Immunohistochemical Expression of Beta-Catenin in Psoriasis

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Abstract

Background: Psoriasis is a common inflammatory skin disease characterized by abnormal keratinocyte proliferation and differentiation, β-catenin is important for epidermal intercellular adherence in addition it also acts as a transcription factor as part of the Wnt signalling pathway.

Objectives: To assess the presence and distribution of β-catenin 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. 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 β-catenin 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 β-catenin 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 β-catenin in all skin layers. There was no significant correlation between the duration of disease and the immunohistochemical staining of β-catenin in different skin layers. Similarly the PASI score did not correlate with the immunohistochemical staining of β-catenin and the used histologic grading score.

Conclusion: In psoriasis there are alterations in the organization of adherence junction proteins especially β-catenin, 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 – β-catenin.

Introduction

PSORIASIS is a common inflammatory skin disease characterized by abnormal keratinocyte proliferation and differentiation, angiogenesis, immune activation and inflammation [1].

In active psoriasis; keratinocyte proliferation outside the basal layer suggests an alteration in cell-cell interactions. The molecular alterations in epidermal barrier function and the mechanisms underlying the perturbed state of proliferation and differentiation in psoriatic epidermis remain poorly understood [2].

β-catenin, a 94-kD is a protein which participates in intercellular adhesion as part of the adherens junctions, as it links E-cadherin to the actin cytoskeleton via a-catenin, so E-cadherin and β-catenin, are thus referred to as E/β protein complex [3].

β-catenin has a dual function as a component of intercellular adherens junctions and also as a transcription factor as part of the Wnt signalling pathway [4]. There is accumulating evidence that β-catenin is also involved in cellular differentiation [5].

Aim of the work:

This work was designed to investigate the role β-catenin in the proliferation of keratinocytes and consequently the pathogenesis of psoriasis vulgaris via the examination of its expression in the psoriatic and nonpsoraitc skin.
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 Beta-catenin expression and distribution in both cases and control groups using anti-β-catenin (clone E-247, 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 β-catenin (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 β-catenin 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 β-catenin 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 β-catenin different skin layers (p-value >0.05). Similarly the PASI score did not correlate with the immunohistochemical staining of β-catenin (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 [9].

β-catenin has a dual function; in cell adhesion as a component of adherens junctions and also as a transcription factor. Movement of β-catenin between the cell membrane and the cytoplasm is dependent on phosphorylation of tyrosine residues which control binding to actin and E-cadherin [8].
This work was designed to investigate the role of $\beta$-catenin 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 $\beta$-catenin was the same in all skin layers among the control group as they had the same mean and standard deviation in all layers ($5.6 \pm 0.8$). This is similar to what was described by some researchers [10-12] who reported that in normal skin tissues, the stain of $\beta$-catenin 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 $\beta$-catenin 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 some authors [13] that found that $\beta$-catenin 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 $\beta$-catenin 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 AJs in the psoriatic epidermis is probably involved in the hyperproliferation of keratinocytes in psoriasis vulgaris, as $\beta$-catenin participates in intercellular adhesion as part of the adherens junctions in addition to being a part of the Wnt/Wingless signaling pathway, in which $\beta$-catenin acts as a transcriptional coactivator and plays a key role in the control of keratinocyte differentiation, prolif-
eratation and development. On the other hand other authors [14,15] believe that the distribution β-catenin 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 cornocytes, is incomplete [16]; also the psoriatic keratinocytes in the mid and upper levels of the epidermis are senescent [17], all these factors may be related to the defective immunostaining for β-catenin in upper spinous and granular layers.

The highly significant negative correlation between the used histologic grading score and immunohistochemical staining of β-catenin mostly refers to the presence of a strong relation between the β-catenin in psoriasis and its histopathologic picture. The more fully developed the lesion the less it will be likely to express β-catenin 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 β-catenin. 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 histological picture.

There was no significant correlation between the duration of disease and the immunohistochemical staining of β-catenin in different skin layers. Similarly the PASI score did not correlate with the immunohistochemical staining of β-catenin (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 β-catenin 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 β-catenin 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 β-catenin, 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**


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