

Skin changes in patients claiming to suffer from “screen dermatitis”: a two-case open-field provocation study

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Abstract: An open-field provocation, in front of an ordinary TV set, of 2 patients regarding themselves as suffering from skin problems due to work at video display terminals (VDTs) is presented. Using immunohistochemistry, in combination with a wide range of antisera directed towards cellular and neurochemical markers, we were able to show a high-to-very high number of somatostatin-immunoreactive dendritic cells as well as histamine-positive mast cells in skin biopsies from the anterior neck taken before the start of the provocation. At the end of the provocation the number of mast cells was unchanged; however, the somatostatin-positive cells had seemingly disappeared. The reason for this latter findings is discussed in terms of loss of immunoreactivity, increase of breakdown, etc. The high number of mast cells present may explain the clinical symptoms of itch, pain, edema and erythema. Naturally, in view of the present public debate, the observed results are highly provocative and, we believe, have to be taken seriously.

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Introduction

Reports of skin complaints in people exposed to video display terminals (VDTs) are becoming an increasing phenomenon in several countries (for refs., see 1). Very little is known about the cause of these health complaints. The symptoms may be grouped into objective ones, including erythema, papules and pustules, as well as subjective ones including sensations of heat, itch, pain, smarting, etc. (2). Clinical dermatologists have regarded the symptoms to be mostly of rosacea or rosacea-like dermatitis nature (cf. 2). A large scale epidemiological study has shown that the subjective facial skin symptoms were more common among VDT-exposed persons, but there were no significant difference between exposed and non-exposed groups in objective skin signs or skin disease (3). The early notion that employees with VDT work might have specific facial histological changes could not be confirmed by Berg et al. in their histopathological study (4). In the

present investigation, the aim was to study possible morphological as well as histochemical changes in the skin before and after an open-field provocation, in front of an ordinary TV set, of 2 patients believing themselves to suffer from skin problems due to work at VDTs, i.e. “screen dermatitis”.

Material and methods

Subjects

Two patients (females; 40 and 54 years of age) claiming to have suffered for several years from “screen dermatitis” were investigated in the study. The patients did not have any other on-going medication or any systemic or dermatological diseases, including acute infections. Routine and special (including peptide radioimmunoassay) laboratory blood tests were performed before and after provocation (see below). Regularly (each 15 min) during the provocation the blood pressure was also monitored.

Provocation situation

The patients arrived in the morning, one at a time, at the clinic (Department of Endocrinology), in an objectively and subjectively unaffected state. They were immediately subjected to the first pair of biopsies and blood tests. Directly following this, they were placed in front of an ordinary household television set (distance 40–50 cm) and the blood pressure analysis was commenced. Care was taken to ensure that the patients were not able to inspect their own mirror-images, thus, they were not in a situation of visual self-suggestion. An interviewer continuously examined the subjective and objective reactions during the provocation. The patients were told to interrupt the on-going provocation at any time, and, finally, when they could not stand further time in front of the TV screen. At this point, the second pair of biopsies and blood tests were taken. Finally, the patients were interviewed after an additional 24–48 hours.

Preparation of tissue

Double punch biopsies (3 mm; 1 cm apart) were taken under local anesthesia with lidocaine (0.5%) without epinephrine from the anterior neck skin (20 mm below angulus mandibulus) before the start of and after the cessation of the provocation (see above). One of the two biopsies was immersed for 2 h at 4°C in a solution of 14% saturated picric acid and 10% formalin. The other biopsy in each pair (to be incubated with the histamine anti-

serum; cf. Ref. 5) was immersed in 4% carbodiimide (1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide; Sigma Chem. Comp., USA) diluted in phosphate buffer (pH 7.4) for 2 h at 4°C. All the tissue was then rinsed for at least 24 h in 0.1 M Sørensen's buffer containing 10% sucrose, 0.01% NaN₃ and 0.02% Bacitracin, and 14 µm sections were cut using a cryostat (Microm, Heidelberg), thawed on to gelatine-coated slides and processed for indirect immunohistochemistry (see below).

Antibodies

Rabbit or mouse antibodies to substance P (SP; 1:400; Amersham), calcitonin gene-related peptide (CGRP; 1:400; Peninsula), neurokinin A (NKA; 1:100; E. Theodorsson-Norheim, Stockholm), galanin (GAL; 1:400; Peninsula), vasoactive intestinal polypeptide (VIP; 1:400; Peninsula), peptide histidine isoleucine amide (PHI; 1:3,200; J. Fahrenkrug, Copenhagen), neuropeptide tyrosine (NPY; 1:400; L. Terenius, Stockholm), enkephalin (ENK; 1:25; Kemila (Sera-Lab)), dynorphin (DYN; 1:400; L. Terenius, Stockholm), somatostatin (SOM; 1:800; R.P. Elde, Minneapolis), protein S-100 (S-100; 1:400; K. Haglid, Göteborg, and L. Olson, Stockholm), neuron-specific enolase (NSE; 1:800; UC), protein gene product 9.5 (PGP 9.5; 1:2,000; UC) and histamine (HIST; 1:2,000; Milab) were used. All antibodies were checked in parallel in positive controls from normal human skin, to avoid any false-negative interpretations.

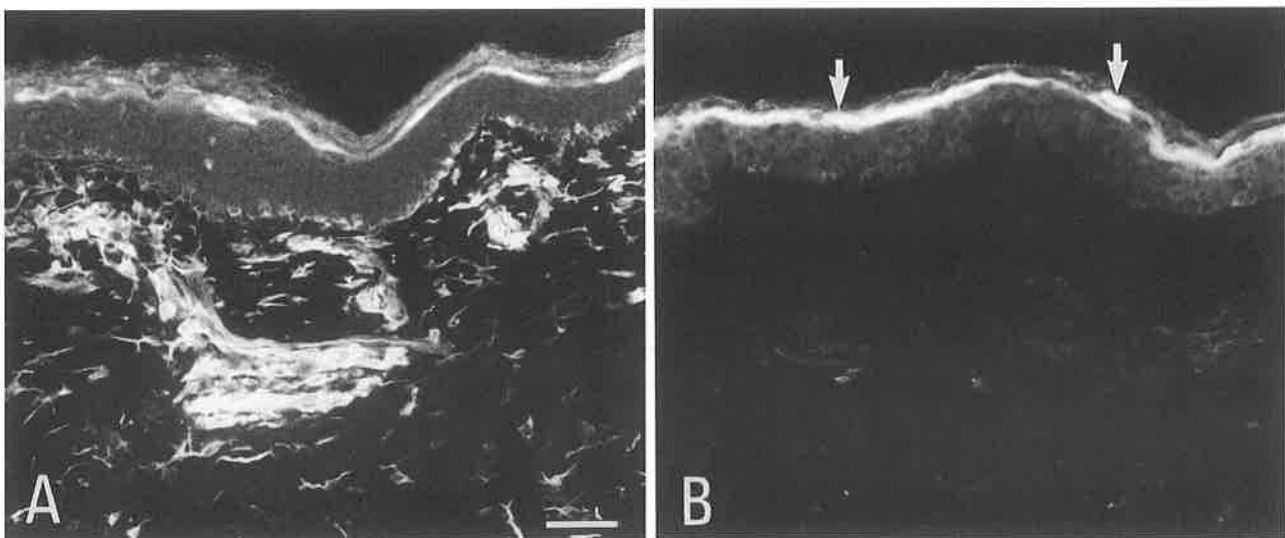


Figure 1A, B. Somatostatin immunohistochemistry. Photomicrographs taken before (A) and after (B) provocation (see text for further details) from patient A. In A, a high number of somatostatin-immunoreactive dendritic cells is seen in the epidermis and dermis. In B, all these cells are seemingly gone, i.e. most probably they have lost their capacity to react with the somatostatin antiserum used. Arrows in B point to unspecific background fluorescence. Bar in A indicates 50 µm.

Immunohistochemistry

The indirect immunofluorescence technique was used. The sections were kept in a humid atmosphere, incubated with the above-mentioned antibodies overnight at 4°C, rinsed in PBS, incubated for 30 min at 37°C in rhodamine (TRITC)-conjugated goat anti-rabbit or anti-mouse IgG (1:80 or 1:40; Boehringer Mannheim), rinsed and mounted. All antibodies were diluted in 0.3% Triton X-100. For observation and photography a Nikon Microphot-FXA or Optiphot fluorescence microscope was used. The material was blind-coded and evaluated by 2 independent observers.

Results

Clinical assessment

Objectively, patient A responded with skin redness already after 10-15 min. This redness was further aggravated until the patient stopped the provocation (after 60 min). The skin was at that moment swollen and gave an impression of general edema. The patient was also sweating somewhat. Furthermore, the patient reported sensations of tingling in the body parts facing the TV screen. At the end of the provocation, the patient complained of dizziness and gave incomplete and inadequate answers to the interviewer's questions. Her speech was also slurred. Patient A was, after a couple of weeks, provoked once more, at which she withstood the situation for 30 min, showing the same objective and subjective symptoms as above.

Patient B, on the other hand, did not reveal any objective or subjective signs at all, apart from some temporal faint reddening of the skin of the neck which only lasted for approx. 10 min. She stopped

the provocation after 3.5 hours without any feelings of illness. The patient was disappointed at not having reacted at all.

Both patients reported profound feelings of subjective illness 24 hours (and onwards) after the provocation. At inspection of patient A 24 h after the end of the provocation, a large number of papules and pustules was seen in the skin of the face.

Immunohistochemistry

In the biopsies taken before provocation a remarkably high number of SOM-immunoreactive dendritic cells was found in the dermis, preferentially around the blood vessels and hair follicles as well as in the basal layer of the epidermis (Figs. 1A and 2A). Furthermore, a profound amount of histamine-positive mast cells could be detected in the carbodiimide-fixed tissue before the start of the provocation (Fig. 3A). The cells were granulated and observed preferentially around the blood vessels.

After provocation, no somatostatin-immunoreactive cells at all could be revealed in either patient A or patient B using the presently employed immunohistochemical method (Figs. 1B and 2B). This observation was the basis for the repetition of the provocation for patient A, i.e. to further establish this finding. Regarding the histamine cells, no changes in morphology, number or fluorescence intensity were observed after the provocation (Fig. 3B), as compared to the pre-provocation state.

There were no difference in the SP, CGRP, NKA, GAL, VIP, PHI, NPY, ENK, DYN, S-100, NSE or PGP 9.5 immunoreactivities before and after the provocation, and the patterns generally looked normal. Furthermore, no changes could be

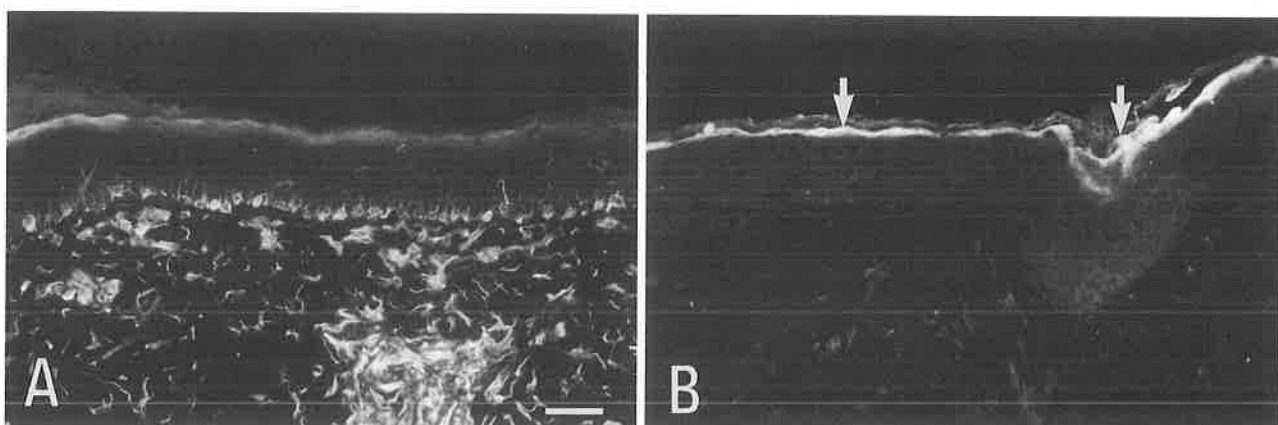


Figure 2A, B. Somatostatin immunohistochemistry. Photomicrographs taken before (A) and after (B) provocation (see text for further details) from patient B. In A, a very high number of somatostatin-immunoreactive dendritic cells is seen in the epidermis and dermis. In B, all these cells are seemingly gone, i.e. most probably they have lost their capacity to react with the somatostatin antiserum used. Arrows in B point to unspecific background fluorescence. Bar in A indicates 50 μ m.

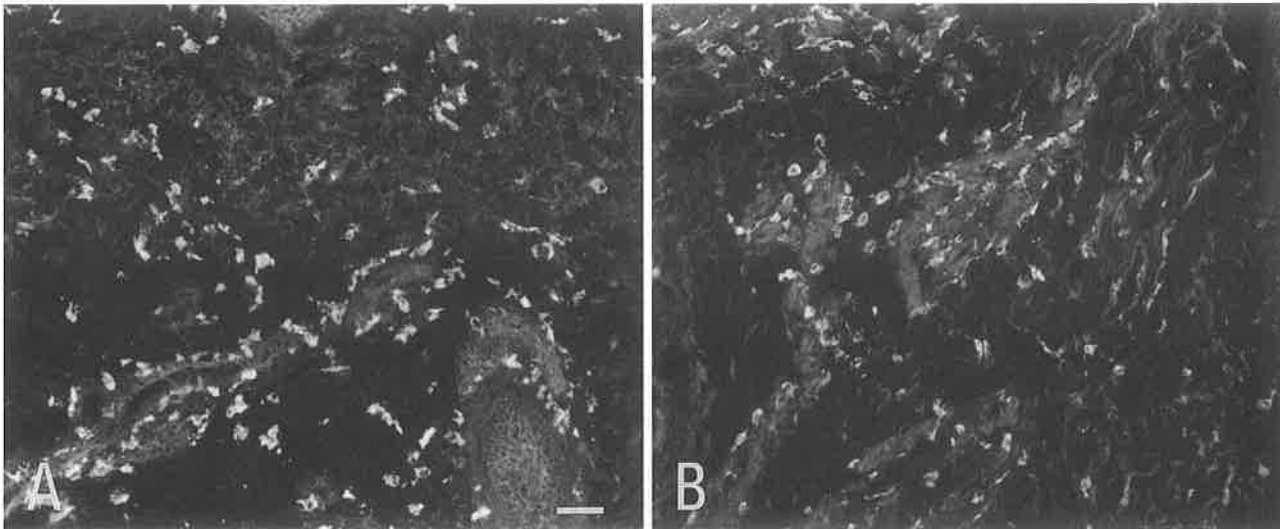


Figure 3A, B. Histamine immunohistochemistry (from patient B). Photomicrographs taken before (A) and after (B) provocation (see text for further details). A high-to-very high number of mast cells is observed both in A and B. There is no clear-cut difference between the two occasions. Bar in A indicates 50 μ m.

seen in the routine blood tests or in the blood pressure monitoring, however, both patients had significant changes in the blood level of pancreatic polypeptide.

Discussion

In the following, our results will be discussed. However, it has to be pointed out that we cannot, based upon the present results, draw any conclusions about the cause of the changes observed. Whether this is due to electric or magnetic fields, a surrounding airborne chemical, stress factors, or something else, still remains an open question. As the basis for an explanation of our present observations, it is tempting to speculate about an effect of the electric and/or magnetic fields emitted by the TV set, but such a correlation can only be obtained in true blind or double-blind experiments.

In the present study, a high number of somatostatin-positive dendritic cells was encountered in the dermis and epidermis of 2 patients claiming to suffer from "screen dermatitis". Compared to our ongoing studies regarding such somatostatin-immunoreactive dendritic cells in normal healthy controls (6; Johansson et al., in preparation), we were immediately struck by the very dense population of these cells, both within the basal layer of the epidermis and around the dermal blood vessels and within the connective tissue.

After the open-field provocation, to our great surprise, the somatostatin-immunoreactive cells were no longer detectable using the presently employed immunohistochemical method. It is our belief that the cells still remained in the tissue, but,

for some unknown reason they were no longer immunoreactive towards the somatostatin antibodies used. The cells may have released their content of somatostatin-like immunoreactivity, or the degradation of the molecule(s) responsible for the immunoreactivity may have been enhanced. However, also direct cytotoxic effects have to be taken into consideration as well as migration of the dendritic cells from the skin to other organs, such as the lymphoid system.

We also investigated the presence of mast cells in the skin using histamine-based immunohistochemistry (cf. Ref. 5). There was no change in number before compared to after the provocation; however, the number of mast cells in their affected areas was remarkably high already from the beginning. Again, it has to be pointed out that the material is too small to allow for any general statement, but, a mastocytosis could very well, due to histamine effects, explain the subjective sensations of itch and pain as well as changes in the blood vessel system leading to edema and erythema reported in this patient category (cf. Refs. 1 and 2). In this context, it must be mentioned that Berg et al. (4) were unable to observe any difference, as compared to normal human skin, in their material.

It is of great importance to note that the 2 patients, subjectively and objectively, from a clinical point of view did not respond in an equal manner during the provocation. In spite of this, our method was sensitive enough to detect the same changes in both patients. With these 2 patients at hand, we cannot fully explain the observed effects as only a Pavlovian-type conditioning reflex or a general stress reaction. It should also be pointed

out that both patients reported profound feelings of subjective illness 24 h (and onwards) after the provocation. It may, therefore, be argued that the time spans generally used for inspection of these patients in earlier studies may very well have been simply too short.

It is evident from our preliminary data that biological changes are present in the patients claiming to suffer from "screen dermatitis". In view of the recent epidemiological studies pointing to a correlation between long-term exposures from magnetic fields and cancer (7, 8), our data ought to be further analyzed. One question that immediately arises is how ordinary healthy normal humans will react in this kind of open-field provocation situation. Blind or double-blind provocations in a controlled environment are also necessary to elucidate possible underlying causes for the changes reported in this investigation.

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References

1. Bergqvist U. Health problems during work with visual display terminals. Doctoral Dissertation, Stockholm, 1994.
2. Berg M. Facial skin complaints and work at visual display units, Epidemiological, clinical and histopathological studies. Doctoral Dissertation, Stockholm, 1989.
3. Berg M, Lidén S, Axelson O. Skin complaints and work at visual display units: an epidemiological study of office employees. *J Am Acad Dermatol* 1990; 22: 621-625.
4. Berg M, Hedblad M-A, Erhardt K. Facial skin complaints and work at visual display units: a histopathological study. *Acta Derm Venereol (Stockh)* 1990; 70: 216-220.
5. Johansson O, Virtanen M, Hilliges M, Yang Q. Histamine immunohistochemistry: a new and highly sensitive method for studying cutaneous mast cells. *Histochem J* 1992; 24: 283-287.
6. Johansson O, Vaalasti A, Hilliges M, et al. Somatostatin-like immunoreactivity in human dendritic cells with special reference to Langerhans cells of the skin. In: Thivolet J, Schmitt D, eds. *The Langerhans Cell*. Paris/London: Colloque INSERM/John Libbey Eurotext Ltd 1988: 261-271.
7. Feychting M, Ahlbom A. Magnetic fields and cancer in people residing near Swedish high voltage power lines. Stockholm: Institutet för miljömedicin, Karolinska Institutet 1992: IMM-rapport 1992: 6.
8. Flodérus B, Persson T, Stenlund C, Wennberg A, Öst Å, Knafe B. Occupational exposure to electromagnetic fields in relation to leukemia and brain tumors: a case-control study in Sweden. *Cancer Causes Contr* 1993; 4: 465-476.