Original Article

Plasmacytoid Dendritic Cell Marker (CD123) Expression in Scarring and Non-scarring Alopecia

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Abstract

Classification of scarring alopecia poses a major problem, as there is considerable clinicopathologic overlap, particularly between lupus erythematosus (LE) and lichen planopilaris (LPP), especially in later stages. CD123 positive plasmacytoid dendritic cells (PDC) have been shown recently to be present in all forms of LE and are touted to be useful in differentiating LE from other scarring alopecias. Their distribution in non-scarring alopecia is not well documented. This is the first study that examines the PDC in both scarring and non-scarring alopecias.

Objective: To study the expression patterns of PDC in cases of both scarring and non-scarring alopecia. **Materials and Methods:** A total of 69 cases of alopecia (48 scarring, 21 non-scarring) were studied for CD123 expression by immunohistochemistry. **Results:** Among the scarring alopecias, 17/20 LE cases showed PDC in contrast to 1/22 LPP cases. This difference was statistically significant (P = 0.0001). 1/2 cases of folliculitis decalvans showed PDC. None of the cases of unclassified scarring alopecia were positive. In the non-scarring group, 19/20 cases of alopecia areata and a single case of trichotillomania lacked PDC. **Conclusion:** The finding of CD123 expressing PDC appears to be a promising parameter in distinguishing LE from other forms of alopecia.

Keywords: CD 123, lupus erythematosus, plasmacytoid dendritic cells, scarring alopecia

Introduction

Plasmacytoid dendritic cells (PDC) play an important role in the induction of autoimmune diseases and various inflammatory skin diseases.[1-3] The precursors of PDC differentiate into mature dendritic cells upon stimulation by IL-3 and CD40 ligand.[1] CD123 represents the monoclonal antibody against the interleukin-3 receptor alpha chain.[4] It is highly expressed on the surface of PDC, which is known to accumulate in the infiltrate of various disorders.[1-3] PDC on stimulation secrets large amount of type I interferons (α and β)[5-7] LE is an autoimmune disorder with an alteration in the function of Plasmacytoid dendritic cells (PDC). Recentstudies have suggested that CD123 positive PDCs are increased in throughout the spectrum of LE.[1] There are diagnostic difficulties in cases of LE and LPP presenting late in the course of the disease with scarring and loss of follicles and DIF is also often negative. The distinction of these two entities is important because treatment options and prognosis differ. This study was carried out to assess the expression of CD123, a PDC marker in both scarring and non-scarring alopecias and its diagnostic utility in LE.

Materials and Methods

Consecutive scalp biopsies were classified into various forms of alopecia based on the standard diagnostic criteria by histopathology and direct immunofluorescence, where done. Vertical sections were used in all cases. Samples with adequate tissue remaining in the block were selected for immunostaining. Sections were cut for immunohistochemistry at 3–4μ from FFPE blocks. Immunohistochemistry for CD123 [Leica clone-NCL-L-CD123] was performed on 69 cases of scarring and non-scarring alopecia.Polymer technology with DAB detection system was used. Heat induced epitoperetrievalwith Tris-EDTA–based buffer (pH 9.0) was done by pressure cooking.

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Table 1: Distribution pattern of CD123 in various forms of alopecia

Disease entity	Positivity	PDC Distribution and Grading				Location of the infiltrate
		Clusters	Lichenoid	scattered	Absent PDC	
LE (20)	17	3+: 5/20 (25%) 2+: 3/20 (15%) 1+: 1/20 (5%)	3+: 1/20(5%)	2+: 2/20 (10%) 1+: 5/20 (25%)	3/20(15%)	Superficial and deep dermal infiltrate, periecrrine and perifollicular
LPP (22)	1	0	0	1+: 1/22 (4.5%)	21/22 (95.5%)	Superficial dermal infiltrate
Unclassified scarring alopecia (4)	0	0	0	0	4/4 (100%)	-
FD (2)	1	2+: 1/2 (50%)	0	0	1/2 (50%)	Superficial and deep dermal infiltrate, perieccrine and perifollicular
Alopecia areata (20)	1	2+: 1/20(5%)	0	0	19/20(95%)	Peribulbar and fibrous streamer
Trichotillomania (1)	0	0	0	0	1/1	-

(LPP-Lichen planopilaris, LE- Lupus erythematosus, FD-Folliculitisdecalvans)

CD123 stains PDCsin the inflammatory infiltrate. It also stains the endothelial cells of the post capillary venules.[8,9] cells. PDC number and cellular density was assessed and presence was graded semi-quantitatively according to the criteria used in a recent study by Tomasini *et al.* as below:

1. Clusters – nodular aggregates containing atleast 10 PDC
2. Lichenoid – PDC either as single or small groups (containing a maximum of four to five PDC) distributed at the dermo-epidermal interface.
3. Scattered- single PDC distributed throughout the infiltrate.
4. None- complete absence of CD123

The following grading scheme was used for the grading of cluster density/relative percentage on the overall infiltrate: a) 1+: 1 cluster/field, with upto 10 CD123 + cells/ 2% of the overall infiltrate b) 2+: 2 clusters/field, with upto 20 CD123+cells/5% of the overall infiltrate c) 3+: 3 clusters/ field, with upto 40 or more CD123+cells/10% of the overall infiltrate.

Tonsil was used as the positive control and the test was interpreted in conjunction with the control.

Fisher's exact test was used to analyze statistical differences in the PDC distribution pattern between

LE and LPP.A two-tailed p value of <0.05 was considered statistically significant. IEC clearance was obtained.

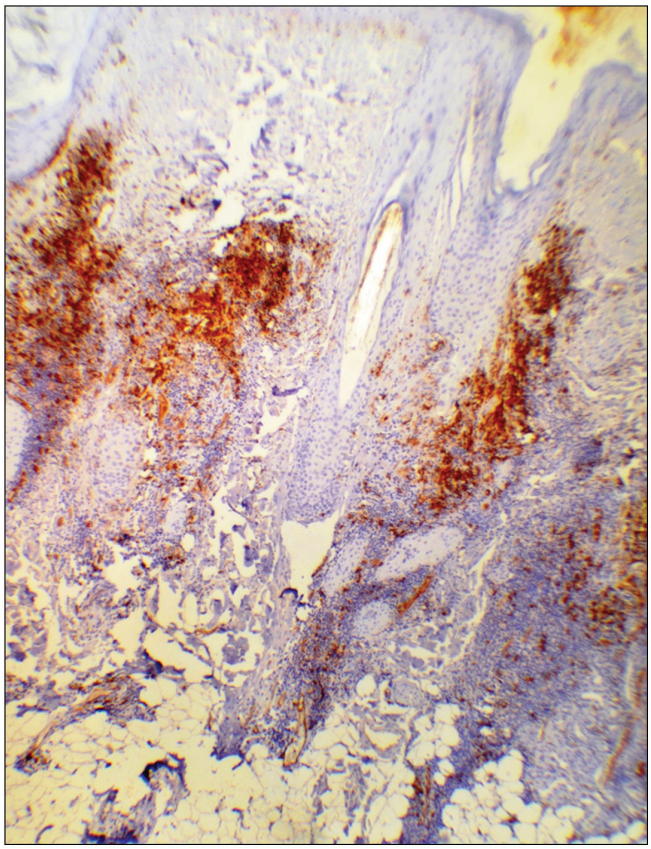

Figure 1: Clusters (3+) of CD123+ cells in LE,(CD 123 X 40)

Results

A total of 69 cases of scarring and non-scarring alopecia were studied. Scarring alopecia included 20 cases of LE, 22 cases of LPP, 4 unclassified/end stage scarring alopecia and 2 cases of Folliculitis decalvans. Non-scarring alopecia included 20 cases of alopecia areata and 1 case of trichotillomania. The staining pattern and grading of the CD 123+ PDCs in the infiltrate was assessed semi-quantitatively. The results are summarized in [Table 1].

In LE, 17/20 (85%) showed positivity for CD123. Clusters of CD123+ cells were located in perifollicular, perieccrine, superficial and deep dermal infiltrates [Figure 1]. In the three cases which were negative, the infiltrate was scanty. In LPP, 21/22 cases were negative [Figure 2] and only one showed scattered 1(+) cells in the superficial dermal infiltrate [Figure 3]. The CD123+ cells in the infiltrate were dense in LE cases as compared to scattered in LPP. Of the 2 cases of folliculitis decalvans, one showed 2+clusters of CD123+ cells in the perieccrine, superficial and deep dermal locations. Four cases of end stage/unclassified scarring alopecia were all negative.

19/20 cases (5%) of alopecia areatawere negative for PDC [Figure 4]. One case showed 2+clusters in the peribulbar infiltrate and in the fibrous streamer [Figure 5]. The HandE slides were reviewed and in this case, the diagnosis remained unchanged. One case of trichotillomania was negative.

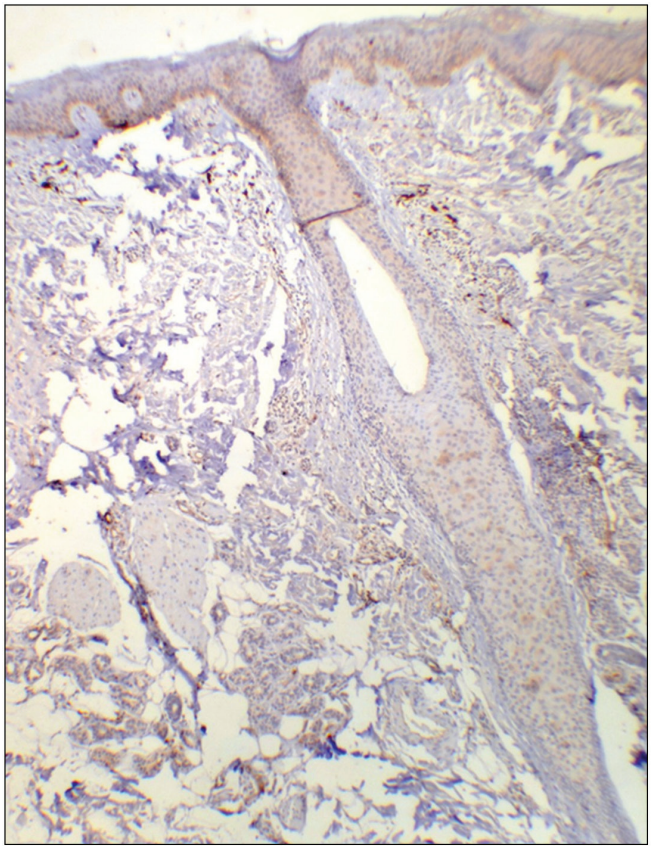

Figure 2: Absence of CD123+ cells in LPP (CD 123 X40)

Fisher's exact test was used to analyse the statistical significance of CD123+ PDC density and grading between LE and LPP group. The two-tailed p value was 0.0001which was statistically significant. ($P < 0.05$)

Discussion

CD123 expression in LE has been described in several studies. Ko *et al.* demonstrated the histopathologic distinction of hypertrophic LE from squamous cell carcinoma and hypertrophic actinic keratosis. A heavy band of CD123-positive cells was present at the epidermal–dermal junction in all cases of hypertrophic LE, and only single or rare scattered clusters of CD123-positive cells were seen in SCC and actinic keratosis.[4] In a study by Farkas *et al*, PDCs were present in 14 out of 15 skin samples from DLE and SLE patients, whereas normal control tissue was negative.[2]

A study by Tomasini *et al*, focused on the distribution patterns of PDC in patients with cutaneous LE and Jessner's lymphocytic infiltrate (LI) of the skin and compared them with other skin diseases.[1] A superficial distribution of PDC was found in SLE and DLE, whereas in tumid LE and reticular erythematous mucinosis it was found in the infiltrate around the deep vascular plexus. A constant perivascular and periadnexal infiltrate with CD123+ cells was noted in LE cases. There was a significant correlation with the intensity of the inflammatory infiltrate, interface changes and the degree of PDC clusters.[1] The study also included 8 cases of scarring alopecia, out of which a single case showed clusters (2+) of CD123 + cells in the interface, superficial and deep perivascular and periadnexal region.[1]

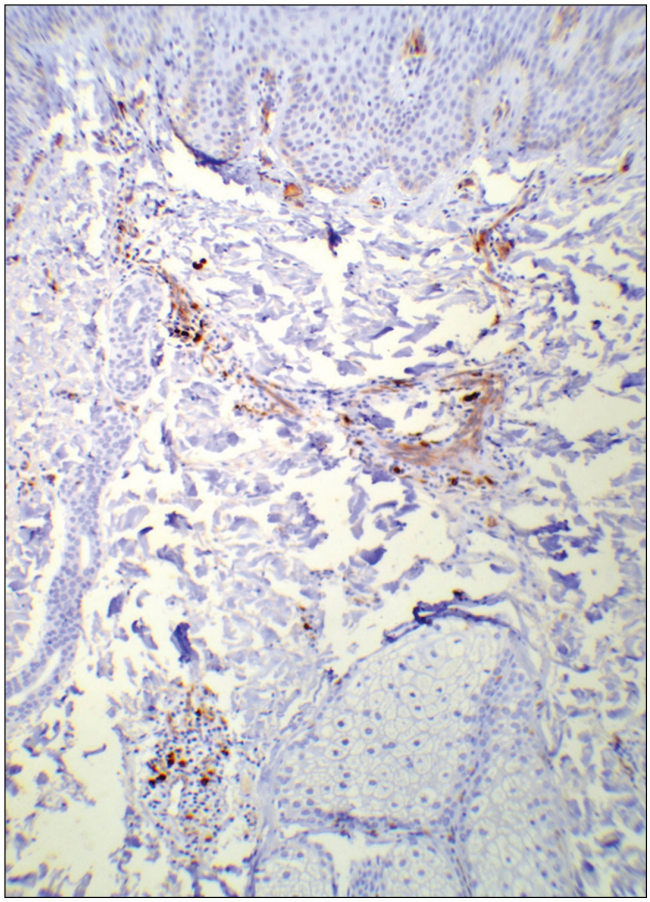

Figure 3: Scattered (1+) CD123+ cells in LPP(CD 123 X40)

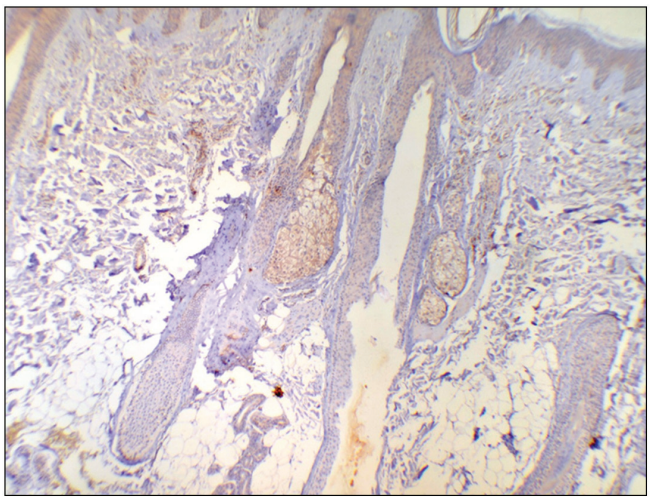

Figure 4: Absence of CD123+ cells in AA, note the catagen follicles (CD 123 X40)

The same criteria were applied in our study to assess the distribution patterns and grading of PDC using CD123 immunohistochemistry in various forms of alopecia.

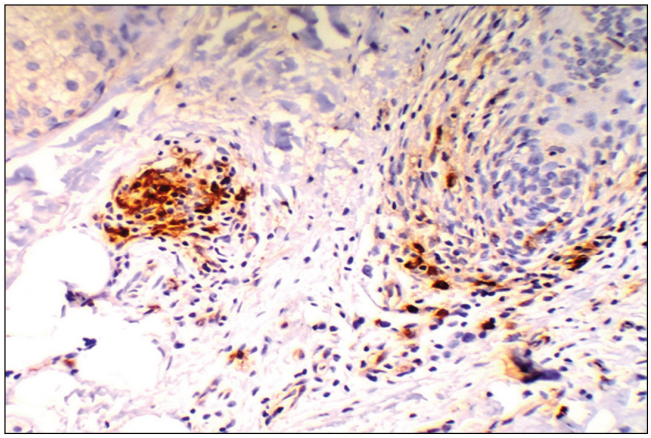

Figure 5: Clusters (2+) of CD123+ cells in the peribulbar infiltrate in AA (CD123 X200)

17/20 cases of LE (85%) showed CD123+ cells in clusters, lichenoid and scattered pattern. The distribution was in the perifollicular, perieccrine, superficial and deep dermal infiltrates which is comparable with other studies.[1,10,11] All 3 cases which were negative showed a paucity of inflammatory infiltrate.

Existence of scattered CD123+ cells has been noted in LP.[12] PDCs were detected as single cells or as small groups in LP, as compared to LE, where they were constantly present in large clusters. In our study, only one caseofLPPshowed scattered CD123+ cells in the superficial dermal location.

The distinct PDC arrangement in LE will serve as a diagnostic tool in the differentiation of LP from LE with a lichenoid pattern.[1]

Also noted in the study were clusters of CD123+ cells in one case each of folliculitis decalvans and AA. The histology of these cases was reviewed and there was no change in the diagnosis.

Rahal *et al.* studied the expression profile of BDCA-2 and MxA in alopecia areata, trichotillomania and Androgenetic alopecia.[13] BDCA-2 is a specific marker for PDC.[14] Myxovirus protein A is a surrogate marker for local tissue type I interferon.[15,16] It is hypothesised that PDC also involved in the pathogenesis of AA in the induction phase of the disease and the distribution pattern was in the peribulbar infiltrate.[13] This could explain the presence of CD123 positive cells in one case of AA. However no literature is available to substantiate the expression in folliculitis decalvans.

The four cases of end-stage scarring alopecia could not be assigned a specific diagnosis owing to marked fibrosis, paucity of infiltrates, absence of epidermal changes of LE and also lacked PDC. This is one the drawbacks of the present study and indicates that in late lesions, diagnostic difficulty persists even with immune markers.

In summary, our study reaffirms the presence of PDC in alopecia due to LE, in comparison with all other scarring and non-scarring alopecias. These findings suggest that CD123 is a highly promising diagnostic marker for alopecia due to LE.

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Conflicts of interest

There are no conflicts of interest.

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