Psoriasin and Follicular Hyperkeratinization in Acne Comedones

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Key Words

Acne · Psoriasin · Hyperkeratinization · Inflammation

Introduction

Regardless of understanding acne as a combination of seborrhea, follicular hyperkeratinization, *Propionibacterium acnes* colonization and perifollicular inflammation, it is still unclear, which is the mechanism of comedo formation. Possibilities include 'irritation' of the follicular lining and sebaceous duct by exogenous compounds, an endogenous hormonal stimulus or even neurological stimulus [1]. The ductal hypercornification can result from hyperproliferation of ductal keratinocytes or a reduced separation of ductal corneocytes [2]. Abnormal keratinocyte differentiation has been associated with a relatively new protein – psoriasin (S100A7), a member of the S100 gene family. S100 proteins are calcium-activated signaling proteins that interact with target proteins to modulate biological processes [3]. Because of their signal transduction role, and role as chemoattractants, S100 proteins are proposed to have an important role in keratinocyte differentiation and in the pathogenesis of psoriasis [4]. In the epidermis, psoriasin is expressed infrequently and at low levels in normal epithelial cells, but can be highly induced in keratinocytes under specific

pathological circumstances [5]. In the meantime, psoriasin has been suggested to be involved in the pathogenesis of inflammatory skin diseases, and its levels were found to increase in response to inflammatory stress. In addition, retinoic acid (RA) and inflammatory agents have been implicated in the upregulation of psoriasin [6, 7]. Psoriasin was shown to be induced not only in psoriatic epidermis [4], but also in keratinocytes after all-*trans*-RA treatment in vitro [8]. In this work we suggest that psoriasin may be involved in the abnormal follicular hyperkeratinization detected in acne lesions.

The purpose of the study was to detect changes of psoriasin expression in acne lesions versus normal skin, especially in the ductus seboglandularis, and to identify a possible psoriasin involvement in acne pathogenesis.

Materials and Methods

We used immunohistochemical investigations of skin samples from acne-prone facial skin, the noninvolved skin of the same patients with acne and from normal human skin without acne with the antibody against psoriasin.

Skin biopsies (3–5 mm) were obtained from acne lesions of the face (acne-involved skin) and the thigh (acne-uninvolved skin) of 33 patients with active acne (18 males and 15 females, aged 15–22 years) of the Outpatient Clinics, 'Seskinės Poliklinika' and the Department of Dermatology, Vilnius University Hospital, Vilnius, Lithuania, and from different skin areas, including the face, of 7 age-matched healthy individuals undergoing routine plastic

Fig. 1. Detection of psoriasin in the epidermis and the ductus seboglandularis of uninvolved skin of acne patients.

Fig. 2. Evaluation of the expression of psoriasin in the epidermis and ductus seboglandularis of (a) acne-involved and (b) acne-uninvolved skin of acne patients and (c) in healthy controls (scale from 0 to 3: 0 = negative; 0.5 = barely discernible; 1 = moderately intensive; 2 = strong staining; 3 = very strong uniform immunostaining).

Fig. 3. Detection of psoriasin in the epidermis and in the sebaceous duct in acne skin samples. Immunohistochemistry was performed as described in Materials and Methods.

surgery. The tissue specimens were incubated with diluted 1:500 primary antibody to psoriasin for 1 h at room temperature. Subsequently slides were reacted with a biotinylated secondary antibody (diluted 1:500) for 30 min and then with a streptavidin enzyme conjugate for 10 min followed by a fuchsin substrate chromogen system for 5–10 min and were counterstained with Mayer's hematoxylin. The negative controls consisted of tissues incubated with antibody diluent instead of the primary antiserum. This

study was conducted according to the ethical standards of the Lithuanian Bioethical Committee for studies involving human subjects (authorization No. 78, protocol No. 1, version No. 1). Immunostaining of SG cells at different stages of differentiation was evaluated semiquantitatively on a scale of 0 to 3: 0 = negative; 0.5 = barely discernible; 1 = moderate intensive; 2 = strong staining; 3 = very strong uniform immunostaining.

Results

We detected marked differences concerning the localization and intensity of staining in keratinocytes of the epidermis and the sebaceous duct. Psoriasin was highly expressed in the epidermis and the ductus seboglandularis of the acne-involved skin. No staining was observed in noninvolved control or normal skin sections (fig. 1, 2). The intensity of staining in acne skin samples increased with the level of keratinocyte differentiation in the epidermis, whereas a strong homogenous staining was observed in the sebaceous duct (fig. 3). Other cutaneous structures, like hair follicles, sweat glands, nerves or blood vessels, were negative for psoriasin in all cases. No staining was observed in control sections stained with preimmune serum antibody diluent.

Discussion

The present study confirmed that psoriasin upregulation is restricted not only to psoriasis and psoriasiform epidermal hyperplasia. It is possible that inflammation in acne skin is a reason for the partial utilization of psoriasin as a chemoattractant agent for recruiting inflammatory cells [9] and cellular RA-binding protein (CRABP-II) as

a modulator of RA activity [10]; likewise it has been thought that it could be in response to RA-induced inflammation [7]. CRABP-II binds RA and is also thought to function as a buffer by sequestering RA or enhancing its degradation, and thus limiting the amount of RA available to the nuclear RA [11]. The concentrations of both calcium and retinoids are critical in regulating epidermal cell differentiation, as suggested by both in vitro and in vivo studies [12]. From the clinical point of view, it is important that the present study, which showed high expression of psoriasin in the ductus seboglandularis in acne, is one more step forward looking to the more comprehensive answers in the pathogenesis of acne and contributes also to the better understanding of biological functions of psoriasin in inflammatory skin diseases under certain conditions in general. Such knowledge might become useful in the development of new strategies to block the local epidermal response of hyperkeratinization and inflammation that characterizes acne.

Conclusions

Psoriasin expression in response to inflammation at high levels in acne might lead to the altered follicular keratinization and the abnormal amount of RA.

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