of skin diseases was not correlated with the immunosuppressive regimen ($P = .43$). Among drug-related skin lesions, hypertrichosis was the most common, followed by gingival hyperplasia, cushingoid features, acne, sebaceous hyperplasia, and striae (Table 1). These lesions did not increase with the duration of posttransplant follow-up period ($P = .18$). Viral wart was the most common infectious skin lesion in these patients, followed by pityriasis versicolor, herpes zoster, herpes simplex, folliculitis, candidiasis, varicella, tuberculosis of lymph nodes, and onychomycosis (Table 1). The mean duration of immunosuppressive therapy was significantly higher in patients with infectious skin diseases ($P < .001$). Solar keratosis was the most frequent among premalignant/malignant lesions which was seen in 20 patients (8.6%). Squamous cell carcinoma was diagnosed more frequently than BCC (Table 1). The risk of skin malignancy increased with the increasing of posttransplant duration ($P = .049$). Other skin lesions seen in these patients were pigmented nevi, eczema, seborrheic dermatitis, skin tags, and epidermal cyst (Table 1). The frequency of skin diseases based on the follow-up duration is shown in Table 2.

Table 1. Skin Lesions in Kidney Transplant Recipients

Skin lesions	Number (%)
Drug-related lesions	
Hypertrichosis	130 (55.8)
Gingival hyperplasia	114 (48.9)
Acne	68 (29.2)
Cushingoid features	63 (27.0)
Sebaceous hyperplasia	29 (12.5)
Striae	2 (0.9)
Total	202 (86.7)
Infectious lesions	
Warts	87 (37.3)
Pityriasis versicolor	58 (24.9)
Herpes zoster	27 (11.6)
Herpes simplex	17 (7.3)
Folliculitis	12 (5.2)
Mucosal candidiasis	11 (4.7)
Varicella	2 (0.9)
Lymphadenitis tuberculosis	1 (0.4)
Onychomycosis	1 (0.4)
Total	114 (48.9)
Premalignant/malignant lesions	
Actinic keratosis	20 (8.6)
Squamous cell carcinoma	7 (3.0)
Basal cell carcinoma	5 (2.2)
Kaposi's sarcoma	1 (0.4)
Total	33 (14.2)
Other lesions	
Eczema	29 (12.5)
Melanocytic nevi	31 (13.3)
Seborrheic dermatitis	15 (6.4)
Skin tags	8 (3.4)
Epidermal cysts	1 (0.4)
Total	226 (97.0)

DISCUSSION

Skin lesions are a significant problem in transplant patients. Rafi and colleagues performed a cross-

Table 2. Frequency of Skin Diseases in Relation to Follow-up Duration*

Follow-up	Number of Patients	Drug-related Lesions	Skin Neoplasms
< 1 year	47	45 (95.7)	1 (2.1)
1 to 5 years	124	119 (96.0)	4 (3.2)
> 5 years	62	62 (100.0)	8 (12.9)

*Values in parentheses are percents.

sectional study on 60 kidney transplant recipients in Saudi Arabia. They observed skin lesions in 90% of the patients including infectious lesions in nearly half of them.[12] Pityriasis versicolor was the most common skin infection (36%), followed by folliculitis (8%) and warts (6%). In a similar study in Puerto Rico, the frequency of skin diseases was reported to be 95% in transplant patients.[13] In the study performed by Bencini and associates on 105 patients, the frequency of skin diseases was 97% and premalignant/malignant skin lesions were seen in 12% of these patients with the preponderance of SCC.[14] Reports from Saudi Arabia, Italy, and India agree with our results.[12,15,16]

Skin lesions in kidney transplant recipients can be divided into 5 groups of drug related, infectious, premalignant, malignant, and miscellaneous.[13,15] Certain miscellaneous skin disorders are not related to neither the renal condition nor the immunosuppression. These include pigmented nevi, skin tags, ichthyosis, and seborrheic dermatitis.[13] Drug-related, infectious, and premalignant/malignant lesions were seen in 202 (86.7%), 114 (48.9%), and 33 (14.2%) patients of our study, respectively. These frequencies agree with the report from India.[16] Lugo-Janer and coworkers and Bencini and colleagues reported infectious lesions as the most common skin manifestation in transplant recipients.[13,14] We found that the risk of infectious lesions increased in proportion to the time elapsed since transplantation. Plain warts were detected in 37.3% of the cases and were considered as the most common infection in the present study, while the prevalence of warts has been reported to be 6.6%, 43%, and 48% in the previous studies.[12,17,18] These differences may be due to the different duration of follow-ups. Therefore, cutaneous lesions infected with human papillomavirus may develop later and are related to the follow-up duration. Pityriasis versicolor has been shown to be a common fungal infection in transplant patients and more common than the general population.[19] Pityriasis versicolor was reported in 24.9% of the patients in this study, 36% in Saudi Arabia, 13.3% in India, 27.4% in Italy, and 36.3% in Turkey.[12,16,19,20]

Hepburn and colleagues performed a study on 52 kidney transplant recipients in New Zealand and reported malignancies in 9 (17.3%) and actinic keratosis in 20 (38.46%) patients which had occurred in the exposed areas to sunlight. They showed that SCC was more frequent than BCC.[17] The frequency of skin cancers is higher in transplant patients and correlates with the posttransplant duration of follow-up and immunosuppressive therapy. In this study SCC was the most common skin malignancy. In a 23-year follow-up study on 793 transplant recipients in Spain, tumors occurred in at least 10% of these patients and included cancers in the skin (46%) and other parts (56%). This study showed that malignancy was an important cause of morbidity and mortality in transplant recipients.[21] In the study by Cohen and coworkers on 580 transplant patients, 59 out of 170 skin lesion biopsies showed malignancy on pathologic examination. Half of these lesions were SCC and they mostly occurred in sun-exposed areas.[22,23] The frequency of malignancies is influenced by age, sex (more frequent in men), duration of the follow-up, immunosuppression with cyclosporine A, color of patient's eyes (more frequent in those with light colors), pretransplant SCC or actinic keratosis, place of residency (tropical areas), smoking, and childhood sunburn.[24-26] Bunney and associates reported no difference between the dermatological effects of two immunosuppressive regimens with azathioprine and cyclosporine A in kidney transplant patients except for hypertrichosis.[27] In the present study, it was concluded that the type of immunosuppressive regimens had no influence on the prevalence of skin diseases in these patients.

CONCLUSION

Transplanted patients are at the risk of skin lesions including skin neoplasms, which is an important

cause of morbidity and mortality among these patients. Therefore, a careful and regular examination of kidney recipients by a dermatologist is mandatory. The physician's advices such as sun avoidance should be a part of the posttransplant care.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Penn I. Tumors of the immunocompromised patient. Annu Rev Med. 1988;39:63-73.
2. Penn I. Cancers complicating organ transplantation. N Engl J Med. 1990;323:1767-9.
3. Carpenter CB, Milford EL, Sayegh MH. Transplantation in the treatment of renal failure. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson AL, editors. Harrison's principles of internal medicine. 16th ed. New York: McGrow-Hill; 2005. p. 1668-74.
4. Berg D, Otley CC. Skin cancer in organ transplant recipients: Epidemiology, pathogenesis, and management. J Am Acad Dermatol. 2002;47:1-17.
5. Jensen P, Hansen S, Moller B, et al. Skin cancer in kidney and heart transplant recipients and different long-term immunosuppressive therapy regimens. J Am Acad Dermatol. 1999;40:177-86.
6. Boyle J, MacKie RM, Briggs JD, Junor BJ, Aitchison TC. Cancer, warts, and sunshine in renal transplant patients. A case-control study. Lancet. 1984;1:702-5.
7. McLelland J, Rees A, Williams G, Chu T. The incidence of immunosuppression-related skin disease in long-term transplant patients. Transplantation. 1988;46:871-4.
8. Gupta AK, Cardella CJ, Haberman HF. Cutaneous malignant neoplasms in patients with renal transplants. Arch Dermatol. 1986;122:1288-93.
9. Hintner H, Fritsch P. Skin neoplasia in the immunodeficient host. The clinical spectrum: Kaposi's sarcoma, lymphoma, skin cancer and melanoma. Curr Probl Dermatol. 1989;18:210-7.
10. Greene MH, Young TI, Clark WH Jr. Malignant melanoma in renal-transplant recipients. Lancet. 1981;1:1196-9.
11. Spencer ES, Andersen HK. Viral infections in renal allograft recipients treated with long-term immunosuppression. Br Med J. 1979;2:829-30.
12. Rafi A, Ghacha R, Sinha A, Issam A, Mohammad I. Spectrum of skin diseases in renal transplant recipients. Dial Transplant. 2001;30:282-5.
13. Lugo-Janer G, Sanchez JL, Santiago-Delpin E. Prevalence and clinical spectrum of skin diseases in kidney transplant recipients. J Am Acad Dermatol. 1991;24:410-4.
14. Bencini PL, Montagnino G, Sala F, De Vecchi A, Crosti C, Tarantino A. Cutaneous lesions in 67 cyclosporin-treated renal transplant recipients. Dermatologica. 1986;172:24-30.
15. Lesnoni La Parola I, Citterio F, Nanni G, Serino F, Borzi MT, Rotoli M. [Skin manifestations in 140 kidney transplants]. Recenti Prog Med. 1992;83:61-3. Italian.
16. Chugh KS, Sharma SC, Singh V, Sakhuja V, Jha V, Gupta KL. Spectrum of dermatological lesions in renal allograft recipients in a tropical environment. Dermatology. 1994;188:108-12.
17. Hepburn DJ, Divakar D, Bailey RR, Macdonald KJ. Cutaneous manifestations of renal transplantation in a New Zealand population. N Z Med J. 1994;107:497-9.
18. Rudlinger R, Smith IW, Bunney MH, Hunter JA. Human papillomavirus infections in a group of renal transplant recipients. Br J Dermatol. 1986;115:681-92.
19. Virgili A, Zampino MR, La Malfa V, Strumia R, Bedani PL. Prevalence of superficial dermatomycoses in 73 renal transplant recipients. Dermatology. 1999;199: 31-4.
20. Gulec AT, Demirbilek M, Seckin D, et al. Superficial fungal infections in 102 renal transplant recipients: a case-control study. J Am Acad Dermatol. 2003;49: 187-92.
21. Dreno B. Skin cancers after transplantation. Nephrol Dial Transplant. 2003;18:1052-8.
22. Cohen EB, Komorowski RA, Clowry LJ. Cutaneous complications in renal transplant recipients. Am J Clin Pathol. 1987;88:32-7.
23. Bordea C, Wojnarowska F, Millard PR, Doll H, Welsh K, Morris PJ. Skin cancers in renal-transplant recipients occur more frequently than previously recognized in a temperate climate. Transplantation. 2004;77:574-9.
24. Marcen R, Pascual J, Tato AM, et al. Influence of immunosuppression on the prevalence of cancer after kidney transplantation. Transplant Proc. 2003;35: 1714-6.
25. Lindelof B, Granath F, Dal H, Brandberg Y, Adami J, Ullen H. Sun habits in kidney transplant recipients with skin cancer: a case-control study of possible causative factors. Acta Derm Venereol. 2003;83:189-93.
26. Ramsay HM, Fryer AA, Hawley CM, Smith AG, Nicol DL, Harden PN. Factors associated with nonmelanoma skin cancer following renal transplantation in Queensland, Australia. J Am Acad Dermatol. 2003;49:397-406.
27. Bunney MH, Benton EC, Barr BB, Smith IW, Anderton JL, Hunter JA. The prevalence of skin disorders in renal allograft recipients receiving cyclosporin A compared with those receiving azathioprine. Nephrol Dial Transplant. 1990;5:379-82.