Immunohistochemical Expression of E-Cadherin in Psoriasis

SOHEIR M. MAHFOUZ, Ph.D.*; SAMIA M. GABAL, M.D.*; MARWA M. FAWZY, M.D.** and HALA M. EL HANBOLI, M.Sc.***
The Departments of Pathology* & Dermatology**, Faculty of Medicine, Cairo University and Fayoum University***

Abstract

Background: Psoriasis is a common inflammatory skin disease characterized by abnormal keratinocyte proliferation and differentiation, E-cadherin is important for epidermal intercellular adherence because it is required for the adhesive properties of keratinocytes and skin differentiation.

Objectives: To assess the presence and distribution of E-cadherin in psoriasis in order to investigate its possible role in the pathogenesis of psoriasis.

Patients and Methods: Thirty patients having psoriasis vulgaris were recruited from the Outpatient Clinic, Dermatology Department, Faculty of Medicine, Cairo University as well as twenty (age and sex matched) volunteers (psoriasis free) with healthy skin appearance as a control group. All patients were subjected to complete history taking with special emphasis on the duration of the disease, dermatological examination and registration of PASI score. Both patients and controls underwent skin biopsy. H&E staining was performed for histopathological examination and a grading system with a numerical value assigned for each biopsy was taken from all cases. Immunohistochemical staining was performed to detect E-cadherin expression and distribution in both cases and control groups.

Results: There was a highly significant difference between cases and control group regarding to immunostaining of E-cadherin in each of (granular, upper spinous, and basal skin layers) with high mean among control, and no significant difference in immunostaining between study groups regarding (lower spinous layer). There was a highly significant negative correlation between the used histologic grading score and immunohistochemical staining of E-cadherin in all skin layers. There was no significant difference in immunostaining between study groups regarding (lower spinous layer). There was a highly significant negative correlation between the duration of disease and the immunohistochemical staining of E-cadherin in different skin layers. Similarly the PASI score did not correlate with the immunohistochemical staining of E-cadherin and the used histologic grading score.

Conclusion: In psoriasis there are alterations in the organization of adherence junction proteins especially E-cadherin, and these alterations could contribute to modify interactions between neighboring cells, leading to inadequate function of the epithelial skin layers, and also enhance the proliferative activity in the affected epidermis.

Key Words: Psoriasis vulgaris – E-cadherin.

Introduction

PSORIASIS vulgaris is a common, chronic, relapsing skin disease and characterized by macroscopic (clinical) and corresponding microscopic (histological) skin alterations and leads to considerable impairment of the quality of life of the affected patients [1].

Keratinocytes have a significant role in the formation of psoriasis plaque. Various types of alterations can be seen in the properties of keratinocytes in the plaques when compared to keratinocytes in healthy epidermis. Proliferation of keratinocytes is raised almost 50-fold but the factors causing the increase are still unknown [2].

Adherens junctions are required for the establishment and maintenance of epithelial layers, mediating intercellular adhesion, sensing the presence of neighboring cells, and anchoring the actin cytoskeleton to protein complexes and the membrane in this region of the cell [3].

E-cadherin is a cell adhesion transmembrane molecule which is a member of a family of functionally related transmembrane glycoproteins that mediate Ca2+ dependent intercellular cellular adhesion [4]. E-cadherin is important for epidermal intercellular adherence because it is required for the adhesive properties of keratinocytes and skin differentiation [5].

Aim of the work:

We aimed by this work to assess the presence and distribution of E-cadherin in psoriasis in order to investigate its possible role in the pathogenesis of psoriasis.
Patients and Methods

Thirty patients having psoriasis vulgaris were recruited from the outpatient clinic, Dermatology Department, Faculty of Medicine, Cairo University from May 2010 to May 2011 (All active therapies were stopped at least 3 weeks prior to inclusion in the study), and twenty (age and sex matched) volunteers (psoriasis free) with healthy skin appearance (attended the dermatology clinic for cosmetic problems) were included in the study as control group.

All patients were subjected to complete history taking with special emphasis on the duration of the disease, dermatological examination and registration of PASI (Psoriasis Area and Severity Index) score according to Feldman and Krueger [6].

Both patients and controls underwent skin biopsy for histopathological and immunohistochemical evaluation.

H&E stain was performed for light microscopy and a grading system and check list with a numerical value assigned to each microscopic criterion for each biopsy was taken from all cases with a total value of 19 according to Trozak [7] histopathological grading system for psoriasis.

Immunohistochemical staining was performed to detect membranous E-cadherin expression and distribution in both cases and control groups using anti-E-cadherin (clone 36B5, Thermo scientific, UK). Semiquantitative assessment of protein expression was performed using a modified H-score in which both intensity and proportion of staining was categorized. Category A indicated the proportion of positive cell staining throughout the section and was assigned a scale from 0 to 3 (0=0-4%; 1=5-24%; 2=25-49%; 3=50-100%). Category B represented the average intensity; the presence of negative, weak, intermediate and strong staining was given a score from 0 to 3. Category A was multiplied by category B to form a multiplicative score. The cases were sorted into three subgroups; H-score 0 referred to negative expression; H-score 1-2 to weak expression; H-score 3-9 to moderate/strong expression [8].

Results

The age of the patients ranged from 20 to 65 years with a mean age 41.36±12.08 years, while that of the control group ranged from 25 to 60 years with a mean age 41.2±10.7 years (age matched groups as p=0.9). Among 30 patients there were 17 males representing 56.7% and 13 females representing 43.3%. The control group (20 individuals) comprised 11 males representing 55% and 9 females representing 45% (sex matched as p=0.96). The duration of the disease varied from 2 months to 25 years with a mean 60.13±71.5 months. PASI score ranged from 7.8 to 37.5 with a mean of 19.3±8.9.

According to the grading system used in this study cases had scores that ranged from 10 to 18 out of a total point score of 19 with a mean of 12.7±2.8.

The expression of E-cadherin (Figs. 1,2) was the same in all skin layers among the control group, while there was a highly significant difference (p-value <0.001) between cases and control group regarding to immunostaining of E-cadherin in each of (granular, upper spinous, and basal skin layers) with high mean among controls. On the other hand there was no significant difference (p-value >0.05) in immunostaining between study groups regarding the lower spinous layer.

The results have also shown that; among the cases, there was a highly significant negative correlation between the used histologic grading score and immunohistochemical staining of E-cadherin in all skin layers (p-value <0.01) (Fig. 3).

There was no significant correlation between the duration of disease and the immunohistochemical staining of E-cadherin in different skin layers (p-value >0.05).

Similarly the PASI score did not correlate with the immunohistochemical staining of E-cadherin (p-value >0.05) and the used histologic grading score (p-value= 0.7).

Discussion

The most characteristic change in psoriasis vulgaris is the markedly increased, persistent, keratinocyte proliferation, and the role of the keratinocytes in psoriasis is beyond doubt but the molecular mechanisms behind the alterations are still poorly understood and the underlying mechanism of excessive epidermal growth is controversial [2].

E-cadherin is important for epidermal intercellular adherence because it is required for the adhesive properties of keratinocytes and skin differentiation [8]. Loss of E-cadherin could therefore lead to progressive hyperproliferation in epidermis [9].
Fig. (1): Membranous E-cadherin expression in normal skin; showing mostly equal diffuse staining in all epidermal skin layers and doesn’t staining the horny layer (H&E X 40).

Fig. (2): Membranous E-cadherin expression in a case of psoriasis; showing decreased staining in the basal cell layer, mostly equal diffuse intense staining in the lower spinous layer and absent staining in granular and horny layers (H&E X 400).

Fig. (3): A case of psoriasis with relatively high histologic grade (17) as shown in its H&E (X 40) photo (A) and its E-cadherin (B) (X 40) membranous staining showing relatively weak stain.

This work was designed to investigate the role of E-cadherin in the proliferation of keratinocytes and consequently the pathogenesis of psoriasis vulgaris via the examination of its expression in the psoriatic and nonpsoriatic skin.

The expression of E-cadherin was the same in all skin layers among the control group as they had the same mean and standard deviation in all layers (7.1 ± 1.22). This is similar to what was described by some researchers [10-12] who both reported that in normal skin tissues, the stain of E-cadherin was detected uniformly within all layers of normal epidermis at the sites of cell-cell junctions.

There was a highly significant difference (p-value <0.001) between cases and control group regarding to immunostaining of E-cadherin in each of (granular, upper spinous, and basal skin layers) with high mean among controls. On the other hand there was no significant difference (p-value >0.05) in immunostaining between study groups regarding the lower spinous layer.

These results are similar to those reported by several researchers [13-15] as they found that E-cadherin showed an irregular and tortuous pattern of distribution in psoriatic epidermal sections, also. The results of Li et al. [11,12] appear to be closest to what we have observed in this study as they also observed that there was a down-regulation of E-cadherin in the granular layer, upper spinous and basal layers with sparing of the lower spinous layer of psoriasis lesional tissue. They hence assumed that the breakdown of adherence junctions in the psoriatic epidermis is probably involved in the hyperproliferation of keratinocytes in psoriasis vulgaris. On the other hand other authors [16,17] believe that the distribution of E-cadherin is the same as in normal skin and hence can play no important role in the pathogenesis of psoriasis.
It is known that in psoriatic epidermis, keratinocytes proliferate and mature rapidly so that terminal differentiation, normally occurring in granular keratinocytes and then squamous corneocytes, is incomplete [18]; also the psoriatic keratinocytes in the mid and upper levels of the epidermis are senescent [19], all these factors may be related to the defective immunostaining for E-cadherin in upper spinous and granular layers. The decreased immunostaining for E-cadherin in basal layer can also be attributed to the presence of mitogenic molecules such as amphiregulin (a potent mitogen for epidermal keratinocytes) that might contribute to the pathogenesis of psoriasis by affecting the integrity of cell-cell junctions through their action of inducing and facilitating neutrophil migration into psoriatic epidermis, at least, in part by disrupting E-cadherin in basal keratinocytes [14].

The highly significant negative correlation between the used histologic grading score and immunohistochemical staining of E-cadherin mostly refers to the presence of a strong relation between the defective E-cadherin in psoriasis and its histopathologic picture. The more fully developed the lesion the less it will be likely to express E-cadherin in all layers except the lower spinous layer.

To the best of our knowledge, there are no previous studies that describe the relationship between the histopathologic picture of psoriasis and immunohistochemical staining of E-cadherin. Such a negative correlation goes hand in hand with the progression of the histologic lesion, indicating a relationship between the loss of such adherence protein and the worsening of the histologic picture.

There was no significant correlation between the duration of disease and the immunohistochemical staining of E-cadherin in different skin layers. Similarly the PASI score did not correlate with the immunohistochemical staining of E-cadherin (p-value >0.05) and the used histologic grading score (p-value= 0.7).

These results mostly indicate that the duration of the disease and the clinical severity of psoriasis according to PASI score have no relation to the severity of E-cadherin proteins defect; they also, show that PASI score bears no relation even to the histologic picture of psoriasis and its grades. However this may not be surprising and may reflect an inherent problem in comparing detailed assessment of single lesions with more general scores that take the whole body surface area into consideration.

On reviewing the literature with regards to these findings, we could not find any studies describing the relation between the degree of immunohistochemical staining of E-cadherin in psoriasis and both the clinical severity and the duration of psoriasis.

Conclusion:
From our results we can conclude that in psoriasis there are alterations in the organization of adherence junction proteins especially E-cadherin, and these alterations could contribute to modify interactions between neighboring cells, leading to inadequate function of the epithelial skin layers, and also enhance the proliferative activity in the affected epidermis.

References


