

Histomorphology of lichenoid tissue reactions: A retrospective study

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Abstract

Objective To analyse variety of disorders comprising of lichenoid tissue reactions on the basis of their respective histomorphological features.

Methods A 2-year retrospective study was conducted on skin biopsies with presence of lichenoid tissue reactions. On histopathological examination, lichenoid reactions were identified in a total of 184 cases, out of which 147 were lichen planus and 37 showed lichenoid eruptions.

Results Out of the total of 184 cases, females (62.5%) were more commonly affected. Most common site of predilection being extremities (34.23%). Among the lichenoid tissue reactions, lichen planus (29.89%) and lichen planus pigmentosus (23.36%) constituted majority of cases. Presence of band-like lymphocytic infiltrate is the most constant histopathological finding of lichenoid tissue reaction followed by basal cell layer vacuolization, hyperkeratosis, hypergranulosis, acanthosis, and pigment incontinence.

Conclusion Thus, histopathology is an essential tool for reaching to a conclusive diagnosis, amongst the vast list of differential diagnosis of lichenoid tissue reactions with similar clinical presentation.

Key message Lichenoid tissue reactions comprises of a variety of inflammatory disorders having a broad spectrum of clinical manifestations. Histopathology, acts as an essential tool for a conclusive diagnosis, to differentiate the vast list of differential diagnosis, that present with similar clinical picture.

Key words

Histopathology; Lichenoid tissue reaction; Lichen planus.

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Introduction

Lichenoid tissue reactions (LTR) represent various inflammatory disorders having a wide spectrum of clinical presentation. They represent a conglomerate of disorders clinically and histopathologically similar to Lichen Planus.¹ Lichenoid tissue reaction have been traditionally subclassified into cell-rich and cell-poor

categories depending upon the intensity of inflammatory infiltrate that butt on the dermoepidermal interface.² Examples of cell-rich lichenoid tissue reaction are lichen planus and its variants, lichen striatus, lichen nitidus and cell-poor lichenoid tissue reaction include some autoimmune connective tissue skin disease, erythema multiforme and acute graft-versus-host skin disease.² Lichen planus is a subacute or chronic inflammatory skin disease involving skin, mucous membrane, hair follicle and nails.³ In skin, it presents as pruritic, planar (flat topped), polygonal, violaceous papules that may coalesce into plaques.³ Some studies have suggested that autoreactive cytotoxic T-cells are the effector cells causing degeneration and destruction of epidermal basal cell layer that is common in lichenoid tissue reaction.²

According to one study, lichen planus constitute 0.38% of dermatological outpatients in India.⁴

Clinical variants of lichen planus are linear, eruptive, atrophic, hypertrophic, annular, vesicular, erosive/ulcerative, lichen planopilaris, lichen planus pigmentosus or actinicus, lichen planus pemphigoides and overlap syndrome with lupus erythematosus.³

Histologically, lichenoid tissue reaction is commonly characterized by lympho-histiocytic inflammatory infiltrate arranged in a band-like fashion along with vacuolar degeneration of basal cell layer.⁵

Despite the large spectrum, a systemic approach can lead to a definite diagnosis.

This study correlates the clinical and histomorphological spectrum of the wide range of disorders showing presence of lichenoid tissue reaction which can help to make a prompt diagnosis and decrease the morbidity associated with these conditions.

Methods

A retrospective study for a duration of 2 years was conducted on the skin biopsy specimens received at Department of Pathology, Hindu Rao Hospital, New-Delhi. Histopathologically, confirmed cases of lichenoid tissue reactions were included and studied in detail from January 2018 to December 2019.

Clinical findings were reviewed and analyzed including the site, duration and type of the lesion and any other additional findings associated with the lesion.

Histopathological features were reviewed and the data retrieved was statistically tabulated.

Results

During the study period, 184 patients with lichenoid tissue reactions were retrieved, out of which 147 had lichen planus and its variants and 37 showed lichenoid eruptions.

Most common age group was 3rd decade followed by 2nd and 4th decade with female preponderance (114 out of 184). The eldest patient was a 66-year-old female, and the youngest was a two year old male patient. 48 patients were below 18 years of age (26.08%).

Most frequent site of lesions were extremities followed by generalized body involvement, scalp, face and neck, oral cavity, trunk and genital area in decreasing order of frequency.

Clinically, most lesions were hyperpigmented (53.26%) and presented most frequently with pruritic papules (40%).

Amongst 147 cases of lichen planus type, classical lichen planus was most frequent with 56 patients and 91 cases were its histopathological variants amongst which lichen planus pigmentosus was most common

Table 1 Histopathological diagnosis of different lichenoid reactions

Diagnosis	n (%)
Lichen planus and variants	
Classical lichen planus	56 (30.43)
Lichen planus pigmentosus	44 (23.91)
Lichen plano pilaris	34 (18.47)
Hypertrophic lichen planus	7 (3.80)
Oral lichen planus	5 (2.71)
Linear atrophic lichen planus	1 (0.54)
Lichenoid eruptions	
Lichen nitidus	9 (4.89)
Lichen simplex chronicus	6 (3.26)
Lichen striatus	5 (2.71)
Lichen sclerosus et atrophica	5 (2.71)
Pityriasis lichenoids chronica	5 (2.71)
Lichen amyloidosis	4 (2.17)
Lichen scrofulosorum	2 (1.08)
Lichen spinulosus	1 (0.54)
Total	184 (100)

constituting 44 patients. The histopathological diagnosis of various cases with lichenoid tissue

A variety of epidermal changes observed in cases of lichenoid tissue reaction in this study is enlisted in **Table 2**.

The histopathological changes in dermis are illustrated in **Table 2**. The most frequent dermal findings were melanin incontinence, followed by lymphohistiocytic band-like inflammatory infiltrate over dermoepidermal interface.

Lichenoid tissue reactions were subdivided into cell-rich and cell-poor categories, based on the severity of inflammation described in **Table 3**.

The characteristic changes present in different conditions of lichenoid tissue reaction are as follows: Lichen planus pigmentosus (**Figure 1**) showed epidermal atrophy (28 cases) and melanin incontinence (39 cases), on histopathological examination. Lichen nitidus showed presence of characteristic claw clutching

Table 2 Epidermal and dermal changes of different lichenoid reactions

Epidermis	No. of Cases	Dermis	No. of cases
Vacuolar basal degeneration cell	113	Melanin incontinence	94
Acanthosis	81	Predominantly lymphocytic infiltrate	87
Hyperkeratosis	69	Perivascular inflammatory infiltrate	60
Hypergranulosis	63	Band like inflammatory infiltrate over DEJ	50
Atrophy	44	Melanophages	47
Parakeratosis	26	Perifollicular inflammatory infiltrate	32
Spongiosis	18	Perifollicular fibrosis	19
Max joseph space	11	Perifollicular basal cell	12
Loss of rete ridges	10	vacuolar degeneration	
Follicular plugging	10	Mixed inflammatory infiltrate	11
Papillomatosis	04	Subepidermal bulla	7
Civatte bodies	03		
Elongated rete ridges (saw tooth)	03		

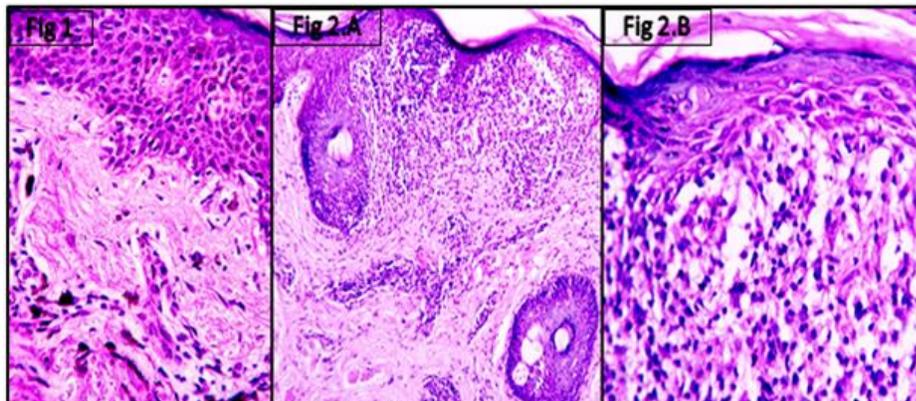


Figure 1 Lichen planus pigmentosus- Melanin incontinence, melanophages in the dermis (100X, H&E);

Figure 2 A&B: Lichen nitidus- Rete ridges clutching the focal dense lymphohistiocytic infiltrate in upper dermis (100X,H&E); Dense lymphohistiocytic infiltrate (400X, H&E)

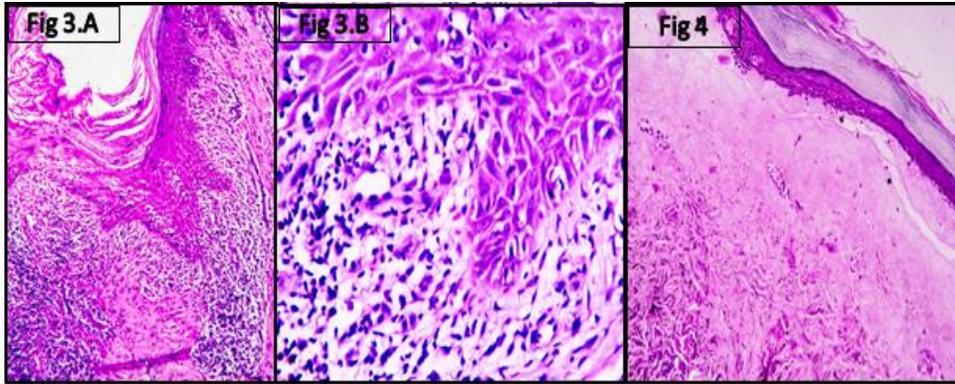


Figure 3 A&B: Hypertrophic lichen planus- Irregular acanthosis, lichenoid infiltrate at the base of hyperplastic epidermis(100X, H&E); Vacuolar degeneration of basal layer (400X,H&E)
Figure 4 Lichen sclerosus et atrophicus- Epidermal atrophy, hyalinosis, dermal edema(100X, H&E)

Table 3 Classification of LTR based on the intensity of inflammatory infiltrate.

<i>Cell-rich LTR</i>	<i>No. of Cases</i>	<i>Cell-poor LTR</i>	<i>No. of cases</i>
Classical lichen planus	56	Linear atrophic Lichen Planus	1
Lichen planus pigmentosus	44	Lichen Simplex Chronicus	6
Hypertrophic lichen planus	7	Lichen Plano Pilaris	34
Oral lichen planus	5	Lichen sclerosus et atrophica	5
Lichen striatus	5	Pityriasis Lichenoids Chronica	5
Lichen nitidus	9		
Lichen amyloidosis	4		
Lichen scrofulosorum	2		
Lichen spinulosus	1		

the ball appearance with expansion of dermal papillae on histopathology (**Figures 2A, 2B**).

Hypertrophic lichen planus (**Figures 3A, 3B**) showed irregular acanthosis (6 cases) in most of the tissue biopsies studied. Lichen sclerosus et atrophicus (**Figure 4**) showed homogenization of collagen in most of the cases. Parakeratosis with acanthosis was seen in most cases of oral lichen planus (**Figures 5A, 5B**). All cases of lichen amyloidosis (**Figures 6A, 6B**) showed amorphous eosinophilic deposits in papillary dermis which showed metachromasia with methyl green stain. Lichen simplex chronicus (**Figure 7**) in histopathology showed longitudinal fibrosis in papillary dermis in most samples. Granuloma along with giant cells, multinucleated histiocytes and minimal necrosis was seen in both the cases of lichen scrofulosorum (**Figures 8A, 8B**).

Discussion

Lichenoid tissue reactions refers to papular skin lesions due to various skin disorders with

different etiologies which can be diagnosed by their distinctive histologic findings. The prototype of lichenoid tissue reaction is lichen planus. These are non-infectious lesions presenting as pruritic, planar (flat topped), polygonal, violaceous papules of different sizes occurring in clusters. In our study, lichen planus and its variants constituted a total of 147 cases (79.89%), among which classical lichen planus (**Figure 9**) were most common, constituting 30.43% (56 cases) of total cases followed by lichen planus pigmentosus (43 cases) and lichen planopilaris (31 cases) (**Figure 10**), consistent with the findings of study done by Parihar *et al.*⁶ The other variants of lichen planus included hypertrophic (7 cases), oral (5 cases) and linear atrophic(1 case) (**Figure 11**). Lichenoid eruptions due to other causes constituted the rest of the 37 cases (20.10%), in which lichen nitidus was most common (9 cases) followed by lichen simplex chronicus (6 cases), 5 cases each of lichen striatus (**Figure 12**), lichen sclerosus et atrophicus and pityriasis lichenoids chronica (**Figure 13**), 4 cases of lichen amyloidosis, 2 cases of lichen scrofulosorum, 1 case of lichen

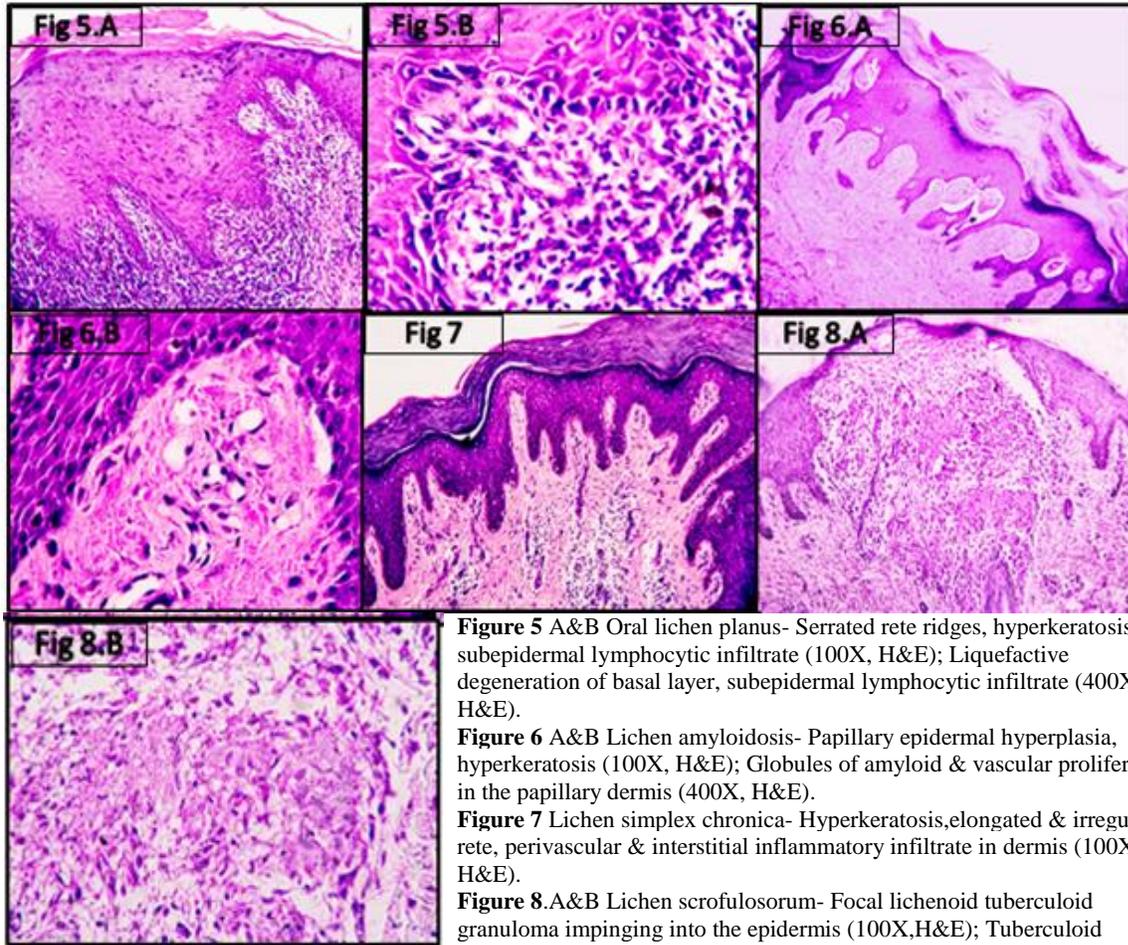


Figure 5 A&B Oral lichen planus- Serrated rete ridges, hyperkeratosis, subepidermal lymphocytic infiltrate (100X, H&E); Liquefactive degeneration of basal layer, subepidermal lymphocytic infiltrate (400X, H&E).

Figure 6 A&B Lichen amyloidosis- Papillary epidermal hyperplasia, hyperkeratosis (100X, H&E); Globules of amyloid & vascular proliferation in the papillary dermis (400X, H&E).

Figure 7 Lichen simplex chronica- Hyperkeratosis, elongated & irregular rete, perivascular & interstitial inflammatory infiltrate in dermis (100X, H&E).

Figure 8. A&B Lichen scrofulosorum- Focal lichenoid tuberculoid granuloma impinging into the epidermis (100X, H&E); Tuberculoid granuloma (400X, H&E).

spinulosus. This finding was comparable to the other studies done on lichen planus by Chauhan *et al.*⁵ Kumar *et al.*⁶

The distribution of different cases in the study conducted by Banushree *et al.*⁷ showed classical lichen planus in 73.3% of the cases, which was followed by lichen planus pigmentosus; 8.3%, follicular lichen planus; 5%, lichen nitidus; 3.3%, each of lichen planus hypertrophicus, lichen planus atrophicus, lichen planus actinicus, benign lichenoid keratosis, lichenoid eruption, and 1.7% being lichen striatus

The present study showed predilection for females as compared to males. This was consistent with various studies quoted in the literature.⁶⁻¹⁰ In the present study most of the cases were in the age group of 2- 50 years of

age, maximum in the 3rd decade, similar to findings of Sehgal *et al.*¹¹ (11- 40 years), Parihar A *et al.*⁴ and Kumar MU *et al.*⁶ where most of the cases were between 1-30 years of age.

In the present study, the most common sites involved by these lesions were upper and lower extremities 34.23% (63 of 184) followed by generalized skin involvement involving multiple sites i.e. head and neck, trunk and extremities seen in 21.73% (40 of 184) cases (**Table 2**) as compared to other studies in which the lower limbs were most commonly affected.^{4,5}

The characteristic clinical features seen in classical lichen planus were pruritic, violaceous papules and plaque, whereas hyperpigmented patches were more common in lichen planus pigmentosus. Lichen planopilaris most commonly showed patchy central scarring

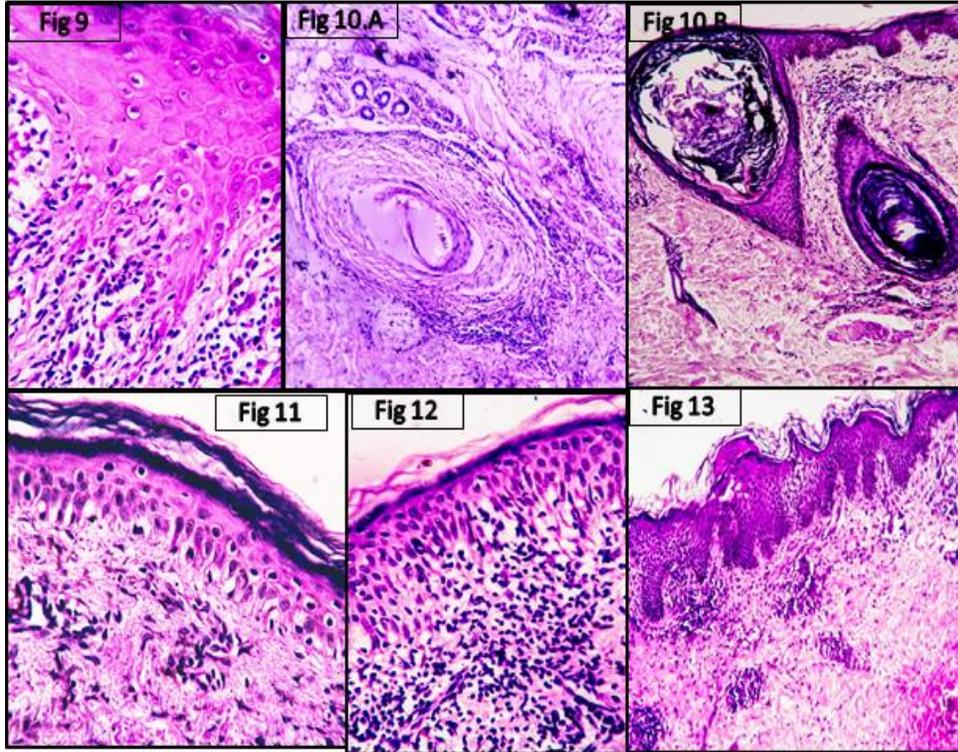


Figure 9 Classical lichen planus- Acanthosis, vacuolar degeneration of basal layer, colloid bodies, dense lymphocytic infiltrate at the dermo-epidermal junction (400X, H&E)

Figure 10 A&B Lichen planopilaris- Perifollicular lymphocytic infiltrate (400X, H&E); Follicular plugging, perifollicular lymphocytic infiltrate (100X,H&E).

Figure 11 Linear atrophic lichen planus- Epidermal atrophy, focal lymphocytic infiltrate in the dermis (400X,H&E).

Figure 12 Lichen striatus- Exocytosis of lymphocytes, subepidermal lymphocytic infiltrate (400X,H&E).

Figure 13 Pityriasis lichenoid chronica- Focal parakeratosis, superficial perivascular inflammatory infiltrate (100X, H&E)

alopecia with hyperpigmented margins. Reticular pattern of the lesions were frequently seen in oral lichen planus.

The histologic findings of lichenoid tissue reactions are mainly explained by autoimmune mechanism involving the plasmacytoid dendritic cell-derived IFN- α mediated cytotoxic T-cell injury to the basal keratinocytes.² This results in a series of degenerative changes at the dermal epidermal junction leading to the presence of inflammatory cell infiltrate mostly comprising of T lymphocytes, macrophages and dendritic cells⁵ at the dermal epidermal junction and vacuolar degeneration of basal cell layer which has an effect on the clinical manifestation associated with the skin lesions.¹²

The amalgamation of different histological features such as type of inflammatory infiltrate and its distribution, vacuolar basal layer degeneration in epidermis, melanin incontinence lead to a diagnosis of lichenoid tissue reaction due to various causes.

Table 4 depicts histopathological comparison of various other similar studies. The epidermal changes seen most frequently in this study were vacuolar basal cell degeneration in 113 (61.4%) cases in consistent with the findings of Maheshwari GR *et al.*¹³ and Chauhan *et al.*⁵ Acanthosis was seen in 81 cases (44.02%) similar to findings of Maheshwari GR *et al.*¹³ (55.5%), Muralidhar *et al.*¹⁴ (56.45%) and Chauhan *et al.*⁵ (60.6%). Hyperkeratosis and

Table 4 Comparison of epidermal and dermal changes with other similar studies.

Parameter	Present study	Maheshwari GR et al. ¹³ (2016)	Muralidhar et al. ¹⁴ (2020)	Chauhan R et al. ⁵ (20215)	Kumar UM et al. ⁶ (2013)
Epidermal changes					
Atrophy	23.91	1.71	1.74	21.21	15.56
Hyperkeratosis	37.5	77.78	80.64	71.21	93.33
Parakeratosis	14.13	18.33	12.9	16.66	6.67
Hypergranulosis	34.23	29	22.58	65.15	
Acanthosis	44.02	55.5	56.45	60.6	83.33
Basal cell vacuolar degeneration	61.41	68.37	95.16	74.24	96.67
Dermal changes					
Max Joseph space	5.97	2.56	4.83	3.03	10
Band like infiltrate	27.17	52	58.06	48.48	93.33
Lymphocytes	47.28	85	100	72.72	100
Melanin	51.08	52.99	90.32	63.63	93.3

hypergranulosis was seen in 69 and 63 cases respectively similar to studies done by other authors.⁵⁻⁷ The dermis predominantly showed lymphocytic infiltration in 47.28% (87 of 184) cases and band-like inflammatory infiltrate in the dermal epidermal junction was seen in (50 of 184) 27.17% cases similar to that of Muralidhar et al;¹⁴ Maheshwari GR et al.¹³ but dissimilar to few other studies.^{6,7,15} Melanin pigment incontinence as a result of damage to the melanocytes in the basal layer was found to be the most frequent histological finding in the dermis in 51.08% (94 of 184) in ours as well as studies done by Maheshwari GR et al.¹³ and Chauhan et al.⁵ (63.63%).

The differential diagnosis of lichen planus has to be ascertained pertaining to its therapeutic and prognostic significance. On the basis of patient's clinical history, presentation of cutaneous lesions, and site predilection of diseases, lichen ruber annularis should be differentiated from morphea or erythema annulare, and lichen ruber linearis from a striated nevus (inflammatory linear verrucous epidermal nevus; ILVEN) or lichen striatus.¹⁶ Squamous cell carcinoma is a rare complication of oral lichen planus and hypertrophic lichen planus, so differentiating hypertrophic lichen planus from classical lichen

planus is utmost important. Lichen planus pigmentosus have been found to be associated with head and neck cancer along with concurrent acrokeratosis paraneoplastica in few instances.¹⁷

Lichen planus generally have a favorable prognosis and relapse rate is 20%. Oral lichen planus and lichen ruber verrucosus persists for several years.¹⁶

Conclusion

Histopathology is an important tool by which a definitive diagnosis of lichenoid tissue reaction can be made. Close cooperation between a clinician and histopathologist is extremely important. One should always keep in mind about all the differential diagnosis while giving a confirmatory diagnosis of lichenoid tissue reaction. A correct diagnosis reduces the morbidity associated with the disease and further enhances its prognosis and patient care.

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Author's contribution

AP, PP, AM, SS, SN, PSK: Contribution to study design, manuscript writing, have given final approval of the version to be publication.

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