

## LETTERS TO THE EDITOR

### Psoriasis and Somatostatin in Serum

Benedikte Geisner<sup>1</sup>, Jørn Skavland<sup>1</sup>, Jan A. Marcusson<sup>1\*</sup>, Olle Johansson<sup>2</sup> and Said Elsayed<sup>1</sup>

<sup>1</sup>Institute of Medicine, Section of Dermatovenereology, Allergy and Research Group, Section of Medical Biochemistry, Haukeland University Hospital, NO-5021 Bergen, Norway, and <sup>2</sup>Experimental Dermatology Unit, Department of Neuroscience, Karolinska Institute, Stockholm, Sweden.

\*E-mail: jan.anders.marcusson@helse-bergen.no

Accepted January 9, 2007.

Sir,

Somatostatin is a polypeptide that is widely distributed throughout the central nervous system (CNS) and in different peripheral tissues (1). Two biologically active forms exist; somatostatin-14 and somatostatin-28, where somatostatin-14 is a part of somatostatin-28 (2). In the CNS somatostatin acts as a neurotransmitter and neuro-hormone and shows generally inhibitory functions. In the periphery its effect is mostly down-regulating on many hormones and neuropeptides. Somatostatin has also an immunoregulatory effect on the T and B cells and other cell types (1, 2).

Somatostatin has been used as treatment of psoriasis (3–8), and the overall impression is that the hormone has a therapeutic efficacy.

The presence of somatostatin has been demonstrated in dendritic cells located in the dermis and epidermis of normal skin and psoriasis lesions (9, 10). Moreover, during various treatments it has been visualized that the number of somatostatin-positive dendritic cells is reduced, along with the healing of the disease, suggesting a role for the hormone (9, 10).

In order to further explore the function of somatostatin in psoriasis, its level in serum was investigated and patients were compared with controls. Furthermore, the amount of somatostatin was correlated with the activity of the disease and the blood levels during treatment were measured.

## MATERIALS AND METHODS

### Patients

Fifteen patients with psoriasis were enrolled, 9 men (median age 55 years, age range 23–73 years) and 6 women (median age 57 years, age range 37–73 years). As controls, 10 healthy subjects were recruited, 7 men (median age 49 years, range 29–64 years) and 3 women (median age 56 years, age range 56–57 years). Their median PASI score (Psoriasis Area and Severity Index) was 6.8 (range 2–13.6).

Five of the patients were followed during treatment with PASI score, somatostatin levels in serum and skin biopsies. Four patients were treated according to the Goeckerman regimen and one with Daivobet™ creme (calciopotriol and betamethasone dipropionate) (Leo Pharma A/S, Ballerup, Denmark). All 5 patients received narrowband ultraviolet (UV)-B. Blood samples were collected before, and after 2 and 4 weeks of treatment. In order to obtain an objective measure of healing, skin biopsies

(4-mm punch) were taken from a target lesion at the same time intervals. Xylocaine (lidocaine) (10 mg/ml) (AstraZeneca, Södertälje, Sweden) was used for anaesthesia. The healing of the psoriasis lesions was assessed by gauging the epidermal thickness (magnification×100).

### Assay for somatostatin

To measure the somatostatin, venous blood was drawn from the patients and controls between 08.00 h and 10.00 h. The decision to collect blood samples at these times was based on the estimation of the somatostatin serum levels in 5 healthy subjects at 09.00 h, 12.00 h and 15.00 h (data not shown). The mean values showed no change between 09.00 h and 12.00 h, but a slight increase between 12.00 h and 15.00 h. It was therefore considered justified to collect the blood samples at the time chosen, between breakfast and lunch. After coagulation the serum was separated, immediately frozen and stored at –70°C until tested. A commercially available somatostatin EIA Kit (Bachem UK, Ltd, Merseyside WA9 3AJ, UK) was used to measure somatostatin-14, somatostatin-28, somatostatin-25 and (des-Ala)-somatostatin-14. Somatostatin analogues were isolated using a hydrophobic non-polar silica (Sorbent C18) column (SEP-columns packed C18, Peninsula laboratories Inc., Sant Carlos CA 94070, USA). No cross-reactivity between substance P, neuropeptide Y, vasoactive intestinal polypeptide, insulin, glucagon and amylin has been demonstrated according to the manufacturer. The procedure suggested by the manufacture was strictly adhered to and the sera from the patients and the controls were simultaneously analysed.

### Statistical methods

The Mann-Whitney *U* test and the Spearman's rank order correlation test were used, as presented in Statistica 7.1 (Statsoft Inc., Tulsa, OK, USA).

## RESULTS

Fig. 1 shows that the patients had significantly higher levels of somatostatin than controls ( $p=0.0171$ ). When the activity of the disease (PASI) was plotted against the somatostatin levels, a non-significant negative correlation ( $r = -0.3582$ ) was found, i.e. the higher psoriasis activity the lower somatostatin level (not shown).

In order to determine whether the somatostatin levels would change during treatment, 5 patients were followed for 4 weeks. During the observation period no change in the mean values of somatostatin was observed, while the healing parameters (PASI score and epidermal thickness) diminished (data not shown).

## DISCUSSION

In untreated psoriasis there are an increased number of somatostatin-containing dendritic cells, both in the epidermis and the dermis of the lesional skin, and their number is decreased during the healing process (9, 10). Accordingly, one would presume that the abundant amount of somatostatin positive dendritic cells in lesional skin would influence the somatostatin level in serum. However, we have only found two earlier reports discussing this issue (8, 11). In those studies another assay was used and showed low levels of somatostatin. On the contrary, our investigation shows that the somatostatin level in the serum of the patients is significantly higher than among controls, suggesting that somatostatin is involved in the pathogenic process and that the role of somatostatin in psoriasis is not fully elucidated. Furthermore, the values are widely spread among the psoriatic patients compared with controls (Fig. 1).

In order to explore this further, the somatostatin levels were plotted against the scoring of disease activity (PASI score) and a non-significant negative correlation was seen.

The somatostatin levels in 5 patients during a 4-week treatment period were also followed. The spread of the somatostatin levels at the beginning was larger than at the end, but there was no change in the mean values over time.

The cells of current interest in psoriasis are the activated T cells in the dermis and epidermis of the lesions (12, 13). At the same location somatostatin-positive dendritic cells have been demonstrated and their number, as well as the number of T cells, is lowered along with the healing (9, 10). We therefore propose that, in the process of clearing psoriasis, the dendritic cells in active lesions secrete somatostatin and, through a paracrine

mechanism, inhibit lymphocyte activity and induce apoptoses of the activated T cells (14). Furthermore, it has been shown that somatostatin also influences the shift from the TH1 to TH2 type of T-cell action, which is also a target mechanism that has been interfered with in order to induce healing (14). Although this study is not conclusive in all aspects, one cannot rule out the role of somatostatin in psoriasis in the light of the recent concept of the pathogenesis and findings in other immunological test systems.

## ACKNOWLEDGEMENTS

The study was supported by Helse-Vest, Norway and the Cancer and Allergy Foundation, Sweden.

## REFERENCES

1. Dasgupta P. Somatostatin analogues; Multipleroles in cellular proliferation, neoplasia and angiogenesis. *Pharmacol Ther* 2004; 102: 61–85.
2. Ten Bokum AMC, Hofland LJ, van Hagen PM. Somatostatin and somatostatin receptors in the immune system. *Eur Cytokine Netw* 2000; 11: 161–176.
3. Weber G, Klughart G, Neidhardt M, Galle K, Frey H, Geiger A. Treatment of psoriasis with somatostatin. *Arch Dermatol Res* 1982; 272: 31–36.
4. Guilhou JJ, Boulanger A, Barneon G, Vic P, Meynadier J, Tardieu JC. Somatostatin treatment of psoriasis. *Arch Dermatol Res* 1982; 274: 249–257.
5. Venier A, De Simone C, Forni L, Ghirlanda G, Uccioli L, Serri F, Frati L. Treatment of severe psoriasis with somatostatin; four years of experience. *Arch Dermatol Res* 1988; 280: S51–S54.
6. Matt LH, Kingston TP, Lowe NJ. Treatment of severe psoriasis with intravenous somatostatin. *J Dermatol Treatm* 1989; 181: 81–82.
7. Camisa C, Maceyko RF, O'Dorisio TM, Schacht GE, Mekhjian HS. Treatment of psoriasis with long-term administration of somatostatin analogue 201-995. *J Am Acad Dermatol* 1989; 21: 139–141.
8. Camisa C. Somatostatin therapy. In: Roenick HH, Maibach H, editors. *Psoriasis*, 2nd edn. New York; Marcel Dekker Inc., 1991: p. 829–846.
9. Johansson O, Hilliges M, Talme T, Marcusson JA, Wetterberg L. Somatostatin immunoreactive cells in lesional psoriatic human skin during peptide T treatment. *Acta Derm Venereol* 1994; 74: 106–109.
10. Talme T, Schultzberg M, Sundquist KG, Marcusson JA. Somatostatin- and factor XIIIa-immunoreactive cells in psoriasis during clobetasol propionate and calcipotriol treatment. *Acta Derm Venereol* 1999; 79: 44–48.
11. Neugebauer D, Weber G. Somatostatinmangel, hyperinsulismus und thrombozytenaggregation bei psoriasis. *Z Hautkrankheiten* 1988; 673: 585–590.
12. Krueger JG, Bowcock A. Psoriasis pathophysiology; current concepts of pathogenesis. *Ann Theum Dis* 2005; 64: 30–36.
13. Lattuada D, Casnici C, Venuto A, Marelli O. The apoptotic effect of somatostatin SMS 201-995 on human lymphocytes. *J Neuroimmunology* 2002; 133: 211–216.
14. Krantic S. Peptides as regulators of the immune system; emphasis on somatostatin. *Peptides* 2000; 21: 1941–1964.

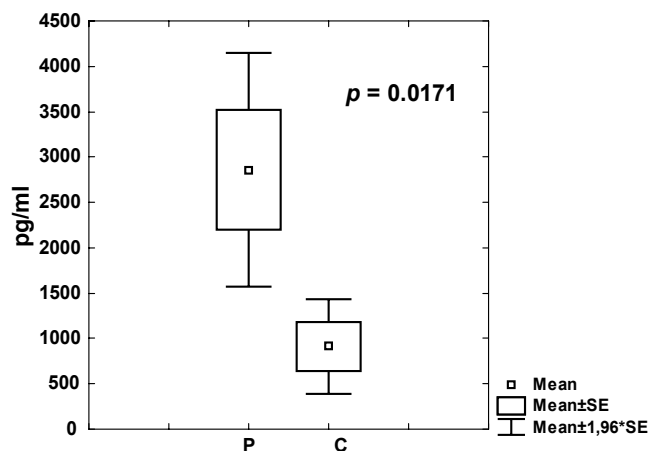


Fig. 1. Somatostatin in the serum of 15 psoriasis patients (P) and 10 healthy controls (C).