Immunohistochemistry profile of inflammatory cells in lichen planopilaris and discoid lupus erythematosus

Mohammad Rahmati Roudsari, MD [1,2]
Farhad Malekzad, MD [1]
Shahram Sabeti, MD [3]
Sarah Ershadi, MD [1]
Forough Yousefi, MD [3]
Mihan Pourabdollah Tonkaboni, MD [3]

1. Faculty of Medicine, Department of Dermatology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Faculty of Medicine, Department of Pathology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding Author:
Shahram Sabeti, MD
Loghman Hakim Hospital,
Makhsoos St., South Karegar Ave,
Tehran, Iran
Email: s_sabeti@sbmu.ac.ir

Conflicts of interest: None to declare

Received: 4 April 2015
Accepted: 21 June 2015

Background: Scarring (cicatricial) alopecia represents a complex group of inflammatory disorders, mainly characterized by destruction of the hair follicle unit. Lichen planopilaris (LPP) and discoid lupus erythematosus (DLE) are the two main causes of primary cicatricial alopecia (PCA), both leading to hair follicle destruction and irreversible alopecia. However, they are different in pathogenesis and sometimes are diagnostically challenging.

Methods: Twenty-eight formalin-fixed paraffin-embedded (FFPE) specimens of skin biopsies from 17 patients with a clinicopathologic diagnosis of LPP and 11 patients diagnosed as DLE were included. Histopathological study was performed with Haematoxylin and Eosin (H&E)-stained slides; then, immunohistochemical staining (IHC) was performed against CD20, CD3, CD4, and CD8 to evaluate and compare the type and distribution pattern of dermal inflammatory infiltrate.

Results: Immunohistochemical findings showed a predominance of T-cells in both groups. CD8+ T-cells were significantly more abundant in LPP (15 cases with 10-50% of infiltration) than DLE (11 cases with <25% of infiltration) with preferential involvement of the perifollicular region (P <0.05). The proportion of CD4+ T-cells in DLE cases was significantly higher than LPP cases (9 cases with 10-50% of infiltration versus 15 cases with 0-10% of infiltration, respectively) (P <0.05) with perivascular and perifollicular distribution.

Conclusions: This study supports the usefulness of IHC for CD4 and CD8 in the differential diagnosis of LPP and DLE in problematic cases.

Keywords: lichen planopilaris, discoid lupus erythematosus, immunohistochemistry, T cell

Iran J Dermatol 2015; 18: 108-115

INTRODUCTION

Cicatricial (scarring) alopecia represents a poorly understood group of hair disorders with a common final pathway of destruction and replacement of the follicular unit by fibrous tissue [1,2]. This group of disorders is classified as primary cicatricial alopecia (PCA) where hair follicle is the primary target and secondary cicatricial alopecia where there is a more general process, such as deep skin infection or thermal burn and hair follicle is involved as a result of spatial contiguity [3,4].

According to the North American Hair Research Society (NAHRS) workshop and the proposed classification, PCA is divided into subgroups based on the predominating inflammatory infiltrates [5,6]. In this classification which mainly relies on

histopathological findings of scalp biopsy specimens, PCA is sub-classified as lymphocytic, neutrophilic, mixed, and nonspecific. Lichen planopilaris (LPP) and discoid lupus erythematosus (DLE) are the two main disorders categorized under lymphocytic cicatricial alopecia whose differentiation could be challenging. Careful clinical evaluation, hair pull test, and methods such as trichoscopy are conventional approaches in alopecia; but skin biopsy, with a 4-mm punch biopsy being the gold standard, can be used for a more definitive diagnosis [7-9]. Some authors have recommended two punch biopsies from affected area; one sectioned transversely and the other one bisected vertically at the time of biopsy, with one half sent for routine histopathology and the other half processed for direct immunofluorescence (DIF) [10].

Effective counselling of patients about the prognosis of their disease and the expected effectiveness of any chosen therapy is extremely challenging. There is more doubt in the field of disease pathogenesis. Some studies have focused on the latter field. It is hypothesized that the permanent destruction of the hair follicles in scarring alopecia may be due to damage to the hair follicle stem cells located in the follicular bulge region [2,11,12]. Some studies suggest that peroxisome proliferator-activated receptor Gamma (PPARγ) has a substantial role in normal function of pilosebaceous units and loss of this factor triggers LPP [13]; this may be useful in disease treatment [14]. Some have investigated the role of altered distribution of integrins in areas involved by LPP [15]. However, most studies are unanimous in the role of inflammatory infiltrates in the PCA pathogenesis inducing subsequent response and follicular damage.

It is widely accepted that PCAs are autoimmune disorders [3]. While some authors suggest that cell-mediated immunity and activated T-lymphocytes target follicular antigens especially in LPP [9], few studies argue against that. Some studies emphasize the type of inflammatory cells which have the main role in disease pathogenesis, such as Langerhans cells [16], or T lymphocytes (CD4+ and CD8+) activated by Langerhans cells in PCA [17].

The present study was undertaken to assess and compare the composition of the inflammatory infiltrate in LPP and DLE using immunohistochemistry (IHC).

PARTICIPANTS AND METHODS

This cross-sectional study was conducted in Loghman Hakim Hospital, Tehran, Iran. The study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences. The data included age, sex, main histopathologic features, and the final diagnosis of the biopsy samples; the latter ones were confirmed via re-examining H&E stained slides. The type and distribution pattern of inflammatory cells were evaluated on IHC slides stained with CD20, CD3, CD4, and CD8 antibodies.

We selected 17 Formalin-fixed, paraffin-embedded (FFPE) samples of patients diagnosed as LPP, and 11 FFPE samples of patients with a diagnosis of DLE. These samples were obtained from the archives of the Pathology Department of Loghman Hakim Hospital, an educational hospital affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran. All samples were collected for diagnostic purposes before 2013. In all cases, diagnostic and morphologic features were evaluated and confirmed through re-examination of H&E stained slides by two expert pathologists. All paraffin blocks were stained with IHC markers CD20, CD3, CD4, and CD8.

The paraffin blocks were stained with ready-to-use (RTU) mouse monoclonal antibodies specific for CD20 (L26, Novocastra, UK), CD3 (PS1, Novocastra, UK), CD4 (1F6, Novocastra, UK), and CD8 (1A5, Novocastra, UK). Positive and negative controls were included in all staining runs.

Briefly, for each block, serial vertical sections in 4-micrometer thickness were prepared and transferred to glass slides. After deparaffinization with xylene and re-hydration through graded alcohols, high temperature antigen retrieval was done using 0.01 M retrieval solution (pH 6.0) for CD20, CD3 and CD8 and 1 mM EDTA retrieval solution (pH 8.0) for CD4. An additional step in preparation for CD4 staining before antigen retrieval was endogenous peroxidase blockade with 0.5% H_2O_2/methanol.

The results of histological examination and IHC studies are reported as frequency and percentage. Statistical analyses were performed using statistical software SPSS (SPSS Inc., Chicago, IL, USA) version 16.0 for Windows. Chi-square or Fisher's exact test were used wherever appropriate. *P*-values less than 0.05 were considered statistically significant.

RESULTS

28 FFPE samples from scarring alopecia patients with a confirmed diagnosis of LPP in 17 cases and DLE in 11 were included in the study. There were 12 females and 5 males (female: male ratio of 2.4:1) in the LPP group compared with 8 females and 3 males (female: male ratio of 2.7:1) in the DLE group (P= 0.99). The mean age of the patients was 38.2±11.0 years (range: 15-53 years) in the LPP group and 36.5±13.0 years (range: 18-59 years) in the DLE group (P= 0.709).

Reexamination of H&E stained slides revealed lichenoid perifolliculitis, perivascular and perifollicular chronic inflammation, and perifollicular fibrosis in all cases of LPP and DLE. While inflammation of the reticular dermis and peri-eccrine lymphocytic infiltrates were observed in all DLE cases, only 23.5% of the LPP cases showed the former and none showed the latter (P < 0.001 for both). Interfollicular epidermal basal vacuolar changes and superficial dermal vascular telangiectasia were present in 90.9% of the DLE cases, whereas the majority of LPP the cases did not show these changes (P<0.001 and P=0.002, respectively). Basement membrane thickening and stromal mucin deposition were other histopathological features frequently observed in DLE, but not in LPP (P = 0.007 and 0.005, respectively). The results of H&E examination of the slides is summarized in Table 1.

Immunohistochemical studies with CD20, CD3, CD4, and CD8 monoclonal antibodies were done to evaluate the type and distribution pattern of dermal infiltrates in LPP and DLE. CD3+ cells were the most abundant inflammatory cells in both groups, followed by CD8+ in LPP and CD20+ in DLE group (Figure 1 and Table 2). While 88.2% of

Table 1. Histopathological findings in H&E slides.

H&E pattern	LPP		DLE		*P*
	+	-	+	-	
Horn plug	10 (58.8%)	7 (41.2%)	6 (54.5%)	5 (45.5%)	0.999
Epidermal atrophy	1 (5.9%)	16 (94.1%)	4 (36.4%)	7 (63.6%)	0.06
Interfollicullar epidermal vacuolar change	3 (17.6%)	14 (82.4%)	10 (90.9%)	1 (9.1%)	<0.001*
Basement membrane thickening	1 (5.9%)	16 (94.1%)	6 (54.5%)	5 (45.5%)	0.007*
Lichenoid perifolliculitis	17 (100%)	0 (0%)	11 (100%)	0 (0%)	—
Pigmentary incontinence	15 (88.2%)	2 (11.8%)	10 (90.9%)	1 (9.1%)	0.823
Stromal mucin deposition	0 (0%)	17 (100%)	5 (45.5%)	6 (54.5%)	0.005*
Superficial dermal vascular telangiectasia	5 (29.4%)	12 (70.6%)	10 (90.9%)	1 (9.1%)	0.002*
Perivascular chronic inflammation	17 (100%)	0 (0%)	11 (100%)	0 (0%)	—
Perifollicular chronic inflammation	17 (100%)	0 (0%)	11 (100%)	0 (0%)	—
Reticular dermis inflammation	4 (23.5%)	13 (76.5%)	11 (100%)	0 (0%)	<0.001*
Perifollicular fibrosis	17 (100%)	0 (0%)	11 (100%)	0 (0%)	—
Perieccrine lymphocytic infiltrate	0 (0%)	17 (100%)	11 (100%)	0 (0%)	<0.001*

LPP: lichen planopilaris; DLE: discoid lupus erythematosus; *P*-values marked by * indicate significant differences.

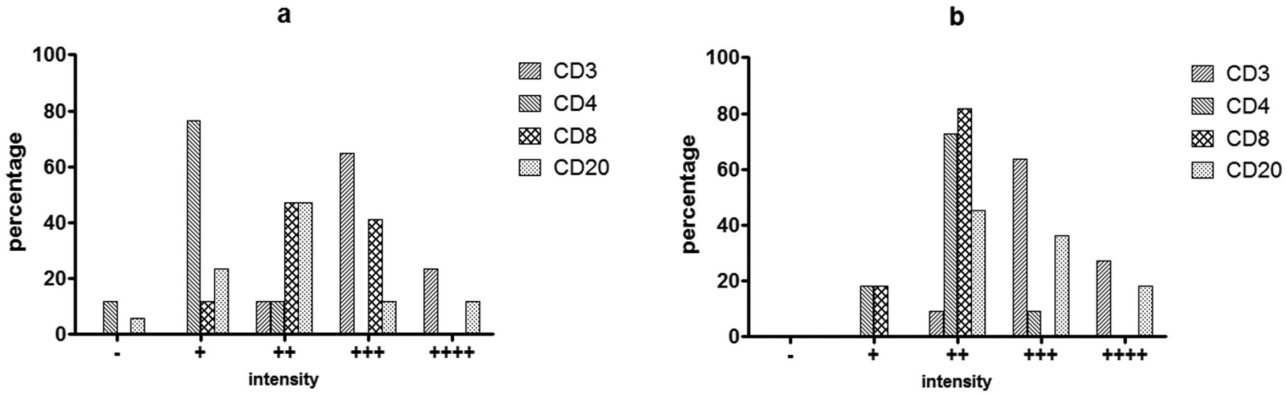

Figure 1. The intensity of immunostaining for CD3, CD4, CD8 and CD20 in: **1.a.** LPP and **1.b.** DLE. The intensity is defined as the percentage of stained cells in proportion to the total cellular infiltration. –: negative; +: weak (0~10%); ++: moderate (10~25%); +++: intense (25~50%); ++++: very intense (> 50%).

Table 2. Number and percentage of cells stained positive for immunohistochemical markers regarding disease category.

		IHC markers							
		CD20		CD3		CD4		CD8	
		LPP	DLE	LPP	DLE	LPP	DLE	LPP	DLE
Intensity	-	1 (5.9%)	0	0	0	2 (11.8%)	0	0	0
	+	4 (23.5%)	0	0	0	13 (76.4%)	2 (18.2%)	2 (11.8%)	2 (18.2%)
	++	8 (47.0%)	5 (45.4%)	2 (11.8%)	1 (9.1%)	2 (11.8%)	8 (72.7%)	8 (47.0%)	9 (81.8%)
	+++	2 (11.8%)	4 (36.4%)	11 (64.7%)	7 (63.6%)	0	1 (9.1%)	7 (41.2%)	0
	++++	2 (11.8%)	2 (18.2%)	4 (23.5%)	3 (27.3%)	0	0	0	0
P		0.256		0.959		0.003*		0.049*	

LPP: lichen planopilaris; DLE: discoid lupus erythematosus. –: negative; +: weak (0~10%); ++: moderate (10~25%); +++: intense (25~50%); ++++: very intense (> 50%) P-values marked by * indicate significant differences.

the cells stained negative or weakly positive for CD4 in LPP, 81.8% of cells stained moderately or intensely in DLE (Figure 2). This difference was significant (P=0.003). The percentage of CD8+ cells was also higher in LPP than DLE with P= 0.049 (Figure 3). Abundance of CD20+ and CD3+ cells showed no significant difference in the studied samples (Figure 4).

In cases diagnosed with DLE, CD20+ cells showed a strong predilection for perifollicular region. CD4+ and CD8+ cells infiltrated perivascular and perifollicular regions almost equally. While perivascular distribution of CD3+ cells was about twice more common than e perifollicular pattern, a mixed pattern was observed in 27.3% of the cases (Table 3). In LPP cases, CD20+ cells showed perifollicular distribution as the most common pattern, followed closely by perivascular distribution. Perifollicular distribution was the predominant pattern in samples stained positive for CD3, CD4, and CD8. Comparing DLE and LPP cases, the distribution pattern of CD20+ and CD3+ cells showed no significant difference. Also, CD4+ lymphocytes preferably infiltrated perifollicular region in both groups. Although CD8+ infiltrate showed a perifollicular tendency in LPP cases, a perivascular distribution was more common in DLE cases. This difference was statistically significant (P = 0.003).

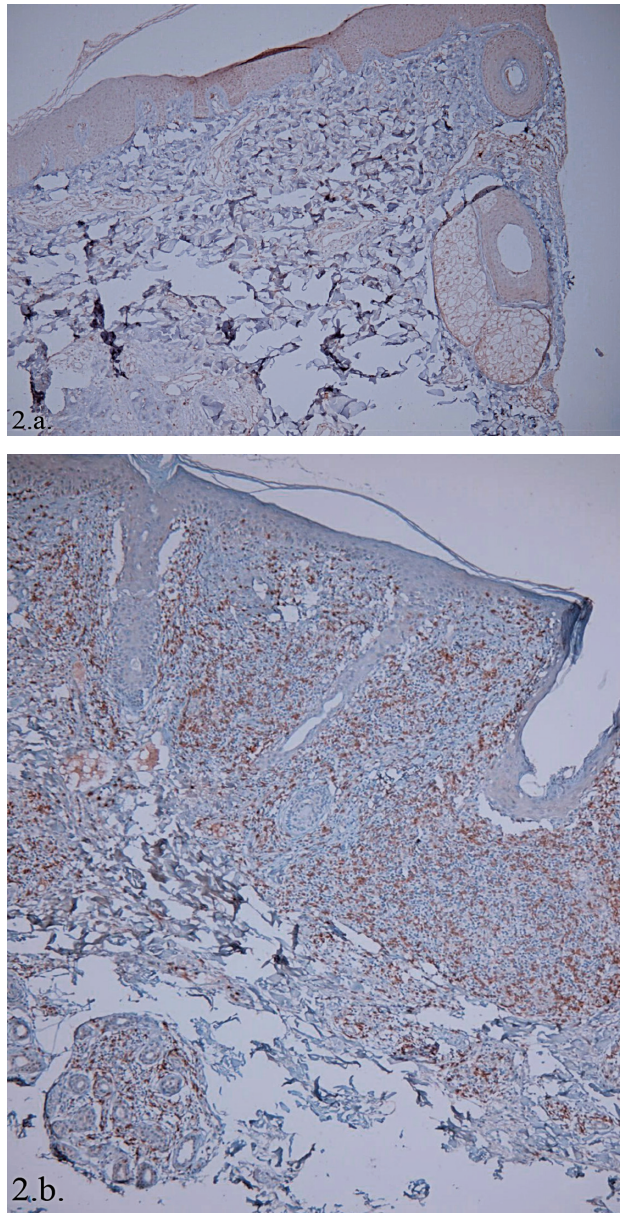

Figure 2. Mild subepithelial and perifollicular infiltration of CD4+ cells is observed in LPP **(2.a)** whereas DLE samples show intensive infiltration of CD4+ cell population in peri-eccrine, perifollicular, subepithelial, perivascular and interstitial areas **(2.b)**.

DISCUSSION

LPP and DLE are considered the main members of primary lymphocytic cicatricial alopecias. These disorders have a tendency to affect middle-aged adults with a female predilection [18,19]. The pathogenesis of lichen planopilaris appears to resemble that of classic lichen planus whereas

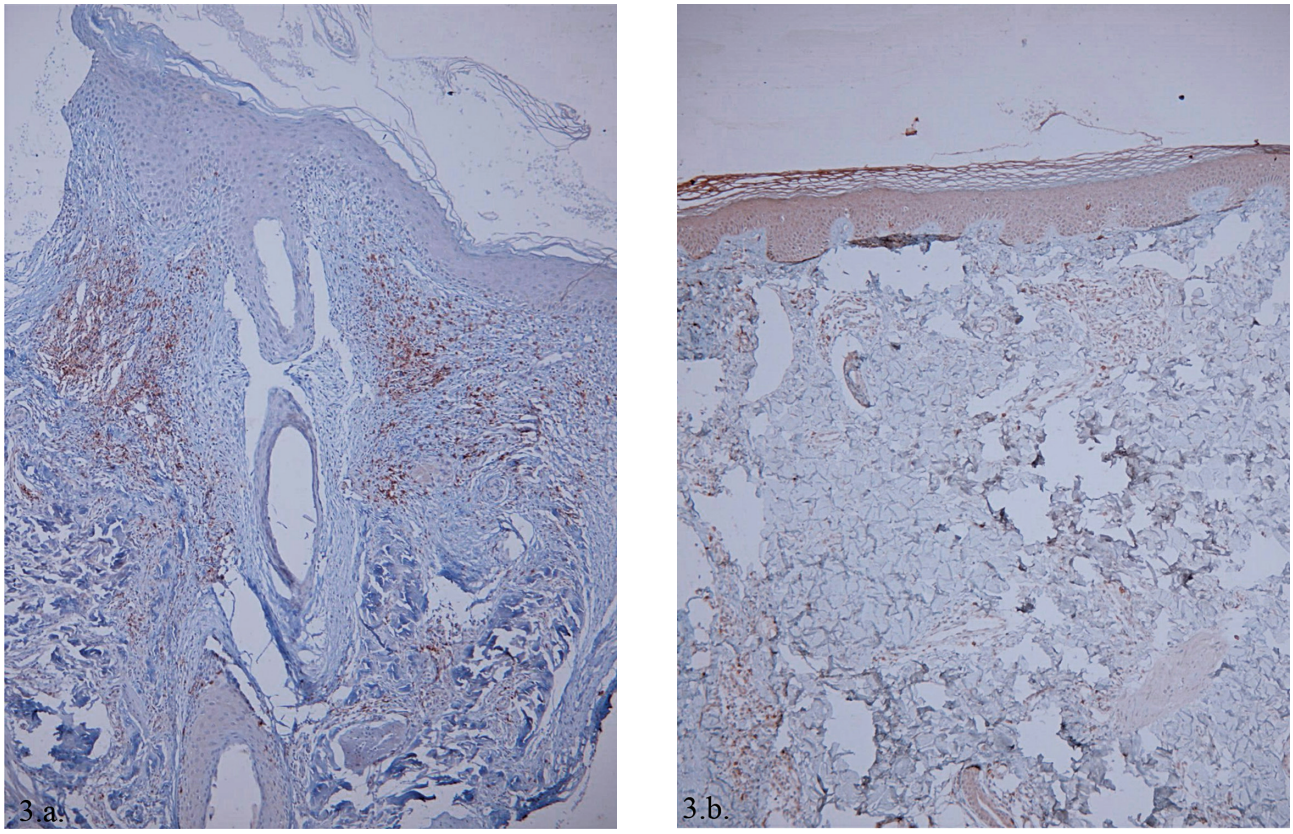

Figure 3. CD8+ cells were more abundant in LPP (**3.a)** than DLE **(3.b)** with perifollicular and subepitjelial involvement in LPP and subepithelial, perivascular and interstitial infiltration in DLE.

the etiology and pathogenesis of DLE are still obscure. It seems that a complex of genetic, environmental, and host factors are involved in the disease evolution [20,21]. Less than 5% of DLE patients progress to systemic lupus erythematosus (SLE) [22]. As we discussed earlier, the clinical and histological features of LPP sometimes overlap with DLE and even become indistinguishable, especially at the end of the disease process. Therefore, careful histopathological and immunohistochemical evaluation would be mandatory to differentiate these diseases.

In this study, we investigated the type and distribution pattern of dermal infiltration in DLE and LPP which might reflect the pathogenesis of the disorders and provide clues to differentiate

Table 3. Distribution pattern of inflammatory cells in DLE and LPP cases.

	Distribution pattern	DLE (%)	LPP (%)	*P*
CD20	Perivascular	4 (36.4)	7 (41.2)	
	Perifollicular	7 (63.6)	8 (47.0)	0.642
	Perivascular+perifollicular	0	1 (5.9)	
CD3	Perivascular	5 (45.4)	4 (23.5)	
	Perifollicular	3 (27.3)	10 (58.8)	
	Perivascular+perifollicular	3 (27.3)	1 (5.9)	0.21
	Perivascular+subepidermal	0	1 (5.9)	
	Perivascular+perifollicular+subepidermal	0	1 (5.9)	
CD4	Perivascular	5 (45.4)	2 (11.8)	0.091
	Perifollicular	6 (54.6)	13 (76.4)	
CD8	Perivascular	6 (54.6)	6 (35.3)	
	Perifollicular	5 (45.4)	10 (58.8)	0.003
	Perifollicular+subepidermal	0	1 (5.9)	

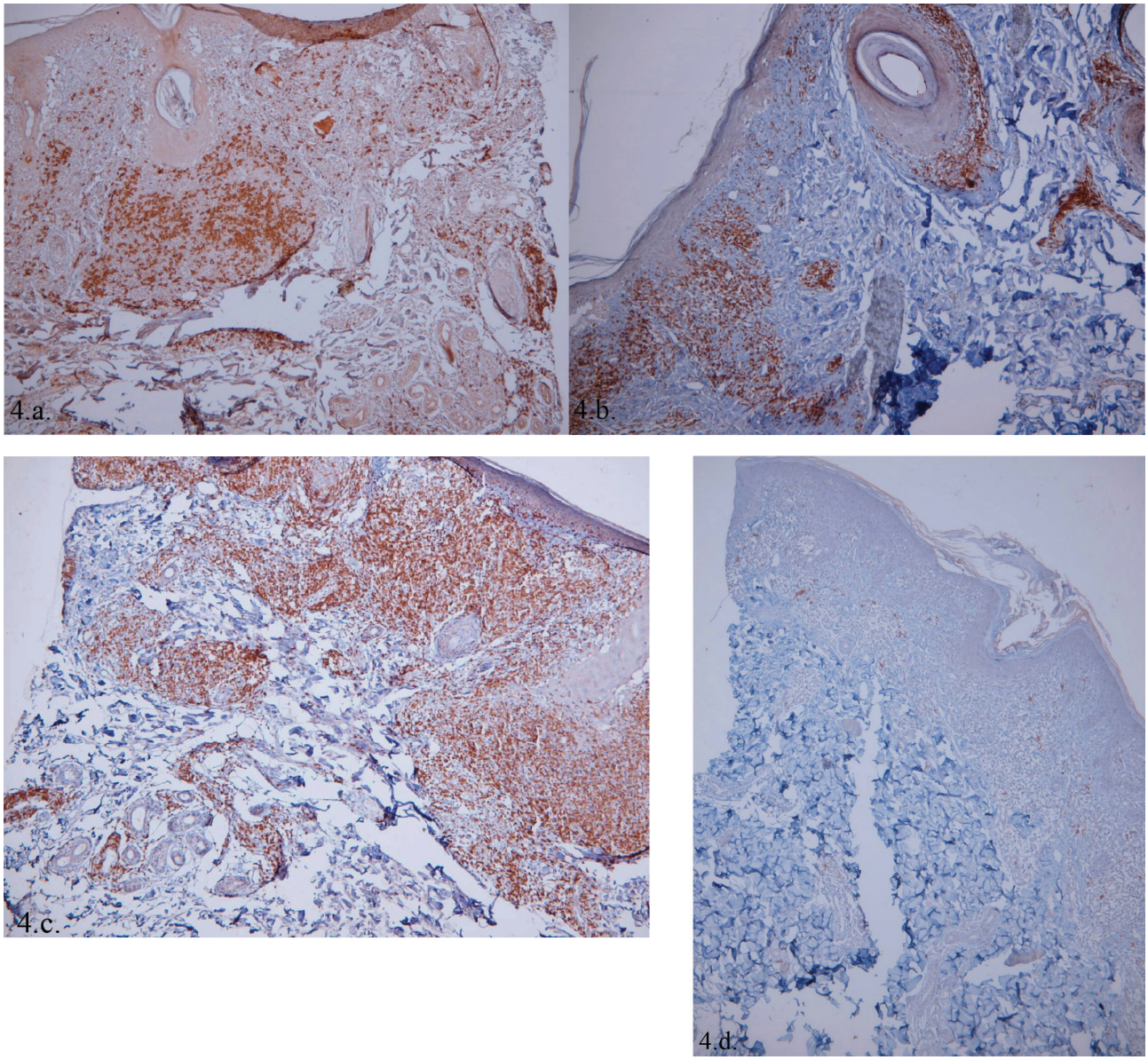

Figure 4. Number of CD3+ and CD20+ cells showed no significant difference between study groups. **4.a.** CD3+ cell infiltration of peri-eccrine, perifollicular, interstitial and subepithelial areas in DLE. **4.b.** CD3+ cell infiltration of subepithelial, perifollicular, perivascular and interstitial areas in LPP. **4.c.** CD20+ cell infiltration of peri-eccrine, perifollicular, interstitial and perivascular areas in DLE. **4.d.** CD20+ cell infiltration of perifollicular and perivascular areas in LPP.

DLE from LPP in difficult cases. Histological examination of 28 samples revealed lichenoid perifolliculitis, pigmentary incontinence, perivascular and perifollicular chronic inflammation and perifollicular fibrosis in both diseases. We noted interfollicular epidermal vacuolar change, basement membrane thickening, superficial dermal telangiectatic vessels, and reticular dermis inflammation more common in DLE than LPP. Ross *et al.* reported periadnexal and interstitial lymphocytic infiltrates, dermal mucin deposition, superficial and deep perivascular infiltration, perifollicular inflammation, thickening of the basement membrane, pigmentary incontinence, epidermal atrophy, and extensive dermal fibrosis as prominent histological changes of DLE. According to that paper, pigmentary incontinence, follicular destruction, lichenoid interface change, and fibrosis of the papillary dermis with adjacent epidermal atrophy were observed in LPP [20]. We noted that unlike DLE, stromal mucin deposition and peri-eccrine inflammation were

absent in LPP skin biopsies which conforms to other studies [2,9].

To determine the composition and distribution of inflammatory infiltration, we used IHC antibodies to detect B-cells (CD20), T-cells (CD3), and T-cell subsets (CD4 and CD8). We observed that CD3+ cells played the major role in LPP, whereas both CD3+ and CD20+ cells were the main inflammatory cell components of DLE. CD8+ cells were significantly more abundant in LPP lesions compared with DLE, while the reverse was true regarding CD4+ cells. Both perivascular and perifollicular infiltrations were commonly recognized in DLE lesions, whereas perifollicular infiltration was the predominant pattern observed in LPP lesions. The tendency of CD8+ cells to infiltrate perifollicular regions was significantly higher in LPP cases compared with DLE. These findings reflect a cell-mediated reaction with the dominancy of CD8+ cells in LPP and CD4+ cells in DLE. This is in accordance with a study conducted by Mobini *et al.* who investigated CD3, CD4, CD8, CD1a and Ki-67 IHC stains in 35 cases of LPP. They found that CD3+ cells comprised the major inflammatory component and CD8+ cells were more abundant than CD4+ cells in LPP [23]. In another study conducted by Lourenço *et al.*, T cells were recognized as the major inflammatory population in lupus erythematosus lesions, with CD20+ B-cells being the minor population. They also reported that CD4+ cells were the main subset of T-cells, followed by CD8+ cells [24]. Tebbe *et al.* also reported that T-cells, mainly of the helper subset, were the main components of dermal infiltration in lupus erythematosus skin lesions. They found B lymphocytes to be rare in the dermis based on CD22 IHC [25]. Hussein *et al.* compared the immune profile of LP and DLE skin lesions with that of the normal skin. They observed heavy infiltration of lesional skin biopsies with dominance of CD3+ cells. They noticed a higher density of CD3+ cells in the perivascular region and dermoepidermal junction in LPP compared with DLE. In contrast, a higher density of CD20+ cells was observed in DLE skin biopsies [26]. However, the results of some studies contradict the findings of the previously mentioned studies. Pozdnyakova *et al.* studied 16 cases of primary scarring alopecia including eight cases of LPP, and a case with chronic cutaneous lupus erythematosus (DLE). They reported that CD4+ T-cells were the dominant component of the inflammatory infiltrates in primary cicatricial alopecia both in the early-active stage and late stage diseases. This study argues against the cell-mediated cytotoxic destruction of follicular bulge stem cells [27]. It is noteworthy that their study population was a diverse group of primary cicatricial alopecia, whereas Mobini *et al.* exclusively studied 35 cases of LPP. In another study by Xie *et al.*, five skin punch biopsies diagnosed as DLE were compared with three normal skin biopsies using a complete IHC panel. They found that the number of cells stained positive for CD3, CD4, CD8, CD20, CD25, and CD57 was higher in DLE samples compared with the normal skin. They reported that the mean percentage of CD8+ cells was slightly higher than CD4+ (37.8% versus 34.5%) in DLE samples, without a statistical significance [28]. It can be argued that this study had a smaller sample size compared with the study conducted by Lourenço *et al*. However, Lourenço *et al.* did not report the percentage of cells stained positive for each marker. In our study, CD4+ cells were slightly more than CD8+ cells in DLE samples, but this difference was not statistically significant, which implies that the ratio of CD4+ to CD8+ cells in DLE is still open to debate and further studies are needed to elucidate the matter.

Our results demonstrate that CD3+ cells with the preponderance of CD8+ subset are the major components of inflammatory infiltration in lichen planopilaris, with a higher tendency to involve the perifollicular region. In DLE lesions, perifollicular and perivascular areas are both infiltrated. Here, CD3+ cells are more abundant, while CD20+ cells and CD4+ cells are more frequently recognized as compared with LPP. These findings can reflect the pathogenesis and contribute to the diagnosis of these two disorders. However, meticulous studies with larger samples and more IHC markers can testify these findings.

Acknowledgments

The authors would like to thank the entire staff of the Department of Pathology, Loghman Hakim Hospital, Tehran, Iran, for helping us with our research. This study was financially supported by the Skin Research Center affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran.

REFERENCES

1. Headington JT. Cicatricial alopecia. Dermatol Clin 1996; 14: 773-82.
2. Harries MJ, Paus R. The pathogenesis of primary cicatricial alopecias. Am J Pathol 2010; 177: 2152-62.
3. Harries MJ, Trueb RM, Tosti A, et al. How not to get scar(r)ed: pointers to the correct diagnosis in patients with suspected primary cicatricial alopecia. Br J Dermatol 2009; 160: 482-501.
4. Sellheyer K, Bergfeld WF. Histopathologic evaluation of alopecias. Am J Dermatopathol 2006; 28: 236-59.
5. Olsen EA, Bergfeld WF, Cotsarelis G, et al. Summary of North American Hair Research Society (NAHRS)-sponsored Workshop on Cicatricial Alopecia, Duke University Medical Center, February 10 and 11, 2001. J Am Acad Dermatol 2003; 48: 103-10.
6. Olsen E, Stenn K, Bergfeld W, et al. Update on cicatricial alopecia. J Investig Dermatol Symp Proc 2003; 8: 18-9.
7. Otberg N, Wu WY, McElwee KJ, et al. Diagnosis and management of primary cicatricial alopecia: part I. Skinmed 2008; 7: 19-26.
8. Gordon KA, Tosti A. Alopecia: evaluation and treatment. Clin Cosmet Investig Dermatol 2011; 4: 101-6.
9. Kang H, Alzolibani AA, Otberg N, et al. Lichen planopilaris. Dermatol Ther 2008; 21: 249-56.
10. Elston DM, McCollough ML, Angeloni VL. Vertical and transverse sections of alopecia biopsy specimens: combining the two to maximize diagnostic yield. J Am Acad Dermatol 1995; 32: 454-7.
11. Cotsarelis G, Millar SE. Towards a molecular understanding of hair loss and its treatment. Trends Mol Med 2001; 7: 293-301.
12. Kloepper JE, Tiede S, Brinckmann J, et al. Immunophenotyping of the human bulge region: the quest to define useful in situ markers for human epithelial hair follicle stem cells and their niche. Exp Dermatol 2008; 17: 592-609.
13. Karnik P, Tekeste Z, McCormick TS, et al. Hair follicle stem cell-specific PPARgamma deletion causes scarring alopecia. J Invest Dermatol 2009; 129: 1243-57.
14. Mirmirani P, Karnik P. Lichen planopilaris treated with a peroxisome proliferator-activated receptor gamma agonist. Arch Dermatol 2009; 145: 1363-6.
15. d'Ovidio R, Sgarra C, Conserva A, et al. Alterated integrin expression in lichen planopilaris. Head Face Med 2007; 3: 11.
16. Moresi JM, Horn TD. Distribution of Langerhans cells in human hair follicle. J Cutan Pathol 1997; 24: 636-40.
17. Assouly P, Reygagne P. Lichen planopilaris: update on diagnosis and treatment. Semin Cutan Med Surg 2009; 28: 3-10.
18. Tan E, Martinka M, Ball N, et al. Primary cicatricial alopecias: clinicopathology of 112 cases. J Am Acad Dermatol 2004; 50: 25-32.
19. Templeton SF, Solomon AR. Scarring alopecia: a classification based on microscopic criteria. J Cutan Pathol 1994; 21: 97-109.
20. Ross EK, Tan E, Shapiro J. Update on primary cicatricial alopecias. J Am Acad Dermatol 2005; 53: 1-37; quiz 8-40.
21. Whiting DA. Cicatricial alopecia: clinico-pathological findings and treatment. Clin Dermatol 2001; 19: 211-25.
22. Hordinsky M. Cicatricial alopecia: discoid lupus erythematosus. Dermatol Ther 2008; 21: 245-8.
23. Mobini N, Tam S, Kamino H. Possible role of the bulge region in the pathogenesis of inflammatory scarring alopecia: lichen planopilaris as the prototype. J Cutan Pathol 2005; 32: 675-9.
24. Lourenco SV, de Carvalho FR, Boggio P, et al. Lupus erythematosus: clinical and histopathological study of oral manifestations and immunohistochemical profile of the inflammatory infiltrate. J Cutan Pathol 2007; 34: 558-64.
25. Tebbe B, Mazur L, Stadler R, et al. Immunohistochemical analysis of chronic discoid and subacute cutaneous lupus erythematosus--relation to immunopathological mechanisms. Br J Dermatol 1995; 132: 25-31.
26. Hussein MR, Aboulhagag NM, Atta HS, et al. Evaluation of the profile of the immune cell infiltrate in lichen planus, discoid lupus erythematosus, and chronic dermatitis. Pathology 2008; 40: 682-93.
27. Pozdnyakova O, Mahalingam M. Involvement of the bulge region in primary scarring alopecia. J Cutan Pathol 2008; 35: 922-5.
28. Xie Y, Jinnin M, Zhang X, et al. Immunohistochemical characterization of the cellular infiltrate in discoid lupus erythematosus. Biosci Trends 2011; 5: 83-8.