Suprabasal Mitotic Index: A Cell Kinetic Aid in Psoriasis Diagnosis

Susan Maria Mendonca, Sumanth Devaraju

Department of Pathology, Kanachur Institute of Medical Sciences, Derlakatte, †Department of Pathology, Father Muller Medical College, Mangalore, Karnataka, India

Abstract

Background: Psoriatic cell kinetic studies attribute psoriatic hyperplasia to increased germinative cell layer and increased mitotic rate causing rapid cell turnover, resulting in suprabasal mitotic activity. The significant Ki-67 and p53 positivity in psoriatic suprabasal layers as opposed to basal layers in normal skin corroborates this finding. Morphology holds importance in differentiating psoriasis among plaque forming lesions as they clinically mimic each other. In this study, the significance of morphologically derived suprabasal mitotic index was evaluated in the diagnosis of psoriatic lesions. Methods: H and E stained paraffin sections of histopathology confirmed cases of psoriasis and its variants \( n = 52 \) were retrieved from archives and studied. For comparison, control group \( n = 30 \) comprising normal skin and other plaque lesions was used. Suprabasal mitoses/100 basal keratinocytes were calculated in both groups and evaluated using Student’s t-test and receiver operator characteristics. Results: The suprabasal mitotic index was significantly higher in psoriatic lesions as compared to controls \( (P < 0.001) \) with lower counts in palmoplantar psoriasis \( n = 14 \). The cutoff of suprabasal mitoses for non-palmoplantar psoriasis was 1/100 keratinocytes with sensitivity, specificity, positive, and negative predictive value of 94.9%, 86.7%, 90.2%, and 92.9%, respectively. The diagnostic accuracy was 91.3%. Palmoplantar psoriasis had comparatively lower values and a diagnostic accuracy of 70.45%. Conclusion: The morphological evaluation of suprabasal mitoses is a reliable and cost-effective cell kinetic tool in diagnosing psoriasis and its variants. This will aid in the differential diagnosis of plaque forming lesions.

Keywords: Palmoplantar, plaque lesions, psoriasis, psoriatic cell kinetics, suprabasal mitoses

Introduction

Psoriasis is a genetically determined, chronic inflammatory, and proliferative disease of the skin that is commonly known to relapse.\(^1\) Psoriasis is characterized by hyperplasia with increased cell turnover.\(^1‑3\) Studies have shown that psoriatic epidermis replaces itself 6-7 times faster than normal skin. Hyperplasia is attributed to increase in germinative cell layer and increased mitotic rate.\(^4\) Histopathological diagnosis can be difficult when psoriatic variants and other plaque lesions are to be differentiated.\(^5\) Ki-67 and p53 studies on psoriatic epidermis have shown that positive keratinocytes were distributed throughout the epidermis as compared to the normal skin where only basal layer showed positivity.\(^5,6\) Suprabasal mitosis is a known morphological feature of psoriasis.\(^1‑2\) The aim of this study is to assess the suprabasal mitotic count and to find its significance as a diagnostic tool in psoriatic skin biopsies.

Methods

Histopathologically diagnosed cases of psoriasis \( n = 52 \) with clinical treatment response correlation were included in the study group, taking note of lesion site. Care was exercised to exclude patients with prior treatment history. Palmoplantar psoriasis cases were chosen based on site and clinical features (well demarcated palmar and/or plantar plaques characterized by erythema and desquamation. Deep, red plaques with adherent and silvery white scales that tend to remain stable for months were the gold standard for the clinical diagnosis of psoriasis.)\(^7‑9\) as well as response to treatment biology. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

How to cite this article: Mendonca SM, Devaraju S. Suprabasal mitotic index: A cell kinetic aid in psoriasis diagnosis. Indian J Dermatopathol Diagn Dermatol 2017;4:2-7.
on follow-up. Hematoxylin and Eosin stained 3-4 u thick paraffin sections were retrieved from archives. Thirty controls were taken comprising normal skin and other plaque forming lesions. Dysplastic/neoplastic skin lesions were excluded from the control group. Two pathologists, who were blinded to clinical history, performed mitotic counting individually. The basal keratinocyte count was estimated by counting basal keratinocytes per high power field and multiplying by the number of high power fields covering the length of the lesion. The suprabasal mitoses were counted for the entire length of lesion. The number of suprabasal mitoses/100 basal keratinocytes was calculated to get suprabasal mitotic index. The same method was used for assessing mitoses in control slides. The average was taken after counting by both pathologists on Penta-Head. The significance of the data was assessed statistically by Student’s t-test, and receiver operator characteristics were used to arrive at a significant cutoff for suprabasal mitotic index.

**Results**

The age group of our patients ranged from 17 to 72 years [Table 1] and included 27 males and 25 females [Table 2]. Psoriasis group [Figures 1-3] comprised 38 cases [Tables 3 and 4] while palmoplantar psoriasis group [Figures 4 and 5] comprised 14 cases [Tables 3 and 5]. Control group comprised thirty cases [Table 6].

The mean value of suprabasal mitoses/100 high power field was 2.86 for psoriasis and 0.47 for controls [Figure 6]. The significant P value as obtained by Student’s t-test was <0.001. Suprabasal mitoses in psoriasis were significantly higher compared to controls. Using receiver operator curve, the cut-off of suprabasal mitoses for psoriasis was calculated to be 1/100 keratinocytes. The sensitivity of this value was 94.9%, and specificity was 86.7%. The positive predictive value was 90.2%, and negative predictive value was 92.9%. The diagnostic accuracy was found to be 91.3% [Table 7].

| Table 1: Age distribution |
|---------------------------|
| Age distribution (years)  |
| 17-72                     |

| Table 2: Sex distribution |
|---------------------------|
| Sex distribution          | Number of Patients |
| Males                     | 27                |
| Females                   | 25                |

| Table 3: Case distribution |
|-----------------------------|
| Case distribution           | Number of cases |
| Psoriasis                   | 38               |
| Palmoplantar psoriasis      | 14               |
The diagnostic accuracy was found to be 70.45%. Hence, palmodplantar psoriasis cutoff was not as good as psoriasis. The morphological evaluation has been the most dependable tool in the diagnosis of skin lesions as they have varied reaction patterns. The psoriatic lesions are no exception with biopsy examination being the mainstay in confirming the diagnosis. The other plaque forming lesions can mimic psoriasis clinically. Hence, histopathological correlation is confirmatory.

Dilated blood vessels, regular epidermal hyperplasia, presence of Munro’s microabscess and/or spongiform pustule of Kogoj have been described to be characteristic features to diagnose psoriasis. However, the presence of marked spongiosis, focal acantholysis, broad globular thickened and confluent rete ridges, blood and fibrin in corneal layer rises diagnostic dilemma.

The psoriatic skin shows a definite transit time of 7 days as compared to 53 days of normal squamous epithelium from basal layer to uppermost layer. The major pathologies in psoriasis are epidermal hyperproliferation with abnormal differentiation and inflammatory infiltration of epidermis and dermis.

The latter pathology correlates with Munro’s microabscess and spongiform pustule of Kogoj, significant diagnostic morphological findings in psoriasis. The former pathology

Table 4: Psoriasis case details

| Age | Sex | Site         | Diagnosis       | Mitotic count | Cells/HPF | Cells counted | Mitotic count/100 cells |
|-----|-----|--------------|-----------------|---------------|-----------|---------------|-------------------------|
| 25  | M   | Chest        | Psoriasis       | 24            | 150       | 1800          | 1.3                    |
| 21  | F   | Elbow        | Psoriasis       | 18            | 120       | 2000          | 0.9                    |
| 38  | M   | Arm          | Psoriasis       | 18            | 120       | 2000          | 0.9                    |
| 46  | M   | Forearm      | Psoriasis       | 46            | 130       | 2200          | 2.09                   |
| 19  | M   | Back         | Psoriasis       | 13            | 70        | 700           | 1.85                   |
| 25  | F   | Leg          | Psoriasis       | 25            | 60        | 700           | 3.5                    |
| 61  | M   | Leg          | Psoriasis       | 25            | 75        | 1000          | 2.5                    |
| 42  | M   | Leg          | Psoriasis       | 21            | 40        | 600           | 3.5                    |
| 61  | M   | Leg          | Psoriasis       | 12            | 60        | 500           | 2.4                    |
| 44  | M   | Leg          | Psoriasis       | 28            | 75        | 2000          | 1.4                    |
| 54  | M   | Site not specified | Psoriasis | 54          | 50        | 750          | 7.2                    |
| 47  | F   | Back         | Psoriasis       | 15            | 60        | 500           | 3                     |
| 48  | M   | Chest        | Psoriasis       | 69            | 50        | 1000          | 6.9                    |
| 29  | F   | Site not specified | Psoriasis | 19          | 45        | 500           | 3.8                    |
| 53  | F   | Abdomen      | Psoriasis       | 12            | 50        | 700           | 1.7                    |
| 24  | M   | Back         | Psoriasis       | 42            | 45        | 900           | 4.66                   |
| 74  | M   | Forearm      | Psoriasis       | 14            | 80        | 1200          | 1.16                   |
| 40  | F   | Forearm      | Psoriasis       | 6             | 80        | 500           | 1.2                    |
| 44  | M   | Arm          | Psoriasis       | 7             | 60        | 750           | 0.9                    |
| 23  | F   | Forearm      | Psoriasis       | 29            | 110       | 1200          | 2.41                   |
| 29  | F   | Leg          | Psoriasis       | 80            | 50        | 800           | 10                    |
| 42  | M   | Forearm      | Psoriasis       | 40            | 60        | 1000          | 4                     |
| 25  | M   | Back         | Psoriasis       | 35            | 90        | 1300          | 2.69                   |
| 27  | M   | Chest        | Psoriasis       | 7             | 60        | 500           | 1.4                    |
| 48  | F   | Leg          | Psoriasis       | 50            | 60        | 1000          | 5                     |
| 42  | M   | Leg          | Psoriasis       | 16            | 50        | 800           | 2                     |
| 62  | M   | Arm          | Pustular Psoriasis | 18           | 50        | 900           | 2                     |
| 50  | F   | Abdomen      | Pustular Psoriasis | 28           | 60        | 650           | 4.3                    |
| 38  | M   | Site not specified | Psoriasis | 18          | 50        | 850           | 2.1                    |
| 67  | M   | Site not specified | Psoriasis | 18          | 100       | 1500          | 1.2                    |
| 23  | F   | Thigh        | Psoriasis       | 12            | 100       | 700           | 1.7                    |
| 19  | M   | Back         | Psoriasis       | 13            | 90        | 900           | 1.44                   |
| 20  | F   | Site not specified | Psoriasis | 9           | 50        | 500           | 1.8                    |
| 38  | M   | Leg          | Psoriasis       | 18            | 50        | 500           | 3.6                    |
| 42  | M   | Leg          | Psoriasis       | 19            | 70        | 1200          | 1.58                   |
| 50  | F   | Site not specified | Psoriasis | 13          | 70        | 500           | 2.6                    |
| 35  | F   | Elbow        | Psoriasis       | 18            | 65        | 800           | 2.25                   |
is represented morphologically by suprabasal mitosis. Although consistently mentioned in many texts, the diagnostic significance of this particular finding is not well documented in the literature. This prompted us to undertake this study on suprabasal mitosis.

Mitosis has been mainstay of evaluation of tumor pathology. It is helping pathologist to diagnose neoplasms and as a part of many grading systems (van Diest et al.)[13] Further works by Doger et al. and Baran et al. had observed by immunohistochemistry that psoriatic epidermis have Ki-67 positive keratinocytes distributed throughout the epidermis as compared to basal layer only positivity in normal skin.[4-6] Mitosis is an indicator of proliferation, and the morphological recognition of mitosis has clear-cut criteria. Hence, morphological evaluation of mitosis can very well replace ancillary studies such as immunohistochemistry and with no additional cost.

**Table 5: Palmoplantar psoriasis case details**

| Age | Sex | Site   | Diagnosis   | Mitotic count | Cells/HPF | Cells counted | Mitotic count/100 cells |
|-----|-----|--------|-------------|---------------|-----------|--------------|------------------------|
| 60  | M   | Foot   | Psoriasis   | 38            | 90        | 1900         | 2                      |
| 65  | M   | Foot   | Psoriasis   | 27            | 60        | 1400         | 1.9                    |
| 52  | F   | Foot   | Psoriasis   | 22            | 110       | 1900         | 1.1                    |
| 72  | M   | Foot   | Psoriasis   | 17            | 120       | 2000         | 0.85                   |
| 45  | F   | Hand   | Psoriasis   | 4             | 60        | 550          | 0.72                   |
| 42  | F   | Sole   | Psoriasis   | 12            | 60        | 1300         | 0.9                    |
| 49  | M   | Hand   | Psoriasis   | 8             | 100       | 1000         | 0.8                    |
| 53  | F   | Foot   | Psoriasis   | 8             | 80        | 2100         | 0.38                   |
| 44  | F   | Foot   | Psoriasis   | 9             | 70        | 1100         | 0.8                    |
| 28  | F   | Foot   | Psoriasis   | 8             | 120       | 1800         | 0.44                   |
| 52  | F   | Foot   | Psoriasis   | 2             | 80        | 500          | 0.4                    |
| 47  | M   | Foot   | Psoriasis   | 23            | 120       | 2400         | 0.95                   |
| 35  | M   | Foot   | Psoriasis   | 22            | 120       | 2300         | 0.95                   |
| 62  | F   | Hand   | Psoriasis   | 16            | 50        | 1000         | 1.6                    |

**Table 6: Control details**

| Age | Sex | Site     | Diagnosis                        | Mitotic count | Cells/HPF | Cells counted | Mitotic count/100 cells |
|-----|-----|----------|----------------------------------|---------------|-----------|--------------|------------------------|
| 29  | M   | Arm      | Chronic eczema                   | 3             | 80        | 1000         | 0.1                    |
| 52  | F   | Chest    | Normal                           | 4             | 50        | 1900         | 0.21                   |
| 20  | F   | Forearm  | Chronic eczema                   | 3             | 70        | 800          | 0.3                    |
| 23  | M   | Back     | Normal                           | 13            | 60        | 1000         | 1.3                    |
| 72  | F   | Forearm  | Lichen planus                    | 4             | 70        | 1700         | 0.23                   |
| 46  | F   | Abdomen  | Epidermal cyst                   | 2             | 40        | 1600         | 0.12                   |
| 70  | M   | Temporal area | Seborrheic Keratosis | 6             | 70        | 700          | 0.8                    |
| 54  | F   | Chest    | Normal                           | 7             | 65        | 2400         | 0.29                   |
| 60  | M   | Back     | Erythroderma secondary to chronic eczema | 7   | 70        | 1300         | 0.53                   |
| 28  | F   | Chest    | Normal                           | 3             | 70        | 1100         | 0.27                   |
| 54  | F   | Forearm  | Hypertrophic lichen planus       | 4             | 60        | 800          | 0.5                    |
| 49  | F   | Abdomen  | Morphea                          | 1             | 40        | 500          | 0.2                    |
| 50  | F   | Chest    | Epidermal cyst                   | 7             | 60        | 1800         | 0.38                   |
| 48  | F   | Chest    | Normal                           | 3             | 100       | 2800         | 0.001                  |
| 48  | F   | Dorsum hand | Lichen planus                  | 4             | 120       | 1800         | 0.002                  |
| 60  | F   | Chest    | Normal                           | 0             | 60        | 1700         | 0                     |
| 25  | F   | Axilla   | Linear epidermal nevus           | 0             | 110       | 8000         | 0                     |
| 59  | F   | Back     | Epidermal nevus                  | 6             | 80        | 2700         | 0.2                    |
| 53  | F   | Back     | Epidermal cyst                   | 3             | 45        | 500          | 0.6                    |
| 49  | F   | Leg      | Lichen planus                    | 8             | 50        | 600          | 1.33                   |
| 48  | M   | Forearm  | Midborderline leprosy            | 5             | 60        | 600          | 0.83                   |
| 48  | F   | Chest    | Normal                           | 1             | 110       | 2200         | 0.04                   |
| 60  | M   | Forearm  | Erythroderma Secondary to Air borne contact dermatitis | 10            | 80        | 1300         | 0.76                   |
| 33  | F   | Neck     | Lichen planus actinicus          | 11            | 45        | 800          | 1.3                    |
| 22  | M   | Axilla   | Striae distensae                 | 19            | 50        | 800          | 2.3                    |
| 38  | F   | Legs     | Hypertrophic lichen planus       | 9             | 80        | 1500         | 0.6                    |
| 47  | F   | Dorsum Hand | Tuberculoid leprosy            | 2             | 70        | 500          | 0.4                    |
| 13  | M   | Arm      | Lichen planus                    | 1             | 50        | 400          | 0.25                   |
| 60  | M   | Knee     | Lichen planus                    | 2             | 70        | 1000         | 0.2                    |
| 41  | M   | Forearm  | Lichen planus                    | 2             | 80        | 1500         | 0.13                   |
Studies by Ralfs et al. on pityriasis rubra pilaris cases, showed a similar rate of epidermal cell production as psoriasis. But as our controls did not comprise this disease entity, it did not affect our observations.

The psoriatic skin changes have no site specificity and show no diurnal variation. Hence, we analyzed lesion from different regions [Figure 8]. However, the consistently lower counts during evaluation in palmoplantar psoriasis prompted us to examine this particular category separately. The absence of sample from palmoplantar region in the study by Fry and McMinn substantiated our observation.

Altered keratin expression is seen in psoriatic epidermis, and changes in keratin gene expression may lead to hyperproliferative status. Thewes et al. found down-regulation of K1 and K10 and upregulation of K6 and K16 in psoriatic epidermis. Leigh IM found K16 and K17 as markers of hyperproliferation in psoriasis. According to them, K16 expression was the most sensitive indicator of psoriasis, with K17 distribution also found in suprabasal mitosis. Swensson et al. had observed specialized keratin expression pattern in human palm and sole (ridged skin) as an adaptation to high physical stress. They found K17-positive, possible stem cells sequester in deeper regions. Taking clue from this finding, the low

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**Table 7: Analytical table of psoriasis group**

| Group                  | Psoriasis |
|------------------------|-----------|
| Suprabasal mitotic index | 2.86      |
| Controls               | 0.47      |
| \( P \)                | <0.001    |
| Sensitivity (%)        | 94.9      |
| Specificity (%)        | 86.7      |
| Positive predictive value (%) | 90.2 |
| Negative predictive value (%) | 92.9 |
| Diagnostic accuracy (%)| 91.3      |

**Table 8: Analytical table of palmoplantar psoriasis group**

| Group                  | Palmoplantar psoriasis |
|------------------------|-------------------------|
| Suprabasal mitotic index | 0.96                    |
| Controls               | 0.47                    |
| \( P \)                | 0.009                   |
| Sensitivity (%)        | 92.9                    |
| Specificity (%)        | 60                      |
| Positive predictive value (%) | 52  |
| Negative predictive value (%) | 94.7 |
| Diagnostic accuracy (%)| 70.45                   |
mitotic count found in palmoplantar psoriasis in our study may be due to deep sequestration.

**CONCLUSION**

The pathogenesis of psoriasis is complex, and understanding of pathogenesis helps in identifying the morphological correlates. This in turn, helps in developing diagnostic criteria. The suprabasal mitotic index represents one such entity and increased suprabasal mitotic index will aid in the histological diagnosis of psoriasis, including palmoplantar psoriasis.

**Financial support and sponsorship**

Nil

**Conflicts of interest**

There are no conflicts of interest

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