Clinical profile and Histopathological spectrum of Interface Dermatitis

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ABSTRACT

Background: Interface Dermatitis is an etiologically diverse and poorly understood group of skin diseases characterized by pathology at the dermo-epidermal junction. The prototype disease is Lichen Planus but there are many other disease entities that exhibit Lichenoid tissue reaction / Interface changes.

Aims: To study the clinical profile and Histopathological spectrum of Interface Dermatitis.

Materials & Methods: This was a prospective study conducted at a tertiary care hospital over a period of eighteen months. A total of Ninety-eight cases clinically suggestive of diseases believed to show interface changes on histology were studied. Clinical details were recorded. Skin biopsies were taken from representative lesions. H&E stained sections were studied in detail for diagnosis and subtyping. Analysis was done in percentages and proportions.

Results: Fifty-three cases (54%) showed IFD on histopathological examination. The most common age range was between 11-40 years and both the sexes were equally affected. Majority of the cases clinically presented as papules and plaques. The most common type of IFD were LP and its variants (52.1%). The most consistent microscopic findings were vacuolar degeneration of basal layer, pigment incontinence and inflammatory infiltrate around DEJ and blood vessels.

Conclusions: IFD includes various diseases which have overlapping clinical as well as histopathological features. A detailed histopathological examination and correlation of the interface changes with clinical diagnosis is helpful in arriving at a definitive diagnosis which is essential for predicting the course of the disease and its optimal management.

Keywords: Interface Dermatitis (IFD), Dermo-epidermal junction (DEJ), Lichenoid infiltrate, Lichenoid tissue reaction (LTR).

Key Messages

The entities under Interface Dermatitis (IFD) have variable clinical pattern and distribution which makes the diagnosis difficult.

Basal cell vacuolar degeneration, leucocytic inflammatory infiltrate at DEJ, pigment incontinence and presence of melanophages are the most common histopathological findings in IFD.

A combination of proper clinical observation and histopathological study gives a conclusive diagnosis that helps in predicting the course of disease and its management.

Introduction

Interface dermatitis (IFD) comprises a group of skin diseases where primary pathology involves “interface” which includes basal layer of the epidermis, the DEJ, the papillary dermis and the adventitial dermis around the adnexal structures. The immunopathogenesis involves T-cell mediated autoimmune attack against the basal keratinocytes resulting in liquefactive degeneration of the basal layer of epidermis. It is characterized by inflammatory infiltrate (usually composed predominantly of lymphocytes) that appears to obscure the dermo-epidermal Junction (DEJ), when sections are observed at low-power examination. At times, Vacuolar interface changes may be the most prominent feature with variable inflammatory infiltrate along the DEJ depending upon the disease and stage of presentation. It has also been referred as Lichenoid Tissue reaction (LTR) by some, though IFD is still the preferred term.\[1,2,3]\]

Plaques and papules along with hyperpigmented macules and patches are the predominant clinical manifestations in IFD. The term “lichenoid” refers to shiny, flat topped, polygonal papules, variable in size and occurring in clusters creating a pattern that resembles lichen growing on a rock.\[4]\]

Although the prototypic skin disease for IFD is Lichen Planus (LP), there are many other conditions which can produce lichenoid dermatitis as a part of their histological presentation. Thus, the group of diseases included in...
IFD are Lichen Planus and its variants, Lichen Simplex Chronicus (LSC), Lichen amyloidosis (LA), Lichenoid drug eruption (LDE), Lichen Sclerosus (LSc), Lichen Sclerosus et Atrophicus (LSEA), Pityriasis Lichenoides (PL), Erythema Multiforme (EM), Lichen Striatus (LS) and Lichen Niditius (LN). They can also be seen in skin disorders associated with systemic illness like Lupus Erythematosus (LE), Dermatomyositis (DM), Polymorphic light eruption (PLE) and the skin changes of potentially fatal disorders such as Graft Versus Host Disease (GVHD), Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). [5,6]

The present study was done to distinguish and recognize the various histological patterns seen in IFD that helps in diagnosis and assessment of disease progression.

Materials & Methods
This was a prospective study done over a period of 18 months in the department of Pathology at a tertiary care hospital and Medical College in Northern India. Approval of the study was taken from the institutional ethical committee before commencing the study. A total 184 skin biopsies were received in the department during the study period. Amongst these 184 biopsies, only 98 cases that mentioned LP & its variants/LSC/LA/LDE/TEN/LSEA/PL/EM/SJS/LN/LS/LE/PLE as clinical diagnosis or one of the differential diagnosis were part of the study. History and clinical findings were recorded. Skin biopsies were taken from representative lesions after taking informed consent. Routinely processed and Haematoxylin & Eosin stained sections were subjected to detailed histopathological examination for diagnosis and subtyping. Special stains like Periodic Acid Schiff (PAS) and Congo red were used where required. Only those biopsies that exhibited interface changes seen as either vacuolar alteration of the basal layer or inflammatory infiltrate at the DEJ or both the features on histopathological examination were included. Analysis was done in percentages and proportions.

Results and observations
Of the 98 cases studied, only 53 cases were confirmed as IFD on histopathology. These cases were subjected to detailed analysis to study clinical profile and histopathological spectrum of IFD. Males and females were almost equally affected (M: F = 1:1.04). The peak incidence was seen equally in the age group of 11-20 years and 31-40 years; each comprising 10/53 cases (19%). The least number of cases were seen in the age group 71 & above (03/53; 5.5%). In the present study, papules and plaques were the dominant lesions followed by macules and pustules. Hyperpigmented macules were common in patients with LP pigmentosus. Waxy papules were seen in LA. Plaques in sun exposed areas were mostly seen in DLE. Pustules were seen in cases of EM, SJS and bullous SLE. The most common site was lower limbs followed by upper limbs and truncal region. Oral and genital region were the least affected areas.

Comparison of the microscopic findings in the present study and the previous studies is shown in Table 2. [7,8,9]

The cases were also categorised according to different classifications proposed by various authors. [10,11] On the basis of intensity of inflammatory infiltrate, they were categorised into Cell Rich and Cell Poor subtype. There were 68.5% cases in Cell-rich category and 31.5% in Cell-poor category as shown in the Table 3. Based on histological changes at the interface, they were categorized as IFD with vacuolar change and IFD with lichenoid inflammation. In the present study, 31.5% of IFD cases showed vacuolar change whereas 68.5% were diagnosed as IFD with lichenoid inflammation as shown in Table 4.

Discussion
The term ‘dermatitis’ means inflammation of the skin. IFD is considered as one of the major inflammatory disorders of the skin. The histopathological findings in most of the entities include basal cell vacuolization, apoptosis of the cell with formation of colloid or Civatte bodies and inflammatory infiltrate at the DEJ. [3] The end result can just be an alteration of orderly row of basal cells and the basement membrane. The microscopic features vary in different disease entities coming under broad category of IFD. The most consistent epidermal findings in this study were hyperkeratosis (89%), hypergranulosis (90.5%), acanthosis (85%) and basal cell vacuolar degeneration (96%). Civatte bodies seen as round, eosinophilic bodies in the lower epidermis and papillary dermis were present in 43.3% of cases. The frequent dermal changes were inflammatory infiltrate at the DEJ (98.1%) and around blood vessels (96%). The infiltrate was predominantly of lympho-mononuclear in nature (58.5%) whereas mixed inflammation was seen in 39.6% cases. Banushree et al and Kumar UM et al. had reported band-like infiltrate over DEJ (almost 100%) as the most common dermal inflammation.
Table 1: DISTRIBUTION OF CASES BASED ON HISTOPATHOLOGICAL DIAGNOSIS (n=53)

| Histopathological Diagnosis                  | Number of cases | Percentage |
|-----------------------------------------------|-----------------|------------|
| **Lichen planus and its variants**            |                 |            |
| Classical lichen planus                       | 14              | 26%        |
| Lichen planus pigmentosus                    | 03              | 5.5%       |
| Follicular lichen planus                     | 01              | 1.8%       |
| Hypertrophic lichen planus                   | 09              | 17%        |
| Oral lichen planus                           | 01              | 1.8%       |
| **Total**                                     | **28**          | **52.1%**  |
| **Lichenoid eruption**                       |                 |            |
| Discoid Lupus erythematosus (DLE)             | 06              | 11.3%      |
| Systemic Lupus erythematosus (SLE)           | 01              | 1.8%       |
| Lichen sclerosus et atrophicus (LSEA)        | 01              | 1.8%       |
| Erythema multiforme (EM)                     | 01              | 1.8%       |
| Lichen nitisus (LN)                          | 01              | 1.8%       |
| Lichen striatus (LS)                         | 01              | 1.8%       |
| Pityriasis lichenoides chronica (PLC)        | 03              | 5.5%       |
| Lichen amyloidosis (LA)                      | 01              | 1.8%       |
| Polymorphic light eruption (PLE)             | 01              | 1.8%       |
| Lichen simplex chronicus (LSC)               | 07              | 13.1%      |
| Steven Johnson syndrome (SJS)                | 01              | 1.8%       |
| Erythroderma                                  | 01              | 1.8%       |
| **TOTAL**                                     | **53**          | **100%**   |

Table 2: MICROSCOPIC FINDINGS AND COMPARISON WITH PREVIOUS STUDIES

| Microscopic Features                           | Present study (n=53) | Chauhan R et al. | Banushree CS et al. | Kumar UM et al. |
|------------------------------------------------|----------------------|------------------|---------------------|-----------------|
| **EPIERMIS**                                   |                      |                  |                     |                 |
| Hyperkeratosis                                 | 89%                  | 71.21%           | 80%                 | 93.3%           |
| Parakeratosis                                  | 53%                  | 16.6%            | 5%                  | 6.6%            |
| Follicular Plugging                            | 45.3%                | 7.57%            | 5%                  | 13.3%           |
| Acanthosis                                     | 85%                  | 60.6%            | 73.3%               | 83.3%           |
| Atrophy                                        | 9.5%                 | 21.2%            | 8.3%                | 15.5%           |
| Spongiosis                                     | 58.5%                | 9.09%            | 70%                 | 67.7%           |
| Hypergranulosis                                | 90.5%                | 65.1%            |                     |                 |
| Vacuolar Basal cell Degeneration               | 96%                  | 74.2%            | 83%                 | 96.6%           |
| Civatte Bodies                                 | 43.3%                | 25.7%            | 80%                 | 21.1%           |
| Papillomatosis                                 | 41.5%                | 3.03%            | 16.6%               | 24.4%           |
| Elongated Rete Ridges                          | 62%                  | 6.06%            | 33.3%               | 60%             |
| Max –Joseph spaces                             | 36%                  | 3.03%            | 13.3%               | 10%             |
| Melanophages                                   | 83%                  | 24.2%            |                     |                 |
| Pigment Incontinence                           | 83%                  | 63.6%            | 93%                 | 93.3%           |
| **DERMIS**                                     |                      |                  |                     |                 |
| Band like infiltrate                            | 38%                  | 48.4%            | 96.6%               | 93.3%           |
| Infiltrate around – DEJ                        | 98.1%                |                  |                     |                 |
| • Mostly lymphomononuclear infiltrate          | 58.5%                | 72.7%            | 100%                | 100%            |
| • Mixed inflammatory infiltrate                | 39.6%                | 27.2%            |                     |                 |
| Perivascular inflammatory infiltrate           | 96%                  | 60.6%            |                     |                 |
| Periadnexal inflammatory infiltrate            | 34%                  | 36.3%            |                     |                 |
Table 3: CLASSIFICATION OF LTR/IFD BASED ON THE INTENSITY OF INFLAMMATORY INFILTRATE (n=53)

| Cell-rich LTR/IFD                  | No. of cases | Percentage |
|------------------------------------|--------------|------------|
| Lichen planus (LP)                 | 15           | 29%        |
| Lichen striatus (LS)               | 01           | 1.8%       |
| Lichen planus pigmentosus          | 03           | 5.5%       |
| Lichen nitidus (LN)                | 01           | 1.8%       |
| Discoid lupus erythematosus (DLE)  | 06           | 11.4%      |
| Hypertrophic lichen planus         | 09           | 17.2%      |
| Lichen amyloidosis (LA)            | 01           | 1.8%       |
| **Total**                          | **36**       | **68.5%**  |

| Cell- poor LTR/IFD                 | No. of cases | Percentage |
|------------------------------------|--------------|------------|
| Lichen sclerosus et atrophicus (LSEA) | 01         | 1.8%       |
| Erythema multiforme (EM)           | 01           | 1.8%       |
| Pityriasis lichenoides chronica (PLC) | 03         | 5.5%       |
| Lichen planopilaris                | 01           | 1.8%       |
| Systemic lupus erythematosus (SLE) | 01           | 1.8%       |
| Steven Johnson syndrome (SJS)      | 01           | 1.8%       |
| Polymorphic light eruption (PLE)   | 01           | 1.8%       |
| Erythroderma                       | 01           | 1.8%       |
| Lichen simplex chronicus (LSC)     | 07           | 13.4%      |
| **Total**                          | **17**       | **31.5%**  |

Table 4: CLASSIFICATION OF LTR/IFD BASED ON THE PREDOMINANT HISTOLOGICAL FEATURES (n=53)

| Prominent lichenoid infiltrate     | No. of cases | Percentage (%) |
|------------------------------------|--------------|----------------|
| Lichen planus (LP)                 | 15           | 29%            |
| Lichen striatus (LS)               | 01           | 1.8%           |
| Lichen planus pigmentosus          | 03           | 5.5%           |
| Lichen nitidus (LN)                | 01           | 1.8%           |
| Discoid lupus erythematosus (DLE)  | 06           | 11.4%          |
| Hypertrophic lichen planus         | 09           | 17.2%          |
| Lichen amyloidosis (LA)            | 01           | 1.8%           |
| **Total**                          | **36**       | **68.5%**      |

| Prominent basal cell vacuolization  | No. of cases | Percentage (%) |
|-------------------------------------|--------------|----------------|
| Lichen sclerosus et atrophicus (LSEA) | 01        | 1.8%           |
| Erythema multiforme (EM)            | 01           | 1.8%           |
| Pityriasis lichenoides chronica (PLC) | 03         | 5.5%           |
| Systemic lupus erythematosus (SLE)  | 01           | 1.8%           |
| Lichen planopilaris                 | 01           | 1.8%           |
| Polymorphic light eruption (PLE)    | 01           | 1.8%           |
| Steven Johnson syndrome (SJS)       | 01           | 1.8%           |
| Erythroderma                        | 01           | 1.8%           |
| Lichen simplex chronicus (LSC)      | 07           | 13.4%          |
| **Total**                           | **17**       | **31.5%**      |
Fig. 1a & 1b - Photomicrograph shows features of classical Lichen Planus seen as basal vacuolar degeneration, Lymphomononuclear infiltrate at DEJ, Civatte bodies (arrowhead) (Fig 1a- H & E, 100X & Fig 1b- H & E, 400X).

Fig. 2. Photomicrograph shows features of Lichen Planus Hypertrophicus (H & E, 100X).

Fig. 3a & 3b- Photomicrograph shows hyperkeratosis with follicular plugging, hydropic basal layer degeneration, inflammatory infiltrate at DEJ (fig 3a- H & E, 100X) and extension of inflammatory infiltrate in the deeper dermis in a case of Discoid Lupus Erythematosus (fig 3b- H & E, 100X).

Fig. 4; Photomicrograph shows features of Lichen Nitidus (H & E, 100X).

Fig. 5: Photomicrograph shows features of Erythema Multiforme (H & E, 100X).
findings.\cite{8,9} However, in the present study band like infiltrate was seen in only 38% cases. In an attempt to analyse this, it was found that band like infiltrate at DEJ was a common finding in classical LP (78.5%). There may be an element of selection bias in the present study as all the cases clinically presenting as Classical LP were not subjected to biopsy by clinician, instead most of the cases with differential diagnosis or where there was diagnostic difficulty were biopsied to achieve the final diagnosis. This could also be one of the reasons behind the differences between the microscopic features in the present study and the previous two studies (Table 2).\cite{8,9} Other dermal findings included pigment incontinence and melanophages in 83% of all cases which was analogous to the findings of Hegde et al.\cite{11} Whereas few studies have reported a much higher percentage of cases exhibiting pigment incontinence.\cite{8,9}

The microscopic features of classical LP in the present study as well as few previous studies include hyperkeratosis, hypergranulosis, elongation of the rete ridges, liquefactive degeneration of basal cells and a band like subepidermal lymphocytic infiltrate that invaded the lower layers of the epidermis (Figure 1a and 1b).\cite{12,13} Other dermal findings included acanthosis, basal cell hydropic degeneration and focal dermal dense infiltrate at the DEJ and thickening of the basement membrane zone (confirmed by PAS staining). In addition, there was mild atrophy and fibrinoid necrosis in the epidermis. This was in agreement with the findings of Alahlafi et al.\cite{16}

Lichen Striatus and Lichen Nitidus was seen in first and second decade of life respectively. In LN the most striking histopathological feature observed was dense lichenoid infiltrate immediately subjacent to the epidermis producing a “claw clutching a ball” appearance as reported in the literature (Figure 4).\cite{15} Lichen Striatus case demonstrated hyperkeratosis, parakeratosis with a few necrotic keratinocytes in the epidermis, vacuolar basal cell degeneration and focal dermal dense infiltrate predominantly lymphomononuclear especially at the DEJ.

LA presented as waxy papules on the extensor aspects of lower extremities in a 52 year old male. Histological features included acanthosis, basal cell hydropic degeneration and presence of small eosinophilic amorphous densities in papillary dermis alongwith mild chronic inflammatory cell infiltrate and pigment incontinence. Amyloid deposits were demonstrated using Congo red and Crystal Violet stains.

The patients diagnosed as EM and SJS presented as bullous lesion which was a typical feature as reported by Weyers et al.\cite{17} The histological findings of EM were lymphocytic infiltrate at the DEJ with exocytosis into the epidermis, scattered necrotic keratinocytes, spongiosis, vacuolar...
The histologic findings were,

conclusive diagnosis of IFD which is necessary for optimal clinical observation and histopathological study gives a disease entity included under IFD. Thus, a combination of histological features are specific and characteristic for each must be present to categorise it as IFD. However, many vacuolar degeneration, inflammatory infiltrate at DEJ, diagnosis difficult. A variable combination of basal cell and distribution of IFD which often makes the clinical pattern

Conclusion

In the present study, one case each of Erythroderma and Polymorphous Light Eruption were also diagnosed. Histologically, they exhibited nonspecific features like hyperkeratosis, epidermal atrophy with flattening of the rete ridges, vacuolar interface changes, loss of elastic fibers, hyalinization of the lamina propria and an underlying lymphocytic infiltrate (Figure 6). Carlson et al. have rather reported variable histological changes like spongiosis, marked lymphocyte exocytosis, dermal infiltration by eosinophils in association with frequent absence of atrophy.[19]

In the present study, one case each of Erythroderma and Polymorphous Light Eruption were also diagnosed. Histologically, they exhibited nonspecific features like hyperkeratosis, epidermal atrophy with flattening of the rete ridges, vacuolar interface changes, loss of elastic fibers, hyalinization of the lamina propria and an underlying lymphocytic infiltrate (Figure 6). Carlson et al. have rather reported variable histological changes like spongiosis, marked lymphocyte exocytosis, dermal infiltration by eosinophils in association with frequent absence of atrophy.[19]

The broad categorization of all the IFD diagnosed cases into Cell Rich /Cell Poor subtype or categorization into IFD with vacuolar change/ IFD with lichenoid inflammation based on interface changes yielded similar results. This broad categorisation can be helpful in narrowing down the diagnosis and in assessing the severity of the disease. Moreover, it can also be of use when a definitive diagnosis cannot be rendered and on the basis of broad categorisation alone the clinician treats the patient. But, this fact still needs to be evaluated by another clinicopathological study in future as the treatment and prognosis differs widely in different diseases of the two broad groups.

Conclusion

There is considerable overlap in the clinical pattern and distribution of IFD which often makes the clinical diagnosis difficult. A variable combination of basal cell vacuolar degeneration, inflammatory infiltrate at DEJ, pigment incontinence and presence of melanophages must be present to categorise it as IFD. However, many histological features are specific and characteristic for each disease entity included under IFD. Thus, a combination of clinical observation and histopathological study gives a conclusive diagnosis of IFD which is necessary for optimal management of the patient.

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