

Skin Diseases in Kidney Transplant Recipients

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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

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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 hypertrichosis, 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

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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,

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) |

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.

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.

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