Non-malignant skin changes in transplant patients

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Introduction

The skin pathology seen in graft recipients is unique because they are usually seen in patients who have a long history of renal disease, where the characteristic lesions seen in pre-terminal failure followed by dialysis-induced skin pathology had developed. The skin changes after renal transplantation partially replace, and partially are superimposed upon, the skin lesions characteristic for these preceding periods.

Skin changes after kidney transplantation

Successful renal transplantation causes a sudden alteration of skin function and subcutaneous pathology. Pre-existing skin pathology changes and a pattern of skin pathology, partly benign, partly malignant, appears. While immunosuppressive drugs cause skin pathology in patients exposed to the same immuno-suppressive drugs as the renal graft recipient, the skin pathology after renal transplantation is unique because of the major pre-existing skin pathology. Our clinical experience would suggest an increased sensitivity of the skin.

Influence on pre-existing skin changes

Decreased sebaceous and sweat gland production normalizes slowly after transplantation [1] and at the same time, the xeroderma which is characteristic of terminal renal failure improves. Ichthyosis is seen in no more than 8% of transplanted patients. In a few cases the increase in sebaceous gland production even leads to seborrhoea. Pruritis tends to disappear: only 2% of transplanted patients complain of pruritus, compared with 50–75% of dialysis patients. The skin also becomes less vulnerable. Skin vulnerability is increased in almost all dialysis patients, but this is seen only in 16% of renal graft recipients [2,3]. Similarly Raynaud’s syndrome tends to disappear. The Raynaud phenomenon can be provoked in no more than 2% of graft recipients, whilst 51% of patients on dialysis complain of Raynaud’s syndrome [4]. Even histological lesions of the vessels disappear. In the dialysis patient, complement and immune globulin deposits are seen in skin vessels, which disappear after successful renal transplantation [5,6]. In cross-sectional studies, Carpal tunnel syndrome is seen in 2% of transplanted patients, compared with 32% of dialysed patients [2], but this may be due to selection bias and true reversibility has not been.

Unfortunately, premature ageing of the skin, i.e. actinic elastosis, is not influenced by renal transplantation. This type of skin pathology, which presents as increased wrinkling and is histologically characterized by deposition of elastotic material, is apparently irreversible.

Dermatoses appearing after transplantation

New dermatoses can appear after transplantation, e.g. lichen ruber planus, urticarial and vesicular exanthemas, facial oedema, or rarely purpura. One of the causes is graft vs host disease, brought about by donor-specific lymphocytes in the graft. Further pathology, partly induced by the immunosuppressive agents, includes hypertrichosis, gingival hyperplasia, seborrhoecic eczema, perioral dermatitis, and porokeratoses [7].

Lichen ruber planus

Lichen ruber planus is a non-infectious inflammatory dermatosis, which may involve skin as well as mucous membranes. It is characterized by flat-topped, violaceous, shiny pruritic papules of the skin (Figure 1) and milky white papules in the mouth. Similar to psoriatic lesions, lichen ruber planus can be provoked by physical and chemical triggers. This is called Koebner’s phenomenon. This explains why the typical lichen ruber planus papules may be seen in excoriated skin. The papules have preferential locations and
follow typical pattern of distribution: flexor aspects of
the wrists, lumbar region, mucosal membranes, and
nails. Nail involvement may lead to destruction of the
nail fold and nail bed with a tendency to onychoschisis.
Destruction of the hair follicles can lead to scarring
alopecia.
In the background population, lichen ruber planus
usually appears between the third to sixth decade; it
may appear at any age in renal transplant recipients.

Seborrhoeic and perioral dermatitis

Seborrhoeic dermatitis is common in the graft recipi-
et. It is characterized by circumscribed red and
scaling skin in regions characterized by a high density
of active sebaceous glands: midfacial region, scalp, and
presternal region. It has been suggested that the fungus
Pityrosporon ovale plays a role in its pathogenesis.
Perioral dermatitis is characterized by discrete
erythematous micropapules that often become con-
fluent, forming inflammatory plaques, especially in the
perioral and periorbital skin.
Predisposing conditions are a seborrhoeic skin type
or gastrointestinal disorders. It is important to exclude
contact allergy to cosmetic preparations and to fluorin-
ated toothpaste. The disease may be markedly aggrav-
ated by topical corticosteroids. It has been suggested
that infection by Candida albicans or bacterial microbes
play an aetiological role and this may explain why
perioral dermatitis is frequent after transplantation.

Porokeratosis

Porokeratosis is a disorder characterized by abnormal
differentiation of the epidermis. The hallmark is the
hyperkeratotic skin lesion with the tendency to centri-
fugal growth. Usually one or more rapidly growing
skin lesions are seen which present initially as a hyper-
keratotic papule, which later exhibits the typical centri-
fugal growth pattern (Figure 2). The characteristic
histological lesion is a focal porokeratosis, the
so-called cornoid lamella. Within this area the cell
nuclei persist up to the horny layer, representing an
immature keratinization.

Graft vs host disease

Graft vs host disease is an immunological reaction
caued by a local interaction between donor lympho-
cytes and host target cells. The characteristic acute cuta-
neous changes range from maculopapular eruptions
to toxic epidermal necrolysis. Chronic changes com-
prise lichenoid eruptions and sclerodermatous changes.
More rarely, keratoconjunctivitis or mucosal involve-
ment with oesophageal and vaginal strictures, gastro-
intestinal pathology, liver involvement, or pulmonary
insufficiency are seen.

Infectious diseases

Apart from cardiovascular complications, infections
are the most frequent complication and cause of death
in the graft recipient. The immunosuppressed state
caued by immunosuppressive drugs, promotes viral
and bacterial infections and predisposes to several
types of malignancies.
The most commom viral infections of the skin
are herpes simplex, Verrucae vulgares (Figure 3) and
Condylomata acuminata.
Herpes simplex virus infection is characterized by
grouped vesicles arising on an erythematous base on
keratinized skin or mucous membranes. The most
frequent presentation is herpes simplex labialis (cold
sore). Immunosuppressed patients may experience
cutaneous or occasionally systemic dissemination of
the disease with involvement of the central nervous
system or inner organs. The herpes simplex virus is a
DNA virus of which two types can be differentiated:
lesions of herpes simplex type I occur on the oral
mucosa and lips, rarely on the face or trunk, whilst the
lesions of herpes simplex type II are seen in the genital
or genitogluteal region.
Verrucae vulgares and C. acuminata are caused by HPV viruses. Verrucae vulgares are typically the result of infection with human papilloma virus types 1, 2, 4, and 7 (Figure 3), Verrucae plantares by HPV 1, 2, and 4, C. acuminata by HPV 6 and 11 and rarely by HPV 16 and 18. Long-standing infection with HPV types 16 and 18 can lead to the development of carcinoma, particularly cervical carcinoma.

Verrucae vulgares typically develop in predilection sites such as hands, fingers, and occasionally face. Warts can be treated using operative curettage, laser surgery or a local immunostimulating drug, imiquimod, which constitutes effective treatment.

Apart from viral infections of the skin, bacterial, and fungal infections of the skin can also develop during immunosuppressive treatment.

Pyoderma, or superficial infection of the skin, bacterial, and fungal infections of the skin can also develop during immunosuppressive treatment.

Pyoderma, or superficial infection of the skin with staphylococci or streptococci is virtually never seen in healthy adults, whilst in children, impetigo contagiosa is not infrequent. In immunosuppressed graft recipients such bacterial skin infections are seen even in adults (Figure 4). Impetigo is characterized by small or large vesicles or bullae on an erythematous basis. The lesion spreads rapidly. After rupture the lesions present as shallow erosions and yellow crusts. Streptococcal infection causes small vesicular lesions. In contrast, staphylococcal infection causes larger bullous eruptions. These infections have a predilection for the skin around the mouth and nose, but scattered lesions can also occur in other locations. Apart from topical treatment, systemic antibiotic therapy is necessary.

The most common fungal infection is tinea pedis. Even before transplantation many patients suffer from dermatophytic infections of the feet. Usually the interdigital area is involved, presenting with itchy, painful fissures and well-demarcated erythema with minute papules at the margin as well as fine white scaling of the sole. This morphology is indicative of fungal infection. Nail involvement leads to yellow, brown discoloration of the nail plate. The nail becomes opaque, thickened, friable, and finally is lifted by the underlying hyperkeratotic debris in the nail bed (Figure 5). Immunosuppressive treatment causes massive deterioration of pre-existing fungal infection (Figure 6). Tinea pedis responds well to topical treatment. In contrast, treatment of tinea unguium, i.e. fungal infection of the nail, is often frustrating. Such treatment has to be administered for between 6 and 9 months.

Conclusion

In summary, on the one hand, in the recipient of a renal allograft, recruitment of uraemia-specific pre-existing skin problems is seen. This benefit is traded off
against the development of alternative skin lesions, caused by immunosuppression. These lesions include bacterial or viral infections on the one hand and malignancy on the other hand.

References