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Epithelial Cell Proliferation of Oral Lichen Planus in Patients Treated with an Aromatic Retinoid

H. Schell, O. P. Hornstein, E. Deinlein
and G. Bauer

*Department of Dermatology, University of
Erlangen-Nürnberg, Federal Republic of Germany*

Received June 8, 1982

Abstract. In 4 patients with lichen planus mucosae (l.p.m.) biopsies were taken from the involved and uninvolved buccal sides before treatment and from the affected side after a 3-week systemic therapy with aromatic retinoid (Ro 10-9359; 50 mg/die). After *in vitro* labelling with ^3H -thymidine the epithelial cell proliferation was determined histo-autoradiographically. In atrophic lesions of l.p.m., increased ^3H -thymidine labelling indices were observed during retinoid therapy. After 3 weeks of treatment the augmented relative portion of labelled basal cells (quotient $\text{LI}_{\text{bas}}/\text{LI}_{\text{suprabas}}$) was found to be lowered, indicating a tendency of proliferating cells to regain normal distribu-

tion in the progenitor compartment of the mucosa epithelium.

Key words: Histo-autoradiography; Lichen planus mucosae; Aromatic retinoid

Abbreviations used

l.p.m.: lichen planus mucosae

LI_{total} : number of labelled cells/100 basal cells

LI_{bas} : number of labelled basal cells/100 basal cells

$\text{LI}_{\text{suprabas}}$: number of labelled suprabasal cells/100 basal cells

$\text{LI}_{\text{bas}}/\text{LI}_{\text{suprabas}}$: mean quotient of individual values of LI_{basal} and $\text{LI}_{\text{suprabasal}}$

With the development of oral retinoids and their successful application to many dermatoses showing aberrant proliferation (2, 3, 4, 13), a new era of dermatologic therapy began which also proved beneficial in erosive lichen planus mucosae (l.p.m.) (1, 7, 11). Due to the improved clinical course, a normalization of the disturbed proliferation and keratinization has been attributed to this therapy in l.p.m. To our knowledge, however, studies concerning epithelial cell proliferation in patients receiving this medication are lacking so far. Hence this study was aimed to determine, before and during therapy with an aromatic retinoid, some cell kinetic parameters in patients with l.p.m.

MATERIAL AND METHODS

Punch biopsies from the buccal mucosa of 4 patients (1 male, 3 female, age 37-64 years) with histologically confirmed l.p.m. were investigated. From each patient, following informed consent, three specimens (4 mm \varnothing , local anaesthesia: 1% solution of Scandicain® without vasoconstrictor) were taken. Before treatment, one biopsy from the involved and the uninvolved (contralateral) buccal mucosa were gathered simultaneously at morning time. After a 3-week therapy with the aromatic retinoid (Ro 10-9359/50 mg/die) another tissue sample was taken from the originally affected buccal mucosa.

Immediately after biopsy, the specimens were incubated in Minimum Essential Medium (MEM, Flow Lab.) containing ^3H -thymidine (spec. act. $5 \mu\text{Ci } ^3\text{H}$ -thymidine/ml) at 37°C and 215.8 kPa (=2.2 bar) O_2 -partial pressure for 60 minutes. Subsequently serial section histo-autoradiographs (5 μm cutting width, stripping film Kodak AR 10, exposure time 14 days at 4°C) were processed. Evaluation of the histo-autoradiographs was performed by copying each serial section using a microprojector. Further details have been published elsewhere (6, 8).

The following data were determined:

1. Number of labelled cells/100 basal cells (^3H -Index, LI_{total})
2. Number of labelled basal cells/100 basal cells (LI_{bas})

Table 1. Cell kinetic data in normal buccal mucosa and in oral mucosa with l.p.m. before and after treatment with aromatic retinoid

$a = LI_{total}$, $b = LI_{bas}$, $c = LI_{suprabas}$, $b/c = LI_{bas}/LI_{suprabas}$. Patients 1 and 2 histologically exhibited the hyperplastic, and patients 3 and 4, the atrophic type of l.p.m.

Pat. no.	Normal buccal mucosa				l.p.m. before medication				l.p.m. after 3 weeks of medication			
	a	b	c	b/c	a	b	c	b/c	a	b	c	b/c
1	28.2	6.0	22.2	0.27	18.1	4.7	13.4	0.35	35.6	13.7	21.9	0.63
2	14.6	4.0	10.6	0.38	40.1	16.1	24.0	0.67	25.9	14.9	11.0	1.35
3	22.1	11.2	10.9	1.03	21.1	9.9	11.2	0.88	28.4	11.7	16.7	0.7
4	21.6	4.7	17.4	0.24	14.7	10.7	4.0	2.60	33.1	15.9	17.2	0.92
M	21.6	6.3	15.3	0.48	23.5	10.4	13.2	1.13	30.8	14.1	16.7	0.9
SD	5.6	3.4	5.6	0.37	11.4	4.7	8.3	1.01	4.4	1.8	4.5	0.33

3. Number of labelled suprabasal cells/100 cells ($LI_{suprabas}$)
4. Quotient of 2 and 3 ($LI_{bas}/LI_{suprabas}$)
5. Labelled cells/1000 μm surface length
6. Basal cells/1000 μm surface length
7. Basal membrane length/1000 μm surface length

COMMENT

The 3H -thymidine labelling index in untreated l.p.m., though found to be elevated after a 3-week retinoid medication, was only slightly raised as compared with normal contralateral buccal mucosa. In a previous study (8) we found, as did other authors (14), when examining a larger number of patients suffering from l.p.m., that the LI_{total} was even more markedly raised. As in other benign oral leukoplakias, a shifting of proliferative activity from the suprabasal to the basal cell layer became evident (5, 6, 8).

Compared with normal mucosa, a higher rate of proliferating cells, proved by the elevated quotient $LI_{bas}/LI_{suprabas}$, was established in the basal cell layer of l.p.m. After 3 weeks of aromatic retinoid therapy, however, a decrease in this quotient was demonstrated. Assuming the pretherapeutic pattern of proliferation to be induced by an untimely differentiation and keratinization of the mucosal epithelium, the retinoid dose administered seems to renormalize the disturbed process of differentiation, as shown in other dermatoses with altered epidermal proliferation (12).

Since the strongly reduced LI of the epithelium increased during retinoid treatment, the data presented in this paper support therapeutic experience with atrophic l.p.m. which is known to be susceptible to oral retinoid treatment (7, 10). However, in acanthotic l.p.m., according to previous findings (8), an elevated LI was demonstrated before medication. While, in atrophic lesions, the lowered items of proliferation were found to be elevated after a 3-week treatment, in the acanthotic lesions the

RESULTS

As shown in Table 1, the means of the cell kinetic data examined in l.p.m. did not, due to the wide scattering range, differ essentially from those in normal mucosa. When comparing the individual values in l.p.m. before and after a 3-week-treatment with the aromatic retinoid, however, a rise of the DNA synthesizing activity was found in the basal as well as suprabasal layers of the epithelium.

Notwithstanding different initial values before oral retinoid therapy, the LI_{total} proved to be elevated after medication in both atrophic ($n=2$) and hyperplastic ($n=2$) l.p.m. lesions, with a rise of the LI_{total} that was particularly striking in atrophic lesions. The increased $LI_{suprabas}$ in the atrophic lesions was remarkable, too, whereas any similar drug-induced changes could hardly be observed in hyperplastic l.p.m. The quotient $LI_{bas}/LI_{suprabas}$ being raised before treatment showed a decrease in one of the atrophic lesions, in contrast to the other one as well as the hyperplastic lesions of l.p.m. (Table 1).

When relating the number of labelled cells to the epithelial surface, no distinct histo-autoradiographic differences could be discerned either before or after 3 weeks of treatment.

suprabasal LI values remained almost unchanged. This may indicate an incipient normalization of the proliferative activity of the epithelium in both atrophic and hyperplastic l.p.m.

Further insight into the subsequent development of the epithelial proliferation pattern during retinoid therapy could not be obtained as the patients, being satisfied with the success of retinoid therapy, refused additional mucosa biopsies. Thus the question remains unsolved as yet, whether and to what extent the dosage influences the degree as well as the velocity of the drug-induced epithelial restitution, as recently shown in epidermal lesions of l.p. (10). Moreover, the small number of biopsies so far available does not allow definite conclusions to be drawn with regard to the basic cellular mechanisms involved in the benefit of aromatic retinoid therapy in oral l.p.

ACKNOWLEDGEMENT

This study was supported by Deutsche Forschungsgemeinschaft (SFB 118/C1). Mrs G. Ritter is gratefully acknowledged for technical assistance.

We are indebted to Hoffmann-La Roche for providing test preparations of Ro 10-9359, out now as Tigason®.

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Assay of Comedolytic Activity in Acne Patients

Otto H. Mills, Jr. and Albert M. Kligman

*Department of Dermatology, University of Pennsylvania,
and the Simon Greenberg Foundation
Philadelphia, PA 19104, USA*

Received April 16, 1982

Abstract. Comedolytic activity was assessed in acne patients by determining the reduction in facial microcomedones using the cyanoacrylate follicular biopsy technique. Microcomedones were counted in five-cm squares after 8 to 12 weeks of treatment.

Only salicylic acid and tretinoin among seven conventional anti-acne medications were found to possess comedolytic activity. The latter was the more effective.

Key words: Comedolytic activity; Acne population; Microcomedone; Tretinoin; Salicylic acid

The initial event in the pathogenesis of acne is the formation of the comedo, an impaction of horny cells in sebaceous follicles. Agents which can prevent this event are effective in moderating the disease.

We have described models for assaying comedolytic drugs. The first utilized comedones in-