Review Article

Lichenoid tissue reaction/interface dermatitis: Recognition, classification, etiology, and clinicopathological overtones

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ABSTRACT

Lichenoid tissue reaction or interface dermatitis embrace several clinical conditions, the prototype of which is lichen planus and its variants, drug induced lichenoid dermatitis, special forms of lichenoid dermatitis, lichenoid dermatitis in lupus erythematosus, and miscellaneous disorders showing lichenoid dermatitis, the salient clinical and histological features of which are described to facilitate their diagnosis. Background of lichenoid reaction pattern has been briefly outlined to enlighten those interested in this entity.

Key words: Classification, interface dermatitis, lichenoid tissue reaction

INTRODUCTION

Lichenoid tissue reaction (LTR) or interface dermatitis (IFD) is some of the commonly encountered clinical and histological presentations in dermatology and pathology. The term interface dermatitis refers to the finding in a skin biopsy of an inflammatory infiltrate that abuts or obscures the dermo-epidermal junction. The term "lichenoid" refers to papular lesion of certain skin disorders of which lichen planus is the prototype. However, this type of reaction can also be seen skin disorders associated with systemic illnesses like lupus erythematosus and the skin changes of potentially fatal disorders such as graft versus host disease, Stevens Johnson syndrome and toxic epidermal necrolysis.

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RECOGNITION AND CLASSIFICATION

The papules of the prototype lichen planus are shiny, flat-topped, and polygonal, of different sizes and occur in clusters creating a pattern that resembles lichen growing on rock.[1] The reaction can be deduced from

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the basic feature of epidermal basal cell damage, whether primary or secondary.[2] On histologic examination, the lichenoid lesions are characterized by an infiltrate of inflammatory cells that fills the papillary dermis in a band like fashion and often obscures the dermo-epidermal junction.

Despite the large spectrum of clinical diseases associated with lichenoid reactions [Table 1], it can lead to a more meaningful diagnosis through organization of the material in a systematic manner. Historically interface dermatitis has been classified based on predominant cell type in the infiltrate, neutrophilic, lymphocytic or lympho-histiocytic. Some authors also prefer to classify the lymphocytic interface dermatitis by the intensity of the interface inflammation into two broad categories. These include cell poor interface dermatitis when only a sparse infiltrate of inflammatory cells is present along the dermo-epidermal junction, or cell rich where a typically heavy band-like infiltrate is seen which obscures the basal layer of epidermis and is often called lichenoid interface dermatitis.[3] A close cooperation of histopathologist and dermatologist is required to reach confirmatory diagnosis of lichenoid dermatoses.

Table 1: Lichenoid tissue reaction/Interface dermatitis: Clinical variants

	Dermatosis
Prototype	Lichen planus: hypertrophic; atrophic, linear, ulcerative, actinic, planopilaris, erythematosus, pemphigoids
	Erythema dyschromicum perstans
	Keratosis lichenoides chronica
	Lupus erythematosus – Lichen planus overlap syndrome
	Lichen nitidus
Others variants	Lichen striatus
	Lichen planus-like keratosis
	Lichenoid drug eruptions
Drug induced	Fixed drug eruptions
	Erythema multiforme
	Toxic epidermal necrolysis
	Lupus erythematosus
	AIDS interface dermatitis
	Graft versus host disease
	Paraneoplastic pemphigus
Miscellaneous	Poikilodermas
	Pityriasis lichenoides
	Lichenoid purpura
	Lichenoid contact dermatitis
	Late secondary syphilis
	Lichen amyloidosis
	Erythroderma
	Lichen photosensitive/phototoxic dermatoses
	Lupus erythematosus: systemic lupus erythematosus, discoid lupus erythematosus, subacute lupus erythematosus, neonatal lupus erythematosus

ETIOLOGY

Lichen planus and lupus erythematosus are the most common and best studied representatives of the lichenoid tissue reaction.[4,5] In lupus erythematosus, basal damage usually is more focal and appears to be secondary, but the events following it are the same. The histologic picture of lichen nitidus is distinctive, but is quite similar to an early lichen planus papule. However, the clinical features of uniform, not enlarging, not confluent round papules, make lichen nitidus a distinctive entity.[6,7] The lichenoid or lichen planus like actinic keratosis, is another example that basal cell damage, though by a neoplastic process, can lead to a typical lichenoid reaction.[8,9] Lichenoid drug reactions caused by an ever increasing list of drugs used in medical therapeutics are the commonest culprit in induction of lichenoid dermatitis or lichenoid photodermatitis.[10] Tropical lichen planus or lichen planus actinicus may be sunlight provoked lichen planus or due to direct damage of epidermal basal layer by ultraviolet rays.[11,12] The current review endeavors to recap the information available thus far in order to facilitate its application in day to day practice.

DERMO–EPIDERMAL INTERACTIONS AND PATHOGENESIS

The basal cell damage is a common denominator of these heterogeneous groups of disorders. The term "interface dermatitis," often used for lichenoid disorders, denotes that the inflammatory infiltrate along with basal cell damage appear to obscure the dermo--epidermal junction. The epidermal basal cell damage leads to cell death and/or vacuolar changes (liquefactive degeneration). The so-called civatte bodies are damaged epidermal cells with shrunken eosinophilic cytoplasm and pyknotic nuclear remnants (apoptosis), However, certain disorders show frank necrosis of the epidermis rather than apoptosis. Filamentous degeneration is another type of cell damage which,[4] may display none of the above changes. Melanin incontinence is another fall out of the damaged basal cells seen more frequently in drug or solar damage induced dermatoses.[2,13-19]

Cell-mediated cytotoxicity is regarded as a major

mechanism of pathogenesis of lichen planus, as evidenced by T cells being the predominant cells in the inflammatory infiltrate.[20] Various factors may precipitate the cell mediated reaction resulting in lichen planus lesions such as, mechanical trauma, systemic drugs, contact sensitivity, infective agents including some viruses.[21] Although the specific antigen of LP is still unclear, the antigen presentation by basal keratinocytes are thought to cause T cell accumulation in the superficial lamina propria, basement membrane disruption, intra-epithelial T-cell migration, and CD8+ cytotoxic cell mediated keratinocyte apoptosis in LP.[22]

There is limited data about the role of cell-mediated cytotoxicity in LP, which is mediated by both cytotoxic T lymphocytes (CTL) and natural killer (NK) cells. The cytoplasm of cytotoxic cells is enriched with granules composed of the potent cytolytic molecule perforin (pore-forming protein) together with serine esterase (granzymes).[23,24] Upon contact with the target cell and activation, CTL and NK cells release perforin and granzymes in a contact zone between target and killer cells. Perforin forms pores in the target cell membrane and thus enables entry of granzymes, responsible for DNA degradation and apoptosis of target cells. Shimizu *et al.*[25] found a significant role of granzyme B-expressing CD8+ T cells in apoptosis of keratinocytes in lichen planus. Massri *et al.*,[26] found higher expression of cytolytic molecule perforin in lesional LP as well as in peripheral blood mononuclear cells, as compared to remission and healthy controls, supporting the hypothesis about the potential role of CD8+ cytolytic effector cells in the exacerbation of disease. Similarly, a variety of clinical and pathologic features uniquely observed in FDE lesions can be explained by the presence of CD8+ intraepidermal T cells, with the effector memory phenotype in the FDE lesion.[27,28]

The possible mechanism involved in the variability of expression of lichenoid tissue reaction depends on the degree and pattern of expression of the intercellular adhesion molecule-1 (ICAM-1). Normal epidermis is resistant to interaction with leukocytes because its keratinocytes have low constitutive expression of ICAM-1. In lichen planus the ICAM-1 expression is limited to the basal keratinocytes while in subacute cutaneous lupus erythematosus, there is a diffuse ICAM-1 expression with basal accentuation.[14,17] This pattern is induced by ultraviolet (UV) radiation possibly mediated by tumor necrosis factor alpha (TNF-alpha). The histogenesis of lichenoid interface dermatoses is diverse, and includes both cell-mediated and humoral immune responses.[29,30] Furthermore, recent work has suggested that a number of different LTR/IFD skin disorders share a common inflammatory signaling pathway involving the actions of plasmacytoid dendritic cell-derived interferon-alpha (IFN-alpha). This signaling pathway appears to amplify cytotoxic T cell injury to the epidermal basal cell compartment. The preceding pathway as well as the other cellular and molecular mechanisms that are thought to be responsible for the prototypic LTR/IFD disorder, lichen planus has recently been reviewed.[31]

The subject of lichen planus (LP) and dental metal allergy long has been debated. An overwhelming majority of the existing literature focuses on mercury and gold salts in relation to oral lichen planus. It is an intriguing revelation and subject of investigations.[32] Accordingly, dental materials like mercury and gold and certain drugs may induce epithelial alterations, resembling oral lichen planus (OLP). Although, these alterations do not have all the clinical and/or the histological features of OLP; yet these lesions are known as oral lichenoid lesions (OLLs). Onset and/or worsening of OLLs/OLP after the administration of anti-hepatitis C virus (HCV) therapy have been highlighted. Furthermore, development of symptomatic OLLs, in consequence to anti-HCV therapy (interferon-alpha and ribavirin), in two human immunodeficiency virus-HCV-coinfected subjects has also been described. An immunological cause related to coinfection and administration of different medications too could be responsible for the onset of OLLs. The new reports, together with the previous ones of a possible association between OLP and/or OLLs and anti-HCV therapy, highlight the absolute need to monitor carefully the human immunodeficiency virus-HCV-coinfected subjects who are about to start the anti-HCV therapy and to define better the clinical and histopathological criteria to distinguish OLP from OLLs.[33]

It is intriguing at this point in time, to enlighten that fludarabine, a purine antimetabolite with potent immunosuppressive properties, has previously been associated with the development of transfusion-associated graft *versus* host disease (TA-GVHD) in patients with hematologic malignancies. Its role as a

risk factor for TA-GVHD in patients without underlying leukemia or lymphoma is uncertain.

However, the increasing use of these drugs in the treatment of autoimmune disease might result in occurrence of TA-GVHD after fludarabine therapy. Such an episode-developing in-patient with systemic lupus erythematosus strongly suggests that this drug is sufficiently immunoablative to be an independent risk factor for TA-GVHD.[34] It is therefore, worthwhile to study this aspect in lichenoid interface dermatosis.

CLINICOPATHOLOGICAL OVERTONES

Lichen planus and its clinical variants

They are fairly common, extensively covered dermatosis encountered worldwide. The clinical and histological features are well documented.[16,29,35-37] The latter is a classic example of the lichenoid interface dermatitis, and is characterized by the basal cell damage in the form of multiple civatte bodies and a band-like infiltrate on the undersurface of the epidermis along with wedge-shaped hypergranulosis with saw toothed rete-ridges[38] [Figure 1]. However, individual histopathological variations [Figure 2] may be seen in the different clinical types of lichen planus[38-44] and have been excellently recorded by Weedon.[29] Ulcerative lesions are usually seen on mucous membranes of the oral cavity, glans penis and vulva.[45] In such instances, the typical histopathological changes are confined largely to the margins of the ulcer.[46-48]

Lichen nitidus

Unlike lichen planus, asymptomatic lesions having predilection for the upper extremities, chest, abdomen, and male genitalia[49-53] clinically characterize it. Previously recorded summertime actinic lichenoid eruption (SALE), may well represent the actinic form of lichen nitidus.[54] The histopathology is picturesque, a dense, well-circumcised subepidermal infiltrate enclosed by a "claw-like" rete ridges.[29,53,55] Overlying epidermis is thinned out with occasional civatte bodies [Figure 3].

Lichen striatus

This, on the other hand, displays papular lesions in a linear, unilateral fashion often following Blaschko's lines, usually occurring in adolescents especially females.[56-58] Its histopathology is marked by hyperkeratosis, parakeratosis, often minute intraepidermal vesicles containing Langerhan's cells and less dense infiltrate of lymphocyte, histiocytes, and melanophages in the mildly edematous dermal papillae[29,56,59-61] [Figure 4]. Hard *et al.*,[61] believe that linear lichen planus and lichen striatus are the opposite ends of a spectrum.

Lichen planus-like keratosis

They are benign lichenoid keratosis present as sudden eruption of solitary or a few violaceous, rusty lesions with thin scale usually present on the arms or presternal areas of middle aged/elderly women.[62-64] The microscopic features are pathognomonic characterized by florid lichenoid reaction, prominent pigment incontinence, and numerous civatte bodies. The dense infiltrate of lymphocytes and macrophages may also show a few plasma cell and eosinophilis.[65] Individual histopathologic variations prompted Jang *et al.*,[66] to classify lichenoid keratosis in three groups, namely, lichen planus-like, seborrheic keratosis-like, and lupus erythematosus-like lichenoid keratosis. The salient histopathological features of the preceding lichenoid interface dermatoses are outlined [Table 2].

Twenty-nail dystrophy

Trachyonychia, a fascinating clinical condition, was brought to focus 25 years ago. Ever since, it has been sparingly reported. Nonetheless, the condition is well recognized, and its diagnosis is made on the basis of clinical features characterized by[67,68] onset in infancy/childhood, and occasionally in adults. The lesions are fairly representative, and are characterized by the alternating elevation and depression (ridging) and/or pitting, lack of luster, roughening likened to sandpaper, splitting, and change to a muddy grayish-white color. Dystrophy is prominent. Several modes of occurrence have been described including an hereditary component. The confirmation of diagnosis is through microscopic pathology corresponding to endogenous eczema/dermatitis, lichen-planus-like or psoriatic-form. It is a self-limiting condition and may occasionally require intervention.

DRUG INDUCED LICHENOID DERMATITIS

The *in vogue* term, lichenoid drug eruptions, is an often encountered drug reaction to a heterogeneous group of ingested and/or injected drugs used in a wide variety of systemic disorders. Ever since the observation of lichen planus-like eruptions occurring in troops who took mepacrine in the World War II,[69] numerous reports[70-103] have recorded this entity in response to different drugs [Table 3]. Wechsler[104] initially reported

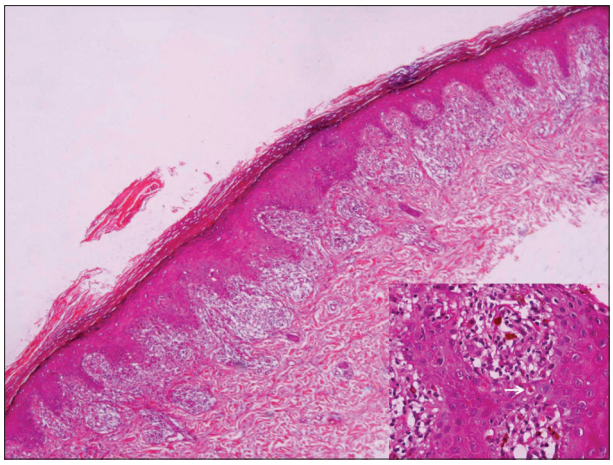

Figure 1: Lichen planus: Section showing hyperkeratosis, hypergranulosis, saw-tooth-like rete and interface dermatitis. High power view showing lichenoid infiltrate and apoptotic keratinocytes (inset, arrow) (H and E, ×40)

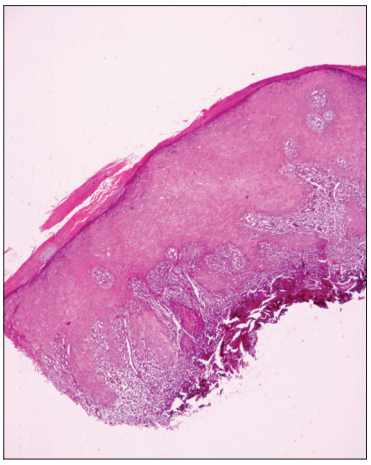

Figure 2: Lichen planus hypertrophicus: Section showing marked hyperkeratosis and epithelial hyperplasia with an otherwise typical band-like infiltrate of lichen planus. (H and E, ×40)

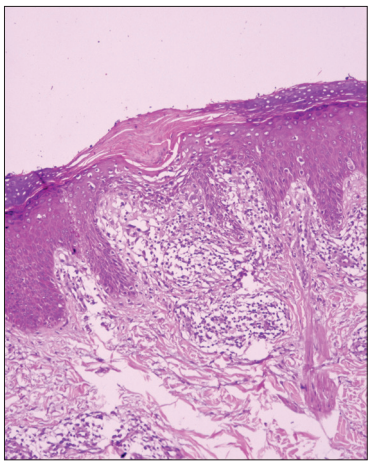

Figure 3: Lichen nitidus: Section from papule showing well circumscribed mixed cell infiltrate in close proximity of epidermis and confined to papillary dermis (H and E, ×100)

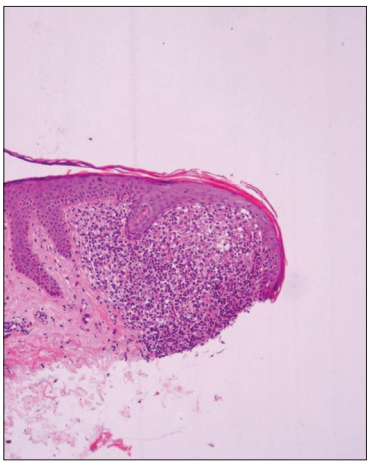

Figure 4: Lichen striatus: Section show features mimicking lichen planus but are focal and may be missed without step sections (H and E, ×40)

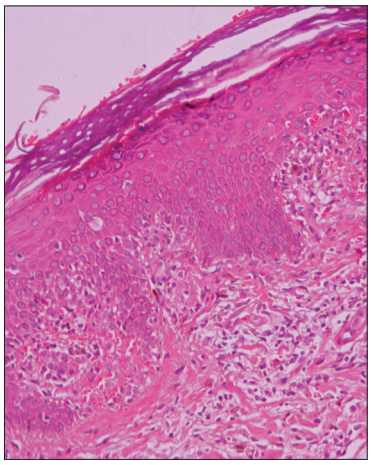

Figure 5: Lichenoid drug eruption: Section showing lichenoid infiltrate similar to lichen planus, but with more numerous eosinophils, parakeratosis and perivascular distribution of infiltrate (H and E, ×200)

photo-lichenoid dermatitis in the year 1954, as a photo allergic reaction to drug(s), presenting a lichenoid pattern on clinical as well as histopathological examination. The lichenoid eruptions/photo-lichenoid eruptions clinically closely mimic lichen planus, but may have some eczematous element and usually leave a pronounced residual pigmentation. Histopathologically, differentiating features of lichenoid eruptions include foci of parakeratosis, mild basal vacuolar changes with a few eosinophils/plasma cells. The degree of melanin incontinence is higher in lichenoid eruption in contrast that of lichen planus[105] [Figure 5]. However, the dermal infiltrate is less dense and less band-like. Photo-lichenoid eruptions, on the other hand, may closely mimic lichen planus.[106]

Table 2: Lichenoid tissue reaction/interface dermatitis salient histopathological features

Disease	Histopathological features
Lichen planus	Prominent civatte bodies, band-like inflammatory infiltrate, wedge-shaped hypergranulosis pigment incontinence. Hypertrophic form has changes limited to the tips of the acanthotic down growths. The infiltrate extends around hair follicles in lichen plano-pilaris
Lichen nitidus	Focal lichenoid lesions; some giant cells; dermal infiltrate often "clasped" by acanthotic down growths.
Lichen striatus	Irregular and discontinuous lichenoid reaction; infiltrate sometimes around follicles, and sweat glands.
Lichen planus-like keratosis	Prominent civatte bodies formation;solar lentigo at margins.
Lichenoid drug eruptions	Focal parakeratosis, eosinophils, plasma cells and melanin incontinence. Deep extension of the infiltrate occurs in photolichenoid lesions.
Fixed drug eruptions	Interface-obscuring infiltrate, extends deeper than erythema multiforme; cell death often above basal layer; neutrophils.
Graft-*versus*-host disease	Basal vacuolation; scattered apoptotic keratinocytes, with attached lymphocytes ('satellite cell necroses') variable lymphocytic infiltrate.
Lupus erythematosus	SLE-prominent vacuolar change and minimal cell death. DLE more cell death, superficial and deep infiltrate, mucin; follicular plugging; basement membrane thickening, Civatte bodies in both.
Dermatomyositis	Resembles acute lupus with vacuolar change, epidermal atrophy, some dermal mucin, superficial and sparse infiltrate.
Poikilodermas	Vacuolar changes; telangiectasia; pigment incontinence; dermal sclerosis.
Pityriasis lichenoides	Acute form lymphocytic vasculitis with epidermal cell death; interface-obscuring infiltrate; focal hemorrhage; focal parakeratosis.
Erythema multiforme	Interface-obscuring infiltrate subepidermal vesiculation and variable epidermal cell death.
Paraneoplastic pemphigus	Erythema multiforme-like changes with suprabasal acantholysis and clefting; sometimes subepidermal clefting.

Table 3: Lichenoid tissue reaction/interface dermatitis drug induced[29]

Disorder	Causitive drugs
Lichenoid eruptions	Amlodipine[65] ACE inhibitors (captopril, enalpril)[66,67] Beta blockers (propranolol, oxprenalol, labetalol)[68-70] Cyanamide[71] Gold salt[72] Interferon alpha-2b intravenous immunoglobulin[73] Levamisole[74] Methyldopa[75] Non-steroidal anti-inflammatory drugs (NSAID)[76] Omeprazole / lansoprazole / pantoprazole[77] Penicillamine[78] Streptomycin[79] Simvastatin[80] Suramin[81]
Photo-distributed lichenoid eruptions	Tiopronin[82] Carbamazepine[83] Chlorpromazine[84] Demeclocycline[85] Diflunisol[86] Diltiazem[87] Enalpril[88] Ethambutol[89] Nimesulide[90] Isoniazid[91] Leflunamide[92] Pyrizinamide[93] Quinine[94] Tetracyclines[95] Quinidine[96] Thiazide[97] Thioridazine[98]

Fixed drug eruptions

A wide variety of drugs have been incriminated.[107] They may probably be induced by drug acting as hapten, binding to keratino/melanocytes producing an immunological reaction, an antibody-dependent cellular cytoid response. Suppressor/cytotoxic lymphocytes attack the drug altered epidermal cells causing the eruption, and thus retain the cutaneous memory in cases of repeated offence by the drug.[107-109] The clinical lesions may mimic lichenoid interface dermatoses.[107] The microscopic pathology of fixed drug eruptions (FDE) shows a prominent vacuolar change in the basal cells, civatte bodies, melanin incontinence, and inflammatory infiltrate often comprising neutrophils approximating the dermo-epidermal junction, extending up to mid-epidermis and dermis.[107-110]

Erythema multiforme and toxic epidermal necrolysis

They are other severe forms of drug eruptions. Histopathology shows changes that of lichenoid dermatitis, conforming to either epidermal, dermal, or mixed pattern. It is characterized by mild-to-moderate lymphocytic infiltrate, a few macrophages, obscuring dermo-epidermal junction, and surrounding the dermal blood vessels up to mid-dermis. Apoptosis with prominent epidermal cell death extending beyond basal cell layer[111-113] is another salient feature. TEN, on the other hand, may reveal a sub-epidermal bulla

beneath a confluent epidermal necrosis. Lymphocytic infiltrate is sparse, and perivascular. Sweat ducts are often involved, and may show a basal cell apoptosis resulting even in necrosis.[114-117]

SPECIAL FORMS OF LICHENOID DERMATITIS

Acquired immunodeficiency syndrome related lichenoid dermatitis

It has been a controversial, infrequently encountered entity.[29] An increased prevalence and severity of cutaneous photosensitivity has been recognized in human immunodeficiency virus (HIV) infection. Lichenoid and/or nonlichenoid eczematous are the two distinct clinical manifestations. Burger and Dhar[118] have studied lichenoid photo eruptions in HIV infection. Systemic and cutaneous immune abnormalities may be relevant in their pathogenesis.[119] Histopathology largely shows a lichenoid reaction pattern depicting interface changes, resembling those of EM/ FDE.[29,119]

Lichenoid reaction to graft versus host disease

Chronic graft versus host disease occurring after 3 months of transplantation or later may resemble lichenoid reactions, affecting the palms, soles, trunk buttocks, and thighs. Oral ulcers and xerostomia may be its accompaniment. The microscopic pathology of the chronic phase may resemble that of lichen planus *albeit* marked by a dense inflammatory infiltrate, and prominent pigment incontinence. Small foci of "columnar epidermal necrosis" may also be a prominent feature.[29,120-122]

Lichenoid eruptions in paraneoplastic pemphigus

They may either occur independently or on previously blistered skin. They are invariably accompanied by severe stomatitis. As the disease gets chronic or after treatment the lichenoid eruptions may overtake the blistering. Unlike, pemphigus vulgaris, they are often seen on the palms, soles, and over paronychial tissue.[123] The microscopic findings resemble EM with lichenoid tissue reaction. Dyskeratotic cell at different level of epidermis is another feature. Subepidermal as well as suprabasal cleft depicting acantholysis have also been recorded.[29,124]

Lichenoid dermatitis in lupus erythematosus

A lichenoid reaction pattern in variable permutation and combination is a common denominator. The clinical features and variants of lupus erythematosus (LE) have been extensively recorded.[123] Some degree of overlap may be seen in its different clinical variants. Discoid lupus erythematosus (DLE) displays a lichenoid reaction pattern with chiefly a peripilosebaceous/ follicular superficial and deep dermal lymphocytic infiltrate. Liquefaction degeneration, scattered civatte bodies, hyperkeratosis, atrophic malpighian layer, and keratotic plugging are succinctly observed[125,126] [Figure 6]. Direct immunofluorescence of involved skin reveals the deposition of IgG and IgM along the basement membrane zone in most cases. The cutaneous lesions of SLE show vacuolar degeneration of the basement membrane, yet civatte bodies are unusual. Fibrinoid material can be deposited in dermis around capillaries and interstitium, which may cause thickening of the basement membrane zone. Special stains may reveal deposition of mucin. Hematoxyphilic bodies, which are usual in the visceral lesions, are rare in the skin lesions. A positive lupus band test is an additional pointer towards diagnosis, which is invariably positive in involved skin.[125,127,128]

The subacute lupus erythematosus displays a wide range of clinical expressions and mild systemic/ serological abnormalities.[29,123] The histopathological features of cutaneous lesions, however, reveal most of the features seen in discoid lupus but with more basal vacuolar changes, epidermal atrophy, dermal edema and superficial mucin in the former. Compared to discoid lupus, it has less pronounced hyperkeratosis, keratotic plugging, pilo-sebaceous atrophy, basement membrane thickening, and cellular infiltrate.[129-131]

MISCELLANEOUS DISORDERS SHOWING LICHENOID DERMATITIS

Late secondary syphilis

Its histopathology may display a lichenoid reaction pattern, the inflammatory infiltrate formed primarily by plasma cells, which are distributed through out the dermis.[1]

Gianotti-Crosti syndrome

It is an uncommon, self-limited, acrodermatitis of childhood, characterized by an erythematous papular eruptions symmetrically distributed on the face and limbs with mild lymphadenopathy. It is thought to be of viral origin. The histopathologic findings are nonspecific, and include focal parakeratosis, mild spongiosis, superficial perivascular infiltrate, papillary dermal edema, and extravasated red blood cells. Interface changes with some basal vacuolization may be present.[132]

Herpes simplex virus (HSV) and varicella-zoster virus (VZV)

They are responsible for various atypical mucocutaneous manifestations in the immunosuppressed population. An altered virus-host cell relationship may be one of the pathomachanisms. Histopathology reveals lichenoid dermatitis. Specific HSV-1, HSV-2, and VZV *in situ* hybridization proved the viral origin of the cutaneous lesions.[133]

Pityriasis lichenoides et varioliformis acuta (PLEVA)

It may show a heavy lymphocytic infiltrate obscuring the dermo-epidermal junction with focal epidermal cell death, and confluent epidermal necrosis. A wedge-shaped dermal infiltrate with apex in deep dermis with variable hemorrhage may be diagnostic.[134]

Poikilodermatous disorders

They are heterogeneous group of disorders, characterized by erythema, mottled pigmentation and epidermal atrophy, complimented histologically by basal vacuolar changes, melanin incontinence and telangiectasia of superficial dermal vessels.[5,29,123] The genodermatoses-like Rothmund–Thomson syndrome,

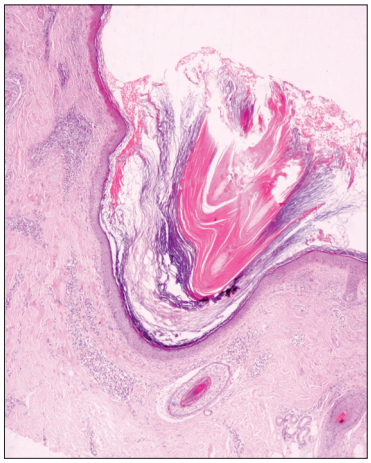

Figure 6: Lupus erythematosus: Section showing hyperkeratosis with follicular plugging with thinning and flattening of epithelium and focal thickening of basement membrane. A predominantly lymphocytic infiltrate is seen around the hair follicles and along dermo--epidermal junction (H and E, ×40)

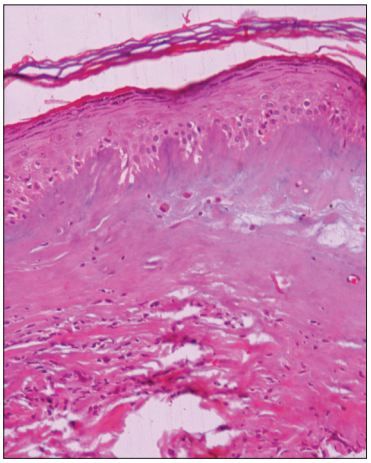

Figure 7: Lichen sclerosus and atrophicus: Section showing hyperkeratosis with atrophy of stratum malphigii, prominent edema, and homogenization of collagen in upper dermis. Early lesion may show interface dermatitis with superficial inflammation in direct contact with epidermis which soon gets separated by edema. (H and E, ×100)

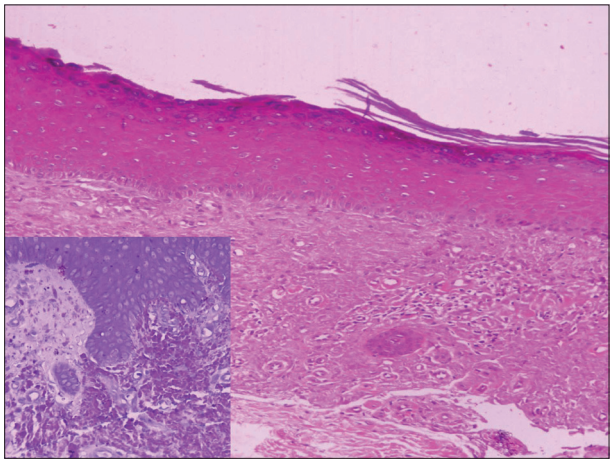

Figure 8: Lichen amyloidosis: Section from lichen amyloidosis showing large acellular homogenous deposits of amyloid in papillary dermis, confirmed on special stains (crystal violet, inset). Smaller amounts of deposits can mimic colloid bodies of lichen planus (H and E, ×100)

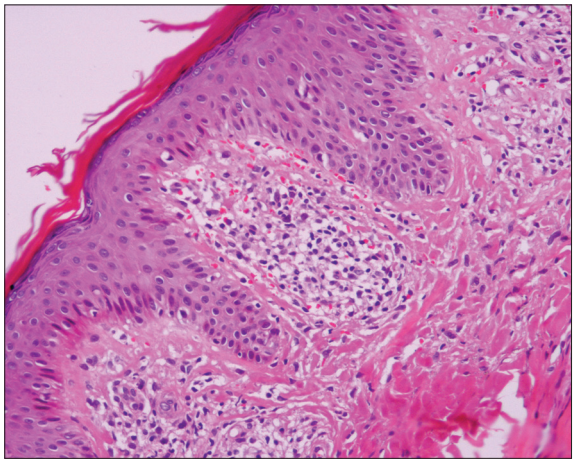

Figure 9: Lichen aureus: Section shows moderate inflammatory infiltrate around the papillary dermal vessels which can cause focal interface dermatitis. Extravasated red blood cells are prominent (H and E, ×200)

Blooms syndrome and dyskeratosis congenital reveal their independent clinical characteristic, and histopathological peculiarities, but with a variable degree of lichenoid reaction. Poikiloderma atrophicans vasculare may represent an early stage of mycosis fungoides.[29,123] Poikiloderma of civatte is now disputed as a distinct entity.[135] Some poikilodermas may be related, in some ways to a graft *versus* host reaction.[136]

Dermatomyositis

Skin lesions have shown a spectrum of histopathological changes, varying from sparse perivascular lymphocytic infiltrate, edema, mucinous changes in the upper dermis, to full-fledged lichenoid reaction pattern with prominent basal vacuolar changes. Occasional civatte bodies and/or neutorphils can be an accompaniment. Severe cases resemble acute lupus erythematosus. Infrequently poikilodermatous features can be an additional with dilated superficial blood vessels and pigment incontinence. Lupus band test is usually negative, although colloid bodies containing IgM may be a salient feature in papillary dermis.[137-139]

Lichen sclerosus (LS)/ lichen sclerosus et atrophicus/ balanitis xerotica obliterans/kraurosis vulvae

It is a chronic inflammatory dermatosis that results in white plaques with epidermal atrophy. It appears to begin as an interface dermatitis. Its early lesions may show a heavy infilammatory infiltrate with vacuolar changes, and apoptotic basal changes. As the disease progresses, the infiltrate is eventually pushed downwards by expanding zone of edema and sclerosis[29] [Figure 7].

Lichenoid contact dermatitis

It shows a patchy band-like dermal infiltrate of lymphocytes with a few eosinophils and a mild basal spongiosis. It usually results from contact with rubber and chemical used in clothing dyes and wine industries.[29]

Progressive pigmented purpuric dermatosis/ Schamberg's disease

It is a chronic discoloration of the skin, which usually affects the legs and often spreads slowly. It may show lichenoid reaction pattern. However, the presence of purpura and deposits of hemosiderin distinguish it from other disorders.[5,29]

Erythroderma and lichen amyloidosis may have prominent pigmented lichenoid tissue reaction.[5,29,123] The latter is recognized by hyperpigmented, lichenified and hyperkeratotic well-formed lesions.[140] Pathologic changes in the form of acanthotic and hyperkeratotic epidermis is cardinal in lichenoid lesions. Eosinophilic cytoid bodies in the epidermis are diagnostic, following histo-chemical stains like congo-red and crystal violet [Figure 8]. The eruption of lymphocyte recovery, initially recorded by Home *et al.*,[141] are now believed to be a form of graft-*versus*-host disease.[142]

Lichen aureus, a variant of pigmented purpuric dermatoses (PPD) is known for persistent, golden, copper-colored, flat-topped papules that appear suddenly. Minute cutaneous blood vassels are the prime target[143,144] [Figure 9].

Lichen spinulosus

It is characterized by round-to-oval patches of grouped follicular papules with rough keratotic centers[145] may yet be another entity, which requires confirmation by microscopic pathology evident as a keratotic plug consisting of laminated corneocytes, occupying a dilated follicle.

CONCLUSIONS

It is worthwhile, at this point in time, to recognize lichenoid tissue reaction/interface dermatitis as an exclusive clinical and/or pathological entity, which has several dermatoses of heterogeneous nature under its ever enlarging domain. Accordingly, it was considered imperative to recapture the precise clinical as well as pathological overtones to exercise the relevant treatment modality.

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Multiple Choice Questions

1. Civatte bodies are defined as
   a. Damaged epidermal cells with shrunken eosinophilic cytoplasm and pyknotic nuclear remnants
   b. Damaged melanocytes shrunken eosinophilic cytoplasm and pyknotic nuclear remnants
   c. Damaged epidermal cells with shrunken basophilic cytoplasm and pyknotic nuclear remnants
   d. Damaged melanocytes with shrunken eosinophilic cytoplasm and pyknotic nuclear remnants

2. Which of the following are the mediators of keratinocyte damage in lichen planus
   a. CD4+ T-cells and NK cells
   b. CD4+ T-cells and dendritic cells
   c. CD8+ T-cells and NK cells
   d. CD8+ T-cells and fibroblasts

3. Which of the following drugs has been incriminated in transfusion- associated graft versus host disease?
   a. Interferon
   b. Adriamycin
   c. Gemcitabine
   d. Fludarabine

4. A dense, well-circumcised sub-epidermal infiltrate enclosed by rete ridges, is a characteristic of
   a. Lichen nitidus
   b. Lichen planus
   c. Dermatomyositis
   d. Discoid lupus erythematosus

5. Which of the following is true for drug induced lichenoid eruption as compared to lichen planus
   a. Melanin incontinence is higher
   b. Denser dermal infiltrate
   c. Absence of parakaratosis
   d. Severe basal cell vacuolation

6. Which of the following is characterized by a lichenoid tissue reaction?
   a. Pemphigus vulgaris
   b. Bullous pemphigoid
   c. Dermatitis herpetiformis
   d. Paraneoplastic pemphigus

7. Lichenoid reaction pattern with chiefly a peri-pilosebaceous /follicular superficial and deep dermal lymphocytic infiltrate is suggestive of
   a. Lichen planus
   b. Dermatomyositis
   c. Lichen nitidus
   d. Discoid lupus erythematosus

8. Lichenoid reaction pattern, the inflammatory infiltrate formed primarily by plasma cells, which are distributed through out the dermis is suggestive of
   a. Syphilis
   b. Graft versus host disease
   c. Toxic epidermal necrolysis
   d. Pityriasis lichenoides et varioliformis acuta

9. Basal vacuolar changes, melanin incontinence and telangiectasia of superficial dermal vessels is a characteristic of
   a. Lichen sclerosus et atrophicus
   b. Schamberg's disease
   c. Poikiloderma
   d. Graft versus host disease

10. Confluent epidermal necrosis, interface dermatitis along with a wedge shaped dermal infiltrate with apex in deep dermis with variable hemorrhage, is a diagnostic feature of
   a. Systemic lupus erythematosus
   b. Lichenoid keratoses
   c. Pityriasis lichenoides et varioliformis acuta
   d. Lichen spinulosus

Answers
1. a, 2. c, 3. d, 4. a, 5. a, 6. d, 7. d, 8. a, 9. c, 10. c