Skin Lesions in Kidney Transplant Patients in Qatar

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SUMMARY

Cutaneous lesions can be a significant problem in kidney transplant recipients (KTR). With the purpose of determining the prevalence and clinical spectrum of skin disease in KTR in Hamad Medical Corporation, 50 KTR were examined for the presence of skin diseases. We classified the dermatological findings as follows: drug-induced, infections, neoplastic and miscellaneous.

Skin lesions are common complication in KTR. The incidence in this study was 94%. The commonest skin lesions were iatrogenic (drug-induced, 86%) followed by infection (52%), and miscellaneous manifestations (8%).

Kaposi's sarcoma (4%) is the most serious complication and it is the only malignant lesion detected in this study. While iatrogenic manifestations decreased with time after kidney transplantation, infectious lesions increased. The prevalence of skin lesions had no significant correlation with the immunosuppressive regimens used.

Introduction

With the advent of effective immunosuppression, kideny transplantation has become an established and successful mode of treating end-stage renal disease.[1] However, renal transplantation requires prolonged use of steroids and immunosuppressive drugs, which may influence the host's immune defence mechanisms and predispose to development of infections and other complications.[2]

Cutaneous lesions can be a significant problem, and various reports have demonstrated that a variety of skin diseases occur commonly in kidney transplant recipients.[3] The length of immunosuppressive therapy and the other risk factors such as old age, skin type, climate, and the residence in high ultraviolet (UV) radiation areas had some influence on the incidence of skin lesions in KTR.[4]

During the past few years, reviews about numerous series of KTR have been carried out[4-6] so that reasonably accurate data have emerged on the incidence of dermatological pathologies in this population.

According to the literature, 75-100% of KTR have some kind of cutaneous lesions manifested by infections, premalignant and malignant lesions, and side effect of the drugs. Moreover, new cutaneous manifestations are periodically reported so that an already complex dermatologic situation related to immunosuppression becomes even more complicated. In many cases the relation of

cutaneous involvement with immunodeficiency is easily explained, but at times it may only be hypothesized.[7]

The aim of this study was to determine the prevalence and the clinical spectrum of skin diseases in 50 kidney transplant recipients followed-up in the kidney transplant clinic at Hamad Medical Corporation in Doha, Qatar.

Patients and Methods

We carried out a dermatological study of 50 KTR (35 males and 15 females). These patients were examined by one dermatologist and were followed-up at our hospital from July to December 1993. The mean age was 40.9 ± 12.1 years (range 14 or 65 years), and the mean interval after transplantation was 39±33 months (range three to 154 months).

There were 22 Qatari patients, 16 non Qatari Arab patients, and 12 non Arab patients. Transplanted kidneys were obtained from foreigners (60%), relatives, (28%) and cadaver (12%).

Several regimens of immunosuppression were used after kidney transplant: 33 patients (66%) used cyclosporin, azathioprine and prednisolone; 13 patients (26%) used cyclosporin and prednisolone; two patients (4%) used azathioprine and prednisolone; one patient (2%) used cyclosporin and azathioprine, and one patient (2%) used cyclosporin alone.

Cyclosporin was given at a dose ranging from 5 to 10mg/kg/day. The dose of azathioprine ranged from 1 to 3mg/kg/day, and the dose of prednisolone ranged from 0.15 to 0.3mg/kg/day.

Thorough history was taken regarding the onset and duration of cutaneous lesions, other medical conditions and previous medication. A complete careful clinical examination of the skin was performed for each patient. Dermatological investigations included appropriate scrapings, cultures or histological examinations when indicated.

The patients were categorized into three groups according to the interval after transplantation; Group A: 15 patients (up to 12 months), Group B: 18 patients (12-60 months), and Group C: 17 patients (more than 60 months).

Results

On the basis of patients' histories, the majority of lesions developed after transplantation. However, it was difficult to determine with certainty the exact time of onset of many skin lesions. Therefore, all lesions present at the time of examination were included in the results.

Forty-seven of 50 KTR (94%) had some kind of cutaneous disease at the time of examination. Dermatological findings were classified as follows:

1. Infectious manifestations: pityriasis versicolor, onychomycosis, candidiasis, warts, and folliculitis.
2. Iatrogenic "drug-related" manifestations hypertrichosis, gingival hyperplasia, fat redistribution, acne, prupura, hyperpigmentation, striae, and xerosis.
3. Miscellaneous manifestations: acanthosis nigricans, urticaria, sebaceous hyperplasia, skin tags and alopecia areata.
4. Malignant lesions : Kaposi's sarcoma.

Forty-three patients (86%) had drug induced skin manifestations, 26 patients (52%) had an infection of the skin, four patients (8%) had miscellaneous lesions, and two patients (4%) had Kaposi's sarcoma (Table 1).

Table 1. Different skin lesions in 50 KTR

	Patients	
	No.	Percentage
Iatrogenic manifestations	43	86%
Infection of the skin	26	52%
Miscellaneous lesions	4	8%
Malignant "kaposi sarcoma"	2	4%

(1) Infectious Manifestations

The prevalence of cutaneous infections was higher in Group C (70.1%) than in Group B

(61.1%) or Group A (40%). In the 26 patients with infective lesions, 29 active infectious manifestations were present at the time of examination. Thirteen (26%) being of pityriasis versicolor, 8 (16%) of warts, 4 (8%) of onychomycosis, 3 (6%) of candidiasis and one (2%) of superficial folliculitis (Table 2). Two patients (one from Group B and the other form Group C) had more than one infectious manifestaiton.

Pityriasis versicolor was not significantly decreased in the prevalence with the duration of immunosuppression (26.7% in Group A, 27.8% in Group B and 23.5% in Group C). Warts were the second most common infectious complication. Their incidence was more frequent in patients who had been immunosuppressed for longer periods. Also, the prevalence and severity of onychomycosis increased with increasing post transplantation interval. Bacterial infections were few and included superficial folliclulitis in one patient (2%) only in Group C (Table 2).

Table 2. Incidence of skin infections in KTR

	Group A (n=15)	Group B (n=18)	Group C (n=17)	All patients (n=50)
Pityriasis versicolor	26.7%	27.8%	23.5%	26%
Warts	6.7%	16.7%	23.5%	16%
Onychomycosis	0	5.6%	17.6%	8%
Candidiasis	6.7%	11.1%	0	6%
Folliculitis	0	0	5.9%	2%
Total percentage	40%	61.15%	70.1%	52%

(2) Iatrogenic Manifestations

There were iatrogenic cutaneous manifestations in 43 patients (86%) at the time of examination. In Group A, 14 patients (93.3%) had two or more iatrogenic lesions. Also, 13 patients (72.2%) in Group B, and 8 patients (47.1%) in Group C had two or more iatrogenic manifestations.

The incidence of iatrogenic manifestations was 100% (15/15) in Group A, 77.7% (14/18) in Group B, and 82.4% (14/17) in Group C (Table 3).

Table 3. Prevalence of iatrogenic manifestations in KTR

	Group A (n=15)	Group B (n=18)	Group C (n=17)	All patients (n=50)
Hypertrichosis	73.3%	55.6%	47.1%	58%
Gingival hyperplasia	66.7%	16.7%	35.3%	38%
Fat redistribution	33.3%	27.8%	17.6%	26%
Acne	20%	27.8%	23.5%	24%
Hyperpigmentation	13.3%	16.7%	11.8%	14%
Purpuras	26.7%	5.6%	5.9%	12%
Striae	0	16.7%	17.6%	12%
Xerosis	6.7%	0	5.9%	4%
Total percentage	100%	77.7%	82.4%	86%

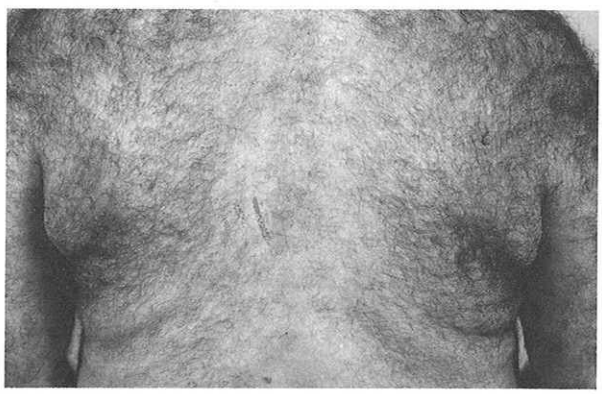

Fig. 1: Hypertrichosis in KTR.

Twenty-nine patients (58%) had hypertrichosis, usually widespread, on the face, ear, upper part of trunk, and upper extremities (Fig. 1). Hypertrichosis showed a declining prevalence as the transplantation interval increased. Gingival hyperplasia was observed in 19 patients (38%). It was so severe in one patient that it necessitated a surgical intervention (Fig. 2). Table 3 enumerates and reports the prevalence of the iatrogenic manifestations and the incidence of each in the three groups.

(3) Miscellaneous Manifestations

Four patients (8%) had six miscellaneous skin lesions. Two patients had more than one miscellaneous cutaneous manifestation. A female patient in Group B had acanthosis nigricans and sebaceous hyperplasia and a male patient in Group C had acanthosis nigricans and multiple skin tags (Table 4).

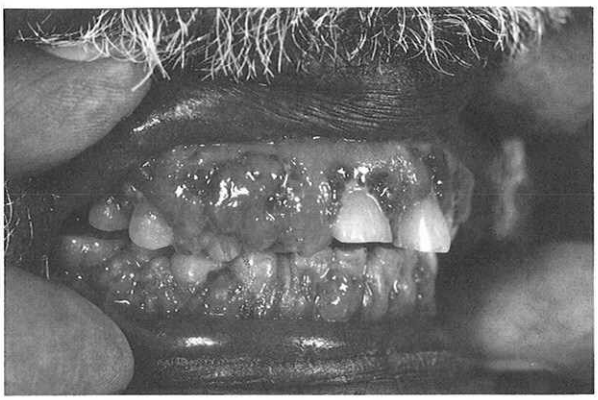

Fig. 2: Gingival hyperplasia in KTR.

Table 4. Prevalence of miscellaneous cutaneous manifestations in KTR

	Group A (n=15)	Group B (n=18)	Group C (n=17)	All patients (n=50)
Acanthosis nigrican	0	5.6%	5.9%	4%
Sebaceous hyperplasia	0	5.6%	0	2%
Skin tags	0	0	5.9%	2%
Alopecia areata	0	0	5.9%	2%
Urticaria	6.7	0	0	2%
Total percentage	6.7%	5.6%	11.8%	8%

(4) Malignant Lesions

Two patients (4%) had Kaposi's sarcoma, one patient belonged to Group A and the other to Group C (Fig. 3).

There was no significant difference in the prevalence of the skin lesions in correlation to the immunosuppressive regimens used (3 drugs therapy versus one or two drugs therapy).

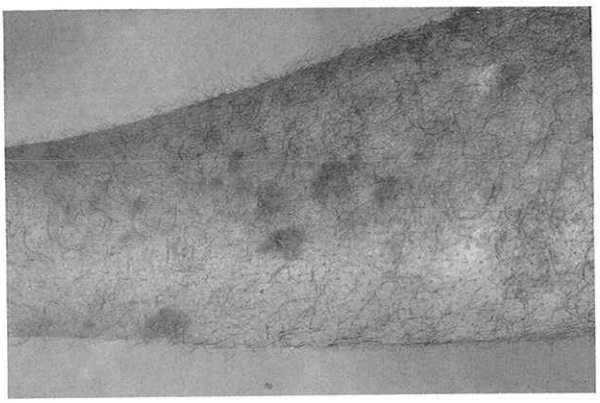

Fig. 3: Kaposi's sarcoma in KTR.

Discussion

The present study shows a high incidence of cutaneous manifestations (94%) in kidney transplant recipients, which confirms and extends the previous reports by other investigators.[2-8] The increased frequency of cutaneous manifestations in these patients rather than in general population in Qatar[9] is a function of the immunosuppressed state, the immunosuppressive drugs or both.[10] In our study, we did not attempt to establish causes, but rather the extent of the problem in a particular population.

We used prevalence as a measure of frequency because it varies directly with both incidence and duration. For chronic lesions, which constitute the majority in KTR, it is a useful tool. Conversely, for acute lesions such as herpes and varicella infection, the prevalence may be misleading.

We tried to compensate for the lack of a sufficiently long-term follow up in our series by dividing the patients into three major groups according to the length of the transplantation interval. This allowed indirect study of the outcome of dermatological lesions as a function of the various post-transplant periods.

Infectious cutaneous manifestations (52%) increased with time after transplantation (Group A 40%, Group B 61.1%, and Group C 70.1%). They were most frequently of pityriasis versicolor (26%) followed by warts (16%),

onychomycosis (8%), candidiasis (6%), and superficial folliculitis (2%).

The incidence and severity of warts increased with time. Pityriasis versicolor infections were almost equally distributed among the different periods showing a trend towards a slight reduction in the third group. Bacterial infections were extremely trivial and only superficial folliculitis was detected in one patient from the third group. These results are in agreement with those of other investigators.[2-8]

The commonest skin lesions in KTR were iatrogenic (drug-induced) manifestations, which were more frequent, early after transplantation, and showed a tendency to improve with time. Hypertrichosis (58%) was the highest incidence followed by gingival hyperplasia (38%). Both are well-known side effects of cyclosporin therapy and tend to resolve with time.[3,11]

There was no significant difference in incidence of steroid-dependent lesions, e.g. acne (24%), purpura (12%), and striae (12%) in the various groups. Whereas purpura decreased with time after transplantation, striae increased. Therefore, in addition to the high dose used in the first months, long term use of low oral steroid dose had an additional toxic effect on the induction of steroid dependent lesions.[2,3] Furthermore, cyclosporin reduces the clearance of prednisolone potentiating its effect.[11]

In this study, miscellaneous cutaneous conditions (8%) were not unusual or different from those expected in general population, and were similar to the results of other investigators.[3,8] Some cutaneous lesions like acanthosis nigricans may resolve spontaneously when sufficient kidney function is restored after successful transplantation.[7]

Although seborrheic dermatitis has recently been reported to associate defective immunity as seen in acquired Immunodeficiency syndrome and related conditions, none of our patients had seborrheic dermatitis. The reason why this disease is not frequently seen in KTR is probably because the immunosuppressive regimen used is not heavy enough to facilitate this disease.[4]

Kaposi's sarcoma (KS) showed a 400 to 500 fold increase in its incidence in KTR compared to patients of the same ethnic origin in a controlled population.[12] KS is mutifactorial and a combination of immunosuppression and/or immunologic stimulation, together with a hereditary predisposition to the disease, are responsible for the major increase in its incidence.[13]

The estimated incidence of KS in KTR in Saudi Arabia was 3.4%[14] and in Australia and New Zealand was 3%.[15] Our result (4%) supported these data. Although treatment with immunosuppressive drugs does predispose to skin cancer, there is no evidence from the clinical trials to suggest that any particular immunosuppressive drug is a dominant risk factor.[16]

In this study, there was no difference in the prevalence of dermatologic side-effects between KTR receiving different therapeutic regimens that was in agreement with the results of other investigators.[4,16,17] It is difficult to differentiate exactly between the effect of steroid and those of cyclosporin on the induction of several cutaneous manifestations.[11] Cyclosporin-treated patients seem to have skin problems similar to those seem with azathioprine and prednisolone.[4]

In conclusion, the high incidence of skin disease in KTR has a significant cause of morbidity in these patients. This stresses the need for close dermatologic surveillance of all transplanted patients and early diagnosis and treatment of any skin lesions.

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