

Original Article



Comparative study of histopathological diagnostic criteria in cutaneous lesions of lichen planus and discoid lupus erythematosus

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Abstract

Background and aims: Lichen planus (LP) and discoid lupus erythematosus (DLE) are two relatively common mucocutaneous lesions whose clinical and histopathological features overlap in some cases. The present study aimed to distinguish between these two lesions histopathologically in order to treat them more accurately.

Methods: In a cross-sectional descriptive-analytical study, 29 and 48 microscopic slides of skin samples of DLE and LP, respectively, were examined in the pathology archive of Al-Zahra hospital of Isfahan from 2008 to 2018. The slides prepared by hematoxylin-eosin staining were examined simultaneously and blindly by three pathologists with a light microscope and compared according to certain histopathological criteria. Then obtained data were analyzed by SPSS version 24 using chi-square, Fisher's exact, Mann-Whitney, and *t* tests ($P < 0.05$).

Results: Based on the findings, the presence of hyperparakeratosis with superficial hyperorthokeratosis, epithelial atrophy, deep perivascular infiltration, presence of edema in the papillary dermis, presence of plasma cells with lymphohistiocytes in inflammatory infiltration, and presence of mucin in the dermis were significantly higher in DLE than in LP ($P < 0.05$). On the other hand, the intensity of lichenoid infiltration, presence of saw tooth hyperplasia of rete ridges, presence of cleft between the epithelium and connective tissue, spongiosis, hyperorthokeratosis alone, and wedge-shaped hypergranulosis were significantly higher in LP than in DLE ($P < 0.05$).

Conclusion: Perieccrine and perifollicular inflammation, presence of Civatte bodies (CBs), abundance of fibrosis, presence of pale keratinocytes, and presence of pseudoepitheliomatous hyperplasia were not the criteria for differential diagnosis of LP and DLE.

Keywords: Lichen planus, Lupus erythematosus, Differential diagnosis, Pathology, Skin

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Introduction

Discoid lupus erythematosus (DLE) and lichen planus (LP) are two distinct lesions in terms of clinical, histopathological, and immunopathological features; however, they have clinicohistopathological overlapping. The diagnosis of oral DLE is often difficult and is clinically and histopathologically very similar to LP (1-4). In the study of Batrani et al, distinctive histopathological features of DLE were perivascular and periadnexal infiltration, increased mucin dermis, epidermal atrophy or pseudoepitheliomatous hyperplasia with pale keratinocytes, and thick basement membrane, while distinctive histopathological features of LP were the presence of dense hyperkeratosis, wedge-shaped hypergranulosis, and epidermal saw tooth hyperplasia (5). These results confirmed the findings of the study by Komori et al whereby the basement membrane thickness in LE was greater than that in LP (6).

In the study of Schiödt and Pindborg, the most important histological differences between LP and DLE were saw tooth appearance of rete pegs in LP in contrast to the alternation of pseudoepitheliomatous hyperplasia and epithelial atrophy in DLE as well as juxtaepithelial band-like infiltration in LP in contrast to the focal deep infiltration in connective tissue in DLE (4). However, in a study by Van der Horst et al, histopathological features in favor of DLE were a combination of hyperkeratosis and follicular plugging, vacuolar degeneration of basal cellular layer, thickening of the basement membrane, perifollicular and perivascular lymphocytic infiltration, and prominent epidermal atrophy (7).

In another study by Annessi et al, the important histopathologically distinctive features were basement membrane thickening, mucin deposits in the reticular dermis, papillary dermal edema, and deep perivascular lymphocytic infiltration in DLE compared with sebaceous

gland atrophy and hypergranulosis in lichen planopilaris (LPP) (8). Inalöz et al reported that hypergranulosis, irregular acanthosis, saw tooth appearance of rete pegs, hydropic degeneration of basal cells with clefts (Max-Joseph spaces), formation of colloid body and band-like dermal lymphocytes occurred more frequently in LP, while basement membrane thickening, hydropic degeneration of basal cells without clefts, and perifollicular and perivascular infiltration were greater in DLE (9). In LP-LE overlap syndrome, Inalöz et al, Schmitz et al, and Jicha et al reported various lesions in a patient that were consistent with LP or DLE (9-11).

In studies by Moure et al and Kumar & Yelikar, extrafollicular hyperkeratosis, perieccrine sweat glands infiltration, thickening of the basement membrane, extrafollicular extensive dermohypodermal partial fibrosis, epidermal atrophy, and vacuolar degeneration of basal epidermal cells were positive in skin lesions of DLE compared with LPP (12,13).

Tandon et al found that reduction or absence of sebaceous glands, lack of perieccrine infiltration, superficial lymphocytic infiltration, low thickness of basement membrane, and mucinous perifollicular fibroplasia in the upper dermis were more distinctive in LPP compared to DLE (14).

In studies by Nico et al and also Karjalainen and Tomich on oral lesions of LE, the most important distinctive histopathological features of DLE from LP were thicker basement membrane, thicker blood vessel walls, deeper perivascular infiltration, edema, and more mucin in lamina propria. In contrast, epithelial atrophy, saw tooth appearance of rete ridges, and presence of Langerhans cells were more prominent in LP than in DLE (15,16). Nambudiri et al showed that interface dermatitis, deep and dense perivascular inflammation, increased interstitial mucin in the dermis, and thicker basement membranes were more prevalent in DLE than in LPP. In contrast, perifollicular inflammation, increased mucin mixed with fibrous tissue in the perifollicular area, perifollicular erythema, and scale combined with lack of follicular plugging or central depigmentation were higher in LPP than in DLE (17).

Therefore, because of overlapping clinicopathological features of LP and DLE, the present study aimed to compare these two lesions from different histopathological aspects for better diagnosis and more accurate treatment.

Materials and Methods

Sample selection

In the present cross-sectional descriptive-analytical study, the recorded samples of LP and DLE were examined in the pathology archive of Alzahra hospital in Isfahan University of Medical Sciences from 2008 to 2018, and samples without the necessary information were excluded from the study. It is noteworthy that histopathological features of oral and cutaneous LP are similar, but the diagnostic criteria for DLE are more present in the skin than in

the mouth; accordingly, a definitive histopathological diagnosis of DLE with oral biopsies was not possible (18-21). Therefore, only skin biopsies of these two lesions were used to remove the diagnostic confounding factors comparing LP and DLE. The present study was performed on 126 microscopic slides of patients diagnosed with skin lesions of LP and DLE. All DLE samples were without clinical systemic signs and symptoms. Out of 126 slides, 49 slides were removed from the study (19 slides due to the presence of a lesion on the scalp, 2 slides due to the presence a lesion in the mucous membrane, 25 slides due to disagreement with the final diagnosis, and 3 slides due to lacking sufficient tissue), and finally 77 slides were selected at magnification of 100 and 400 under a light microscope (Olympus Bx41TE, Tokyo, Japan). The selected slides had significant tissue and were stained with hematoxylin-eosin including 29 slides of DLE (37.7%) and 48 slides of LP (62.3%).

Consideration of samples

The prepared slides were considered simultaneously by two oral and maxillofacial pathologists and a dermatopathologist based on certain histopathological criteria such as saw tooth hyperplasia of rete ridges, pseudoepitheliomatous hyperplasia, pale keratinocytes, orthokeratotic hyperkeratosis, wedge-shaped hypergranulosis, atrophy of the epidermis, perivascular and periadnexal (e.g., hair follicles, sebaceous glands, and sweat glands) infiltration, accumulation of keratin in the orifice of the hair follicle (follicular plugging), band-like juxtaepithelial infiltration of lymphocytes, presence of cleft between the epithelium and connective tissue (Max-Joseph space), papillary subepithelial edema (sometimes to the point of vesicle formation), spongiosis, hydropic degeneration of basal cellular layer, deep dermal infiltration, and Civatte bodies (CBs). In addition, clinical characteristics of patients such as age, sex, presence of oral involvement, site of skin involvement (scalp, arm, abdomen, legs, wrist, and the like), and clinical differential diagnosis of lesions were extracted from the patient file.

Statistical analysis

The obtained data were analyzed using SPSS software version 24 and statistical tests of chi-square, Fisher's exact, Mann-Whitney, and *t*-student. It should be noted that scalp specimens were excluded from the present study for a more accurate comparison.

Results

Based on the obtained accessory clinical findings, both DLE and LP skin lesions were more common in women. The Mean age of DLE was 41.58 ± 16.58 years which most of them were in the face and mean age of LP was 44.83 ± 18.09 years which most of them were in the extremities. Therefore, there was a significant difference between the two lesions only in terms of the site of involvement ($P < 0.001$).

Based on the obtained histopathological findings, the presence of hyperparakeratosis with hyperorthokeratosis at the surface of the lesion, epithelial atrophy, deep perivascular infiltration, presence of edema in the papillary dermis, presence of plasma cell cells with lymphohistiocytes in the inflammatory infiltration, and presence of mucin in the dermis were significantly higher in DLE than in LP ($P < 0.05$). On the other hand, the intensity of lichenoid infiltration, presence of saw tooth hyperplasia of the rete ridges, presence of cleft between the epithelium and connective tissue (Max-Joseph space), spongiosis, hyperorthokeratosis alone, and wedge-shaped hypergranulosis were significantly higher in LP than in DLE ($P < 0.05$). However, the prevalence of age and sex, periecrine and perifollicular inflammation, presence of CBs, frequency of fibrosis, presence of pale keratinocytes, and presence of pseudoepitheliomatous hyperplasia did not differ significantly between the lesions and, therefore, could not be criteria for differentiating LP and DLE (Table 1 and Figures 1 to 4).

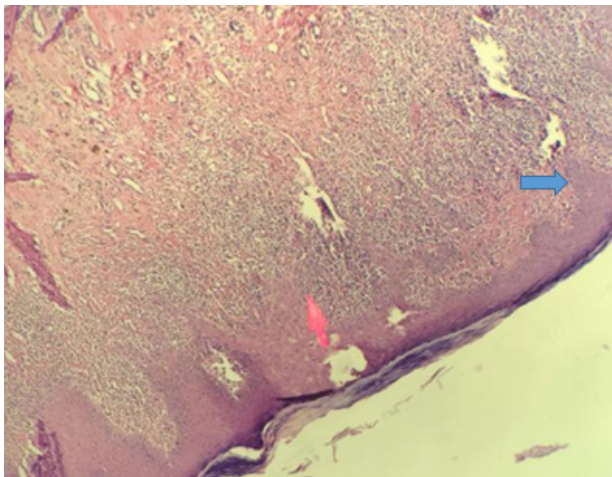


Figure 1. Lichenoid infiltration and hydropic degeneration of basal cells (pink arrow), saw tooth hyperplasia of rete ridges (blue arrow) in cutaneous LP (magnification $\times 100$). Note: LP: Lichen planus.

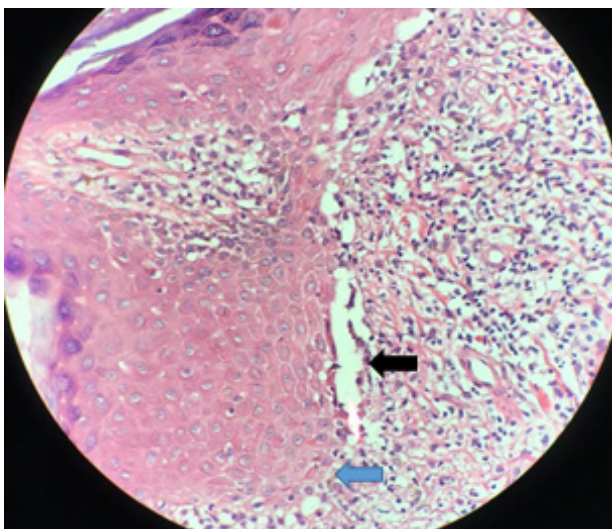


Figure 2. Presence of cleft between epithelium and basement membrane (Max-Joseph space) (black arrow), and hydropic degeneration of basal cells (blue arrow) in cutaneous LP (magnification $\times 400$). Note: LP: Lichen planus.

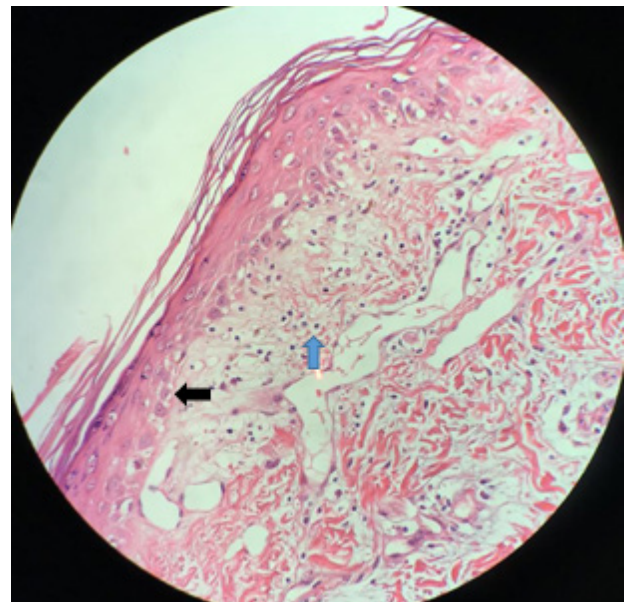


Figure 3. Presence of edema in papillary dermis (blue arrow), and hydropic degeneration of basal cells (black arrow) in cutaneous DLE (magnification $\times 400$). Note: DLE: Discoid lupus erythematosus.

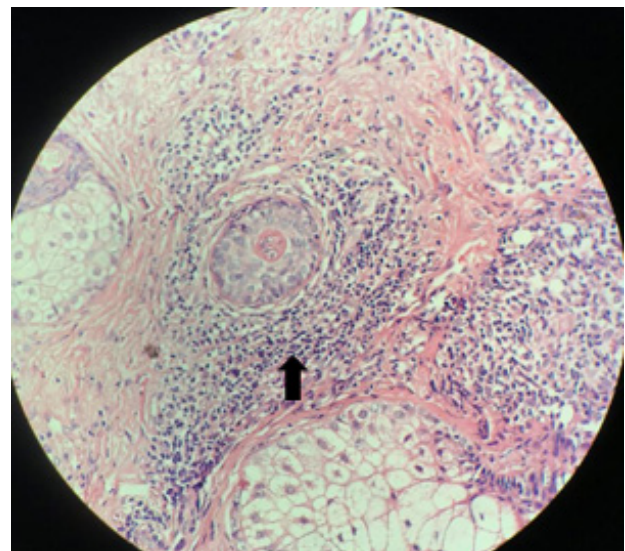


Figure 4. Presence of perifollicular inflammation (black arrow) in cutaneous DLE (magnification $\times 400$). Note: DLE: Discoid lupus erythematosus.

Discussion

Due to the overlap of clinical and histopathological features of LP and DLE, the present study compared each clinical and, especially histopathological, features of the two lesions separately which are presented below:

Frequency of LP and DLE skin lesions by sex and age

In the present study, both LP and DLE lesions tended to occur more frequently in women, which is similar to the study by Asadi Kani et al and Rahmati Roudsari et al on comparing DLE and LPP and also consistent with the study by Inalöz et al, Crowson and Magro, and Szczech et al on the DLE (9, 22-25). In a review study by Ahmed et al, contrary to the present study, the sexual prevalence of LP was reported to be the same, which may be due to differences in the number of samples in the two

Table 1. Comparison of characteristics of DLE and LP

	Variable	DLE	LP	P value	
Not significant	Gender (Female)	17 (58.6)	26 (54.2)	0.703	
	Age	41.58±16.58	44.83±18.09	0.434	
	Perieccrine inflammation	1 (3.4)	4 (8.3)	0.645	
	Perifollicular inflammation	18 (62.1)	20 (41.7)	0.083	
	Civatte body	12 (41.4)	13 (27.1)	0.194	
	Fibrous tissue	8 (27.6)	6 (12.5)	0.096	
	Pallor keratinocytes	19 (65.5)	28 (58.3)	0.531	
	Pseudoepitheliomatous hyperplasia	0	6 (12.5)	0.087	
Site of involvement					
In favor of each of DLE or LP per site	Head and neck	25 (86.2)	13 (27.1)	<0.001	
	Upper limbs	1 (3.4)	7 (14.6)		
	Lower limbs	0 (0)	18 (38.5)		
	Trunk and genital	3 (10.3)	10 (20.8)		
In favor of DLE	Hyperparakeratosis with Hyperorthokeratosis	18 (62.1)	9 (18.8)	<0.001	
	Epithelial atrophy	20 (69)	18 (37.5)	0.007	
	Deep perivascular infiltration	17 (58.6)	3 (6.3)	<0.001	
	Presence of edema in papillary dermis	13 (44.8)	1 (2.1)	<0.001	
	Presence of plasma cells with lymphohistiocytes	11 (37.9)	1 (2.1)	<0.001	
	Presence of mucin in derm	4 (13.8)	0 (0)	0.018	
Intensity of lichenoid infiltration					
In favor of LP	Low	15 (51.7)	8 (16.7)	<0.001	
	Moderate	11 (37.9)	29 (60.4)		
	Severe	0 (0)	10 (20.8)		
	Saw tooth hyperplasia of rete ridges	1 (3.4)	24 (50)		<0.001
	Cleft between epithelium and connective tissue (Max-Joseph space)	7 (24.1)	25 (52.1)		0.016
	Spongiosis	8 (27.6)	24 (50)		0.053
	Hyperorthokeratosis alone	7(24.1)	38(79.2)		<0.001
	Wedge shaped hypergranulosis	2 (6.9)	33 (68.8)		<0.001

Note. DLE: Discoid lupus erythematosus; LP: Lichen planus.

studies (26).

The present study reported that the mean age of patients with DLE and cutaneous LP was 41.58 ± 16.58 and 44.83 ± 18.09 years, respectively, which is almost similar to the study findings of the study by Asadi Kani et al, Parihar et al, and Ahmed et al (22,26,27).

Frequency of LP and DLE skin lesions according to the site of involvement

In the present study, skin involvement in LP was more common in the extremities and face, respectively, while it was more common in the face and trunk, respectively, with regard to DLE. In DLE, the lesions occurred significantly more in the head and neck area. Likewise, in a review study, Crowson and Magro reported more DLE involvement in the head and neck area (around the eyes and ears) in line with the present study (24). In their study, Arps and Patel also stated that hypertrophic DLE was more likely to occur in the face and arms, while hypertrophic LP was more likely to develop skin lesions in the lower extremities, which confirms the results of the

present study (28).

Comparison of lichenoid infiltration (juxtaepithelial lymphocytic band) rate in LP and DLE skin lesions

In the present study, moderate and severe lichenoid infiltration was higher in LP than in DLE, and lichenoid infiltration was often as low presentation in DLE. Similar to the present study, a study on LPP and DLE lesions by Asadi Kani et al reported that moderate, severe, and low lichenoid infiltration in LPP was greater than that in DLE (22). By examining six cases of ulcerated LP and DLE, Batrani et al reported dense lichenoid infiltration in all three cases of LP compared with two cases of DLE (5). Grabbe and Kolde also observed more of these findings in LP, but suggested that they may also be present in DLE (29). Andreasen and Ahmed et al, similar to the present study, reported lichenoid infiltration as a diagnostic feature of LP (26,30). In line with the present study, Komori et al observed moderate to severe lichenoid infiltration in LP with definite limits in all lesions (6).

Comparison of the presence of saw tooth hyperplasia of rete ridges in LP and DLE skin lesions

In the present study, saw tooth hyperplasia of rete ridges was observed in 50% of LP specimens, while saw tooth hyperplasia of rete ridges was not visible in 96.6% of DLE specimens, and the frequency of presence of saw tooth hyperplasia of rete ridge in LP specimens was significantly higher compared with DLE specimens. Therefore, saw tooth hyperplasia of the rete ridges can be considered as a criterion for histopathological differentiation of LP from DLE.

In line with the present study, Schiødt and Pindborg (1976), World Health Organization, Elder, Patterson, Calonje, Batrani et al, and Ahmed et al observed saw tooth hyperplasia of rete ridges in a higher percentage of LP compared with DLE and reported it as a diagnostic feature of LP (2,3,4,5,26,31,32). However, in contrast to the present study, Karjalainen and Tomich in their study of oral LP and LE and Schiødt (1984) in their study of oral DLE reported that saw tooth hyperplasia of the rete ridges in DLE was slightly higher than in LP, but they did not recognize it to have diagnostic value (16,33). In their study, Karjalainen and Tomich stated that rete ridges were more prone to atrophy in LPs (16). This difference may be due to the study of different specimens, and perhaps most of the LP specimens examined in the mentioned studies were non-reticular LPs. In a study by Andreasen, examining all types of LPs, the reticular type had a greater degree of saw tooth hyperplasia of the rete ridges than other types of LPs (30).

Comparison of the frequency of basal layer hydropic degeneration in LP and DLE skin lesions

In the present study, hydropic degeneration of the basal layer was seen in all LP and DLE samples. Asadi Kani et al reported more hydropic degeneration of the basal layer in DLE samples (84.62%) than in LPP samples (45.45%), which may be due to a comparative study containing LPP samples (22), because hydropic degeneration in LPP is more evident in the basal cells of the hair follicles than in the basal cells of the epidermis. Although Andreasen confirmed basal layer hydroponic degeneration as a diagnostic criterion for oral LP; nevertheless, he observed rather marked variations in histological appearance of clinical types of oral LP and, apart from lichenoid infiltration, found none of the other histological features of oral LP to be a constant finding in all cases (30). In line with the present study, Karjalainen and Tomich as well as Schiødt (1984) reported this process equally in both lesions and did not consider it as one of their differentiation criteria (16, 33). Kumar and Yelikar found that this feature in DLE was slightly higher than in LP (13). Further, in line with the present study, Komori et al observed basal layer hydropic degeneration in all LP and lupus erythematosus (LE) lesions (6).

Comparison of the frequency of pseudoepitheliomatous hyperplasia in LP and DLE skin lesions

In the present study, pseudoepitheliomatous hyperplasia was observed in 12.5% of LP samples compared to none of the DLE samples, but this difference was not statistically significant. By examining three cases of LP and three cases of oral DLE, Batrani et al observed pseudoepitheliomatous hyperplasia in two cases of DLE and no case in LP, reporting it as a distinctive feature of these two lesions in favor of DLE (5). Schiødt (1984) also considered the presence of pseudoepitheliomatous hyperplasia to have a high diagnostic value in the diagnosis of DLE, but he also found it is very difficult to diagnose pseudoepitheliomatous hyperplasia by itself because the improper placement of the sample in paraffin mold can lead to a false-positive result of the presence of pseudoepitheliomatous hyperplasia (33), and this can be one of the reasons for the difference between the present study and the previously mentioned studies.

Comparison of the cleft between epithelium and connective tissue in LP and DLE skin lesions

In the present study, 52.08% of LP cases had a cleft between the epithelium and connective tissue (Max-Joseph space), and this rate was significantly higher than that of DLE. In line with the present study, Ahmed et al and Inalöz et al described the presence of a cleft in the basement membrane due to lysis of keratinocytes (Max-Joseph space) as a feature observed in LP (9,26). Komori et al also reported the presence of a cleft with the floor of the basement membrane attached to the dermis in all cases of patients with LP and attributed it to hydropic degeneration of the basal layer, eventually leading to fluid accumulation (6).

Comparison of the presence of epithelial atrophy in LP and DLE skin lesions

In the present study, epithelial atrophy was significantly higher in DLE (69%) than in LP (37.5%). Consistent with the present study, Batrani et al, Rahmati Roudsari et al, Moure et al, Asadi Kani et al, and Kumar and Yelikar reported more epithelial atrophy in DLE than in LP (5,12,13,22,23). Batrani et al, Schiødt and Pindborg (1976), and Schiødt (1984) considered epithelial atrophy to have diagnostic value for the differential diagnosis of DLE from LP (4,5,33). In contrast to the present study, Karjalainen and Tomich reported more atrophy of rete pegs in oral LP (16). In addition, Grabbe and Kolde in a review study found epithelial atrophy in both LP and DLE. This difference may be due to the fact that the LP cases studied by Grabbe and Kolde were mostly atrophic LPs or the lesion has survived a long life at the time of diagnosis (29).

Different opinions have been expressed about the presence of epithelial atrophy in oral LP and DLE lesions, and there is no consensus on this issue. Andreasen believed that only young specimens of reticular and papular types

of oral LP showed typical histopathological features of skin lesions. In young lesions, inflammation and focal epithelial hyperplasia and hyperkeratosis can show the appearance of Wickham striae in the clinical view, while epithelial atrophy is more likely to be observed in older lesions (30).

Schiødt's recommendations for the differential diagnosis of oral DLE from reticular LP include the atrophy of rete ridges, deep inflammatory infiltration, edema in the papillary dermis, and thickening of the basement membrane in DLE, which has also been confirmed by Elder, Patterson, Calonje, and the World Health Organization (2,3,31-33).

Comparison of the presence of pale keratinocytes in LP and DLE skin lesions

In the present study, pale keratinocytes were higher in DLE (65.5%) than in LP (58.3%), but this difference was not statistically significant. In their study, Karjalainen and Tomich described these pale keratinocytes as vacuolization of keratinocytes (16), and Eversole et al called them koilocytes which will be also seen in hairy leukoplakia and other white lesions (34). Furthermore, Batrani et al studied six cases of LP and DLE and observed pale keratinocytes in 2 cases of DLE compared to no cases of LP, so they reported pale keratinocyte as one of the distinguishing features of these two lesions. However, they did not perform a statistical test due to the small number of samples (5).

Comparison of the frequency of spongiosis in LP and DLE skin lesions

The present study reported epidermal spongiosis in 50% of LP cases compared to 27.6% of DLE cases, which was significantly higher in LP than in DLE. Compared to other studies, only Nico et al examined spongiosis in oral cases of these two lesions, reporting the presence of spongiosis in both LP and DLE lesions with no significant difference (15).

Comparison of the frequency of keratinization in LP and DLE skin lesions

In the present study, hyperorthokeratinization alone was significantly higher in LP samples, while hyperparakeratinization alone and hyperparakeratinization with hyperorthokeratinization were significantly higher in DLE samples compared to LP. Andreasen observed hyperparakeratosis in 86% of LP oral lesions in his study (30). In contrast, Ellis observed hyperparakeratosis in only 12% of LP skin lesions (35). In their study on all three cases of cutaneous LP, Batrani et al reported hyperorthokeratosis and introduced it as a prominent feature of LP and a discriminating characteristic from DLE (5). However, in their study on LPP and DLE lesions, Asadi Kani et al reported the prevalence of hyperorthokeratosis in LPP (87.01%) less than in DLE (96.15%) and observed more parakeratosis

in LPP (22). By examining several patients with oral DLE and oral LP lesions, Schiødt (1984) did not consider both hyperparakeratosis and hyperorthokeratosis to be of diagnostic value for differentiating between the two diseases as they often occur in DLE and LP. However, keratotic plugging and keratotic pearl were significantly more associated with DLE diagnosis compared to LP diagnosis (33).

Comparison of the frequency of wedge-shaped hypergranulosis in LP and DLE skin lesions

In the present study, wedge-shaped hypergranulosis was significantly higher in LP than in DLE. Observing wedge-shaped hypergranulosis in all cases of oral LP compared to none cases of oral DLE, Batrani et al introduced this feature as one of the distinctive features of these two lesions (5). Asadi Kani et al also reported more epidermal hypergranulosis in LPP cases than in DLE cases (22). Arps and Patel, in line with the present study, believe that hypergranulosis is more likely to occur in LP (28). Likewise, Grabbe and Kolde in a review study reported this feature more frequently in LP cases but did not consider its presence impossible in DLE samples (29).

Comparison of the frequency of inflammatory infiltration in LP and DLE skin lesions

In the present study, superficial and superficial-mid dermal perivascular infiltration was significantly higher in LP than in DLE. Superficial-mid and deep dermal perivascular infiltration was also significantly higher in DLE samples than in LP cases. In their study, consistent with the present study, Batrani et al observed deep dermal perivascular infiltration of the lesion, more in cutaneous DLE cases and expressed it as a characteristic of DLE for differential diagnosis from LP specimens, although it was also considered to be due to the secondary reaction to the ulcerated margins (5). In their study on oral LE and LPs, Karjalainen and Tomich reported detectable perivascular infiltration in the majority (60%) of LE samples compared with 6% of LP samples. More importantly, all LE cases showed a large number of scattered and diffuse inflammatory cells in deeper parts of connective tissue in contrast to LP cases. In addition, the majority of LEs in their study showed a relatively dense accumulation of inflammatory cells beneath the epithelium, but this infiltration, like LP, was not well defined and band-like, instead, it was diffused with an indistinct or fading margin (16). In line with the present study, Asadi Kani et al reported deep perivascular infiltration in DLE samples than in LPP samples and Moure et al observed perivascular and perieccrine infiltration as a contributing factor in the differential diagnosis of DLE from LPP (12,22). In the same way, Crowson and Magro found moderate to severe deep perivascular infiltration and peri-adnexal infiltration in DLE and Komori reported perivascular and peri-adnexal infiltration among the characteristics of DLE (6,24). Schiødt (1984) also reported focal deep

perivascular infiltration among the characteristics of DLE (33). In contrast, Rahmati Roudsari et al found perivascular infiltration in all cases of DLE and LPP (23).

According to the results of the present study, perifollicular inflammation in DLE was slightly higher than in LP, but this difference was not statistically significant. Perieccrine inflammation was also higher in LP than in DLE but was not statistically significant. The presence of perifollicular and perieccrine inflammation at the same time was more common in DLE than in LP, but this difference was not statistically significant, and it is not possible to differentiate between DLE and LP based on this feature. However, by studying LPP and DLE, Rahmati Roudsari et al and Asadi Kani et al observed perifollicular and perivascular inflammation in DLE and LPP similarly or almost similarly and observed perieccrine inflammation only or more in DLE (22,23). Likewise, Moure et al as well as Kumar and Yelikar reported perifolliculitis in both lesions and perieccrine inflammation only in DLE (12,13). This difference may be due to the investigation of LPP in these studies. Batrani et al also reported periadnexal infiltration among differentiating features of DLE from LP (5). According to the results of this study and the insufficient depth of most DLE cases in some histopathological studies, a sufficient incisal biopsy is necessary instead of a punch biopsy for accurate diagnosis because the punch biopsy may confuse the diagnosis (4). In addition to the appropriate depth, Batrani et al have recommended in their study that it is better to perform an adequate biopsy of the edges of the lesion rather than the center, which is not diagnostic in most cases (5).

Comparison of inflammatory cell abundance in infiltration in LP and DLE skin lesions

According to the results of the present study, the rate of lymphohistiocytes in both LP and DLE lesions was higher than in other cells. This rate was significantly higher in LP than in DLE. The rate of lymphohistiocytes-plasma cells was significantly higher in DLE than in LP. In DLE samples, cases with infiltration of lymphohistiocytes and lymphohistiocytes-plasma cells were reported rather equally. The results of this study also showed the significant presence of more infiltration of lymphohistiocytes-plasma cells and neutrophils in DLE than in LP. In line with the present study, by examining oral and cutaneous lesions of LP and LE, Asadi Kani et al and also Komori et al reported scattered histiocytes, in addition of lymphocytes in the both lesions. Moreover, other inflammatory cells such as neutrophils and plasma cells were also observed in both lesions (6,22). However, similar to the present study, in the study by Asadi Kani et al, neutrophils and plasma cells were more commonly observed with lymphocytes in DLE specimens (22). By comparing several oral cases of LP and DLE, Batrani et al reported the presence of plasma cells variably in both groups and attributed this feature to ulceration, similar to other features such as papillary dermal edema, telangiectasia, and capillary

proliferation, which occur possibly to a secondary change in response to ulceration(5). The present study, together with the confirmation of several recent studies, suggests that the presence of plasma cells among inflammatory cell infiltrates may confirm the diagnosis of DLE.

Comparison of frequency of edema in papillary dermis in LP and DLE skin lesions

According to the results of the present study, edema in the papillary dermis was observed to a greater extent in DLE than in LP, and this difference was statistically significant. In line with the present study, Karjalainen and Tomich reported more edema in the papillary dermis in cases of oral LE than in oral LP. They stated that the high edema in LE could be due to the following reasons: Due to inflammatory infiltration with certain limits in LP, this edema can be hidden, and on the other hand, more severe and widespread inflammation in LE can lead to vascular changes, fibrinoid necrosis, increased permeability, and eventually edema in the papillary dermis (16). In line with the present study, Ahmed et al in a review study as well as Komori et al reported the highest rate of edema in the papillary dermis in LE (6,26). In contrast, in a study on a limited number of cases of oral LP and DLE, Batrani et al observed edema in the papillary dermis in three cases of LP and two cases of oral DLE and identified this feature as one of the histopathological features seen in both lesions and stated that this feature can be secondary to ulceration of the lesion or the site of involvement (5).

Comparison of high frequency of Civatte bodies in LPP and D skin lesions

In the present study, a high frequency of CBs was observed in a larger number of DLEs compared to LPs, but this difference was not statistically significant. Since no similar study has been conducted on the frequency of CBs, it was not possible to compare the results with the research conducted by other researchers.

Comparison of the frequency of fibrosis in LP and DLE skin lesions

According to the results of the present study, dermal fibrosis was significantly higher in DLE than in LP, but this difference was not statistically significant, although it was close to significant ($P=0.096$). In line with the present study, Kumar and Yelikar also reported the relatively positive presence of fibrosis in the dermis of DLE samples (13). Similarly, in their study, Crowson and Magro found that samples of DLE that have been diagnosed for a long time were more likely to have fibrosis in their dermis (24). In LPPs (88.31%), Asadi Kani et al reported more follicular tract fibrosis (footprints or fibrotic pathways at the site of destroyed follicles) than in DLEs (46.15%) (22). Although Moure et al did not identify tract fibrosis as a factor for the differential diagnosis of LPP from DLE, they did report extrafollicular fibrosis as a contributing factor in the diagnosis of DLE (12).

Comparison of mucin frequency in LP and DLE skin lesions

In the present study, mucin density was significantly higher in DLE than in LP. In the study of Rahmati Roudsari et al, Asadi Kani et al, and Batrani et al, the mucin in the dermis of DLE samples was higher than that of LP samples (5, 22, 23). Batrani et al, Asadi Kani et al, Arps and Patel, as well as Karjalainen and Tomich introduced this feature as a diagnostic feature of DLE (5,16,22,28). Vincent and Chan also observed mucin in the superficial and deep reticular dermis in LE significantly more frequently than in LP and considered it as a diagnostic feature of LE, but they characterized that mucin in the papillary dermis failed to distinguish between the lesions (36). In confirmation, Batrani et al noted that due to secondary changes arising from ulceration of the LP and DLE (e.g., the formation of granulation and scar tissues), mucin is often present in these tissues. Therefore, mucin should be evaluated in the interstitial reticular dermis away from the superficial areas (papillary dermis) or granulation and scar tissues (5). However, in their study examining cutaneous LP and DLE, Grabbe and Kolde found similar levels of mucin in both lesions (29). This difference may be contributed to the difference between the place of study of mucin in their study, other studies, and present study. In general, by further confirming the previous studies, the present study suggests that the presence of mucin in the reticular dermis may be a differential diagnostic feature of DLE from LP.

Conclusion

According to obtained results, in the histopathologic differential diagnosis of LP and DLE the presence of CBs, perieccrine and perifollicular inflammation, abundance of fibrosis, presence of pale keratinocytes, and presence of pseudoepitheliomatous hyperplasia cannot be used as diagnostic criteria.

Suggestions

Considering the overlap between clinical and histopathological features of DLE and LP, for accurate diagnosis of these lesions in suspected or unknown cases, in addition to conventional clinical and histopathological findings, it can be used from findings of specific staining, immunohistochemistry, immunofluorescence, and if necessary, serologic and hematologic tests.

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Authors' Contributions

PD conducted the study concept, study design, literature review, histopathological study, statistical analysis, discussion, manuscript preparation, and editing. FK contributed to the literature review, histopathological study, and discussion. FM conducted

histopathological study and cooperated in preparation of samples. TM cooperated in preparation of samples and literature review.

Conflict of Interests

The authors declare that they have no conflict of interests.

Ethical Approval

This study was approved by the Ethics Committee of Isfahan University of Medical Sciences with ethical code of IR.Mui. Research.Rec.1398.299.

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