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Original Research Article

A Study on Diagnostic Utility of Ki-67 Immunostaining in Differentiation of Psoriasis Vs Other Psoriasiform Dermatitis

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Abstract:

Introduction: Psoriasiform dermatoses refers to a group of disorders and the disease coming under this group of disorders have a very common histological and clinical presentation from psoriasis itself. In psoriasis there is accelerated epithelial turnover and these keratinocytes are resistant to apoptosis. Hence, a nuclear Ki67 protein is expected to be increased in psoriasis in comparison to other psoriasiform reaction. Our study is intended to analyse the clinical features and histopathology of Psoriasiform Dematoses and to evaluate the immunohistochemical expression of Ki67 in Psoriasiform Dermatoses and to evaluate the diagnostic utility of Ki67.

Methodology: This is a study on evaluation of clinical features and histomorphology of Psoriasiform Dermatoses with immunohistochemical evaluation undertaken in the department of pathology in a tertiary care teaching hospital over a period of 1 year. A punch biopsy including both lesional and perilesional area was taken so as to compare the normal and the diseased skin. The biopsy is kept in 10% neutral buffered formalin immediately in a well-closed container and transported to the histopathology lab with adequate measures. Immunohistochemical staining for anti-Ki67 antibody marker is done as per procedure.

Results: In the present study out of 50 cases, psoriasis constituted the most common psoriasiform dermatoses cases constituting 40% followed by parapsoriasis 20%. In the present study moderate to severe ki67 % expression was seen most commonly among parapsoriasis cases. Mild and moderate ki67 % expression was seen in pityriasis rubra pilaris. Lichen simplex chronicus also showed with mild ki67 % and moderate ki67% expression. Both pityriasis rosea and chronic superficial dermatitis showed nil to minimal expression in all of cases.

Conclusion: In the present study, psoriasis constituted the most common case of psoriasiform dermatoses lesion followed by parapsoriasis and pityriasis rubra pilaris. Among expression of Ki67 immunohistochemistry, Psoriasis has the highest percentage of expression. All the cases of histopathologically confirmed psoriasis cases showed moderate to severe percentage of anti Ki67 antibody expression in the basal and suprabasal keratinocytes. Expression of Ki67 is positive in 75% of total cases of parapsoriasis when constituted the most common case with moderate Ki67 expression among non-psoriasiform psoriatic dermatoses cases.

Keywords: Ki 67 expression, psoriasis, psoriasiform dermatitis.

Introduction

Psoriasis has been known as a chronic disease in history for many decades. The history of psoriasis is itself very interesting because of the various etiological factors associated with psoriasis. This is due to the fact that etiology of psoriasis is still a puzzle but many studies have tried to unfold this mystery by putting up a lot of etiological factors.

Psoriasiform dermatoses is a special unique term. This special term refers to a group of disorders and the disease coming under this group of disorders have a very common histological and clinical presentation from psoriasis itself [1,2]. This group of disorder includes many separate entities belonging to several unrelated disorders of the integument. These disorders either in the beginning of the disease or in the progression/ resolution phase, exhibit lesions resembling psoriasis [3,4].

The most important validatory point is Psoriasis is the prototype of psoriasiform reaction pattern [5]. Coming to the incidence of Psoriasis it is found to be twice to thrice as common in males when compared to females. As many studies have

suggested the most common age group of presentation of psoriasis is from 30s to 40s6. Children younger than 18 and elderly adults over 70 have a very less incidence of psoriasis. Histologically, psoriasis vulgaris needs to be differentiated from the collection of disorders called psoriasiform dermatoses. All the diseases under these disorders clinically and or histologically the differential diagnosis in this group simulates psoriasis [7,8,9].

Management differs for each subset of PD (psoriasiform dermatoses). The clinical features for each of them are also varied and an accurate diagnosis would be made possible with the help of histopathological evaluation. Following are some of the most diagnostic histopathological feature of psoriasis, There is congestion and vasodilatation in the papillary dermis, Psoriasiform epidermal hyperplasia, Munros micro abcess / kogojs abscess [10,11]

Increase in mitotic activity of epidermis leads to increased proliferation and elongation of rete ridges. The cytokines and other mediators from the vasodilated blood vessels and capillaries lead to the hyperproliferation of epidermal keratinocytes [5]. This gives us a hyperproliferated epidermis noted as psoriasiform epidermal hyperplasia. All the differentials present in the psoriasiform dermatoses group is characterized by regular epidermal hyperplasia. But these features are absent when biopsy is taken from early lesions.

According to Nickoloff, Ki67 is the protein which is found to be expressed by keratinocytes. These ki67 protein are resistant to apoptosis. Hence, there is a high possibility for hyperproliferation where there is an aberrant expression of Ki67 protein. Histopathological criteria for psoriasis has been well established in many studies and articles. However, there is a diagnostic dilemma when one is confronted with psoriasiform patterns versus true psoriasis lesions.

In psoriasis there is accelerated epithelial turnover and these keratinocytes are resistant to apoptosis. Hence, a nuclear Ki67 protein is expected to be increased in psoriasis in comparison to other psoriasiform reaction. Our study is intended to analyse the clinical features and histopathology of Psoriasiform Dematoses and to evaluate the immunohistochemical expression of Ki67 in Psoriasiform Dermatoses and to evaluate the diagnostic utility of Ki67 immunostaining in differentiation of Psoriasis and other Psoriasiform Dermatoses

Materials and Methods

This is a study on evaluation of clinical features and histomorphology of Psoriasiform Dermatoses with immunohistochemical evaluation undertaken in the department of pathology in a tertiary care teaching hospital over a period of 1 year.

After obtaining written understandable and consent as mentioned in the consent format from the patients, skin biopsies are obtained from the patients. These skin biopsies are done by the dermatologists as a outpatient procedure. There is practice of doing skin punch biopsies as a routine diagnostic procedure.

A detailed clinical history was taken from the patient where special emphasis is laid on duration of illness, symptoms, site of involvement, distribution of lesions, past history. History of drug intake and general medical conditions.

A punch biopsy including both lesional and perilesional area was taken so as to compare the normal and the diseased skin. The biopsy is kept in 10% neutral buffered formalin immediately in a well-closed container and transported to the histopathology lab with adequate measures.

The skin biopsy specimens are received in Department of Pathology, CMCH in 10% neutral buffered formalin. Specimens are left in the fixative for adequate time. After adequate fixation tissue processing is done as routine in the issue processor, four to five micron thick sections are cut from paraffin blocks using microtome cutting and are subjected to Hematoxylin and Eosin staining. Necessary slides which are coated are used for immunohistochemistry evaluation. Immunohistochemical staining for anti-Ki67 antibody marker is done as per procedure. The slides are read under compound microscope and photographed for future reference.

Results

The present study was conducted over a period of 12 months from June 2019 to May 2020 in the Department of Pathology, Coimbatore Medical College and Hospital, Coimbatore, Tamilnadu.

A total of 382 various skin biopsies were received in the Department of Pathology during the study period, out of which Psoriasiform Dermatoses lesions along with the Non Psoriasis Psoriasiform Dermatoses case constituted 13.08 % (50 cases) of the skin biopsies received.

Table 1: Showing frequency distribution of various Psoriasiform dermatoses

Disease	Frequency	Percentage
Psoriasis	20	40%
Parapsoriasis	10	20%
Pityriasis Rubra Pilaris	8	16%
Lichen simplex chronicus	5	10%
Pityriasis rosea	4	8%
Chronic superficial dermatitis	3	6%
Total	50	100%

In the present study (table 1) shows distribution of various psoriasiform dermatoses cases. In the present study out of 50 cases , psoriasis constituted the most common psoriasiform dermatoses cases constituting 40% [n=20] followed by parapsoriasis 20% [n=10], pityriasis rubra pilaris 16% [n=8], lichen simplex chronicus 10% [n=5], pityriasis rosea 8% [n=4] and chronic superficial dermatitis 6%[n=3]

Out of 50 cases, in the present study male accounted for 65% of cases. Psoriasis, parapsoriasis, pityriasis rubra pilaris and lichen simplex chronicus showed predominantly male predominance [62.5%, 75%, 66.6% and 100% respectively]. Pityriasis rosea showed female predominance [100%], also chronic superficial dermatitis [66.6%].

Psoriasis presented most commonly in age group of 31-45 years [50%], parapsoriasis presented most commonly in age group of 31-45 years [37.5%], pityriasis rubra pilaris presented equally in three age groups of 18-30 years, 31-45 years and 46-60 years [33.3% each] , lichen simplex chronicus presented most commonly in 31-45 years [50%] and chronic superficial dermatitis presented equally in three age groups 18-30 years, 31-45 years and 46-60 years [33.3% each] .

In the present study, most common presentation of cutaneous lesion was in the upper and lower limbs [45%]. Upper and lower limbs involvement was seen most commonly in psoriasis [62.5%] and chronic superficial dermatitis [66.6%]. Next common presentation was seen all over the body [40%]. In all over the body most common diseases were parapsoriasis [75%], pityriasis rubra pilaris [66.6%] and pityriasis rosea [66.6%]. Lichen simplex chronicus showed most common presentation in axilla and groin [50%].

Coming to complaints, in psoriasifrom dematoses lesions, scaling was the chief complaint in psoriasis (62.5%), pityriasis rubra pilaris (66.6%). Rashes was the most common complaint in parapsoriais (100%) and pityriasis rosea (66.6%). Itching was the most common complaint in lichen simplex chronicus (66.6%) and chronic superficial dermatitis (66.6%).

We also evaluate cutaneous lesion and plaques were seen as the common cutaneous lesion in psoriasis (68.7%), pityriasis rubra pilaris (83.3%) and lichen simplex chronicus (50%). Scaling is seen exclusively in psoriasis (25%), erythema is seen in all cases of chronic superficial dermatitis (100%). Patches are seen exclusively in pityriasis rosea (100%).

In the current study, oral mucosal involvement was seen most commonly in psoriasis (62.5%). Oral mucosal involvement was completely absent in pityriasis rubra pilaris, pityriasis rosea and chronic superficial dermatitis.

Table 2: Showing epidermal changes in histopathological examination of various psoriasiform dermatose

Disease	Hyperkeratosis	Acanthosis	Psoriasiform hyper-plasia	Suprapapillary thinning	Downward elonga-tion of rete ridges	Spongiosis	Basal vacuolar change	Epidermotrophism of lymphocytes	Alternate or-thokeratosis and	Follicular plugging
Psoriasis	5	16	20	14	26	0	0	0	0	0
Parapsoriasis	0	10	10	3	5	5	3	5	0	0
Pityriasis Rubra Pilaris	8	2	3	0	2	3	3	0	5	3
Lichen simplex chronicus	3	1	1	0	0	0	0	0	0	0
Pityriasis rosea	0	4	4	0	0	3	0	2	0	0
Chronic superficial dermatitis	1	1	1	0	0	3	2	2	0	0

In the present study psoriasiform hyperplasia, downward elongation of rete ridges are both seen in all of cases of psoriasis. Other features seen in psoriasis are acanthosis and suprapapillary thinning seen in 16 cases (80%) of all psoriasis cases. Hyperkeratosis is seen in 5 cases (25%).

Most common histological finding seen in epidermis of parapsoriasis cases are acanthosis (100%), psoriasiform hyperplasia (100%) followed by downward elongation of rete ridges, epidermotrophism of lymphocytes and spongiosis in 5 cases (50%) of all parapsoriasis cases. Pityriasis rubra pilaris shows hyperkeratosis in 8 cases (100%) and alternating orthokeratosis and parakeratosis in 5 cases followed by psoriasiform hyperplasia, spongiosis, follicular plugging and basal vacuolar change in 3 cases.

Lichen simplex chronicus shows hyperkeratosis in 3 cases and acanthosis and psoriasiform hyperplasia in each 1 case. Pityriasis rosea shows acanthosis and psoriasiform hyperplasiain all 4 cases (100%). It also shows spongiosis in 3 cases and epidermotrophism of lymphocytes in 2 cases. The most common epidermal histological feature of chronic superficial dermatitis is spongiosis seen in 3 cases (100%) followed by basal vacuolar change and acanthosis with psoriasiform hyperplasia in 1 case.

KI67 Expression

The below table shows percentage of Ki67 antibody expression among the psoriasis cases.

Mild Ki67 index was seen in 3 of psoriasis cases and severe Ki67% expression was seen in 17 of psoriasis cases.

Table 3: Anti Ki67 antibody immunohistochemical expression among Non Psoraisis Psoriasiform Dermatoses cases

Disease	Mild ki67	Moderate ki67	Severe ki67	Total
Parapsoriasis	0	7	3	10
Pityriasis rubra pilaris	4	4	0	8
Lichen simplex chronicus	3	2	0	5
Pityriasis rosea	4	0	0	4
Chronic superficial dermatitis	3	0	0	3

In the present study moderate to severe ki67 % expression was seen most commonly among parapsoriasis cases. Mild and moderate ki67 % expression was seen in pityriasis rubra pilaris. Lichen simplex chronicus also showed with mild ki67 % and moderate ki67% expression. Both pityriasis rosea and chronic superficial dermatitis showed nil to minimal expression in all of cases.

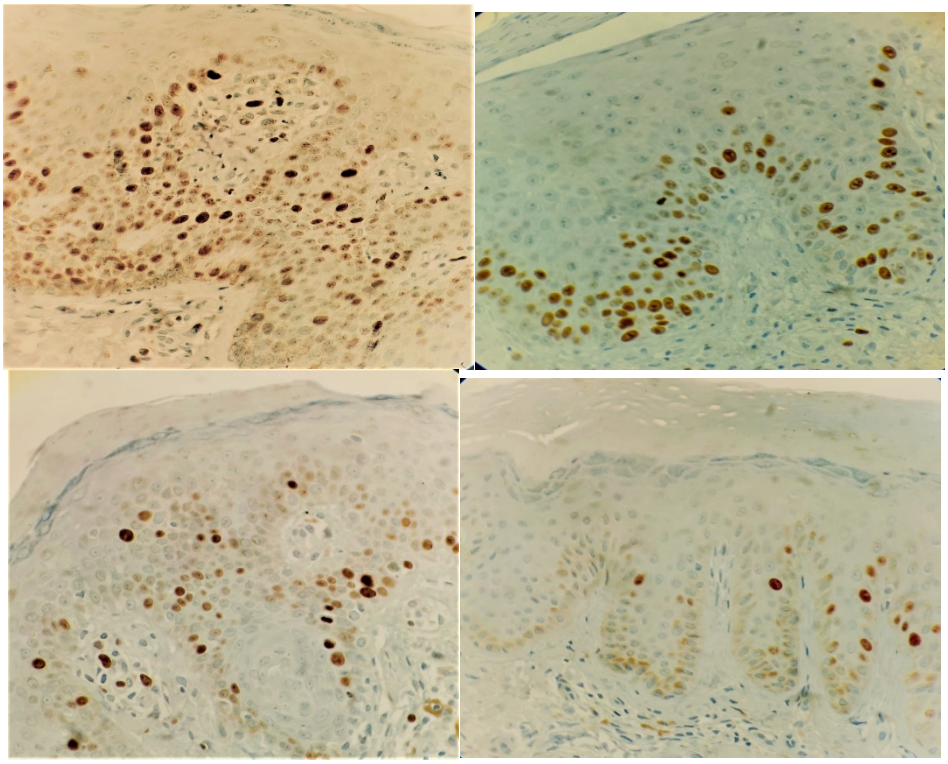

Figure 1: A: Severe B: Moderate C: Mild D:Nil expression of Ki-67

Discussion

The accurate diagnosis of any erythematous skin lesion resembling psoriasis is important both clinically and histopathologically for its effective treatment and evaluation of its prognostic significance. Most of the psoriasiform skin lesions have a similar clinical presentation, thereby making histopathological study and immunohistochemical evaluation as the gold standard for the final diagnosis of these differentials. [12] The present study was conducted to compare the clinical presentation including age, sex, clinical features, and histopathological findings along with immunohistochemical correlation of all the differential diagnosis of Psoriasiform dermatoses reactions.

Out of all the psoriasiform lesions, the common lesions encountered in the present study are Psoriasis, Parapsoriasis, Pityriasis Rubra Pilaris, Lichen simplex chronicus, Pityriasis Rosea and Chronic Superficial Dermatitis. In the present study, Psoriasis was the most common psoriasiform dermatoses lesion which was similar to Alexander et al [13]. A characteristic pattern of epidermal hyperplasia was the most common feature seen in psoriasis case in the current study which is also mentioned as the same in Farmer and Hood classification of psoriasiform lesions [14].

Elder at al [15] classified psoriasis according to predominant dermal inflammatory infiltrate which was in correlation with the present study that neutrophilic dermal infiltrate is a prominent finding in psoriasis cases. This finding is similar to that of Gordon, Johnson and Chopra et al who also found neutrophils as prominent inflammatory infiltrate in psoriasis cases. Tirumalae R et al [16] mentioned in their study that all other diseases other than psoriasis exhibit an uneven psoriasiform pattern i.e., rete ridges are of uneven lengths and thickness with thick suprapapillary plates.

In the present study psoriasis cases showed acanthosis in 16 cases which was similar to studies by Lal et al a in which acanthosis was seen in 100% of cases and in studies of Gordon et al [17]. Lal et al [18], Gordon et al showed that acanthosis is seen in 100% of psoriasis cases and Mehta et al [19] mentioned that 93.10% of psoriasis cases featured acanthosis. This finding is similar to the data in my present study. In the present study neutrophilic infiltrate was identified in 50% of all psoriasis cases.

Pityriasis rubra pilaris is characterized by horizontal and vertical alternating areas of ortho and para keratosis along with follicular plugging, which was similar to the present study.

In the present study we have performed immunohistochemical studies using antiKi67 antibody in samples of normal skin, psoriasis and also in cases of non-psoriasiform psoriatic dermatoses. Expression of Ki67 is found to be higher in Psoriasis group when compared with the non-psoriasiform psoriasis dermatoses group and was very minimal in the normal skin group. This is in concordance with many studies particularly by Jayalakshmy P et al in his study [20]

Total basal layer cell counts were taken to calculate Ki67 percentage expression. The keratinocytes of psoriatic skin reaches the skin surface from the basal layer in just 6-8 days. This is comparatively very high because the turn over time in normal skin is almost 30 days. In some studies, Ki67 was even used to elucidate why psoriasis does not transform into malignancy.

In our study, we made a comparative analysis of Ki67 expression between psoriasiform dermatoses and non-psoriasiform psoriatic dermatoses cases. Ki67 marker is widely used in many studies to detect S1, G2 and M phase defects of the cell cycle. Overexpression of Ki67 in the epidermis of psoriatic lesion was higher than that of non-lesional skin. This is a significant finding, which points out epidermal hyperproliferation. Our study coincides with the finding of Ki67 overexpression in psoriasis as suggested by Batinac et al. in his study [2].

Positive Ki67 was found in the epidermis and viewed by brown colouration created in the nuclei of epidermal cells. In each of the sample cases, high percentage expression (25%) was considered positive. Positive and negative staining results were different between psoriasiform dermatitis and other non-psoriasiform dermatoses cases.

There is also a marked difference between psoriasis and psoriasiform dermatoses cases in Ki67 expression. Batinac et al [21] demonstrated a prominent rise in Ki67 expression in psoriatic skin than normal (17.05 vs 3.65). Another study proved simultaneously that samples of psoriasis cases with high Ki67 expression also showed a higher expression of p53 antibody which is in concordance with my study. Amin and Azin study also showed that the expression of Ki67 between psoriatic lesions and non-involved skin was statistically different which is true in case of my study. [22]

The study of Sezer et al, where determination of 75% as cut off in suprabasal /total epidermal cell count ratio for Ki67 expression for the differentiation between psoriasis and pityriasis rubra pilaris .All the psoriatic patients showed positivity higher than 75%. In my present study, all

the cases of psoriasis showed Ki67 express of more than 80%.

Conclusion

In the present study, psoriasis constituted the most common case of psoriasiform dermatoses lesion followed by parapsoriasis and pityriasis rubra pilaris. All the psoriasiform dermatoses cases along with non-psoriasiform psoriatic dermatoses cases were most common in the third to fourth decade. Psoriasiform hyperplasia and downward elongation of rete ridges were identified in all of cases of psoriasis. Acanthosis and psoriasiform hyperplasia were seen in 100% of cases of psoriasis and pityriasis rosea. Hyperkeratosis was the most common histopathological feature in Pityriasis rubra pilaris and lichen simplex chronicus.

Among expression of Ki67 immunohistochemistry, Psoriasis has the highest percentage of expression. All the cases of histopathologically confirmed psoriasis cases showed moderate to severe percentage of anti Ki67 antibody expression in the basal and suprabasal keratinocytes. Expression of Ki67 is positive in 75% of total cases of parapsoriasis when constituted the most common case with moderate Ki67 expression among non-psoriasiform psoriatic dermatoses cases. Pityriasis rosea and chronic superficial dermatitis showed no/minimal expression with anti Ki67 antibody.

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