

A Histopathological Study: ñ-Sign, The Visual Clues In The Diagnosis Of Psoriasis In A Tertiary Care Centre - An Observational Study

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Abstract:

Introduction: Psoriasis is a common chronic inflammatory skin disease that affects >60 million worldwide. The “ñ-sign” may be a visual clue for the histopathological diagnosis of psoriasis which aids in giving a definitive diagnosis in comparison with other inflammatory skin disorders.

Objectives: To determine the visual clues (ñ-sign) in the histopathological diagnosis of psoriasis and compare the histopathological findings between papulosquamous skin disorders and psoriasis.

Methodology: A retrospective observational study was done on all skin punch biopsy samples received as papulosquamous disorders. The ñ-sign was evaluated in the test group in comparison with the control group.

Results: 36 cases were clinically diagnosed as psoriasis while the rest of them (24) were diagnosed as papulosquamous disorders (n=60). Of the 36 cases of psoriasis, 33 were diagnosed as psoriasis on histopathology. The ñ-sign was present in 31 (93.9%) cases and was absent in 2 cases (6.1%) of test group (P <0.001). The combination of ñ sign with hypogranulosis was present in 6 cases (18.2%), ñ-sign with neutrophil infiltration was present in 7 cases (21.2%) and ñ-sign with hypogranulosis and neutrophilic infiltrate was present in 14 cases (42.4%) of test group respectively. Only ñ-sign was present in 4 cases (12.1%) of the test group. Sensitivity and specificity of ñ-sign in the test group were 93.9% and 100% respectively.

Conclusion: These visual clues (ñ-sign) help the pathologists and dermatologists in aiding a definitive diagnosis of psoriasis in early diagnosis and treatment of the same as they share similar features with inflammatory skin disorders.

Key Words: Psoriasis, papulosquamous disorders, histopathology, ñ-sign.

INTRODUCTION:

Psoriasis is a common chronic inflammatory skin disease that affects > 60 million worldwide. Clinically, psoriasis is presented as papulosquamous lesions and mainly shows a psoriasiform reaction pattern on histopathological examination.^[1] Classical histologic results can vary markedly throughout the clinical evolution of psoriasis. The clinical and histopathologic diagnosis of inflammatory skin disorders can be challenging and overlapping with psoriasis.^[2] Skin punch biopsies of mature psoriatic lesions shows regular acanthosis, elongation of the rete ridges with a thin suprapapillary epidermis, dilated vessels in the upper dermis and hyperkeratosis with parakeratosis.^[3,4] Under these circumstances, it is helpful to identify the more specific histopathologic sign (“visual clues”) to indicate the possibility of psoriasis. Recently, Camporro et al discovered “ñ sign” as a visual clue for the histopathologic diagnosis of psoriasis. The ñ-sign includes the sum of two histological criteria: a) the tilde represents a wavy laminar, parakeratotic and separated stratum corneum b) The ‘n’ denotes epidermal hyperplasia and regularly elongated rete ridges.^[1,2] In the present study, we analyzed hematoxylin-and-eosin-stained sections of clinically diagnosed papulosquamous lesions of skin.

Objectives of the study:

1. To detect the visual clues (ñ-sign) in the histopathological diagnosis of psoriasis.
2. To compare the histopathological findings between psoriasis and other papulosquamous skin disorders.

MATERIALS AND METHODS:

Study Design And Case Selection:

It is a hospital based retrospective observational study performed in the department of Pathology at Sri Siddhartha Institute of Medical Sciences and Research Centre, T. Begur, Nelamangala, Bangalore.

Inclusion criteria: All skin punch biopsy specimens of papulosquamous disorders received for histopathological examination in the department of pathology at Sri Siddhartha Institute of Medical Sciences and Research Centre, T. Begur, Nelamangala, Bengaluru from April 2023 to July 2024.

Exclusion criteria: Inadequate samples.

The study was approved by the Institutional Ethics committee at Sri Siddhartha Institute of Medical Sciences and Research Centre T. Begur, Nelamangala. (Ref. No.: SSIMS&RC/IEC/PG/006-2024-25)

Data collection:

All skin punch biopsy samples received in the department of Pathology, clinically diagnosed as psoriasis and other papulosquamous disorders in the department of Dermatology from April 2023 to July 2024. The clinical data were collected from the biopsy requisition forms. These specimens were analysed based on clinical and histopathological features. All psoriasis cases were considered as test and other papulosquamous disorders were considered as control.

In the present study, two observers independently analyzed the biopsy sections to determine the detailed histopathology and the presence or absence of the $\bar{n}$ sign along with following patterns: 1) $\bar{n}$ sign with hypogranulosis. 2) $\bar{n}$ sign with neutrophilic infiltration. 3) $\bar{n}$ sign with hypogranulosis + neutrophilic infiltration.

Statistical Analysis:

All the data collected was entered in Microsoft excel and analysed using statistical software SPSS version 23.0. Data is summarised using frequency and percentage. Graphical representation is used where ever required. All the quantitative variables are presented with mean and standard deviation/median with quartiles. Chi square test was used to compare categorical variables.

RESULTS:

Clinical information:

Total 60 skin punch biopsy sections were included in this study. Of these patients, 36 (60%) cases were clinically diagnosed as psoriasis while the rest of them (24 cases 40%) were diagnosed as other papulosquamous disorders as shown in Fig 1. Of the 36 (60%) cases of psoriasis, 33 (55%) were diagnosed as psoriasis on histopathology Fig 2. The $\bar{n}$ -sign was present in 31 (93.9%) cases and was absent in 2 cases (6.1%) of test group Fig 3. ($P < 0.001$). The combination of $\bar{n}$ sign with hypogranulosis was present in 6 (18.2%) cases, $\bar{n}$ -sign with neutrophil infiltration was present in 7 (21.2%) cases and $\bar{n}$ -sign with hypogranulosis and neutrophilic infiltrate was present in 14 (42.4%) cases of test group respectively. Only $\bar{n}$ -sign was present in 4 (12.1%) cases of the test group Table 1. Sensitivity and specificity of $\bar{n}$ -sign in the test group were 93.9% and 100% respectively Table 2.

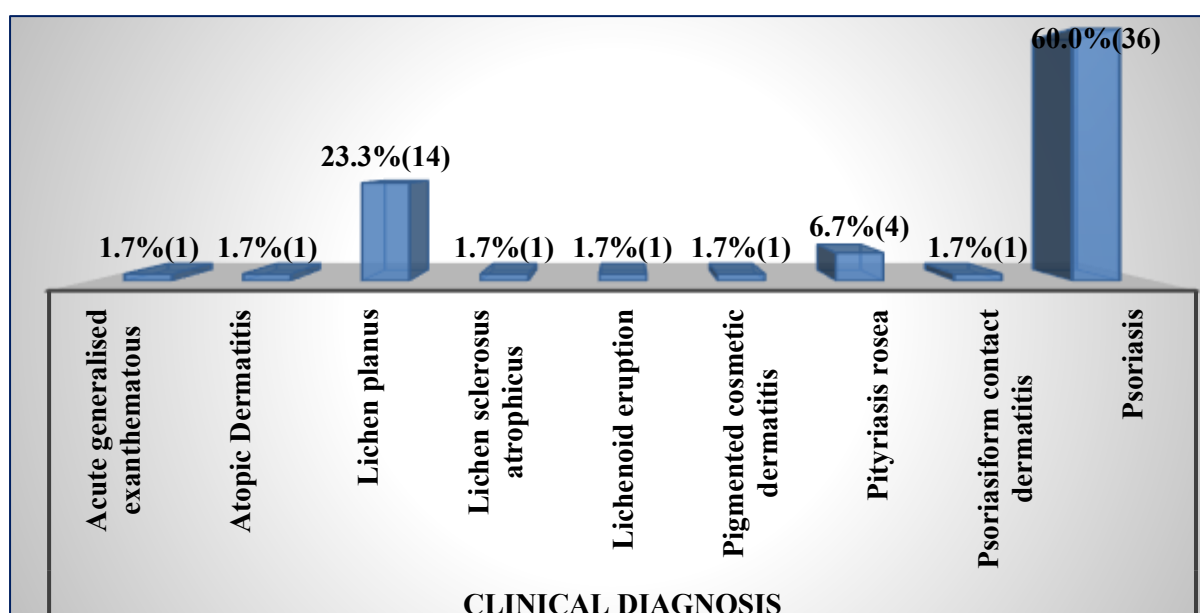


Figure 1: Distribution of clinically diagnosed papulosquamous lesions of skin

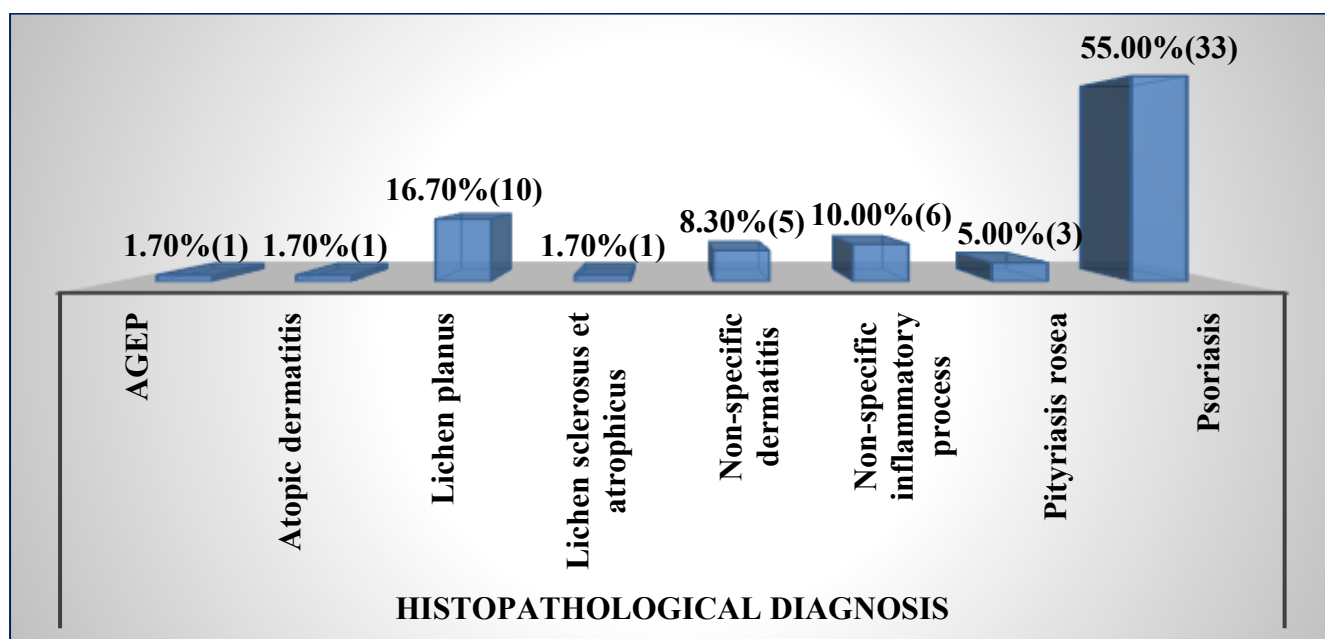


Figure 2: Distribution of histopathological diagnosis of all papulosquamous lesions of skin

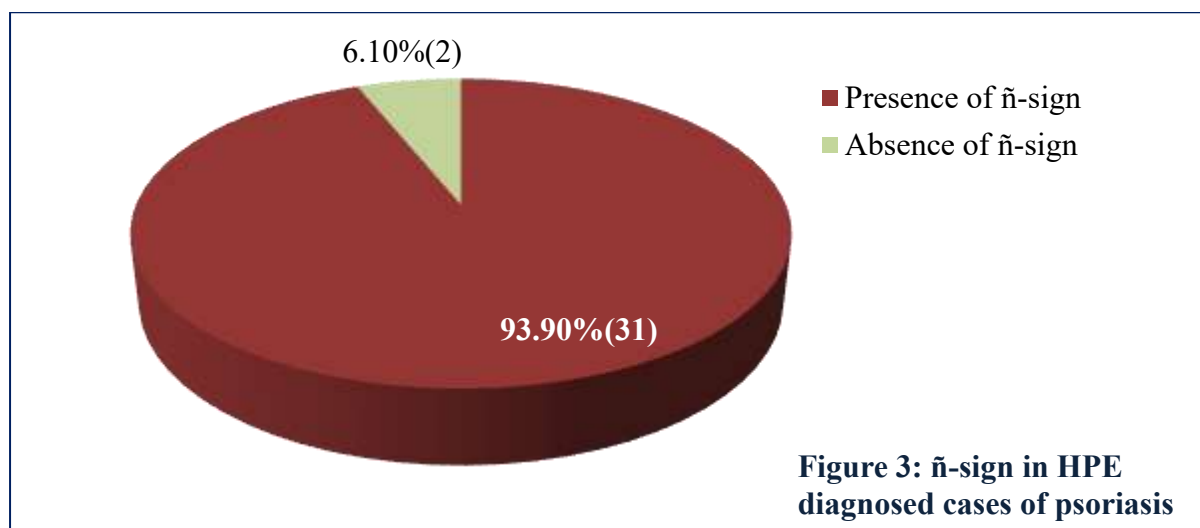


Figure 3: ñ-sign in HPE diagnosed cases of psoriasis

Parameters	Case group	Control group						
	Psoriasis 55.00% (33)	Lichen planus 16.70% (10)	Non-specific inflammatory process 10.00% (6)	Non-specific dermatitis 8.30% (5)	Pityriasis rosea 5.00% (3)	Atopic dermatitis 1.70% (1)	AGEP 1.70% (1)	Lichen sclerosus et
ñ sign	12.10 % (4)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)

PSORIASIS		Sen		Spe		PPV		NPV		p value		Result	
PARAMETER		93.9%		100.0%		100.0%		93.1%		<0.001		HS	
ñ sign + hypogranulosis	18.20 % (6)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	
ñ sign + neutrophilic infiltration	21.20 % (7)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	
ñ sign + hypogranulosis and neutrophilic infiltration	42.40 % (14)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	
Total	93.90 % (31)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	00% (00)	

Table 1: Histopathological diagnosis of all papulosquamous lesions of skin showing ñ-sign**Detailed histologic features of psoriasis**

The detailed histologic features of psoriasis are summarized in **Table 3**

EPIDERMAL FINDINGS	HISTOPATHOLOGICAL=Psoriasis(33)	
	Count	N %
Parakeratosis	28	84.8%
Hyperkeratosis	30	90.9%
Spongiosis	31	93.9%
Suprapapillary thinning	24	72.7%
Clubbing of rete ridge	29	87.9%
Munro's microabscess	19	57.6%
Spongiform pustules of Kogoj	18	54.5%
Hypogranulosis	21	63.6%
Hypergranulosis	11	33.3%
Neutrophilic exocytosis	19	57.6%
Regular acanthosis	31	93.9%

Vacuolar degeneration of basal layer	3	9.1%
Pustule	2	6.1%
Irregular acanthosis	1	3.0%
Papillomatosis	1	3.0%
Lymphocytic exocytosis	1	3.0%
Orthokeratosis	1	3.0%

Table 3: Epidermal findings in HPE diagnosed cases of psoriasis**Prevalence of the ñ sign in the psoriasis and control groups**

The ñ sign was present in 31 (93.90%) of 33 biopsy sections in the psoriasis group and complete absent in 27 (45%) biopsy sections in the control group (Table 1). The prevalence of the ñ sign was highly specific in the psoriasis group ($P < 0.001$), with a sensitivity of 93.9% and specificity of 100.0%. ñ-sign was only present in psoriasis means that the ñ-sign has high specificity as a predictive clue.

DISCUSSION:

In pathology, the diagnostic process is based on the recognition of histologic patterns and their correlation with clinical data. Morphologic clues composed of some specific histopathological features may help reach a definitive histopathological diagnosis. The pathological diagnosis of inflammatory skin disorders is based on the recognition of histological patterns and their correlations with clinical data. This pattern recognition helps pathologists to reach a final pathological diagnosis and can be extremely useful in daily clinical practice.

Song H et al^[1] and Camporro et al^[2] recently discovered that the ñ-sign could be a visual clue for the histopathologic diagnosis of psoriasis. Song H et al^[1] (n=100) concluded that only ñ-sign present in 79 (79.0%) cases, ñ-sign + hypogranulosis in 72 (72.0%) cases, ñ-sign + neutrophilic infiltration in 74 (74.0%) cases and ñ-sign + hypogranulosis and neutrophilic infiltration seen in 67 (67.0%) cases which is concordant with our study. Camporro et al^[2] (n=67) concluded that ñ-sign is present in 54 (80.6%) cases. (Table: 4)

Parameters	Song H et al ^[1] n=100	Camporro et al. ^[2] n=67	Present study n=33
ñ-sign	79 (79.0%)	54 (80.6%)	4 (12.10%)
ñ-sign + hypogranulosis	72 (72.0%)	-	6 (18.20%)
ñ-sign + neutrophilic infiltration	74 (74.0%)	-	7 (21.20%)
ñ-sign + hypogranulosis and neutrophilic infiltration	67 (67.0%)	-	14 (42.40%)

Table 4: Others Study Showing Ñ-Sign In Psoriasis

COLOUR PICTURES:



Figure 5: (H&E-400X) Parakeratosis, hyperkeratosis, clubbing of rete ridges, regular acanthosis and suprapapillary thinning.



Figure 6: (H&E x 100) ñ-sign in psoriasis



Figure 7: (H&E x 100) ñ-sign with hypogranulosis

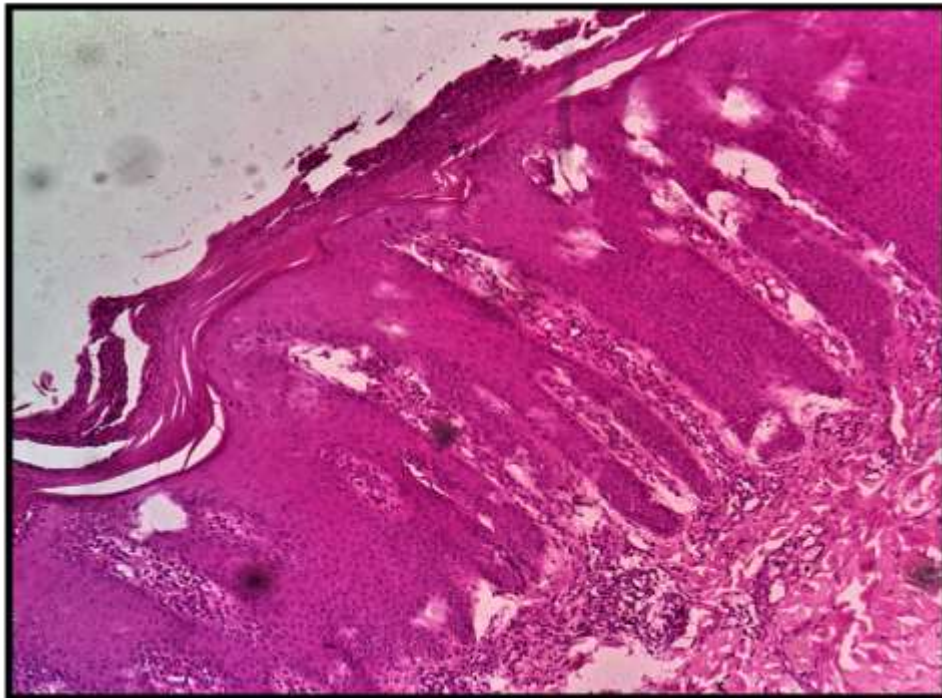


Figure 8: (H&E x 100) ñ-sign with hypogranulosis & neutrophilic infiltration

CONCLUSION:

The ñ-sign could be a useful visual clue for pathologists and dermatologist to distinguish between psoriasis and other inflammatory skin disorders. Recognizing histopathological patterns could be the first step in narrowing differential diagnosis. However, a definitive diagnosis requires further correlation to prove the ñ-sign in psoriasis

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