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Histopathological Spectrum of Interface Dermatitis in a Tertiary Care Center

Jwalanta Poudel [1*], Abhimanyu Jha [2], Usha Manandhar [3], Upama Paudel [4], Uma Bhatta [5]
[1] Consultant Pathologist, Department of Pathology, Bir Hospital, Kathmandu, Nepal
[2] Professor, Department of Pathology, Institute of Medicine, T.U.T.H, Kathmandu, Nepal
[3] Lecturer, Department of Pathology, Institute of Medicine, T.U.T.H, Kathmandu, Nepal
[4] Associate Professor, Department of Dermatology, Institute of Medicine, T.U.T.H, Kathmandu, Nepal
[5] PGY-1, Department of Pathology and Laboratory Medicine, University of Tennessee Health Science Center, Memphis, Tennessee

* Corresponding Author: **Jwalanta Poudel**

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Abstract
Background: Interface dermatitis (ID) is a histomorphological tissue reaction pattern that involves dermoepidermal junction of skin. Varieties of cutaneous lesions fall under primary ID which has to be differentiated from secondary ID.
Aim: This study was undertaken to evaluate the histopathological spectrum of ID and compare them in relation to age, sex and anatomical site along with clinicopathological correlation.
Material and method: This is a one year prospective cross sectional study done at Department of Pathology of Tribhuvan University Teaching Hospital, which included 69 cases of skin biopsies with histological features of ID.
Results: Out of 650 skin biopsies, 69 cases were diagnosed as primary ID. Most common age of presentation was 21-40 years. Male to female ratio was 1:1.5. Lichen planus and variants were the commonest ID (63.8%) with widest anatomical distribution, followed by discoid lupus erythematosus (15.9%) and pityriasis lichenoides chronica (8.7%). The most consistent histopathological findings of IDs were basal layer vacuolation and interface inflammation. Clinicopathological concordance was seen in 79.7% of cases.
Conclusion: Distinctive histopathological features of basal layer vacuolation and interface inflammation involving dermoepidermal junction were valuable in arriving at diagnosis of various lesions of interface dermatitis. However, histopathological categorization of ID should be done in a clinical context because of overlapping clinical and histological features and for guiding appropriate therapy.

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1. Introduction

There are various tissue reaction pattern that characterizes inflammatory dermatosis, namely lichenoid (interface), spongiotic, vesiculobullous, granulomatous and vasculopathic reaction pattern [1]. Interface dermatitis is the characteristic histomorphological tissue reaction pattern that involves dermoepiderrmal junction.

Interface dermatitis is defined by two major inflammatory patterns that primarily involves dermo-epidermal zone [2]. First one is lichenoid dermatitis which includes superficial, dense, band-like infiltrates of lymphocytes abutting dermo-epidermal junction and obscuring the interface. The second pattern is characterized by vacuolar dermatitis which includes vacuolar degeneration of basal keratinocytes. However, there is considerable overlap between both of these patterns and damage to the basal keratinocytes and basement membrane zone is the final outcome. So, the primary changes in interface dermatitis includes: inflammatory

infiltration at dermo-epidermal junction, vacuolar changes of basal keratinocytes, apoptotic keratinocytes (Civatte or colloid bodies) and pigment incontinence [3]. Secondary changes which is seen in the epidermis and in the dermis are useful for the differential diagnosis of various disease that show interface tissue reaction. In addition, clinicopathological correlation is mandatory in histopathological evaluation of interface dermatoses which can be further emphasized by the fact that many neoplastic, infectious and other inflammatory conditions can also have secondary interface changes.

Thus, the objective of our study is to evaluate the histopathological spectrum of ID and compare them in relation to age, sex and anatomical site along with clinicopathological correlation.

2. Materials and Methods

The present study is a hospital based cross sectional prospective study done in department of pathology of Tribhuvan University Teaching Hospital. This study was conducted for a period of one year. During this period, a total of 69 cases of skin biopsies with histological features of ID were studied. Biopsy was taken in the department of dermatology of the same hospital. All biopsies were fixed in formalin and then processed in histopathology section, slides were then stained with hematoxylin and eosin and other special stains wherever required, followed by microscopic examination under the light microscopy for epidermal and dermal changes.

3. Results

In the present study, Primary interface dermatitis were seen in 69 of all skin biopsy specimens. Frequency of interface dermatitis increased with increasing age from second decade to fourth decade with maximum number of cases seen in 31-40 years of age and thereafter the frequency decreased with increasing age. (Fig. 1).

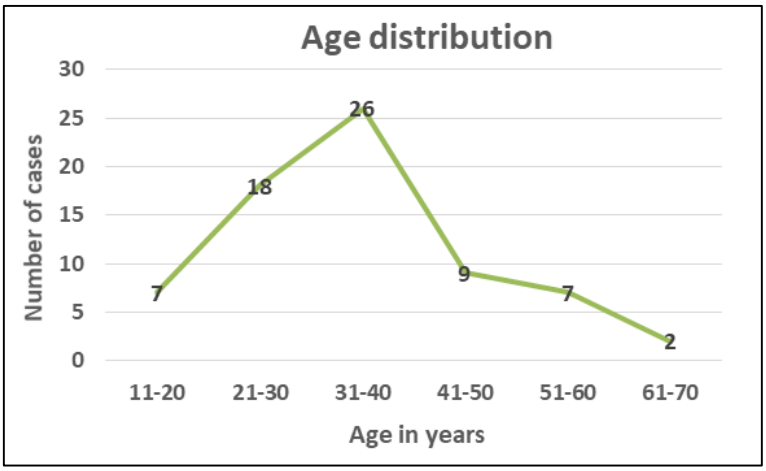

Fig 1: Age distribution of interface dermatitis

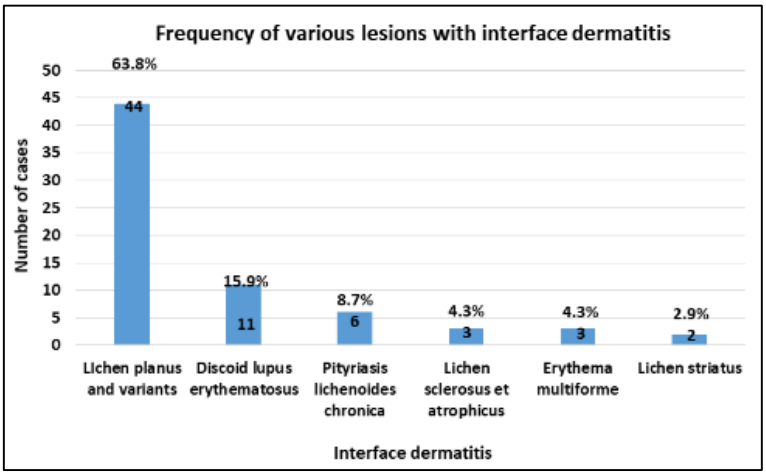

Fig 2: Frequency of various lesions with interface dermatitis

Lichen planus and variants were the most common lesion that presented as primary interface dermatitis, followed by discoid lupus erythematosus and pityriasis lichenoides chronica (Fig. 2).

Table 1: Anatomical distribution of various lesions with interface dermatitis

S.N	Anatomical Location	Number of cases of Interface dermatitis (%)						
		Lichen planus and variants	Discoid lupus erythematosus	Pityriasis lichenoides chronica	Lichen striatus	Lichen sclerosus et atrophicus	Erythema Multiforme	Total
1	Scalp	06 (13.6)	02 (18.1)	-	-	-	-	08 (11.5)

2	Oral cavity	12 (27.2)	-	-	-	-	-	12 (17.3)
3	Face	04 (9.09)	08 (72.7)	-	-	-	-	12 (17.3)
4	Neck	02 (4.54)	01 (2.27)	01 (16.6)	01 (50)	-	-	05 (7.24)
5	Trunk	05 (11.3)	-	02 (33.3)	-	-	01 (33.3)	08 (11.5)
6	Palms & soles	-	-	-	-	-	01 (33.3)	01 (1.44)
7	Nail matrix	01 (2.27)	-	-	-	-	-	01 (1.44)
8	Upper extremities	07 (15.9)	-	02 (33.3)	-	-	-	09 (13.0)
9	Lower extremities	03 (6.81)	-	01 (16.6)	01 (50)	-	01 (33.3)	06 (8.69)
10	Genitalia	04 (9.09)	-	-	-	03 (100)	-	07 (10.1)
	Total	44	11	06	02	03	03	69

Oral cavity and face were the most common sites of involvement with 12 cases each, followed by upper extremities, scalp, trunk and genitalia. Palms and soles and nail matrix were least common sites involved by interface dermatitis. (Table 1).

Lichen planus and variants showed wide anatomical distribution involving almost all the sites except palms and soles with oral cavity being the most common site. (Table 1).

Neck and lower extremities were the most common locations involved by most types of interface dermatitis. Except lichen sclerosus et atrophicus and erythema multiforme, neck was involved by all the four types of interface dermatitis. (Table 1).

Face and scalp were the most common sites involved by DLE. Similarly, trunk and upper extremities were the most common sites of involvement by PLC (Table 1).

Table 2: Age distribution of various lesions with interface dermatitis

S.N	Age (years)	Number of cases of Interface dermatitis						
		Lichen planus and variants	Discoid lupus erythematosus	Pityriasis lichenoides chronica	Lichen sclerosus et atrophicus	Erythema multiforme	Lichen striatus	Total
1	0-10	-	-	-	-	-	-	-
2	11-20	03	-	03	-	-	01	07
3	21-30	11	05	-	-	01	01	18
4	31-40	17	04	02	02	01	-	26
5	41-50	06	02	-	01	-	-	09
6	51-60	05	-	01	-	01	-	07
7	61-70	02	-	-	-	-	-	02
Total		44	11	6	3	3	2	69

Interface dermatitis involved all the age groups ranging from second to seventh decade of life with youngest being 11 years and 65 years being the oldest. Children below 10 years of age were spared (Table 2).

Lichen planus and variants showed widest age distribution involving second to seventh decade of life with peak at second to third decade of life. Maximum cases of DLE was seen in third to fourth decade of life (Table 2).

Table 3: Sex distribution of various lesions with interface dermatitis

Number of cases (%)					
S.N	Diagnosis	Male	Female	Total	
1	Lichen planus and variants	18 (41)	26 (59)	44	100%
2	Discoid lupus erythematosus	02 (18)	09 (82)	11	
3	Pityriasis lichenoides chronica	02 (33)	04 (67)	06	
4	Erythema multiforme	02 (67)	01 (33)	03	
5	Lichen sclerosus et atrophicus	01 (33)	02 (67)	03	
6	Lichen striatus	02 (100)	00 (00)	02	
Total		27 (39)	42 (61)	69	

Overall interface dermatitis showed female predominance. However, erythema multiforme was common in male and there was no cases of lichen striatus in female (Table 3).

Table 4: Histopathological spectrum of various interface dermatitis

S.N	Histopathological findings	Number of cases of interface dermatitis					
		Lichen planus and variants	Discoid lupus erythematosus	Pityriasis lichenoides chronica	Lichen sriatus	Lichen sclerosus et atrophicus	Erythema multiforme
		44 cases	11 cases	06 cases	02 cases	03 cases	03 cases
1	Parakeratosis	08	-	05	02	-	-
2	Orthokeratosis	26	02	01	-	01	01
3	Hypergranulosis	23	-	-	-	-	-
4	Atrophy	05	08	-	-	02	-
5	Papillomatosis	02	01	-	-	-	-
6	Civatte bodies	24	03	01	-	-	03
7	Acanthosis	29	01	03	02	-	-
8	Follicular plugging	02	11	-	-	-	-

9	Basal layer vacuolation	44	11	06	02	03	03
10	Interface inflammation (Dense band like)	33	01	-	02	03	03
11	Interface inflammation (Focal)	09	10	06	-	-	-
12	Pigment incontinence	23	06	02	01	01	-
13	Perivascular infiltrates	10	11	06	02	-	-
14	Basement membrane thickening	-	08	-	-	-	-
15	Dermal mucin	-	11	-	-	-	-
16	Periadnexal infiltrates	-	11	-	02	-	-
17	Spongiosis	-	-	05	02	-	03
18	Dermal sclerosis	-	-	-	-	03	-

Orthokeratosis, basal layer vacuolation, interface inflammation, Civatte bodies and pigment incontinence were the most consistent findings in lichen planus and variants, followed by hypergranulosis and acanthosis. (Table 4).

In all the cases of DLE, basal layer vacuolation, interface inflammation, follicular plugging, dermal mucin, perivascular and periadnexal infiltrates were seen. Papillomatosis, acanthosis and dense band like interface inflammation were noted in a single case (Table 4).

Basal layer vacuolation, focal interface inflammation and perivascular infiltrates were seen in all the six cases of PLC. Parakeratosis and spongiosis were seen in five of the six cases and one case showed Civatte bodies and orthokeratosis (Table 4).

Except pigment incontinence, basal layer vacuolation, interface inflammation, parakeratosis, acanthosis, spongiosis, perivascular infiltrates and periadnexal infiltrates were seen in both the cases of LS. (Table 4).

Basal layer vacuolation, dense band like interface inflammation and dermal sclerosis were seen in all the three cases of lichen sclerosus et atrophicus. Orthokeratosis and pigment incontinence were seen only in one case and atrophy was not seen in one case of LSEA. (Table 4).

Except orthokeratosis, basal layer vacuolation, dense band like interface inflammation, spongiosis and civatte bodies were seen in all the three cases of EM. (Table 4).

Table 5: Clinicopathological correlation

Correlation	Number of cases	(%)
Concordant	55	79.7
Discordant	4	5.79
Cases diagnosed only on histology	10	14.4

Cases with multiple clinical differential diagnosis were correlated with histopathological findings and if histopathological diagnosis is compatible with any one of the differential diagnosis provided was considered to be clinicopathologically concordant. Histopathological diagnosis was compatible with clinical diagnosis in 55 cases (79.7%), discordance between clinical and histopathological diagnosis was seen in four cases (5.79%). Cases diagnosed only by histological findings with no clinical information constituted 10 (14.49%) cases (Table 5).

4. Discussion

Interface dermatitis is the common tissue reaction pattern that occurs in various skin disorders characterized primarily by lichenoid and vacuolar interface dermatitis [2]. Clinically, it represents heterogeneous groups of dermatoses which can be categorized as primary interface dermatitis and includes lichen planus, lupus erythmatosus, lichenoid drug eruptions, pityriasis lichenoides, lichen sclerosus et atrophicus, fixed drug eruption, lichen striatus and lichen nitidus. There are four components of interface that includes basal layer of epidermis, dermoepidermal junction, papillary dermis in contact with basement membrane and the adventitial dermis around the adnexal structures [4]. Common histopathological changes that occurs in interface dermatitis includes basal layer vacuolation, inflammatory infiltrates obscuring dermoepidermal junction, necrotic keratinocytes and pigment incontinence [3].

In the present one year study, 69 cases of interface dermatitis were identified with six types of primary interface dermatitis namely, LP and variants, DLE, PLC, lichen sclerosus et atrophicus, erythema multiforme and lichen striatus (Fig. 2). In a study by Hegde and Khadilkar comprising 125 cases of ID, similar findings were seen, however, in their study DLE was not identified [5]. Findings similar to present study were also seen in the studies of Suguna BV and Malathi *et al*. [6, 7]. In this study, lichen planus and variants was the most common lesion (63.8%, 44 cases). This was similar to the studies by Hegde *et al* with 63.2% (79 cases) [5]. Several other studies showed lichen planus and variants being the most common lesion of interface dermatitis [4, 6, 7, 8]. In present study, LP and variants was followed by DLE (15.9%, 11 cases) and PLC (8.7%, 6 cases). Suguna BV showed similar finding with most common ID being LP and variants followed by DLE (13.3%, 12 cases) and PLC with (12.2%, 11 cases) [6]. In our study, lichen sclerosus et atrophicus and erythema multiforme each constituted three cases (4.3% each). Two cases (2.9%) of lichen striatus were also seen. Hegde *et al* noted four cases (3.2%) of erythema multiforme and two cases (1.6%) of lichen sclerosus in their study [5]. Malathi *et al* identified six cases (11%) of lichen sclerosus et atrophicus, two cases (3.8%) of erythema multiforme and one case (1.8%) of lichen straitus in their study [7].

Oral cavity (17.39%) and face (17.39%) were the most common sites involved by interface dermatitis altogether constituting 34.7% of cases followed by upper extremities (13.04%), trunk (11.5%), scalp (11.5%) and genitalia (10.1%) in our study. Among IDs, oral cavity was involved only by lichen planus and they were categorized classically under specific variant of lichen planus termed oral lichen planus. Lichen planus showed wide anatomical distribution involving almost all the sites except palms and soles (Table 1). Palmoplantar regions are the rare site of involvement.

59% cases of lichen planus and variants were seen in female in our study which is similar to finding of Parihar *et al* consisting of 54.5% of cases in female [9]. In a literature review by Boyd and Neldner, cutaneous lichen planus was seen in 55% to 65% of cases in female [10]. Majority of cases were seen in the age group of 31-40 years in this study which is same as in the study of Malathi *et al*. [7].

In this study, classical lichen planus showed basal layer vacuolation, band like dense infiltration, orthokeratosis and hypergranulosis in all the cases. Other common histological

features included acanthosis in 84.61% and Civatte bodies in 69.23% of our cases. Pigment incontinence was observed in 38.46% of our cases. In a study done by Srivani *et al*, basal layer vacuolation was seen in all of their 50 cases, Civatte bodies in 76% and acanthosis was seen in 70% of classical lichen planus in their study [11]. In a study of Parihar *et al*, orthokeratosis was seen in all the cases and hypergranulosis was observed in 96.5% of cases [9].

Out of 11 cases of DLE in this study, nine cases were seen in female. Similar findings were seen in the study of Bajaj *et al* with a female preponderance of 65.5% (n=110) [12]. In the present study, face was the most common site of involvement by DLE (73%) followed by scalp (18%) and neck (2%). Similar findings were seen in a study of Bajaj *et al*, face was the most common site affected (54.5%) followed by scalp (23.6%) and neck (9.1%). Most cases of DLE (45.5%) in our study was seen in the third decade of life (Table 2). In the study of Bajaj *et al* 44% of cases were seen in 21-30 years of age [12].

In the present study, DLE showed basal layer vacuolation, interface inflammation, follicular plugging, dermal mucin, perivascular and periadnexal infiltrates in all the cases, this was consistent with the findings described in most of the literatures [13, 14]. One of our cases showed marked acanthosis and papillomatosis which was compatible with hypertrophic variant of DLE [15, 16].

In our study, out of six cases of pityriasis lichenoides chronica (PLC), 50% cases were seen in 11-20 years of age (Table 2). In the study of Nair P involving 39 cases of PLC, 27% cases were seen in 11-20 years of age followed by 23.5% of cases in 31-40 years of age [17]. Four out of six cases of PLC in our study was seen in female. In the study of Nair P, PLC was common in male involving 54% of cases. Upper extremities and trunk were the common sites involved in PLC constituting 66.6% of our cases, similar finding was observed by Nair P with most cases involving trunk and upper extremities (37.2%) [17]. Histopathological findings of PLC showed basal layer vacuolation, focal interface inflammation with exocytosis and perivascular infiltrates in all the six of our cases. In addition parakeratosis and spongiosis were seen in five cases and acanthosis in three cases. A study done by Nair P *et al*, basal layer vacuolation and perivascular infiltrates were found in all of their 39 cases followed by spongiosis, exocytosis, acanthosis and parakeratosis [17].

We identified two cases of lichen striatus and both the cases were seen in male. Male predominance with male to female ratio of 3:1 in lichen striatus was seen in the study of Hauber *et al*. [18]. Both of our cases was seen in 11-30 years age group. Histopathology of lichen striatus showed basal layer vacuolation, dense band like interface inflammation, parakeratosis, acanthosis, spongiosis, perivascular and periadnexal infiltrates in both of our cases as mentioned in various literatures [19, 20].

In our study, three cases of lichen sclerosus et atrophicus were identified and all were seen in genitalia. Two cases were seen in female and one in male. In a study by Malathi *et al* similar finding was seen with 83.3% of cases in females [7]. In our study, all the cases of LSEA was seen in 31-50 years of age. LSEA is most frequent in genital region in both the sexes [14]. Histology of LSEA showed basal layer vacuolation, dense band like inflammation and dermal sclerosis in all the cases in our study. In a study by Carlson *et al*, all of their cases showed dermal sclerosis, vacuolar interface changes, and lymphocytic infiltration underlying the sclerosis [21].

Three cases of erythema multiforme (EM) were seen in this study and two cases were seen in male and one in female. In a study by Howland *et al* involving 42 cases of EM, 23 cases were seen in male and 19 in female [22]. In this study, one case each was seen in trunk, palm and lower extremity. Two of three cases were seen in 21-40 years of age and one case was seen in 51-60 years of age. In a study of Hegde *et al*, three out of four cases were seen in 41-50 years of age and one case in 21-30 years [5]. Histopathology of EM in all of our cases showed basal layer vacuolation, Civatte bodies, spongiosis and focal interface inflammation. Orthokeratosis was seen in one case. In a study by Suguna BV, all the four cases of EM showed hyperkeratosis, parakeratosis and basal layer vacuolation. [6].

In our study, histopathological diagnosis was compatible with clinical diagnosis in 55 cases (79.7%) and discordance between clinical and histopathological diagnosis was noted in four cases (5.7%). In a study by Pawar *et al*, clinical concordance was seen in 82.64% cases and discordance in 17.36% cases [8]. Study of Malathi *et al* showed clinicopathologic concordance in 83.33% and discordance in 14.81% of cases [7].

Cases diagnosed only by specific histological findings with no clinical information constituted 10 (14.49%) cases in our study.

5. Conclusion

Interface dermatitis was a common histological diagnosis in skin biopsies. It was seen predominantly in female and showed wide age distribution with peak at third to fourth decade of life and sparing children below 11 years of age. Lichen planus and variants constituted majority of interface dermatitis followed by DLE and PLC. Although, any anatomical sites can be involved, widest distribution was seen in lichen planus and variants. Basal layer vacuolation and interface inflammation were the most consistent histological findings. Histopathological examination combined with clinical findings is the best approach to establish the specific diagnosis.

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