Evolution of a pragmatic algorithm based approach for sub-categorization of Interface dermatitis- A Clinico-Pathological study

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Abstract

Background: Interface dermatitis is a morphological pattern of inflammatory dermatoses characterized by significant histological alterations involving the dermo-epidermal junction. Based on the degree of inflammation and degenerations of the basal layer, it is broadly categorized into vacuolar and lichenoid sub-types. The dermal changes may be confined to the superficial layers only or may involve the deeper dermis as well. Diagnostic entities having diverse etiologies and prognostic significance may present with this morphological pattern warranting a proper diagnosis for effective management.

Aims: 1. To study histomorphology of inflammatory dermatoses presenting with interface pattern
2. To evolve algorithms for further categorization of interface dermatitis

Methods: A prospective study was carried out at a tertiary care hospital for a period of three years. All skin biopsies showing interface dermatitis were evaluated giving due importance to additional changes in epidermis and dermis.

Results: A total of seventy four cases of inflammatory dermatoses presenting with interface pattern were encountered. Majority of the cases were seen in adults in the age group of 30 to 60 years, with slight female preponderance (53.4%). Lichen planus and its variants accounted for the bulk (68.9%) of the cases. All the cases were further stratified based on epidermal changes. Diagnostic algorithms were developed taking into account the epidermal and dermal changes for initial approach to all cases.

Conclusion: A thorough evaluation of epidermal alterations and strong correlation with clinical findings aid in contemplating proper diagnosis for cases presenting with interface pattern of dermatitis.

Keywords: Interface; Lichenoid eruptions; Histopathology; Algorithms.

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Introduction

The pathologic diagnosis of inflammatory skin diseases can be challenging, particularly in a general surgical pathology practice where skin biopsies are seen less frequently.[1]

A number of uncommon, clinically diverse inflammatory skin diseases are grouped under a common term “Interface dermatitis”, which refers to the finding in a skin biopsy of an inflammatory infiltrate that abuts or obscures the dermo-epidermal junction (DEJ).[2]

Additional changes of the epidermis & papillary dermis are used for the differential diagnosis of the various diseases that exhibit interface changes.

Material and Methods

A prospective study of skin biopsies was carried out at the department of Pathology in a tertiary care center for a period of three years from 2012 to 2014. All skin biopsies of inflammatory nature obtained by punch or excisional biopsy were fixed with 10% formalin and submitted for processing after gross examination. The sections were stained with routine hematoxylin and eosin (H&E) stain followed by special stains wherever required. Cases showing interface pattern of inflammation were included in the study. These cases were further studied in detail giving importance to additional epidermal and dermal alterations to evolve a series of algorithms. Descriptive statistical measures like percentages and proportions were utilized to present the data.

Results

A total of 74 cases showing “interface pattern” of inflammation were studied amongst 207 reported cases of inflammatory skin disorders during the period. Majority of the cases (61.6%) were in the age group of 30 to 60 years, with slight female preponderance (53.4%). The cases were broadly grouped into vacuolar and lichenoid categories of interface dermatitis. Each category was further sub-divided into two categories based on the extent of dermal involvement into superficial only or superficial and deep. Lichen planus and its variants accounted for the bulk (68.9%) with

almost all cases showing typical epidermal features and characteristic lichenoid infiltrate. The various diagnostic entities encountered in the present study are shown in table 1. The epidermal and dermal alterations are shown in table 2 and table 3 respectively. The characteristic histo-morphological findings for prototypical examples of each category of interface dermatitis are shown in figures 1, 2, 3 and 4.

Table 1: Various diagnostic entities encountered in the present study.

Diagnostic entities	**Number of cases**
Vacuolar superficial	
Lichen sclerosus et atrophicus (LSEA)	5
Erythema multiforme (EM)	2
Vacuolar superficial and deep	
Discoid lupus erythematosus (DLE)	5
Verrucous DLE	1
Pityriasis Lichenoides(PL)	
Pityriasis lichenoides chronica (PLC)	2
Pityriasis lichenoides et varioliformis acuta (PLEVA)	1
Fixed drug eruption (FDE)	1
Lichenoid superficial	
Lichen planus (LP)	36
Hypertrophic lichen planus (Hyp LP)	6
Overlap LP/DLE	4
Lichen planus like keratosis	2
Lichen planus with Lichen planopilaris	2
Pigmented lichen planus	2
Lichen planopilaris	1
Lichen planus pemphigoides	1
Lichenoid drug eruption (LDE)	1
Lichenoid superficial and deep	
Secondary syphilis (Sec Syph)	2
Total	74

Table 2: Epidermal changes in the present study.

	EM [2]	PL [3]	FDE [1]	LP [36]	DLE [5]	Overlap LP/DLE[4]	LDE [1]	Hyp LP [6]	Sec Syph [2]	LSEA [5]
Hyperkeratosis	-	-	1	35	3	4	1	6	1	5
Parakeratosis	-	3	-	8	2	1	1	2	-	-
Hypergranulosis	-	1	-	35	-	2	-	4	-	-
Follicular Plugging	-	-	-	2	3	2	-	-	-	1
Acanthosis	-	1	-	35	-	3	1	6	1	1
Atrophy	-	-	-	-	3	1	-	-	-	5
Spongiosis	1	1	-	10	-	1	1	1	-	-
Basal vacuolation	2	3	1	36	3	4	1	5	2	4
Keratinocyte necrosis/Apoptosis	2	3	-	25	-	2	1	4	-	-
Rete elongation	-	-	-	15	-	3	1	-	-	-

Table 3: Dermal changes in the present study.

		EM [2]	PL [3]	FDE [1]	LP [36]	DLE [5]	Overlap LP/DLE [4]	LDE [1]	Hyp LP [6]	Sec Syph [2]	LSEA [5]
Severity (DEJ Infiltrate)	Mild		2			3	3				3
	Moderate	2		1	8	1	1	1	3		2
	Severe		1		28	1			3	2	
Distribution	Band-like		1		36	2	2		5	2	1
	Patchy	2	2	1		3	2	1	1		4
Type of Infiltrate	Lymphocyte	2	3	1	36	5	4	1	6	2	5
	Neutrophil	1	2		-	-	-		1	-	-
	Eosinophil	-	-	1	-	-	-	1	-	-	-
	Plasma cell	1	-		-	-	1		-	1	-
	Histiocyte	-	-	1	20	-	3	1	4	1	-
Pigment incontinence		-	-	1	25	1	3	-	5	-	2
Perivascular infiltrate		2	3	1	11	5	3	1	4	2	4
Periappendageal infiltrate		-	-	-	3	4	3	-	1	2	-
Dermal edema		-	-	-	-	3	1	-	-	-	5
Dermal sclerosis		-	-	-	-	1	-	-	-	-	5

Table 4: Table showing prototypical examples of Cell poor and Cell rich interface dermatitis

Prototypes of Cell-Poor Interface Dermatitis
Erythema multiforme
Systemic lupus erythematosus
Dermatomyositis
Mixed connective tissue disease
Graft-versus-host disease
Morbiliform viral exanthem
Morbiliform drug reaction
Prototypes of Cell-Rich Interface Dermatitis
Idiopathic lichenoid disorders
Lichen planus
Lichen nitidus
Lichen striatus
Discoid lupus erythematosus
Anti-Ro–positive systemic lupus erythematosus
Mixed connective tissue disease
Lichenoid and granulomatous dermatitis
Lichenoid purpura
Lichenoid and fixed drug reaction

Table 5: Classification of interface dermatitis based on epidermal changes.

Category	Diagnoses
Interface dermatitis with acute cytotoxic change	Erythema multiforme Fixed drug eruption Pityriasis lichenoides
Interface dermatitis with premature terminal differentiation	Lichen planus Lichenoid drug eruption Lichen striatus Lichenoid keratosis Discoid lupus erythematosus Graft versus host diseases Dermatomyositis
Interface dermatitis with psoriasiform hyperplasia	Lichenoid purpura Bullous pemphigoid Urticarial pemphigoid Secondary syphilis Porokeratosis of Mibelli Acrodermatitis chronica atrophicans
Interface dermatitis with irregular epidermal hyperplasia	Hypertrophic LP Verrucous DLE Some drug eruptions
Interface dermatitis with epidermal atrophy	Lichen sclerosus et atrophicus

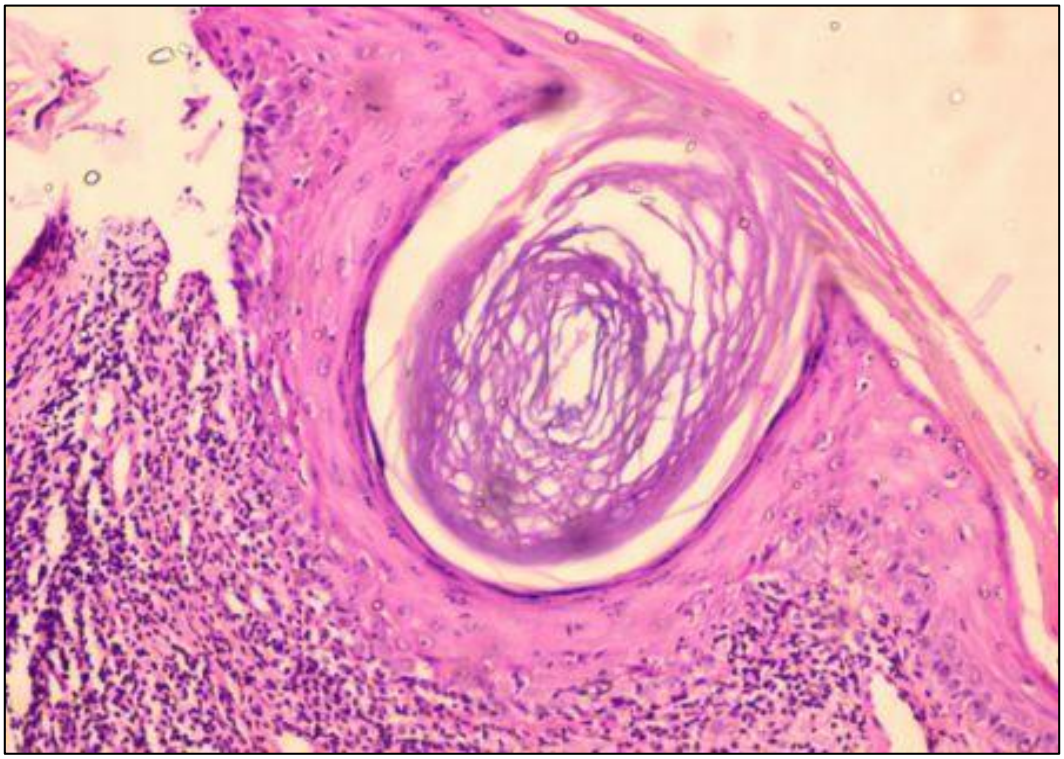

Figure 1: Discoid lupus Erythematosus-Photomicrograph showing follicular plugging, Basal cell vacuolar degeneration and perifollicular inflammation (H&E stain, X100)

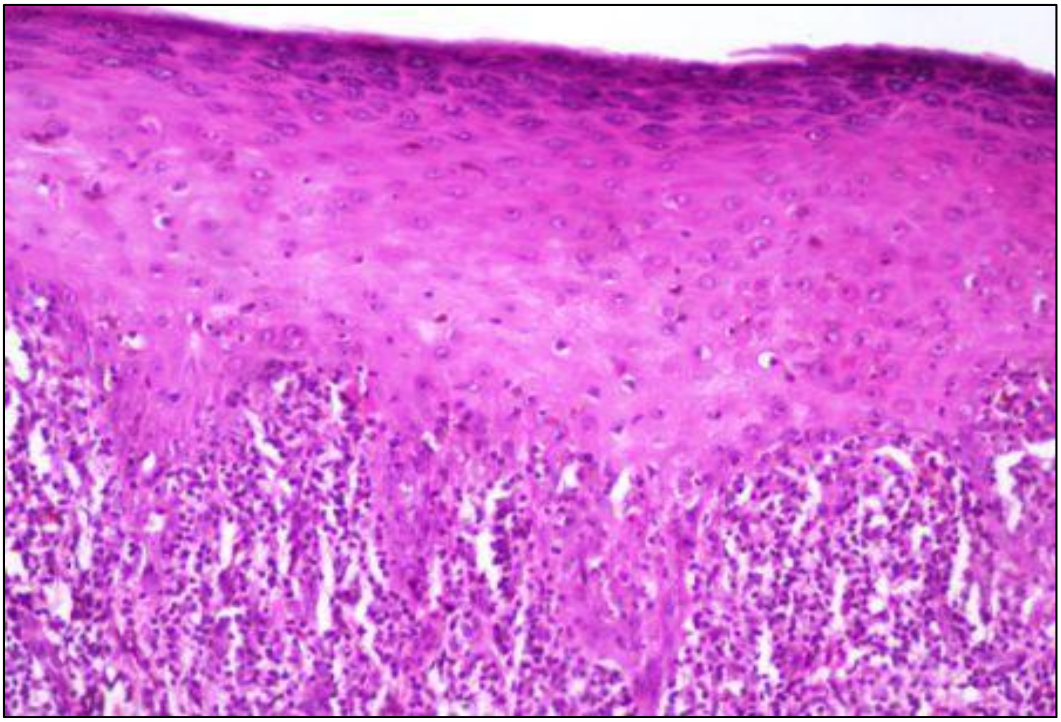

Figure 2: Lichen planus-Photomicrograph showing wedge shaped hypergranulosis, basal cell degeneration, saw toothed rete ridges and lichenoid infiltrate (H&E stain, X100)

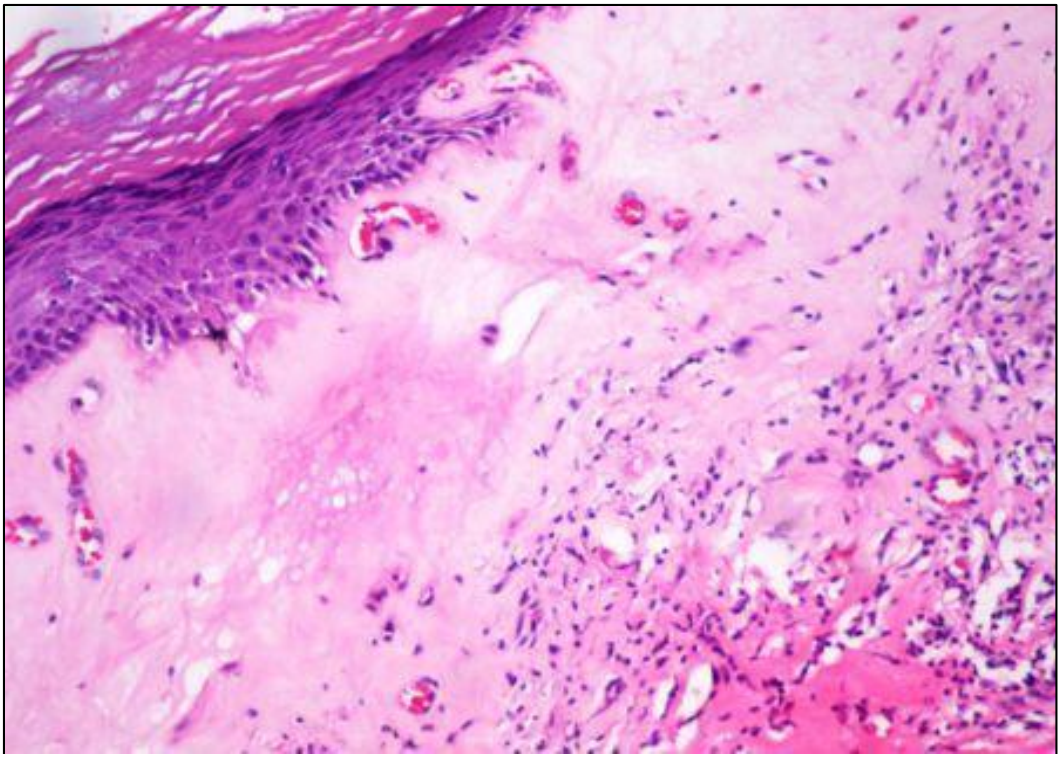

Figure 3: Lichen sclerosis et atrophicus-Photomicrograph showing epidermal atrophy, basal cell vacuolar degeneration, dermal edema and sclerosis (H&E stain, X100)

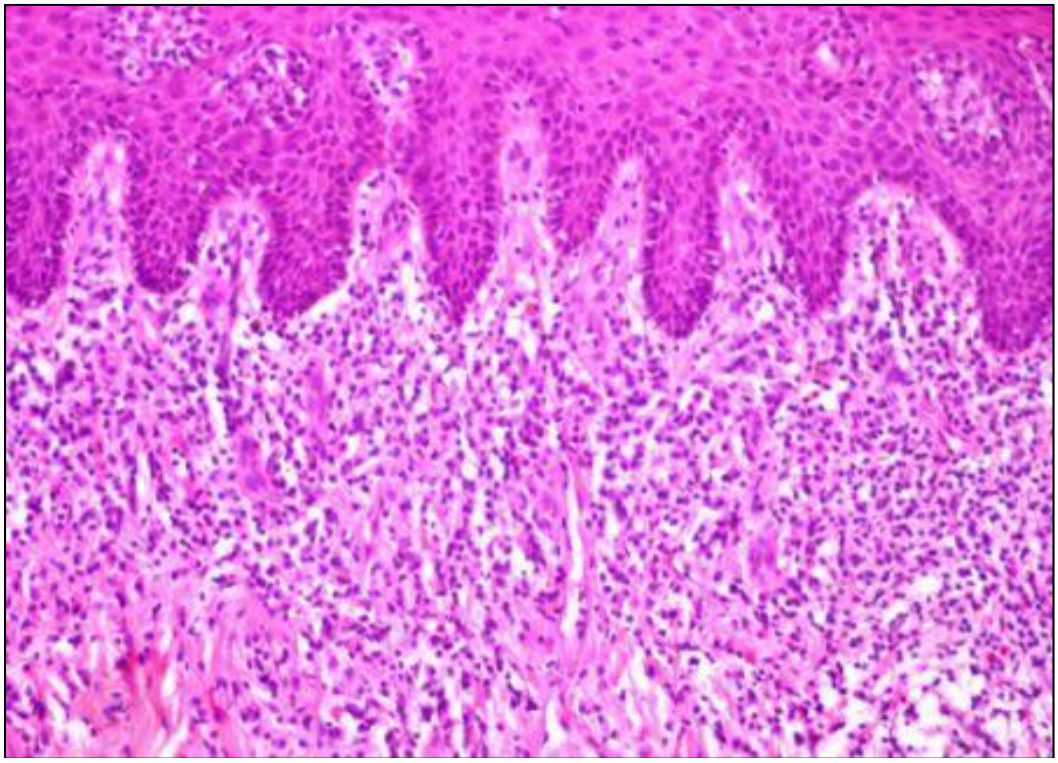

Figure 4: Secondary syphilis-Photomicrograph showing psoriasiform epidermal hyperplasia and plasma cell rich infiltrate at dermo-epidermal junction (H&E stain, X100)

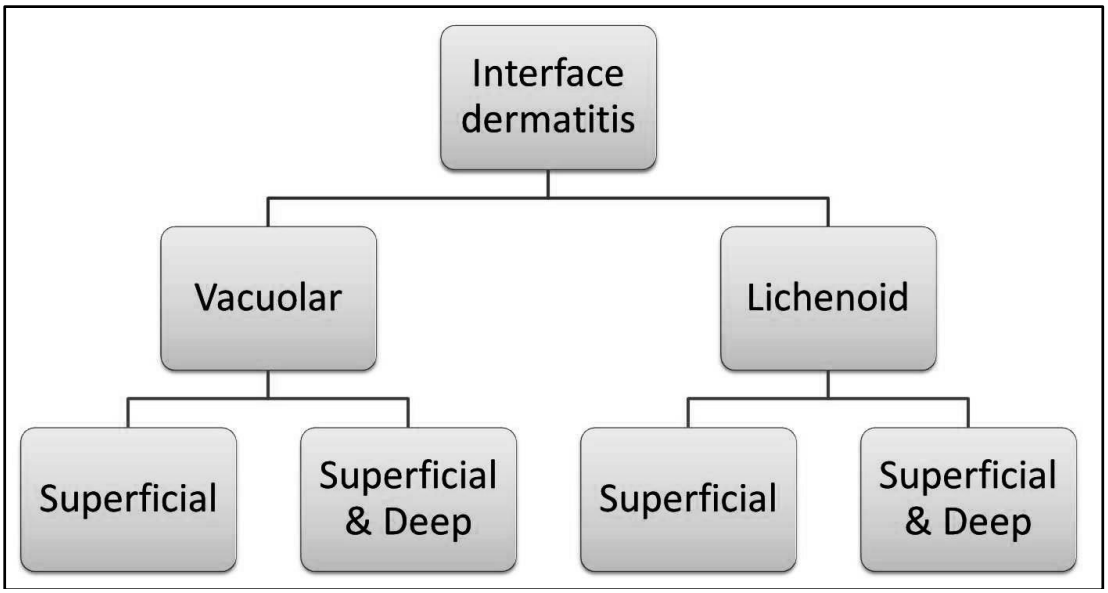

Figure 5: Algorithm showing patterns of interface dermatitis

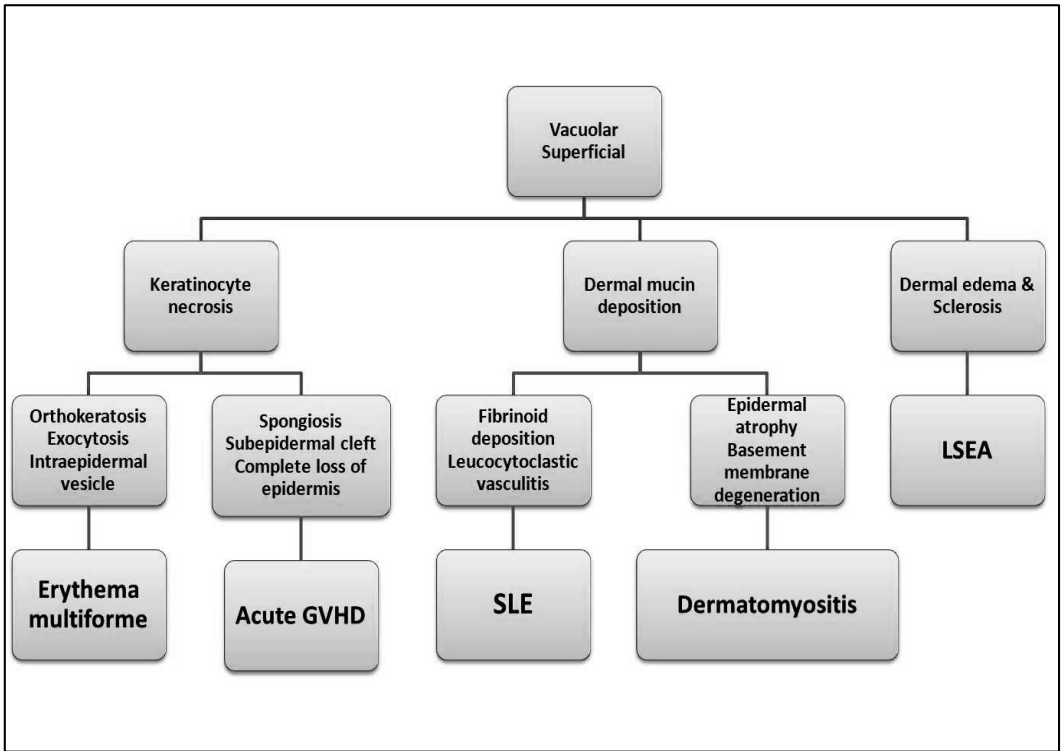

Figure 6: Algorithm showing conditions with vacuolar pattern and superficial inflammation

GVHD-graft versus host disease, SLE-systemic lupus erythematosus,

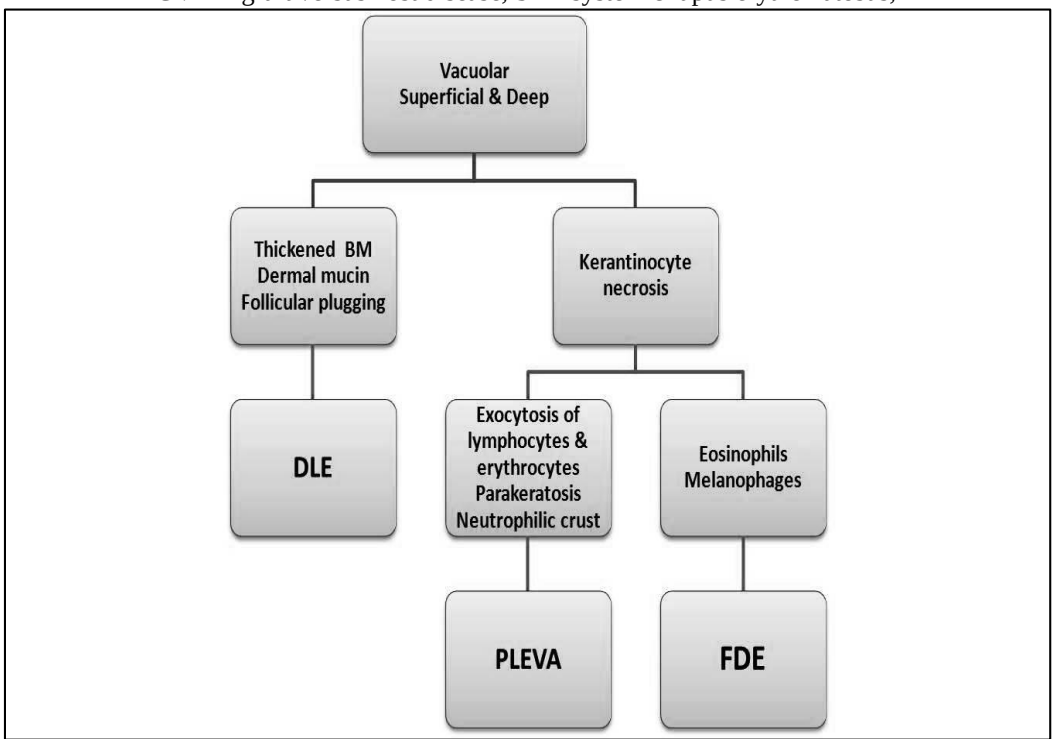

Figure 7: Algorithm showing conditions with vacuolar pattern with superficial and deep inflammation

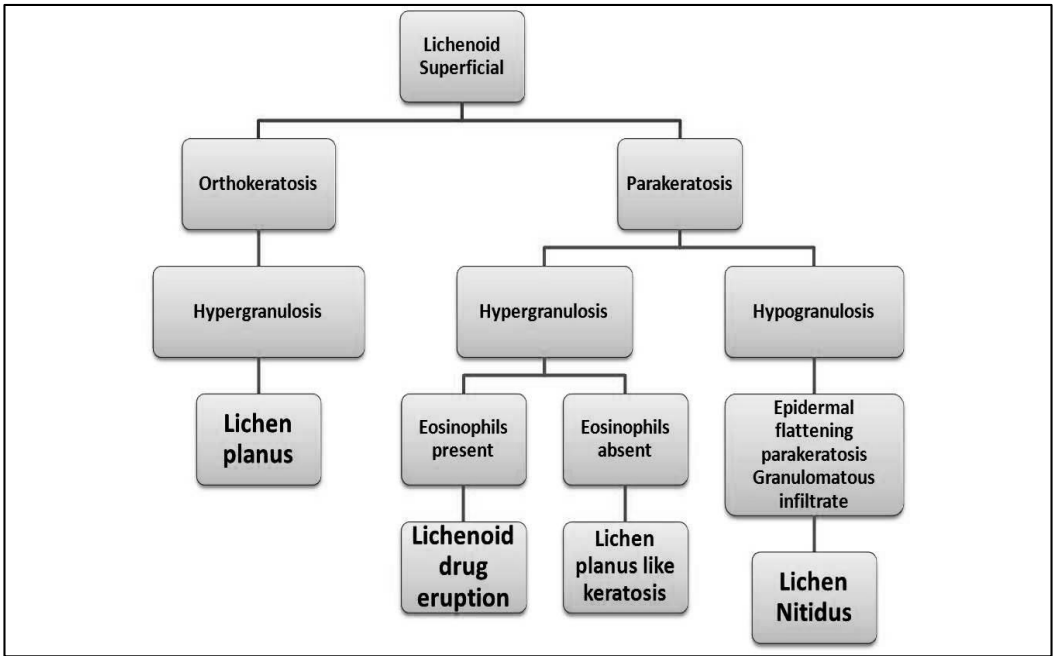

Figure 8: Algorithm showing conditions with lichenoid pattern with superficial inflammation

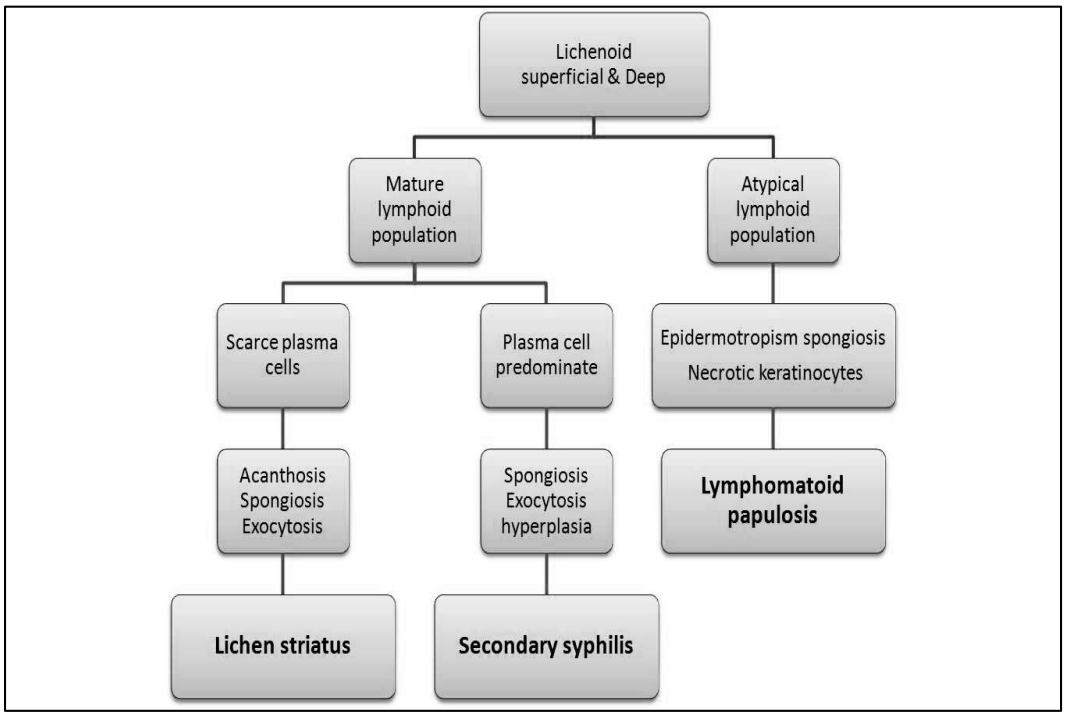

Figure 9: Algorithm showing conditions with lichenoid pattern with superficial and deep inflammation

Discussion

Interface dermatitis includes conditions in which the primary pathology involves the "interface," i.e., the dermo-epidermal junction. The components of this "interface" include the basal layer of the epidermis, the dermo-epidermal junction, the papillary dermis, and the adventitial dermis around the adnexal structures. These constituents function as a single anatomico-physiological unit and pathological alterations of any of these result in changes that affect all the individual constituents.[3] Traditionally, interface dermatitis has been divided into cell rich and cell poor dermatitis[4] as shown in table 4. A variety of conditions have been described in literature like mycosis fungoides, poikiloderma, leprosy and some neoplasms, where interface changes are secondary and are not required for the diagnosis. Such conditions are not included in the present study.

Le Boit PE[5] has proposed a classification of interface dermatitis based on epidermal changes into five categories as shown in table 5. We have made an attempt to categorize the entities encountered in our study using these criteria and discuss their histomorphology.

In the present study, we encountered 6 cases showing acute cytotoxic changes of epidermal keratinocytes with vacuolar degeneration of the basal layer. Two cases of erythema multiforme were seen which showed necrotic keratinocytes at various levels of epidermis with orthokeratotic hyperkeratosis and these findings are comparable to those described by Mei-Chun Chiang et al., [6] Howland et al.,[7] Tonnesen et al.,[8] and Cote et al.[9] We studied a case of fixed drug eruption (FDE) following administration of phenobarbitone, demonstrating characteristic histological features of compact orthokeratotic hyperkeratosis with vacuolar degeneration of basal layer and a dermal infiltrate rich in eosinophils. These findings comply with the histomorphology of FDE described by Wiwat Korkij et al.[10], Sehgal et al.[11] and Lee et al.[12] in their review.

We studied 3 cases of pityriasis lichenoides, of which one case had more pronounced epidermal changes in the form of parakeratosis, keratinocyte necrosis and exocytosis of lymphocytes and erythrocytes. The interface changes and dermal inflammation were also more marked in this case warranting a diagnosis of pityriasis lichenoides et varioliformis acuta (PLEVA). These findings were in accordance to the histomorphological findings described by Nair et al.[13] in their study of 12 cases of PLEVA and the studies of Hood et al.[14]and Longley et al.[15] The other two cases had similar changes in a more subtle form and were reported as pityriasis lichenoides chronica (PLC). One of the cases showed basal cell vacuolization in addition to other characteristic features of PLC, whereas the other case did not have basal cell vacuolization, indicating the fact that the disease was in a later phase of evolution, not demonstrating the characteristic interface histomorphology.

Majority of the cases (54 cases) in our study showed a pattern of premature terminal differentiation of the epidermis associated with a dense lichenoid infiltrate. Bulk of the cases in this category comprised of lichen planus and its variants, demonstrating hypergranulosis and compact orthokeratotic in addition. The histomorphological features have been elucidated in greater detail by various authors like Diliamy[16], Ellis[17], Hamid et al.[18], Scully et al.[19]and Boyd et al.[20]. We studied 5 cases of discoid lupus erythematosus (DLE), which had focal areas of epidermal atrophy and acanthosis, follicular plugging with a thickened basement membrane and an increase in dermal mucin. These features were consistent with the histology of DLE described by Al-Saif et al.[21] and Al-Waiz et al.[22] in their studies. There were seen 4 cases having overlapping features of lichen planus and DLE and as such were categorized as "Overlap-syndrome". We encountered a single case of lichenoid drug eruption which in addition to generalized features of interface dermatitis also showed parakeratosis and inflammatory infiltrate rich in eosinophils.

Six cases of hypertrophic lichen planus and a single case of verrucous DLE showed marked irregular epidermal hyperplasia apart from the characteristic histologic morphology.

Psoriasiform hyperplasia as an additional epidermal feature in interface dermatoses has been described in entities like bullous pemphigoid, secondary syphilis, porokeratosis of Mibelli, acrodermatitis chronic atrophicans, early lesions of lichen sclerosus et atrophicus (LSEA). Two cases of secondary syphilis were seen in the present study which in addition to classical histomorphology, also had regular psoriasiform elongation of epidermis, with features of interface dermatitis as described by Jeerapaet et al.[23]and Abell et al.[24]

In the present study, 5 cases of LSEA were seen which were characterized by orthokeratotic hyperkeratosis, follicular plugging, atrophy of stratum malpighii with hydropic degeneration of basal layer, pronounced edema and homogenization of collagen in the upper dermis, and an inflammatory infiltrate in the mid-dermis. The presence of a zone of hyalinization just beneath the epidermis separating the basal layer from the mid-dermal chronic inflammatory band qualifies all the 5 cases in our study to be in the chronic phase of the disease process. Histomorphology of lichen sclerosus has been described by Chalmers RJG et al.[25], Jasaitiene D et al.[26]and Aynaud et al.[27]

Based on the histo-morphological features, we propose a series of simplified algorithms as shown in figures 5,6,7,8 and 9, which can be utilized to narrow down the differential diagnoses in skin biopsies with interface pattern of dermatitis. These algorithms have been formulated using hallmark features and as such additional features may be encountered in individual cases. As the histologic characteristics of dermatological lesions are overlapping, these algorithms are not infallible and should be used in correlation with clinical findings. The algorithmic approach described in the present study is a holistic one, taking into account all the previously published classification schemes for interface dermatitis. At the same time, an attempt is made by the study group to keep the algorithms in a simplified manner, for the sake of utility in a centre with busy dermatopathology practice.

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