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DIAGNOSTIC UTILITY OF KI 67 AND CYCLIN D1 IMMUNOSTAINING IN DIFFERENTIATION OF PSORIASIS VS OTHER PSORIASIFORM DERMATITIS

Pathology

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ABSTRACT

Psoriasis and other psoriasiform dermatoses (PD) are characterised by overlapping clinical and histopathological characteristics and are often confused with each other leading to erroneous diagnoses and prolonged treatment. **Aim:** To study the morphology of psoriasis and other psoriasiform conditions and to study the expression of Ki67 and Cyclin D1 in distinguishing psoriasis from the other psoriasiform dermatitis lesions. **Methods:** A study was performed on paraffin blocks of 28 psoriasis and 22 psoriasiform dermatitis patients between 2018 and 2020. The selected formalin fixed paraffin embedded tissues from each biopsy specimen were cut into 3-5 µm section and were stained with hematoxylin and eosin. Primary antihuman antibodies against Ki67 and Cyclin D1 were applied on all the cases. **Results:** Mean staining of Ki 67 was higher compared with Cyclin D1 in psoriasis than other psoriasiform dermatitis which was statistically significant. Likewise, a higher mean staining of Cyclin D1 was observed in Psoriasis patients which was again statistically significant. **Conclusion:** The present study showed the expression of Ki67 biomarker in comparison to cyclin D1 higher in psoriasis as compared to the other psoriasiform dermatitis lesions.

KEYWORDS

Immunohistochemistry; Psoriasis; Psoriasiform dermatitis, Ki67; Cyclin D1

INTRODUCTION

Psoriasis is a chronic papulosquamous disease of unknown aetiology with unpredictable course of remission and exacerbations.[1] Both genetic and environmental factors are thought to play a role in initiation and progression of the disease.[2,3]

Psoriasis and psoriasiform dermatitis acquire considerable importance owing to the frequency of occurrence. Clinical history and examination is necessary for diagnosis and since these diseases are characterized by similar morphological characteristics, it is feasible to consider them as a group.

Typical lesions are chronic, recurring, scaly papules, and plaques. Pustular eruptions and erythroderma can occur. Clinical presentation varies among individuals, from those with only a few localized plaques to those with generalized skin involvement. Psoriatic erythroderma is psoriasis involving the entire skin. Psoriatic arthritis occurs in 10 to 25% of patients.

Each clinical presentation has different histopathological features, hence understanding the histopathology is important for confirmation of the clinical diagnosis.

Recently, many studies are carried out by the pathologists and dermatologists to determine more criterias which would be significant in determining the course of psoriasis and also the outcome of treatment modalities, based on immunohistochemistry.[4] Depending on the form of psoriasis and severity of the pathological processes, there is difference in the expression of immunohistochemical markers involved in cell proliferation, vascularization, apoptosis and inflammation. The immunohistochemical markers studied and of significance include CD3, CD68, Ki-67, VEGF, CD34, P63 and S100.

Immunohistochemistry scoring

The immunohistochemistry scoring results were based on staining intensity and frequency of distribution of immunopositive cells. The tissue samples were considered positive when nuclear staining was detected in ≥10% of the cells.

Ki-67 monoclonal antibody (mAb) has been suggested to react only with proliferating cells. In order to study epidermal proliferating cells, immunohistological staining was performed with Ki-67. Cyclin D1 is a regulatory subunit of the cyclin-dependent kinase Cdk4/6, which is involved in the regulation of proliferation and development in mammals.[5]

A distinct brown nuclear staining was considered as positive and cytoplasmic staining was disregarded.

The percentage of positive cells was determined after evaluating the entire lesion present in the slide. The mean percentage of positive tumour cells for each marker was determined in 5 fields per section at high magnification.

The scores indicating the percentage of positive cells and staining intensity were multiplied to produce a semiquantitative immunohistochemical score.

RESULTS

The present study was conducted on 50 patients of psoriasis, and psoriasiform dermatitis, received in the Department of Pathology, Government Medical College, Amritsar. The relevant clinical history was recorded. The Skin biopsies were fixed, then processed and embedded in paraffin wax to prepare blocks. For the histopathological diagnosis of psoriasis and psoriasiform dermatitis, one section was stained by hematoxylin and eosin and the other section was subjected to IHC staining after the confirmation of the diagnosis on histopathology. The following results were obtained.

Table 1: Table Showing Age & Gender Wise Distribution

Age group (years)	No. of cases	Psoriasis (28)		Psoriasiform Dermatitis (22)	
		M	F	M	F
<=20	5	-	3 (60%)	-	2 (40%)
21-40	20	7 (35%)	4 (20%)	3 (15%)	6 (30%)
41-60	21	12 (57%)	-	5	6 (30%)
61-80	4	2 (50%)	-	2 (50%)	-
Total	50	21 (42%)	7 (14%)	10 (20%)	12 (24%)

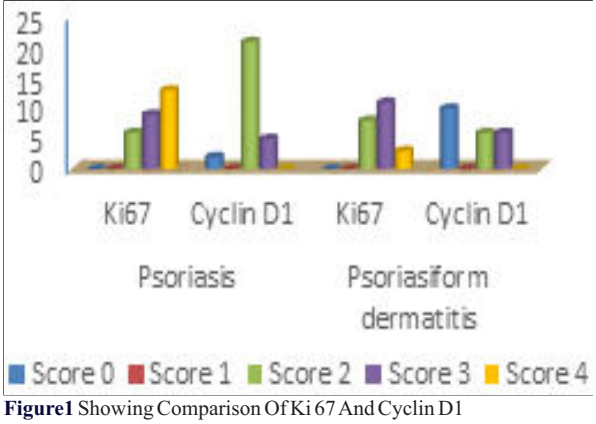


Figure1 Showing Comparison Of Ki 67 And Cyclin D1

Table 2: Table Showing Comparison Of Ki67 And Cyclin D1 Score

	Ki 67					Cyclin D1			
	Score 0	Score 1	Score 2	Score 3	Score 4	Score 0	Score 1	Score 3	Score 4
Psoriasis	0	0	6 (21.43%)	9 (32.14%)	13 (46.43%)	2 (7.14%)	0	21 (75%)	5 (17.86%)
Psoriasiform dermatitis	0	0	8 (36.36%)	11 (50%)	03 (13.64%)	10 (45.45%)	0	6 (27.27%)	6 (27.27%)

P-VALUE: Ki 67 0.040 Cyclin D1 0.001

Ki67 and Cyclin D1 cell counts in psoriasis and psoriasiform dermatitis were compared and it was seen as in table and figure that positively stained cell count was higher in psoriasis compared to PD.

DISCUSSION

Psoriasis with its varied clinical features mimics many other skin lesions and as a prototype of Psoriasiform Dermatitis needs distinction from the other entities.

The age group most commonly affected in our study was 21 to 40 years (42%) followed by the cases in the age group 41 -60 years (40%). This bimodal incidence found in the present study is similar to the findings in the previous literature which find that these lesions are more commonly found in the age group of less than 30 years and 30-50 years. Psoriasis and PD are the lesions of male preponderance and likewise our study also found these lesions to be predominant in males (62%) In a study done by Dogra and Yadav (15), it was seen that Psoriasis is twice more common in males compared to females.

Psoriasis is characterized by epidermal hyperproliferation and expression of Ki67 is widely used to differentiate it from the normal skin and other skin lesions and also from the Psoriasiform Dermatitis lesions. Cyclin D1 plays a central role in the regulation of proliferation linking the extracellular signalling environment to cell cycle progression. In the present study, the use of Ki67 and Cyclin D1 was done to aid in the differentiation of Psoriasis from Psoriasiform Dermatitis.

Study By Prakashiny S , Vindu Srivastava, the most common histologic findings were hyperkeratosis (83.33%), parakeratosis (67.7%), acanthosis (71.8%), elongated rete pegs (59.37%), diminished or absent granular layer (39.58%), suprapapillary thinning (39.58%), munromicroabscess (6.25), spongioform pustules of kogoj (4.16%) Dermal changes like inflammation and congested capillaries were found to be 75%.

WY Ma, L Zhuang et al,[6] in the year 2012, reported that Ki67 positivity index of psoriatic patients was higher as compared to the normal patients. Dorota Jesionek kupnika et al (2013)[7] in study of 100 patients clinically and histologically diagnosed with psoriasis were observed and an increased expression of ki67 in psoriatic lesions was seen. The ki67 positivity ranged from 0 to 30% in psoriatic patients as against 0 to 10% in normal skin.

In the study by Maha Mohamed Amin and Zeinab Abdel Azim (2012), overexpression of 67 in epidermis of psoriatic lesions was significantly higher than non lesional skin ($p \leq 0.001$) which points out epidermal Hyperproliferation and also coincides with that observed by jun-min, et al.[8] Also, Ki 67 positive inflammatory cells are in the epidermis and Ki 67 negative dermal cells are in agreement with nickoloff and Griffiths.[9]

In Prakashiny S , Vindu Srivastava (2017) study, the mean positivity index of ki67 was observed to be 20.93% in psoriasis which is in close relation with the above 2 studies.

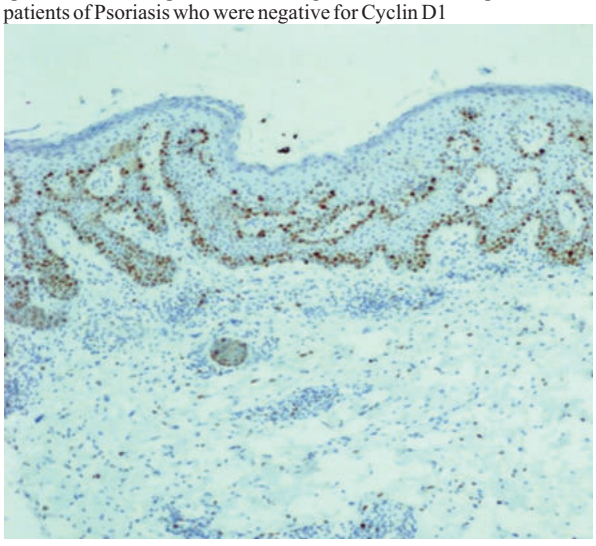
In study by sung AE kim et al (2017) on 20 patients with psoriasis showed increased expression of cyclin D1 was found in psoriasis which was in agreement with the previous studies.[10,11,12]

The upregulation of cyclin D1 is well-established in hyperproliferative tissues[13,14] In the study by sung ae kim et al, cyclin D1 was overexpressed in thick plaques of chronic psoriasis. Cyclin D1 immunoreactivity in chronic psoriasis was demonstrated as strong positive staining among several normal stained nuclei and at regular intervals in the basal layer. This finding is in agreement with previous studies, which also found increased cyclin D1 expression in psoriasis.[11,12,13] However, further studies are warranted to elucidate whether the cells in basal layers that were strongly positively stained for cyclin D1 are psoriatic stem cells or transient amplifying cells, which are important in the hyperproliferation of the epidermis.

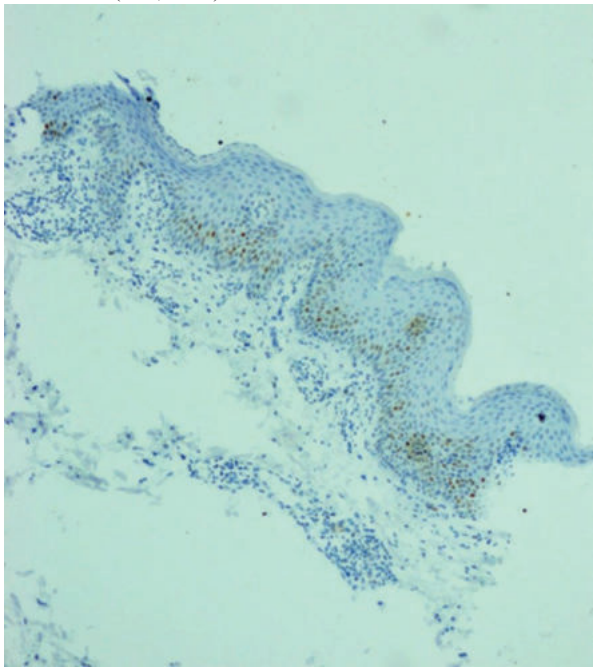
CONCLUSION

Psoriasis is a hyperproliferative skin disorder with increased epidermal turnover compared with other psoriasiform dermatitis. The diagnosis of psoriasis and psoriasiform dermatitis is made mostly on morphology and aided by IHC. We studied the role of proliferation markers, Ki-67 and Cyclin D1 by their expression levels in the epidermis to differentiate psoriasis from other psoriasiform dermatitis. Ki-67 is found to be a more sensitive marker than Cyclin D1 on the basis of epidermal immunoreactive cells, which could be useful for dermatopathologists in differentiating psoriasis from other psoriasiform dermatitis.

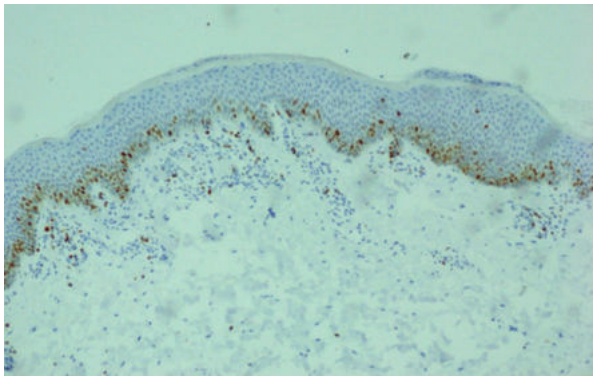
1. Ki67 quantity score staining is more in Psoriasis than PD
2. Cyclin D1 quantity score is more in Psoriasis than PD
3. On comparing the two markers, Cyclin D1 was found to be more specific as 10 PD patients were negative for it in comparison to 2 patients of Psoriasis who were negative for Cyclin D1



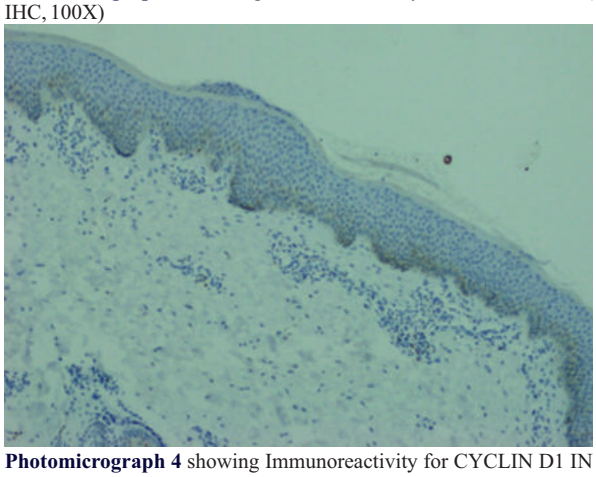
Photomicrograph1 showing Immunoreactivity for KI 67 IN PSORIASIS (IHC, 400X)



Photomicrograph 2 showing Immunoreactivity for CYCLIN D1 IN PSORIASIS (IHC, 100X)



Photomicrograph 3 Showing Immunoreactivity For Ki 67 IN PD (IHC, 100X)



Photomicrograph 4 showing Immunoreactivity for CYCLIN D1 IN PD (IHC, 100X)

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