

Interface dermatitis-Clinicopathologic Spectrum

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Abstract

Introduction: Interface dermatitis (ID) includes numerous skin dermatoses which have in common salient histopathological features but varied clinical presentation that have traditionally been referred to as the lichenoid tissue reaction/ID. The primary morphologic change is noted at the dermoepidermal junction with secondary subsequent changes in the epidermis. The prototypic skin disease in this category is lichen planus (LP) and its variants. Several other inflammatory, infective and neoplastic conditions may show interface change.

Aim: The present study was planned to correlate the significance of Interface dermatitis with their clinico-pathological aspects.

Methodology: The material for the present retrospective study consisted of skin biopsy samples received from the outpatient department of dermatology. The study was done for a period of six years from 2009 to 2015.

Results: In the present study, a total of 54 cases were analysed which clinically presented as papulosquamous disorders. Majority of the cases were seen in women. On histopathological diagnosis majority were LP and its variants. The most consistent histopathological feature noted was basal cell vacuolar degeneration in the epidermis along with a band of lymphocytic inflammatory infiltrate and pigment incontinence in the dermis. Clinicopathologic concordance was seen in 45 cases (83.33%) and discordance in 8 cases (14.81%).

Conclusion: Thus, combination of the histologic details, in correlation with the clinical data helps in arriving at a specific diagnosis of various ID.

Keywords: Clinicopathologic correlation, Interface dermatitis, Lichenoid tissue reaction, Papulosquamous disorders.

Introduction

In dermatopathology one of the biggest challenge is to make a specific diagnosis of inflammatory skin diseases⁽¹⁾, interface dermatitis (ID) is one such disorder often presenting in dermatopathology⁽²⁾. The term interface dermatitis refers to the presence of an inflammatory infiltrate obscuring the dermo-epidermal junction⁽³⁾. The interface functions as a single anatomico-physiological unit and includes the basal layer of epidermis, the dermo-epidermal junction, the papillary dermis and the adventitial dermis around the neck cell structures. Hence, pathological alterations involving any one of the components would result in changes that can affect all components⁽⁴⁾.

The interface change is observed among a wide range of inflammatory skin diseases but with considerable overlap of histologic features.1/The histopathologic changes could include some or all of the primary and secondary changes⁽⁴⁾.

The prominent primary changes are basal cell vacuolisation, apoptotic keratinocytes and obscuring of dermo-epidermal junction by lymphocytes. The basal cell vacuolisation leads to partial or complete destruction of the basal cells. These cells can present as ballooned cells or completely be replaced by cells displaying spinous processes (squamatization). These changes finally culminate in cleft formation and subepidermal vesicles. The colloid/civatte bodies are the anucleate apoptotic keratinocytes seen as small, round, eosinophilic hyaline structures in the basal layer, upper papillary dermis & in the stratum corneum either

in single or clumps or as whorls. The interface reaction is described as obscuring the dermo-epidermal junction by ingress of inflammatory cells (lymphocytes). The density of the inflammatory infiltrate varies from pauc-inflammatory to dense band-like "lichenoid infiltrate" depending on the type and stage of ID⁽³⁾.

The subsequent secondary changes include epidermal and dermal changes⁽³⁾. Le Biot has stated that the categorisation of ID on the basis of epidermal changes ensures diagnostic consistency⁽¹⁾.

- The acute cytotoxic type (Eg: Erythema multiforme) consists of basal cell vacuolization with lymphocytic infiltration of lower epidermis and the presence of scattered individual necrotic keratinocytes. Epidermal keratinization is unaffected.
- The premature terminal differentiation type (Eg: lichen planus, DLE) displays thick granular layer, compact stratum corneum and dense lichenoid lymphocytic infiltrate. Lichen planus displays focal hypergranulosis and a thick compact orthokeratotic stratum corneum.
- Marked Irregular epidermal hyperplasia-Seen in hypertrophic LP and verrucous DLE.
- ID with psoriasiform hyperplasia type: Seen in lichen striatus (LS) and developed lesions of pityriasis lichenoides 1/ (PL).
- ID with epidermal atrophy, which represents late atrophic phase of several dermatoses Eg: Lichen sclerosis et atrophicus (LS et atrophicus)⁽⁴⁾.

The skin lesions present usually on flexor surfaces of forearms, legs, glans penis as pruritic, polygonal, violaceous, shiny, flat-topped papules of variable sizes in clusters creating a pattern resembling lichen growing on a rock⁽⁵⁾. The oral lesions present as ulcerative lesions⁽⁶⁾.

The primary pathological event is autoimmune attack by T-Cells, with cytotoxic T-lymphocytes being the cause of epidermal basal cell injury. In the lymphocytic infiltrate CD8 cells are more than CD4 cells⁽⁷⁾. Thus, perforin and granzyme expressing CD8 cells in both cutaneous and oral LP have been suggested to play a primary role in keratinocyte apoptosis⁽³⁾. Increased numbers of gamma-delta T-cells are often present along the dermo-epidermal junction, which respond to a broad array of microbial pathogens including those with super-antigen properties, a clue to the possible infection-triggered etiology of LP⁽⁷⁾.

Thus, this study was undertaken with the objective of determining the histomorphological spectrum of changes in various types of ID and correlates them with the clinical features.

Methodology

A retrospective descriptive study was conducted in the pathology department of a teaching hospital from July 2009 to April 2015 after taking permission from

Institutional Ethical Committee. A total of 54 patients diagnosed as inflammatory diseases belonging to interface dermatitis were included in the study. All cases which showed interface changes secondary to infective, inflammatory or neoplastic aetiology were excluded from the present study. Four mm punch biopsy were routinely formalin-fixed and processed. The 5-micron thick sections were stained with haematoxylin and eosin. All the slides were examined for histopathological changes. The clinico-pathological correlation for individual cases was analysed. The data was collected and tabulated in Microsoft excel sheet. The percentages were calculated for purpose of comparison. The clinical details and other investigation reports of the cases were obtained from individual case requisitions submitted to the department of pathology and medical records department.

Results

In the present study, majority of the patients presented as itchy, scaly skin lesions of papules and plaques. The lesions were commonly present in a generalised manner over extremities. One case presented as solitary eroded pus discharging lesion over the inner aspect of lower lip. Another female patient had presented as a papulosquamous vulvar lesion.

Table 1: Types of skin manifestations clinically observed

Diagnosis	Papules	Plaques	Macules	Pustules	Total
LP & Variants	16	10	-	01	27
LS et. atrophicus	06	02	-	-	08
DLE	04	02	01	-	07
LSC	02	03	01	-	06
PL	02	01	-	-	03
EM	-	01	-	01	02
Lichen striatus	01	-	-	-	01
Total	31	19	02	02	54

*LP: Lichen Planus; LSC: Lichen simplex chronicus; DLE : Discoid lupus erythematosus LS: Lichen sclerosis; PL: Pityriasislichenoides; EM : Erythema multiforme; 1/LS: Lichen striatus.

Out of 54 cases studied, the most common type (27 of 54; 50%) of ID was lichen planus (LP) and its variants (Fig. 1), followed by lichen sclerosis et atrophicus (LS et atrophicus) with 8 cases (14.8%). Discoid lupus erythematosus (DLE) (Fig. 2) constituted 7 cases (12.9%) followed by 6 cases (11.1%) of lichen simplex chronicus (LSC), and 3 cases (5.6%) of pitriyasislichenoids (PL). The lesser common type was erythema multiforme (EM) with (02 of 54; 3.8%) and a single case of lichen striatus (LS) (1.8%).

Table 2: Distribution of different types of interface dermatitis (ID)

Type of ID	No. of cases (%)
LP and its variants	27 (50.0)
LSC	08 (14.8)
DLE	07 (12.9)
LS et atrophicus	06 (11.1)
PL	03 (5.60)
EM	02 (3.80)
Lichen straitus	01 (1.80)
Total	54 (100)

*LP: Lichen Planus; LSC: Lichen simplex chronicus; DLE: Discoid lupus erthametosis LS: Lichen sclerosis; PL: Pityriasislichenoides; EM: Erythema multiforme; I/LS: Lichen striatus.

In the present study, majority of the cases presented in the age group of 31-40 years (38.9%) followed by in 21-30 years (20.4%) and 11-20 years (14.8%). Three cases (5.6%) were in the age group 1-10 years with the youngest case being a 6-year old male child. The oldest patient in our study was an 80-year female patient. (Table 3)

Among the 54 cases, 32 (59.3%) were females with an over allfemale predominance observed. The overall ratio of male to female patients in the study was 1:1.57. However, in DLE and PL more cases were seen in males, whereas, in EM the ratio was equal. (Table 4)

In our study, clinicopathologic concordance was seen in 45 cases (83.3%) and discordance in 8 cases (14.81%).

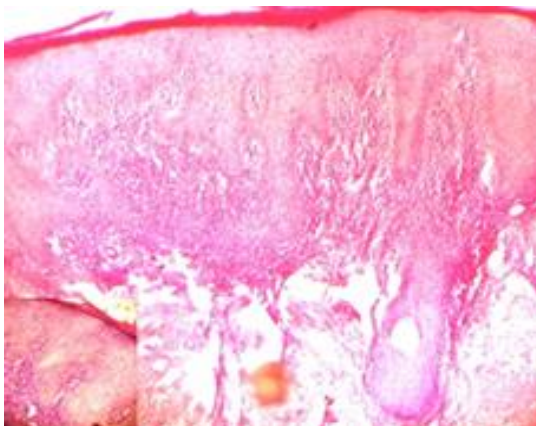


Fig. 1: Microphotograph showing lichenoid infiltrate at the dermoepidermal junction (H & E, 4x); inset; Lichenoid infiltrate (H & E, 40x)

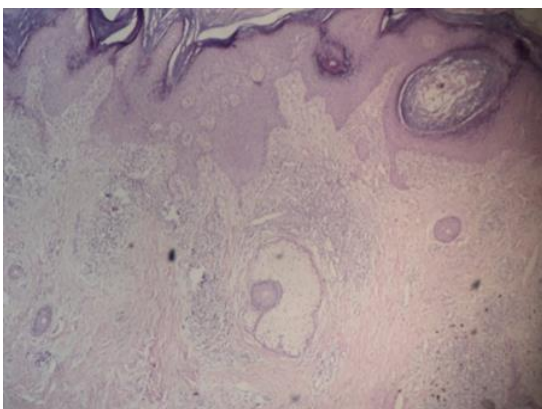


Fig. 2: Microphotograph showing follicular plugging, peri-adenexal and dermo-epidermal junction lympho-plasmacytic infiltrate in DLE (H & E, 4x)

Discussion

The lichenoid tissue reaction (as defined by Pinkus, 1973) is characterized by an epidermal basal cell morphological change that has been variously described as being "liquefactive/hydronic/vacuolar, that is, intimately associated with a massive infiltration of band-like array of mononuclear inflammatory cells in the papillary and mid dermis⁽⁷⁾. Varying elements of lichenoid histologic features are noticed in many clinically distinct dermatoses. However, there are subtle differences that define the particular variant⁽⁶⁾. As minimum criteria, a variable combination of leukocytic infiltration in the dermis, vacuolar change of the basal epidermis, accumulation of melanophages in the upper dermis and necrosis of keratinocytes has been recommended/suggested for a diagnosis of ID⁽⁸⁾.

In the present study, 54 cases of ID were analyzed along with the clinicopathologic correlation. LP and its clinical variants constituted the major (50%) proportion of cases. This was followed by cases of LSC, DLE and LS. ID can affect any age group⁽⁸⁾. In the present study, the age ranged from 6 to 71 years.1/Majority of the cases were in the age group of 31-40 years (38.9%). (Table 3) The youngest case was a six years old child of LP and the oldest patient was an 80 years female patient of LS. In the study findings of Hegde and Khadilkar, majority of the cases were in the age group of 41-50 years (23.2%)⁽⁸⁾. However, Mahesh and co-authors in their study had reported majority of cases in the younger age group (1-30 yrs.). In their study, the youngest patient was a 1-year female and the oldest was a 71-year old male⁽⁵⁾.

The overall gender distribution of cases of ID in our study showed a female preponderance with (59.3%). (Table 4) There was a male/female ratio of 1:1.57, which was comparable with the findings of Hegde and Khadilkar (1:1.3)⁽⁸⁾. Male predominance was noted in our cases of DLE & PL, while; in EM equal sex ratio was noted. In another study the authors found a male/female ratio of 0.73⁽⁵⁾.

The clinical manifestations of ID are variable⁽⁸⁾. In our study of 54 cases, the commonest clinical presentation was papules and plaques with 72.2%. Also, pruritus was the commonly reported. One female patient presented with ulcerative lesions of lower lip. In their study of 125 cases, the authors found predominant papulo-squamous lesions (97.6%)⁽⁸⁾.

In our study of 54 skin biopsy of ID cases, the most uniform and consistent histopathological changes were noted in the epidermis and was basal cell vacuolar degeneration, while in the dermis it was band of lymphocytic inflammatory infiltrate and pigment incontinence (Fig. 3, Fig. 4). Spongiosis and hyperkeratosis were the next frequent change with acanthosis and saw toothed rete in equal number of cases. (Table 5) Most of the changes were comparable

with changes observed in the study by Hegde and authors. In our study, the epidermal changes included vacuolar degeneration of basal cell layer, with hyperkeratosis, spongiosis, acanthosis & saw toothed rete ridges. Singly, scattered apoptotic colloid bodies were seen in 18 cases of ID (Fig. 5). 1/Hegde and co-authors in all their cases of ID noted liquefactive degeneration of basal cell layer⁽⁸⁾.

The primary histologic event appears to be a T-cell mediated liquefactive degeneration of the basal epidermis preceding a sequence of degenerative changes within the epidermis⁽⁸⁾.

In the present study, interface inflammation was observed in all the cases of ID. In the dermis, the inflammatory infiltrate was composed of exclusively lymphocytes in 70.3% of cases. 1/Mixed infiltrate of lymphocytes, histiocytes, plasma cells and eosinophils was noted in 21% cases. Melanin incontinence was observed in 75.9% cases. The authors in their analysis of 125 ID cases have reported a comparable finding of 71.2% of lymphocytic infiltration, while; mixed infiltrate was seen in 11.2% cases. 1/Melanin incontinence was observed in all their cases⁽⁸⁾.

Lichenoid infiltrates may be a manifestation of active viral infection, HIV-related dermatoses or with superantigen reaction, secondary syphilis or in leprosy. Also noted in early plaque stage of mycosis fungoides, urticarial pemphigoid, lichenoid purpura and neoplastic conditions like cutaneous T-cell dyscrasias and

lymphomas^(3,4). In HIV patients various inflammatory dermatoses may develop and present as itchy multifocal plaques & patchy erythematous, scaly lesions, over time becoming violaceous with pronounced hyperpigmentation with accentuation in the face and neck regions. The histopathological changes reported in viral cytopathic changes are a fairly brisk angiocentric superficial & deep lymphocytic infiltrate with minimal epidermal injury⁽³⁾. These interface changes are always secondary and do not form the part of histologic criteria of primary ID⁽⁴⁾. Thus, a correlation of interface changes with the clinical diagnosis often helps in arriving at a definitive diagnosis of the various lichenoid disorders⁽⁹⁾.

In our study, clinicopathological concordance was seen in 45 cases (83.33%) and discordance in 8 cases (14.81%). In their study, the authors Hegde and Khadilkar found a clinicopathological concordance in 109 cases (87.2%) and discordance in 16 cases (12.8%)⁽⁸⁾.

In view of the paucity of these lesions in routine histopathology practise, few studies are available in the literature. (Table 6) The treatment of this diverse group of disorders is guided by the degree of symptomatology, disability and associated systemic illness. This further accentuates the need to have set criteria to guide the histopathologist in reporting these lesions with confidence.

Table 3: Age distribution of Interface dermatitis (ID)

Diagnosis	Age groups							
	1-10	11-20	21-30	31-40	41-50	51-60	61-70	Total
LP & its variants	3	2	2	14	1	4	1	27
LSC	-	3	2	1	-	-	2	08
DLE	-	1	2	3	1	-	-	07
LS et atrophicus	-	1	3	1	-	-	1	06
PL	-	-	2	1	-	-	-	03
EM	-	-	-	1	1	-	-	02
Lichen straitus	-	1	-	-	-	-	-	01
Total	3	8	11	21	3	4	4	54

*LP: Lichen Planus; LSC: Lichen simplex chronicus; DLE: Discoid lupus erythematosus LS: Lichen sclerosis; PL: Pityriasis lichenoides; EM: Erythema multiforme; 1/LS: Lichen striatus.

Table 4: Gender distribution of ID

Diagnosis	Males	Females	Total
LP and its variants	9	18	27
LSC	2	6	8
DLE	5	2	7
LS et atrophicus	1	5	6
PL	2	1	3
EM	1	1	2
Lichen straitus	-	1	1

Total	21	34	55
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1/*LP: Lichen Planus; LSC: Lichen simplex chronicus; DLE: Discoid lupus erthametosis LS: Lichen sclerosis; PL: Pityriasislichenoides; EM: Erythema multiforme.

Table 5: Spectrum of histomorphological changes in the epidermis and dermis in various ID

Histopathological Changes	No. of Cases (n=54)
Epidermis	
Parakeratosis	14
Hyperkeratosis	39
Acanthosis	28
Atrophy	15
Spongiosis	38
Papillomatosis	06
Saw-toothed rete ridges	28
Civatte bodies	16
Liquefactive degeneration of basal layer	47
Max-Joseph space	16
Follicular plugging	09
Dermis	
Band-like configuration hugging the interface	30
Mostly lymphocyte	38
Melanin incontinence	41
Plasma cells	06
Eosinophils	04

Table 6: Comparison of various clinico-pathological features among various studies.

Sl. no	Study (year)	Predominant features				
		Age group (In Years)	Gender (%)	Diagnosis (%)	Epidermal change	Dermal Change
01	Desai SR et al (2014) ¹⁰	30-40	Not mentioned	Lichen Planus and variants (38.3%)	Basal cell changes	Inflammatory infiltrate and melanin incontinence
02	Hegde et al (2014) ⁸	41-50 (23.2%)	Female (57.6%)	Lichen planus and variants (63.2%)	Basal cell vacuolardegeneration	Inflammatory infiltrate and melanin incontinence
03	Maheswari GR et al (2016) ¹¹	10-19	Female (58.9%)	Lichen Planus	Hyperkeratosis	Inflammatory infiltrate
04	Kulkarni I/V et al (2016) ¹²	30-60 (61.6%)	Female (53.4%)	Lichen planus& variants (68.9%)	Basal cell vacuolardegeneration	Inflammatory infiltrate
05	Present study (2016)	31-40 (38.8%)	Female (59.3%)	Lichen planus and variants (50%)	Basal cell vacuolardegeneration	Inflammatory infiltrate and melanin incontinence

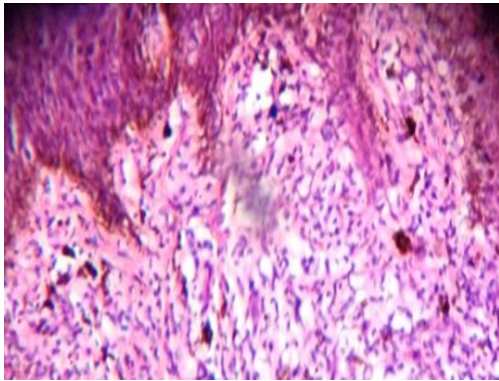


Fig. 3: microphotograph showing pigment incontinence in the dermis with focal basal cell vacuolar degeneration (H & E, 40x)

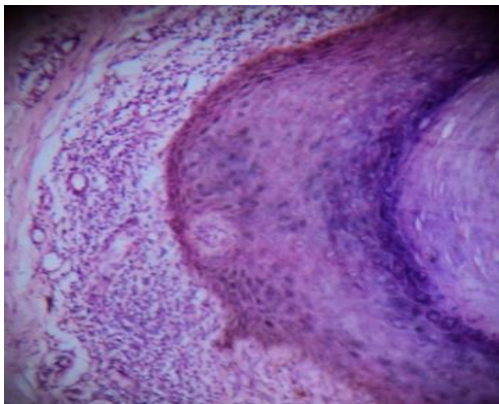


Fig. 4: Microphotograph showing acanthosis, hypergranulosis & orthokeratosis with lymphocytic infiltrate at dermo-epidermal junction in Lichen Planus (H & E, 40x)

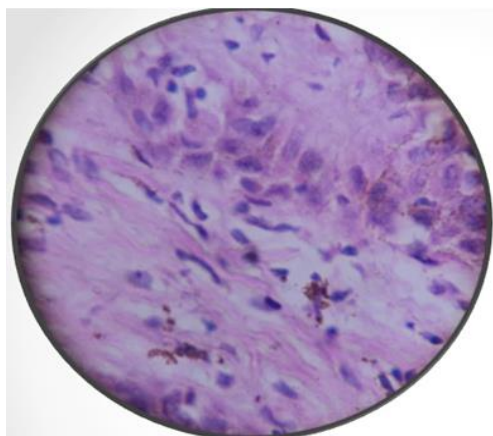


Fig. 5: Microphotograph showing scattered lymphocytes, pigment incontinence in the papillary dermis with vacuolar alteration of the basal layer & Civatte bodies (H & E, 100x)

Conclusion

ID is an exclusive clinicopathologic entity, which consists of several dermatoses of heterogenous nature. Considerable variation exists in the histologic expression of specific diseases depending on the body site sampled; adequacy of the sample and the most important stage of evolution of the lesion should be sampled. So, a close cooperation of histopathologist and dermatologist becomes necessary for precise diagnosis of various lichenoid disorders.

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