Epidermal Urocanic Acid in Discoid Lupus Erythematosus

Sir,

Ultraviolet radiation (UVR) induces isomerization of *trans*-urocanic acid (UCA), a natural component of human skin, into *cis*-UCA, which has been shown to suppress both delayed hypersensitivity and contact hypersensitivity (1).

An autoantigen-specific T-cell-mediated mechanism has been proposed in both chronic cutaneous lupus erythematosus, presenting mostly as discoid lupus erythematosus (DLE), and polymorphous light eruption (PLE) (2, 3). A subnormal epidermal UCA content might theoretically lead to disease exacerbation of T-cell-mediated disorders due to less *cis*-UCA-mediated suppression of cell-mediated autoimmune processes. To study this possibility, we examined the epidermal UCA contents of patients with DLE and compared the results with data obtained from PLE patients and control persons.

PATIENTS AND METHODS

Patients

DLE patients (7 males, 9 females, mean age 44 years, age range 17–71 years), PLE patients (3 males, 9 females, mean age 46 years, age range 29–64 years) and non-photosensitive healthy individuals (10 males, 14 females, mean age 45 years, age range 17–71 years) were included in the study. The diagnoses were based on clinical, histological (4) and serological findings. All DLE patients had been or were on antimalarial medication (either chloroquine 250 mg daily or hydroxychloroquine 300 mg daily). Eleven DLE patients were sampled while using antimalarial medication and 12 DLE patients while not using medication. Thus, 7 patients were sampled twice, with or without medication. The use of medication had lasted from 1 to 48 weeks and the abstinence for at least 5 weeks. In all PLE patients, the PLE rash had occurred during the preceding summer. None of the PLE patients was on antimalarial medication during or for at least 6 months before the study. Eight of 16 DLE patients presented with a history of PLE type skin lesions, a coincidence recently noted to be rather common in DLE (5).

Sampling and UCA analysis

In all patients and control persons, samples were collected from buttock skin. In the DLE patients, the back of the hand and in the PLE patients, healthy-looking extensor forearm skin, previously affected by PLE rash, was also examined. The back of the hand and the forearm were sampled in control patients in 19 and 12 cases, respectively. All 12 PLE patients, 5 DLE patients and 9 control persons were sampled only during the winter (from December to early March), 5 DLE patients and 15 control persons only during the sunny season (from late March to the end of June) and 6 DLE patients both during the winter and the sunny season.

The samples were taken using the chamber method, stored for a maximum period of 6 months at $-20^{\circ}C$ and subjected to high-performance liquid chromatography (HPLC) analysis of *cis*- and *trans*-UCA isomers, as outlined earlier (6). Mean values of the triplicate samples were calculated and used as data for compiling the figure in this report.

Statistical analysis

As the data were not normally distributed, the Mann–Whitney U test was used for comparison between groups. Statistical analysis was performed with Statistica® for Windows (Version 5.1, StatSoft, Inc, Tulsa, Okla, USA). Values of $p<0.05$ were considered statistically significant.

RESULTS

The median *cis*-UCA content, but not the total UCA content, in UVR-protected buttock skin, was significantly lower in non-medicated DLE patients than in control persons and in PLE patients (Fig. 1). The *cis*-UCA results of the DLE patients with a history of PLE did not differ from those without such history.

In DLE patients with antimalarial medication, numerically higher *cis*- and total UCA contents in buttock skin were found, compared with the patients without medication, but the differences did not reach statistical significance.

The *cis*- or total UCA contents of DLE patients in sun-exposed skin, i.e. the back of the hand during the sunny season, did not differ significantly from those of control persons. However, the median *cis*-UCA content, but not the median total UCA content, in the back of the hand was significantly higher during the sunny season than in the winter, both in DLE patients ($p=0.00007$) and control

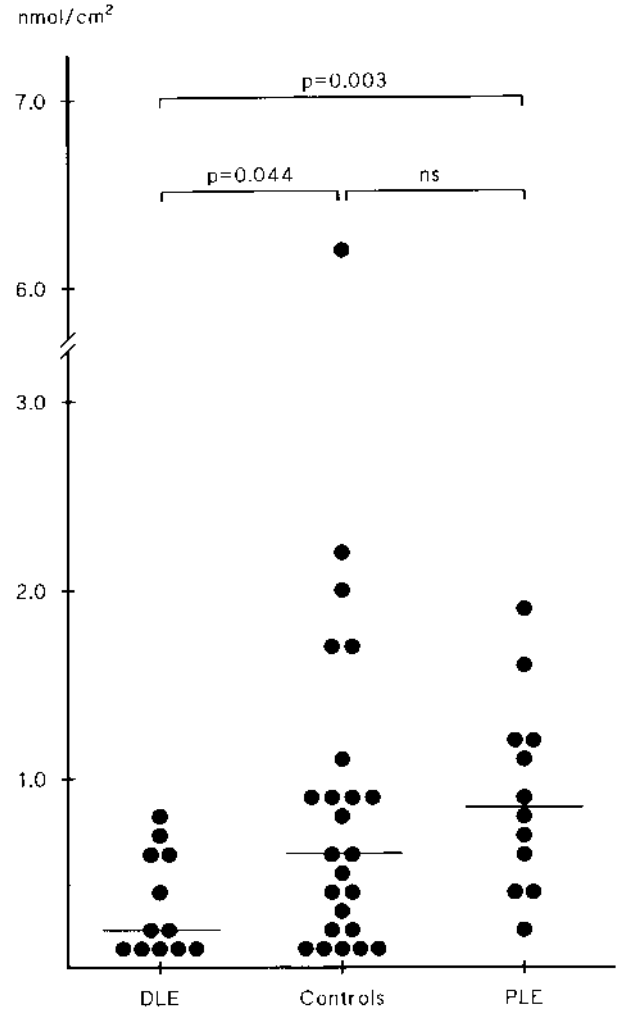

Fig. 1. Cis-UCA contents in buttock skin in non-medicated patients with discoid lupus erythematosus (DLE) and polymorphous light eruption (PLE) and in controls. Bars represent medians of *cis*-UCA in each group. ns = not statistically significant difference.

persons ($p = 0.033$). Eight of the 11 DLE patients sampled during the sunny season and 1 of 11 sampled during the winter were using antimalarial medication.

The forearm *cis*- and total UCA contents of the PLE patients did not differ significantly from those of control persons.

DISCUSSION

Cis-UCA has a suppressive effect on delayed hypersensitivity (1). Thus, the lowered epidermal *cis*-UCA content in UVR-protected buttock skin of DLE patients, demonstrated in our study, agrees with the proposal that DLE skin symptoms are caused by an augmented T-cell-mediated mechanism (2). Unexpectedly, contradictory results were found in PLE, which is also proposed to be mediated by a delayed hypersensitivity reaction (3).

We do not believe that sampling during different seasons skewed the results of non-protected buttock skin, since the *cis*- or total UCA values of control persons were unaffected by sun exposure of other skin sites (data not shown). In a recent Danish study, it was observed that the total UCA content in buttock skin was lower and the percentage of *cis*-UCA elevated during the summer compared with other seasons. Our differing result may be due to differing sampling period during the sunny season, i.e. before July in the present study vs. after July in the Danish study (7).

Unlike in UVR-protected buttock skin, there were no differences in *cis*-UCA contents between DLE patients and control persons in sun-exposed skin of the back of the hand. This may be due to the disease process itself. However, the possibility of a normalizing effect of antimalarial medication must also be considered, since the *cis*-UCA contents also tended to be higher in UVR-protected buttock skin of DLE patients on antimalarial medication than in non-medicated DLE patients.

ACKNOWLEDGEMENT

This study was supported by a grant from the Medical Research Fund of Tampere University Hospital, Tampere, Finland.

REFERENCES

1. Noonan FP, De Fabo EC. Immunosuppression by ultraviolet B radiation: initiation by urocanic acid. Immunol Today 1992; 13: 250–254.
2. Sontheimer RD. Photoimmunology of lupus erythematosus and dermatomyositis: a speculative review. Photochem Photobiol 1996; 63: 583–594.
3. Norris PG, Morris J, McGibbon DM, et al. Polymorphic light eruption: an immunopathological study of evolving lesions. Br J Dermatol 1989; 120: 173–183.
4. van Braag MCG, Boom BW, Vermeer BJ. Diagnosis and treatment of polymorphous light eruption. Int J Dermatol 1994; 33: 233–239.
5. Nyberg F, Hasan T, Puska P, Stephansson E, Häkkinen M, Ranki A, et al. Occurrence of polymorphous light eruption in lupus erythematosus. Br J Dermatol 1997; 136: 217–221.
6. Jansen CT, Lammintausta K, Pasanen P, Neuvonen K, Varjonen E, Kalimo K, et al. A non-invasive chamber sampling technique for HPLC analysis of human epidermal urocanic acid isomers. Acta Derm Venereol 1991; 71: 143–145.
7. de Fine Olivarius F, Wulf HC, Crosby J, Norval M. Seasonal variation in urocanic acid isomers in human skin. Photochem Photobiol 1997; 66: 119–123.

Accepted March 21, 1999.

Taina Hasan[1], Paavo Pasanen[2] and Christer T. Jansen[3]
[1]Department of Dermatology, University of Tampere and Tampere University Hospital, PO Box 2000, FIN-33521, Tampere, Finland (E-mail: thasan@tays.fi), [2]Department of Chemistry, University of Turku and [3]Department of Dermatology, Turku University Central Hospital, Turku, Finland.

Chloramphenicol Induced Acute Generalized Exanthematous Pustulosis Proved by Patch Test and Systemic Provocation

Sir,

Acute generalized exanthematous pustulosis (AGEP) is characterized by sudden onset of high fever, generalized scarlatiniform erythema covered by numerous non-follicular small superficial sterile pustules, blood leukocytosis with neutrophilia, and acute evolution (1–2). The main causative agent is drugs, but chloramphenicol has been rarely implicated (3).

Patch tests were performed in several cases of AGEP and results showing eczematous or pustular reaction were considered positive (2). Systemic provocation proved the cause in 1 case sensitive to isoniazid (4).

We here report a case of AGEP in which chloramphenicol was shown to be the cause by both patch test and oral provocation with a lowered dose.

CASE REPORT

A 36-year-old Korean woman had treated her rhinitis with acetaminophen and codeine for 2 days and with chloramphenicol for less than 1 day in June 1998. After ingestion of the former drugs 5 times and injection of the latter drug twice, pruritic, deeply erythematous and oedematous patches developed suddenly on almost her entire body, accompanied by mild fever (37.5°C). She also intermittently felt a burning sensation. The skin lesions became worse the next day, showing marked facial oedema and superimposed tiny superficial pustules. She had treated her rhinitis before, but had never had skin lesions. The laboratory findings were unremarkable, except for blood neutrophilia (8,500/μl) and glucosuria (more than 2g/dl), which normalized after 2 days. After administration of oral prednisolone, the skin lesions improved rapidly with disappearance of the facial oedema and fever the next day and of the pustules after a few days. Mild shallow desquamation followed. Patch tests were