Skin and Oral Mucosal Changes in Patients Infected with Human Immunodeficiency Virus

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During a 6-month-period, 150 patients infected with Human Immunodeficiency Virus (HIV) were repeatedly examined by dermatologists and dentists for lesions of skin and oral mucosa. The most frequently encountered diseases were: oral hairy leukoplakia (21%), dermatophytosis (including tinea unguium/tinea pedis et inguinalis) (20%), seborrheic dermatitis (19%), viral infections (10%), oral candidiasis (7%), acne vulgaris (6%), and folliculitis (5%). A variety of other manifestations were seen, with frequencies less than 5%. Herpes zoster was seen in 3% of the patients, indicating a rate of 60/1 000 per annum. The presence of seborrheic dermatitis was statistically associated with low T-helper lymphocyte count. Patients with low T-helper lymphocyte count had on average twice as many mucocutaneous lesions as patients with a normal or moderately decreased count. Any one of the manifestations seborrheic dermatitis, oral candidiasis or oral hairy leukoplakia was associated with a greater average number of additional mucocutaneous changes than seen in patients exhibiting none of these three conditions. The high proportion of HIV-infected patients with cutaneous and oral lesions underlines the importance of referring the patients to dermatologists and dentists for examination. Prospective examinations of the study population remain to elucidate the prognostic significance of mucocutaneous manifestations of HIV-infected patients. *Key words: Skin diseases; Oral lesions; AIDS.*

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Since the recognition of the HIV infection as the cause of AIDS and ARC, increasing evidence has accumulated pointing to a high prevalence of certain skin and mucosal lesions in infected individuals (1–5).

Previous studies have indicated that oral lesions, especially oral candidiasis and hairy leukoplakia, are the result of immunosuppression caused by HIV (6–8). We have performed an interdisciplinary study, where dermatologists and dentists repeatedly examined a group of HIV-infected individuals, with the purpose of gaining a cross-sectional impression of the prevalence of skin lesions and lesions of the oral mucosa and to create a basis for future studies on the prognostic significance of the manifestations.

MATERIAL AND METHODS

From December 1986 to May 1987 inclusive, 150 HIV-infected patients were seen regularly at the dermatological out-patient clinic. All patients had antibodies against HIV by ELISA and Western blot techniques. 144 were men, and of these 132 were homo/bisexuals, 12 were heterosexuals, of whom 11 were intravenous drug abusers. There were 6 women; 5 of these were intravenous drug abusers, and one was from central Africa. Seven of the patients (4.7%) had or developed AIDS during the examination period.

All patients were examined repeatedly by senior dermatologists and a dentist (mean number of visits = 3). Dermatophyte and candida infections were diagnosed by fungal scrapings for microscopy

and culture. Hairy leukoplakia was diagnosed by the clinical appearance (typically vertical white bared-like lesions on the lateral aspects of the tongue and on the buccal mucosal membrane (7)) and lack of effect of extensive antifungal therapy.

Biopsy samples were taken from 13 patients with characteristic lesions and histophathology confirmed the diagnosis. The patients were grouped according to their T-helper lymphocyte count—those with values above the lower normal limit and those with a low or decreased number. In our laboratory the lower normal limit is 400×10^6/l. Patients with a T-helper value below 200×10^6/l were regarded as having severely impaired immune function. For statistical testing we used χ^2-test and Mann-Whitney's test. A p-value of <0.05 was considered statistically significant.

RESULTS AND COMMENTS

The findings are shown in Table I. A wide variety of lesions were disclosed, the most frequent being: oral hairy leukoplakia (21%), dermatophytosis (including tinea unguium/ tinea pedis et inguinalis) (20%), seborrheic dermatitis (19%), viral infections (10%), and oral candidiasis (7%).

The prevalence of seborrheic dermatitis was similar to that reported earlier (1, 4, 5, 9). The disease occurred significantly more often in patients with low T-helper cell counts ($p<0.05$) (Table I). Oral candidiasis occurred in 3/12 (25%) of patients with a low T-helper cell count, but as they were so few, there was no statistically significant difference.

Patients with a low T-helper cell count had on average twice as many mucocutaneous lesions as patients with normal or only moderately decreased T-helper cell counts (Table II). Seborrheic dermatitis, oral candidiasis and oral hairy leukoplakia were associated with a greater average number of additional mucocutaneous lesions than seen among patients exhibiting none of these conditions (Table III).

Table I. *Mucocutaneous findings in 150 HIV infected patients, grouped according to low or normal T-helper lymphocyte count*

Diagnosis	Total $N=150$	Leu 3a+≥ 200×10^6/l ($n=138$)	Leu 3a+< 200×10^6/l ($n=12$)
Oral hairy leukoplakia	32 (21%)	29 (21%)	3 (25%)
Seborrheic dermatitis	28 (19%)	21 (15%)	7 (58%)*
Tinea unguium	18 (12%)	14 (10%)	4 (33%)
Tinea pedis, inguinalis	12 (8%)	11 (8%)	1 (8%)
Oral candidiasis	11 (7%)	8 (6%)	3 (25%)
Acne vulgaris	9(6%)	8 (6%)	1 (8%)
Folliculitis (truncal)	7 (5%)	6 (4%)	1 (8%)
Psoriasis	5 (3%)	5 (4%)	–
Herpes zoster	5 (3%)	5 (4%)	–
Cheilitis angularis	4 (3%)	4 (3%)	–
Pityriasis versicolor	4 (3%)	4 (3%)	–
Herpes simplex	4 (3%)	4 (3%)	–
Condylomata accuminata	4 (3%)	4 (3%)	–
Aphthous ulceration	4 (3%)	3 (2%)	1 (8%)
Asteatotic eczema	3 (2%)	2 (2%)	1 (8%)
Dry skin	3 (2%)	2 (2%)	1 (8%)
Hair disease	2 (1%)	1 (1%)	1 (8%)
Molluscum contagiosum	2 (1%)	2 (2%)	–
Rashes (unknown)	1 (1%)	–	1 (8%)
Syphilis	1 (1%)	1 (1%)	–
Others	6 (4%)	6 (4%)	–

* $p<0.05$ (χ^2-test).

Table II. *Number of mucocutaneous changes in relation to the T-helper lymphocyte count*

	Average number of mucocutaneous conditions
Leu 3a+ $<200\times10^6$/l (n=12)	2.17*
Leu 3a+ $\geq200\times10^6$/l (n=138)	1.01

Leu 3a+ = T-helper lymphocyte count.
* $p<0.002$ (Mann-Whitney test).

Table III. *Number of mucocutaneous changes in patients with and without cutaneous manifestation*

	Average number of other mucocutaneous conditions
a) Seborrhoeic dermatitis (n=28)	1.26*
b) Oral candidiasis (n=11)	1.90**
c) Oral hairy leukoplakia (n=32)	1.10***
d) Non a, b, c (n=97)	0.57

* $p<0.01$, ** $p<0.002$, *** $p<0.02$ (Mann-Whitney test).

As oral lesions seem to be prevalent among HIV-infected patients, regular examinations of these patients by specially trained dentists should be performed. Oral hairy leukoplakia and/or oral candidiasis in otherwise healthy individuals should be considered as indicators of an underlying immune defect caused by HIV.

Many patients revealed skin and nail mycoses, in accordance with the findings of another recent study (9). The significance of this must await further investigation. Three of the 7 AIDS patients had tinea unguium of the white subungual type (10). Herpes zoster was recorded in 3% of the patients during a 6-month period, indicating a rate of 60/1 000 per annum, which is 21-fold greater than the rate in the 20–50-year-old general population of the USA (11, 12). Our results are supported by a retrospective study of 300 patients with AIDS-Kaposi's sarcoma that revealed a prevalence of 8% of herpes zoster (13).

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Eruptive Seborrheic Keratoses Associated with Erythrodermic Pityriasis Rubra Pilaris

Possible Role of Retinoid Therapy

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A 74-year-old female patient with an erythrodermic pityriasis rubra pilaris developed multiple seborrheic keratoses during the early stage of the skin disorder. There was no evidence of an underlying internal malignancy. Initially, the patient was treated with etretinate. The seborrheic keratoses all faded away during the next 3–4 months without any specific treatment. The possible role of retinoid treatment in the resolution of seborrheic keratoses is discussed. *Key words: Erythrodermia; Sign of Leser-Trélat; Retinoids.* (Received December 12, 1988.)

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The sudden appearance of multiple seborrheic keratoses or the sudden increase in number and size of pre-existing seborrheic keratoses can be a manifestation of an underlying malignancy. This relationship is known as the sign of Leser-Trélat (1).

If strict criteria for this sign are applied, it is evident that in very few reported cases does the course of the seborrheic keratoses reflect the course of the tumour. It has therefore been questioned whether the association represents a genuine paraneoplastic sign (2). Statistical confirmation of the association is lacking, since only instances with a concurrent tumour are reported. Little is known about the frequency of seborrheic keratoses changing or growing without evidence of an underlying malignancy. Seborrheic keratoses or acanthomas resembling seborrheic keratoses may arise during the course of an erythrodermic condition (3, 4). The paucity of published descriptions of this association suggests that it is either very rare or else ignored by clinicians. We report here a typical case.