Lichen planopilaris: histopathological survey of 70 vertical sections of scalp biopsies

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Background: Lichen planopilaris (LPP) is the most common form of immune-mediated scarring alopecia. We evaluated the histopathologic features of LPP in vertical sections of scalp biopsies and compared findings between the scarring and non-scarring phases of the disease.

Methods: From June 2019 to June 2020, vertically sectioned scalp biopsies of 70 new cases of LPP were examined (H&E) according to North American Hair Research Society criteria. Furthermore, patients were divided into two groups based on either the presence or the absence of vertical fibrous bands, and other histopathological features were compared between these two groups.

Results: Characteristic findings of LPP were perifollicular lymphocytic infiltration (97.1%), follicular interface degeneration (60%), and perifollicular plasmacytic infiltration (21.4%). Vacuolar degeneration in the dermo-epidermal junction (38.6%), perifollicular lamellar fibroplasia (67.1%), loss of sebaceous glands (87.1%), perifollicular cleft formation (28.6%), and vertical fibrous tracts (65.7%) were also found. Furthermore, we found a significant correlation between the presence of fibrous tracts with both loss of sebaceous glands ($P = 0.005$) and the presence of lamellar fibroplasia ($P = 0.015$).

Conclusion: The most common findings in the histopathological examination of LPP slides are perifollicular lymphocytic infiltration and loss of the sebaceous glands. Furthermore, sebaceous gland loss and perifollicular lamellar fibroplasia correlate with the scarring phase of LPP.

Keywords: lichen planus, alopecia, autoimmunity

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INTRODUCTION

Lichen planopilaris (LPP) is the most common form of immune-mediated scarring alopecia. It presents as multiple, atrophic, ill-defined patchy alopecia accompanied by perifollicular erythema, follicular keratosis, and disappearance of follicular orifices [1,2]. A lymphocyte lichenoid inflammatory reaction targeting the superficial portion of the folliculosebaceous apparatus is the histopathologic finding of LPP. The diagnosis is usually based on clinical and histopathological findings [1,2]. Cutaneous lesions of lichen planus may be present in up to 28% of cases [1,3]. Furthermore, other clinical features such as follicular papules on the trunk and extremities can be seen, like in Graham–Little syndrome, a clinical

entity in which hair loss affects the scalp, eyebrows, axillae, or pubic area [4,5]. Another subtype of LPP, frontal fibrosing alopecia, presents as progressive frontal recession initially reported by Kossard *et al.* in post and premenopausal women [2,4,6-8]. In FFA, the hairline, eyebrows, and even peripheral body hairs are affected [9].

Histopathologically, the features of LPP and its variants are similar, irrespective of their clinical presentation. In early lesions, there is a vacuolar interface change with a moderately dense perifollicular lichenoid lymphocytic cell infiltration at the level of the infundibulum and isthmus [10]. Occasionally, the interfollicular epidermis may have an associated lichenoid infiltration. One of the reasons for performing this study was to evaluate the presence or absence of plasma cells in the inflammatory infiltrate of LPP because plasma cells are crucial in the histopathologic diagnosis of connective tissue diseases, especially DLE. We wanted to determine whether these cells are present in LPP and, if so, assess its severity. In advanced lesions, concentric perifollicular lamellar fibrosis (Figure 1) occurs, and the lichenoid infiltration backs away from the follicle [10]. Furthermore, clefting between the follicular epithelium and the stroma may be seen in long-standing lesions. In end-stage LPP, loss of elastic fibers in a superficial dermal wedge-shaped scar can be seen, which is better demarcated with the Verhoeff–van Gieson elastic stain [5] (Figure 2). Likewise, mucinous perifollicular fibroplasia with the absence of interfollicular dermal mucin in the upper dermis has been described

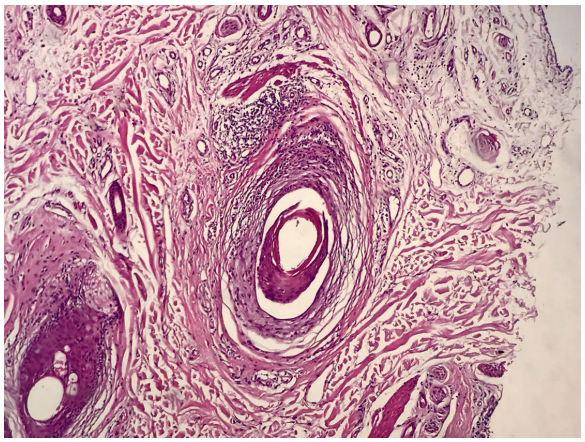

Figure 1. Concentric perifollicular fibrosis, asymmetrical atrophy of follicular epithelium, and an artifactual cleft between the epithelium and stroma (H&E, ×10).

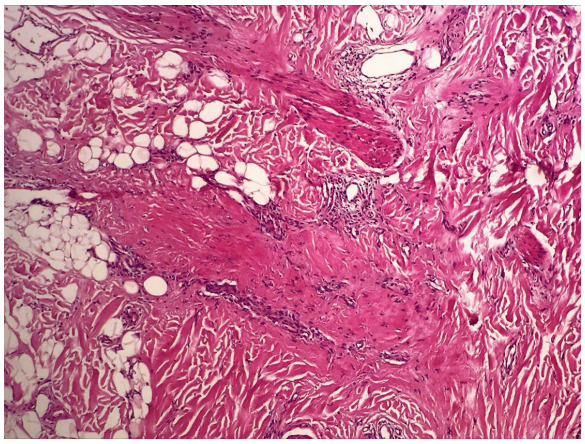

Figure 2. Complete disappearance of folliculosebaceous structure and vertical fibrous tract formation (H&E, ×10).

in vertical sections. Direct immunofluorescence highlights the presence of colloid bodies in the peri-infundibular/isthmic area staining with IgM (less frequently with IgG, IgA, and C3). There is a shaggy or linear band of fibrinogen deposition along the basement membrane zone of affected follicles, while the interfollicular epidermis is negative for immunoreactants [11].

The standard material for evaluating alopecia is two punch biopsies: one for horizontal sections and the other for vertical sections. All of the findings of authoritative scientific books are based on both horizontal and vertical sections. However, one biopsy is usually taken in Iran, which is cut vertically. Hence, we decided to evaluate histologic findings of LPP only on vertical sections. In this study, we have focused on the histopathological diagnostic criteria of LPP in vertical sections of scalp biopsies taken from clinicopathologically confirmed disease cases. We wanted to find histopathologic clues that warn the immediate arrival of disease to the irreversible (scarring) phase requiring fast and intense treatment.

MATERIALS AND METHODS

From June 2019 to June 2020, 70 slides of scalp biopsies diagnosed as LPP in the dermatopathology department of Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran, were selected. Three dermatopathologists reviewed the H&E stained vertical sections according to the North American Hair Research Society (NAHRS) criteria. Finally, the slides were divided into two groups based on

the presence or absence of vertical hairless fibrous bands as the most important clue for the complete destruction of folliculosebaceous units and entry of the disease into the irreversible phase. Then, other histopathologic features were compared between these two groups.

Statistical analysis was conducted in SPSS version 21 (SPSS Inc., Chicago, IL, USA) using Pearson's chi-squared test, Fisher's exact test, and the two-samples t-test. A significance level of 0.05 was considered in all cases. Besides, in multivariate analysis, only variables were modeled that were significant in univariate analysis.

RESULTS

Seventy slides from cases with a definite diagnosis of LPP were selected, and their medical records and pathological slides were evaluated. The mean age of the patients was 40.6 ± 12.3 years, and 41 (58.6%) patients were female. All the patients were new cases of LPP and were not using any relevant treatments for LPP.

Regarding histopathologic findings, follicular vacuolar degeneration was presented in 42 (60%) patients. Likewise, perifollicular lamellar fibroplasia (Figure 1), including mucinous and non-mucinous fibroplasia, was seen in 47 (67.1%) slides. Furthermore, vacuolar degeneration in the Dermo-Epidermal Junction (DEJ) was found in 27 (38.6%) patients. Interestingly, mild to moderate perifollicular lymphocytic infiltration, loss of sebaceous glands, and hairless vertical fibrous bands were found in 68 (97.1%), 61 (87.1%), and 46 (65.7%) slides, respectively (Figure 2). Perifollicular cleft formation was seen in 20 (28.6%), and perifollicular plasmacytic infiltration (often mild, scattered) was seen in 15 (21.4%) patients. Regarding mucin deposition, perifollicular mucinous fibroplasia was seen in 28 (40%), while interfollicular mucin was absent from all samples. Moreover, secondary pathological changes including melanophages in the papillary dermis and foreign body granulomas were present in 45 (64.3%) and 3 (4.3%) patients, respectively (Table 1).

In the univariate analysis, we found a significant relationship between the presence of fibrous tracts with both sebaceous gland loss (P = 0.001, CI: 22.5 [2.61-194-27]) and the presence of perifollicular lamellar fibroplasia (P = 0.002, CI: 9.26 [1.94-43.48]).

Table 1. The frequency and percentage of different histopathological features in 70 lichen planopilaris biopsies

Histopathological feature	Frequency N (%)
Dermal mucin deposition	0 (0%)
Foreign body granulomas	3 (4.3%)
Perifollicular plasmacytic infiltration	15 (21.4%)
Perifollicular cleft formation	20 (28.6%)
Vacuolar degeneration of dermo-epidermal junction	27 (38.6%)
Perifollicular mucinous lamellar fibroplasia	28 (40%)
Follicular vacuolar degeneration	42 (60%)
Melanophages	45 (64.3%)
Hairless vertical tract fibrosis	46 (65.7%)
Perifollicular lamellar fibroplasia (mucinous & non-mucinous)	47 (67.1%)
Loss of sebaceous glands	61 (87.1%)
Perifollicular lymphocytic infiltration	68 (97.1%)

In other words, the chances of fibrous tract presence (scarring phase) in patients with loss of sebaceous glands and perifollicular lamellar fibroplasia were 22.5 and 9.26 times more, respectively. Moreover, based on the multivariate analysis and by considering variables that were significant in univariate analysis, the logistic regression model also showed a significant correlation between the presence of the fibrous tracts with both loss of sebaceous glands (P = 0.006, CI: 60.75 [5.9, Inf]) and perifollicular lamellar fibrosis (P = 0.042, CI: 29.02 [2.05, Inf]) (Table 2).

DISCUSSION

In the present study, we report the histopathological features of the vertical sections of 70 slides with a definite diagnosis of lichen planopilaris (LPP). The most important finding of the present study is the correlation of the scarring phase of LPP with the presence of perifollicular lamellar fibroplasia and the absence of sebaceous glands.

The histopathological features of LPP have been evaluated in previous reports. The most comprehensive articles about the histopathological criteria of LPP are the research of Tayyebi *et al.* [12] on 44 patients and Tandon *et al.* [13] on 27 LPP scalp biopsies. The most common feature in our study was the presence of perifollicular lymphocytic infiltration (97.1%). This feature was found in 77.3% of both Tayyebi *et al.* and Tandon *et al.* cases. Furthermore, the loss of sebaceous glands was seen in 87.1% of our patients, while Tayyebi *et al.*

Table 2. Comparison of histopathological criteria between the scarring and non-scarring phase of lichen planopilaris

Analyzed parameters	Status	Fibrosis tract N (%)	Unadjusted OR (95% CI)	Unadjusted *P*-value*	Adjusted OR (95% CI)	*P*-value*
Sex	Female	28 (68.3%)	0.76 (0.28-2.06)	0.589	-	-
	Male	18 (62.1%)				
	Negative	25 (89.3%)				
Perifollicular lamellar fibroplasia	Positive	25 (53.2%)	9.26 (1.94-43.48)	0.002	29.02 (2.05, Inf)	0.042
	Negative	21 (91.3%)				
Mucinous lamellar fibroplasia	Positive	15 (53.6%)	0.409 (0.149-1.127)	0.123	-	-
	Negative	31 (73.8%)				
Dermal mucin deposition	Positive	0 (0%)	-	-	-	-
	Negative	46 (65.7%)				
Vacuolar degeneration in dermo-epidermal junction	Positive	18 (66.7%)	1.07 (0.388-2.961)	0.894	-	-
	Negative	28 (65.1%)				
Loss of sebaceous glands	Positive	45 (73.8%)	22.5 (2.61-194-27)	<0.001	60.75 (5.9, Inf)	0.006
	Negative	1 (11.1%)				
Perifollicular plasmacytic infiltration	Positive	10 (66.7%)	1.06 (0.32-3.54)	0.93	-	-
	Negative	36 (65.5%)				
Foreign body granulomas	Positive	1 (33.3%)	0.24 (0.021-2.84)	0.269	-	-
	Negative	45 (67.2%)				
Perifollicular cleft formation	Positive	10 (50%)	0.389 (0.133-1.136)	0.08	-	-
	Negative	36 (72%)				
	Negative	24 (85.7%)				
Melanophage	Positive	27 (60%)	0.474(0.159-1.415)	0.177	-	-
	Negative	19 (76%)				

*Adjusted *P*-value based on multivariate logistic regression.

and Tandon *et al.* detected this critical feature in 52% and 70% of samples, respectively [12,13]. We also found a higher percentage of perifollicular lamellar fibroplasia in our study (67.1% vs. 11-15.9%). This difference can be attributed to the advanced nature of the disease in our cases. Likewise, vertical fibrous tracts, melanophages in the papillary dermis, perifollicular cleft formation, and perifollicular plasmacytic infiltration were detected in 65.7%, 64.3%, 28.6%, and 21.4% of cases, respectively; these features were absent in other studies. Follicular interface degeneration in our study was comparable with Tayyebi *et al.* (60% vs. 61.3%, respectively). In the meantime, interface degeneration in the interfollicular epidermis was 38.6% in our study, 50.6% in Tayyebi *et al.*, and 11% in Tandon *et al.*'s investigation. Regarding mucin deposition, perifollicular mucinous change was 40% in our study, 50% in Tayyebi *et al.*, and 37% in Tandon *et al.*'s work. While we did not find any sample with interfollicular mucin disposition, Tayyebi *et al.* reported this feature in 2.3% of their patients [12,13].

Lichen planopilaris is the most common subtype of cicatricial alopecia. The main histopathological differential diagnosis of LPP is discoid lupus erythematosus (DLE). Although basal vacuolar degeneration can be seen in up to one-fourth of LPP patients (similar to DLE patients), the absence of interstitial mucin deposition, deep inflammation (including peri-eccrine glands), and lack of a positive direct immunofluorescence result in the dermo-epidermal junction can differentiate between LPP and DLE [14]. It is well-understood that affected hair follicles are entirely destroyed unless proper treatment is started in the early phase of the disease. However, the pathological stage in which the destruction of the hair follicle becomes irreversible is not unraveled yet.

In the present study, by comparing the scarring and non-scarring phases of LPP, we found a higher chance of the presence of fibrous tracts in the scarring phase in those with sebaceous gland loss and perifollicular lamellar fibroplasia (22.5 and 9 times, respectively). The invasion of the sebaceous glands by the immune system in the initial phase of LPP was formerly shown by Harries *et al.* This finding can explain the relation between sebaceous gland loss and the scarring phase of LPP [15,16]. In addition to histopathological importance, this

finding can be practically used in the clinical approach and may be implicated in the treatment decision. In other words, if the pathologist does not find these two mentioned histopathological features, it means that starting a fast and effective treatment may prevent the scarring phase.

The retrospective nature of the disease was the major limitation of the study. Our study found that the predominant findings in the histopathological examination of LPP slides were perifollicular lymphocytic infiltration and loss of sebaceous glands. Furthermore, sebaceous gland loss and perifollicular lamellar fibroplasia correlated with the scarring phase of LPP. Further studies with a higher number of cases focusing on the molecular and Immunohistochemical aspects of this disease may shed light on the pathogenesis of LPP and its different clinicopathological stages. Although the standard approach to the diagnosis of LPP, like other alopecias, requires two biopsy specimens, based on the findings of our study, evaluation of vertical sections alone will provide acceptable information to the pathologist to make a diagnosis. However, in the early stages of LPP, we always need both horizontal and vertical sections.

CONCLUSION

We conclude that the most common findings in the histopathological examination of LPP slides are perifollicular lymphocytic infiltration and loss of sebaceous glands. Furthermore, sebaceous gland loss and perifollicular lamellar fibroplasia correlate with the scarring phase of LPP.

Acknowledgment

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest: None declared.

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