Original Article

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Pathology Section

Immunoexpression of CD1a and Histopathology in Lesional and Non Lesional Skin in Psoriasis: A Cross-sectional Study

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ABSTRACT

Introduction: Psoriasis is a long-lasting autoimmune disease mediated by T-lymphocytes and dendritic cells. Langerhans cells are a unique population of dendritic cells found in the epidermis, where they can be identified by Cluster of Differentiation 1a (CD1a) positivity. They play an important role in the pathogenesis of psoriasis.

Aim: To evaluate the utility of immunoexpression of CD1a in the early diagnosis of psoriasis and to study the histopathology of skin biopsies from clinically diagnosed cases of psoriasis.

Materials and Methods: A cross-sectional study was conducted from September 2017 to August 2019 at Gandhi Hospital, Secunderabad, Telangana, India. Skin biopsies were taken from 50 patients with psoriasis from the Outpatient Department (OPD). Histopathological features in early psoriasis were studied, and CD1a immunoexpression in lesional, perilesional, and distant skin was analysed. The data were analysed using Student's t-test with the Statistical Package for the Social Sciences (SPSS) software.

Results: Half of the cases were found in two age groups: 51-60 years (15 patients, 30%) and 11-20 years (10 patients, 20%). The majority of the cases were males (36 patients, 72%). Most of the biopsies were taken from the lower limb (24 patients, 48%), followed by the back (13 patients, 26%). In this study, the average number of CD1a positive Langerhans cells was highest (54.92±5.26) in perilesional skin compared to lesional skin (30±3.96), which was statistically significant (p-value=0.04).

Conclusion: Based on the observations in this study, a strong positive reaction of CD1a in perilesional skin can be used to diagnose psoriasis in the early clinical stages, before full-blown clinical psoriatic plaques have appeared. Early diagnosis may prompt physicians to initiate treatment early.

Keywords: Cluster of differentiation 1a, Epidermis, Langerhans cell, Perilesional skin

INTRODUCTION

Psoriasis is a chronic, relapsing inflammatory disease that affects the skin, nails, and mucous membranes. Skin involvement is characterised by pink to red scaly papules and plaques [1]. Psoriasis vulgaris is the classic presentation, but there are multiple variants of the disease. In typical cases, a clinical diagnosis can be made without the need for a cutaneous biopsy. However, in atypical presentations, less common variants, or cases where the disease has been partially treated or altered by secondary changes, the pathologist may play a role in establishing the diagnosis of psoriasis. In these cases, the pathologic findings may be modified.

Psoriasis has now been recognised as an immune-mediated inflammatory disorder [2]. Studies have supported the concept that interactions between dendritic cells, T-cells, keratinocytes, neutrophils, and the cytokines released from immune cells contribute to the initiation and perpetuation of the cutaneous inflammation that is characteristic of psoriasis. Dendritic cells, including Langerhans cells, which are a subset of dendritic cells found in the epidermis and are characterised by CD1a expression, are involved in the pathogenesis of psoriasis [3,4]. Langerhans cells play an important role in the initial events that lead to the cytokine cascade resulting in keratinocyte proliferation and the development of psoriatic lesions [5].

The main aim of this study was to assess the immunoexpression of CD1a in lesional, perilesional, and distant skin of clinically diagnosed cases of psoriasis. Additionally, this study aimed to gain a thorough understanding of the histopathology of psoriasis in order to recognise the features of psoriasis even when they are incomplete or partially obscured, or in early stages of the disease.

MATERIALS AND METHODS

A cross-sectional study of histopathology and CD1a positivity in psoriasis was conducted from September 2017 to August 2019 for a period of 24 months in Department of Pathology, Gandhi Medical College, Secunderabad, Telangana, India. Skin biopsies were taken from 50 clinically diagnosed cases of psoriasis from the OPD, after obtaining Ethics Committee Approval (No. IEC/GMC/2017/No:180 dated: 05/08/2017).

Inclusion criteria: Clinically diagnosed cases of plaque psoriasis with no prior treatment and a duration of symptoms less than three months were included in the study.

Exclusion criteria: Patients with symptoms lasting more than three months and those who had received prior treatment were excluded from the study. Informed consent was obtained from all the patients. Clinical parameters such as age, sex, and site of involvement were recorded. Punch biopsies were taken from 50 patients with typical plaque-type psoriasis, including samples from the periphery of the psoriatic plaque (lesional skin), adjacent normal-appearing skin (perilesional skin), and 2 cm or more distant from the lesions (distant area skin).

The skin biopsies were fixed in 10% formalin and processed for embedding in liquid paraffin. Sections of 3-5 µm thickness were obtained using a rotary microtome. Two microsections were mounted on slides, one on an albumin-coated slide for Haematoxylin and Eosin (H&E) staining and the other on a Poly-L-Lysine coated slide for immunohistochemical staining. Slides for Immunohistochemistry (IHC) were subjected to antigen retrieval, washed with phosphate-buffered saline, and incubated with the primary antibody, FLEX monoclonal mouse Anti-human CD1a Clone 010, manufactured by Dako, Agilent technologies, Inc, USA. The negative control used was FLEX negative control, Mouse (code IR750).

A comprehensive analysis of the histopathological features of psoriasis and CD1a positivity in lesional, perilesional, and distant skin was performed. The CD1a-positive staining of Langerhans cell membrane was identified by the detection of brown colour, with a cytoplasmic and/or membranous staining pattern. For the counting of CD1a-positive cells, 10 high-power fields (40×) were photographed, and the cells were independently counted by two pathologists in each field. The mean values were calculated for each tissue sample. The interobserver variability was substantial (kappa value 0.75). The mean values of cells in perilesional, lesional, and distant skin for each patient were tabulated. The overall mean number of cells collectively in different types of lesions in all cases was calculated and presented as the mean cell number/square millimeter for analysis.

STATISTICAL ANALYSIS

The results were summarised and statistically analysed using student's t-test. The software used was IBM SPSS version 25. Descriptive data were presented as frequency, and percentage. Comparisons were made using Student's t-test. A p-value<0.05 was considered as statistically significant.

RESULTS

The study included patients ranging from 5-70 years old. The highest number of cases (15 patients, 30%) was found in the 51-60 years age group, followed by the 11-20 years age group (10 patients, 20%) [Table/Fig-1]. The mean age of the patients was 39.84 years. Out of the 50 cases, the majority were males (36 patients, 72%), resulting in a male to female ratio of 2.57:1. Biopsies were predominantly taken from the lower limb (24 patients, 48%), followed by the back (13 patients, 26%) [Table/Fig-2].

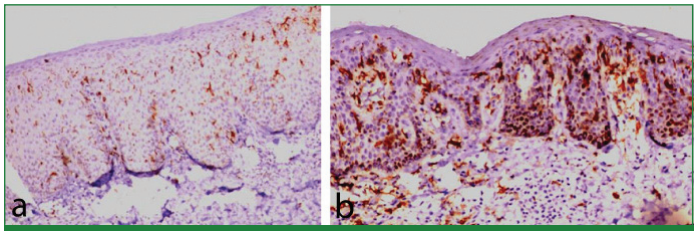
Age (years)	N (%)
1-10	2 (4)
11-20	10 (20)
21-30	5 (10)
31-40	8 (16)
41-50	5 (10)
51-60	15 (30)
>60	5 (10)
Total	50 (100)

[Table/Fig-1]: Age wise distribution of cases.

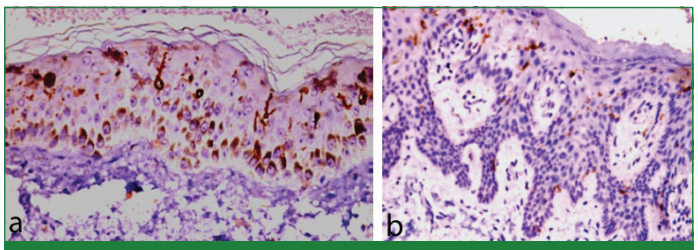
Biopsy site	N (%)
Upper limb	6 (12)
Lower limb	24 (48)
Back	13 (26)
Trunk	7 (14)
Total	50 (100)

[Table/Fig-2]: Biopsy site.

CD1a-positive staining was observed in lesional skin, perilesional skin, and distant area skin, identified by the brown colour of the CD1a Langerhans cell membrane [Table/Fig-3]. The average number of CD1a-positive Langerhans cells was highest in the perilesional area of the psoriatic plaque (54.92±5.26) and moderately increased the plaque lesion (30±3.96) [Table/Fig-4]. This difference was statistically significant (p-value=0.04) [Table/Fig-5]. Additionally, the average number of CD1a-positive cells in distant skin was significantly lower than in perilesional and lesional skin (p-value 0.03 and 0.04, respectively). Histopathological evaluation of perilesional skin showed early-stage changes [Table/Fig-6], while well-defined psoriatic plaque (lesional skin) showed advanced-stage changes [Table/Fig-7].



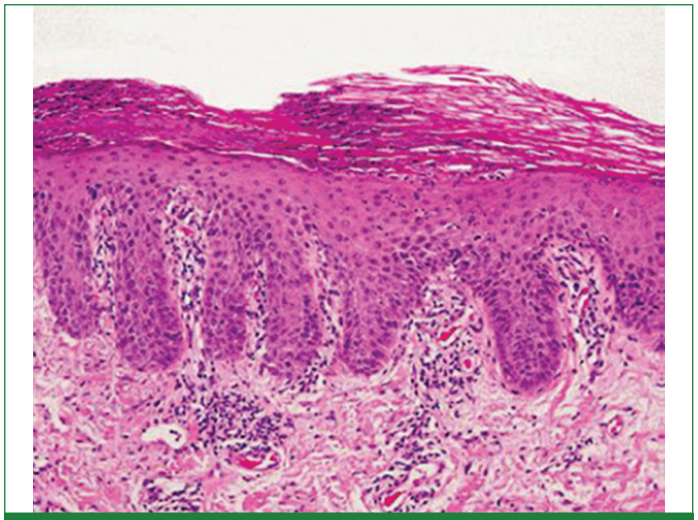
[Table/Fig-3]: CD1a positivity in (10×): a) lesional skin; b) perilesional skin (10x).



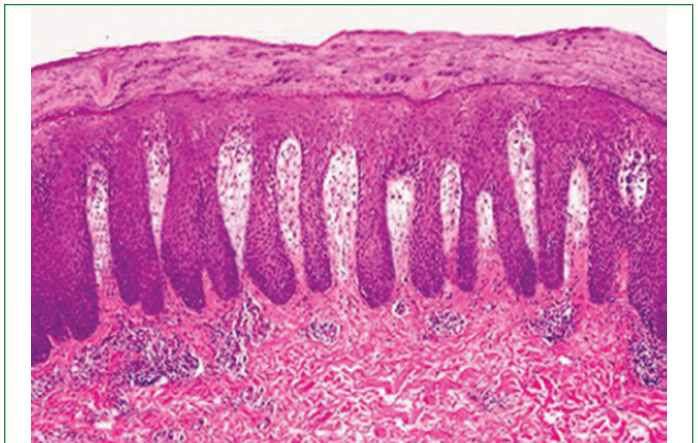
[Table/Fig-4]: High number of CD1a positive langerhans cells (40×) in (a) perilesional skin compared to (b) lesional skin.

Site of biopsy	Average no. of cells	Mean difference	p-value
Perilesional	54.92±5.26	24.92	0.04
Lesional	30±3.96		
Perilesional	54.92±5.26	44.92	0.03
Distant	10±1.26		
Lesional	30±3.96	20	0.04
Distant	10±1.26		

[Table/Fig-5]: Comparative analysis of CD1a immune expression between lesional, perilesional and distant skin.
The data was analysed with Student-t test



[Table/Fig-6]: Early Psoriasis. Mounds of parakeratosis with neutrophils, thin granular layer, moderate acanthosis, focal spongiosis, increased mitotic figures, dilated blood vessels at the tip of the dermal papillae, and perivascular infiltrate of lymphocytes and a few neutrophils (40x).



[Table/Fig-7]: Advanced Psoriasis. Markedly elongated rete ridges, absent granular layer, parakeratosis with neutrophils and dilated tortuous vessels in the dermal papillae (10x).

DISCUSSION

Psoriasis is a common papulo-squamous, immune-mediated inflammatory disorder [1]. Pathologists should be familiar with the histopathological features of psoriasis to assist clinicians in diagnosing psoriasis, even in cases with atypical lesions or in the early stages of the disease. Langerhans cells, which strongly express CD1a, play an important role in the pathogenesis of psoriasis. This study aims to gain a thorough understanding of the histopathology of psoriasis and to study the CD1a positivity of Langerhans cells in lesional, perilesional, and distant skin.

In this study, skin biopsies were taken from 50 cases of psoriasis. Out of the 50 patients, nearly half of them (25 patients, 50%) were in the 51-60 years and 11-20 years age groups. This was consistent with large population studies by Langley RG et al., and Smith AE et al., where most new cases were found in late teens to 20s and 50s to 60s [6,7]. Twelve patients (24%) were <20 years of age. The prevalence of psoriasis in children was reported as 3.8% by Seyhan M et al., [8]. However, in India, most patients present in their third or fourth decade [9-11]. This discrepancy was likely due to the fact that this study is hospital-based rather than a population study. According to Naldi L, psoriasis is slightly more prevalent among males compared to females [12]. In India, psoriasis is twice as common in males compared to females [13]. In this study, the male to female ratio was 2.57:1. Biopsies were taken from the lower limb and back in nearly three-fourths of the cases, which are common sites of initial psoriatic lesions.

A thorough histopathological evaluation of the lesional skin, perilesional skin, and distant area was conducted. The normal-appearing skin adjacent to the plaque (perilesional skin) and the earliest pinhead-sized macules or smooth-surfaced papules showed subtle histologic changes, with a preponderance of dermal changes. These changes were termed as early-stage changes. The early stage showed elongation and dilatation of blood vessels in the papillary dermis, with associated oedema and lymphocytic infiltrate (perivascular cuffing). The epidermis during this phase appeared normal [Table/Fig-6].

Typical changes at the edge of a well-defined psoriatic plaque (lesional skin) were termed as advanced stage changes. Histologically, lesional skin showed acanthosis, parakeratosis, elongation of rete ridges, suprapapillary thinning, spongiform pustules of Kogoj, absent granular layer, Munro microabscesses, elongation and oedema of the dermal papillae, and dilated and tortuous capillaries [Table/Fig-7]. These findings were consistent with various studies on the histopathology of psoriasis [14,15].

In psoriasis, T-cells, Langerhans cells, and cytokines have been suggested to play a key role in the pathogenesis of the disease [16]. Langerhans cells are antigen-presenting dendritic cells in the epidermis, and their presence is thought to be essential for the progression of psoriasis. In this study, the number of CD1a-positive Langerhans cells was highest in perilesional skin compared to lesional and distant skin. This suggests that Langerhans cells play an active role in inflammation in the perilesional epidermis and the formation of psoriatic plaques. These observations also suggest that Langerhans cells increase in number in the epidermis during the early stages of plaque formation in psoriasis.

A study by Komine M et al., also showed increased density and number of CD1a-positive cells in the epidermis of normal-appearing skin adjacent to the plaque (perilesional skin) compared to the epidermis of the skin within the plaque (lesional skin) or normal-appearing skin (distant skin) [17]. They concluded that Langerhans cells are involved in provoking epidermal inflammation in the perilesional epidermis and have a pathogenic role in the formation of psoriatic plaques.

A study by Gilleaudeau P et al., showed that CD1a-positive Langerhans cells were increased in number in psoriatic lesions compared to healthy controls and uninvolved skin of psoriatic patients, and there was no difference in numbers between the skin of healthy controls and uninvolved skin of psoriatic patients [18].

Meena N et al., concluded that CD1a cells were more concentrated in the epidermis compared to the dermis in both lesional and distant skin, as well as compared to the epidermis of healthy control skin [19]. The degree of CD1a cell infiltration was similar in the epidermis of both lesional and distant skin, which is in contrast to present study.

Alshenawy HA and Hasby EA reported that the number of positive CD1a, CD11c, and CD86 cells were increased in perilesional and psoriatic skin compared to distant skin, and they were the least in normal control skin. They concluded that dendritic cells have an important role in the initiation of the plaque in perilesional skin [20]. A study on mice by Kim JH et al., reported that treatment with blocking antibodies against CD1a alleviated skin inflammation [21]. Hardman CS et al., showed that a therapeutically targetable CD1a-dependent pathway can prevent cutaneous inflammation [22]. Based on the observations of present study, the strong positive reaction of CD1a in perilesional skin can be used to diagnose psoriasis in early clinical stages where full-blown clinical psoriatic plaques have not appeared, in atypical cases of psoriasis, less common variants of psoriasis, partially treated cases of psoriasis, or cases of psoriasis with secondary changes where a definite clinical diagnosis of psoriasis cannot be made. Early diagnosis might prompt physicians to start treatment early.

Limitation(s)

Present study had small size. There is a need for IHC staining with other markers like Langerin, CD11c, and CD86 to validate the results of this study, which were not done in this study.

CONCLUSION(S)

Skin biopsy and IHC staining are not routinely required for the diagnosis of psoriasis. However, strong CD1a positivity in perilesional skin can be used to diagnose psoriasis in atypical and early cases, prompting physicians to start treatment early.

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