Histopathology

Histopathology 2019, **74**, 908–916. DOI: 10.1111/his.13817

Utility of CD123 immunohistochemistry in differentiating lupus erythematosus from cutaneous T cell lymphoma

Stephanie J T Chen,[1,2] Julie Y Tse,[3] Paul W Harms,[1,4] Alexandra C Hristov[1,4] & May P Chan[1,4]

[1]*Department of Pathology, University of Michigan, Ann Arbor, MI,* [2]*Department of Pathology, University of Iowa, Iowa City, IA,* [3]*Department of Pathology, Tufts Medical Center, Boston, MA, and* [4]*Department of Dermatology, University of Michigan, Ann Arbor, MI, USA*

Date of submission 17 November 2018
Accepted for publication 30 December 2018
Published online *Article Accepted* 31 December 2018

Chen S J T, Tse J Y, Harms P W, Hristov A C & Chan M P
(2019) *Histopathology* **74**, 908–916. https://doi.org/10.1111/his.13817

Utility of CD123 immunohistochemistry in differentiating lupus erythematosus from cutaneous T cell lymphoma

Aims: Histopathological overlap between lupus erythematosus and certain types of cutaneous T cell lymphoma (CTCL) is well documented. $CD123^+$ plasmacytoid dendritic cells (PDCs) are typically increased in lupus erythematosus, but have not been well studied in CTCL. We aimed to compare CD123 immunostaining and histopathological features in these conditions.

Methods and results: Skin biopsies of cutaneous lupus erythematosus (CLE, $n = 18$), lupus erythematosus panniculitis (LEP, $n = 17$), mycosis fungoides (MF, $n = 25$) and subcutaneous panniculitis-like T cell lymphoma (SPTCL, $n = 9$) were retrospectively reviewed and immunostained with CD123. Percentage, distribution and clustering of $CD123^+$ cells were compared between CLE and MF and between LEP and SPTCL using χ^2 and two-tailed *t*-tests. A higher percentage of $CD123^+$ cells was observed in CLE than MF ($P < 0.01$), more frequently comprising ≥20% of the entire infiltrate ($P < 0.01$) and forming clusters ($P < 0.01$). Similarly, LEP showed a higher percentage of $CD123^+$ cells than SPTCL ($P = 0.01$), more frequently comprising ≥20% of the infiltrate ($P = 0.04$) and forming clusters ($P = 0.01$). Basal vacuolar change or dyskeratosis was observed in all CLE cases and in 48% cases of MF cases ($P = 0.05$). Plasma cells were readily identified in 76% cases of LEP but in none of the SPTCL cases ($P = 0.01$). Adipocyte rimming by lymphocytes, hyaline fat necrosis and fibrinoid/grungy necrosis did not significantly differ between LEP and SPTCL. Dermal mucin also failed to distinguish between groups.

Conclusions: CD123 immunostaining is helpful in differentiating CLE from MF and LEP from SPTCL, but should be interpreted in conjunction with clinicopathological features and other ancillary studies to ensure accurate diagnosis.

Keywords: CD123, cutaneous T cell lymphoma, lupus erythematosus, mycosis fungoides, plasmacytoid dendritic cells, subcutaneous panniculitis-like T cell lymphoma

Introduction

Histopathological overlap between cutaneous/subcutaneous lupus erythematosus and cutaneous T cell lymphoma (CTCL) is well recognised, and may present a diagnostic challenge. Although mycosis fungoides (MF) is readily diagnosed when fully developed, classic features such as Pautrier microabscesses are often lacking in early cases.[1–3] Such cases may mimic various inflammatory dermatoses such as eczematous dermatitis, connective tissue disease, pigmented purpuric dermatosis and lichen sclerosus.[4–6] Of these, cutaneous lupus erythematosus (CLE) may enter the differential diagnosis of MF when interface

Address for correspondence: M P Chan MD, University of Michigan, NCRC Building 35, 2800 Plymouth Road, Ann Arbor, MI 48109, USA. e-mail: mpchan@med.umich.edu

changes[1–3,7–10] or dyskeratotic keratinocytes[2,3,8] are present. Conversely, some cases of CLE may show a robust lymphomatoid infiltrate at the dermo-epidermal junction and around blood vessels, potentially raising concern for MF.[6,10,11]

Even more notoriously challenging is the distinction between lupus erythematosus panniculitis (LEP) and subcutaneous panniculitis-like T cell lymphoma (SPTCL).[12–19] Several authors have reported misdiagnosis of LEP as SPTCL and vice versa.[14,15,20,21] Specifically, interface changes and other classic features of LEP have been reported in SPTCL.[13,18,22,23] The striking similarities of LEP and SPTCL have led some authors to propose that these entities may belong on a spectrum of T cell dyscrasia.[12,16] A European Organisation for Research and Treatment of Cancer study group reported that 19% of the patients with SPTCL had an associated autoimmune disease, with one-third of those having systemic lupus erythematosus.[15] These findings further support a possible link between LEP and SPTCL.

Plasmacytoid dendritic cells (PDCs), most commonly stained with CD123, are rarely present in normal skin.[24–26] The distribution and quantification of $CD123^+$ PDCs have been studied in a variety of inflammatory dermatoses.[18,26–33] Increased density and clustering of PDCs have been noted in all forms of lupus erythematosus,[24,26,30,31,34,35] including LEP.[18,19,36] In contrast, their density and distribution have been less rigorously studied in CTCL. Only three prior studies have examined PDCs in SPTCL, all of which found PDC clusters in significantly fewer cases of SPTCL than in LEP.[18,29,37] Another two studies have utilised the BDCA2/CD303 antibody to detect PDCs, in addition to other dendritic cell types, in various stages of MF and Sezary syndrome.[38,39]

The goal of this study was to compare CD123 immunostaining and various histopathological features in lupus erythematosus (CLE and LEP) and CTCL (MF and SPTCL).

Materials and methods

After approval by the Institutional Review Board, the pathology database at University of Michigan was searched for skin biopsies diagnosed as CLE (discoid, subacute cutaneous or systemic), LEP, MF and SPTCL between 2000 and 2017. An additional case of SPTCL was obtained from Tufts Medical Center. All cases were diagnosed originally based on clinicopathological correlation, with supporting immunohistochemical and T cell receptor (TCR) gene rearrangement studies as needed. Clinical data were obtained from electronic medical records.

Haematoxylin and eosin (H&E)-stained sections of CLE and MF cases were evaluated for the following features: basal vacuolation with associated lymphocytes and/or dyskeratotic keratinocytes, Pautrier microabscesses, melanin incontinence, increased dermal mucin and readily identifiable plasma cells. For LEP and SPTCL the following were evaluated: basal vacuolation with associated lymphocytes and/or dyskeratotic keratinocytes, increased dermal mucin, adipocyte 'rimming' by lymphocytes, readily identifiable plasma cells, hyaline fat necrosis and fibrinoid/grungy fat necrosis (fibrinoid necrosis containing karyorrhectic debris).

CD123 immunohistochemistry was performed on all cases. The majority of cases were immunostained at the University of Michigan research laboratory using the following protocol: 4-μm thick sections were deparaffinised and heat-induced epitope retrieval was performed using the Dako PT Link with a proprietary Tris-ethylenediamine tetraacetic acid (EDTA) buffer pH 9 from Dako (Carpenteria, CA, USA; FLEX retrieval solution, high pH). After blocking endogenous peroxidase activity, the slides were incubated for 120 min at room temperature with a mouse monoclonal CD123 antibody (7G3; BD Pharmingen, Franklin Lakes, NJ, USA) and subsequently detected on the EnVision $FLEX^+$ mouse diaminobenzidine (DAB) detection system (Dako). A small subset of cases was immunostained at the time of original diagnosis using the same antibody on the BenchMark ULTRA slide staining platform (Ventana Medical Systems, Tucson, AZ, USA), according to standard protocols validated in our clinical immunohistochemistry laboratory. Protein expression was detected using the ultraView Universal DAB Detection Kit (Ventana).

Plasmacytoid dendritic cells were identified by strong and crisp CD123 staining of small, round to oval cells outside of blood vessels. The percentage of $CD123^+$ PDCs of the entire infiltrate was assessed semiquantitatively from 0 to 100%. Clusters of $CD123^+$ PDCs were defined as tight aggregates of $\geq$15 $CD123^+$ PDCs. Subcutaneous location of PDC clusters and intra-epidermal PDCs were additionally recorded. Other immunohistochemical findings were recorded from the original pathology reports.

Histopathological and CD123 immunohistochemical findings were compared between groups: CLE versus MF and LEP versus SPTCL; χ^2 and two-tailed *t*-tests were used for categorical and continuous data,

respectively. A $P \leq 0.05$ was considered statistically significant.

Results

Eighteen CLE biopsies from 18 patients, 25 MF biopsies from 23 patients, 17 LEP biopsies from 14 patients and nine SPTCL biopsies from nine patients were identified. Patients with CTCL (mean age = 66 years) were generally older than those with lupus erythematosus (mean = 45 years) ($P < 0.01$). Female predominance was observed in the lupus group (male-to-female ratio = 1:2.5), whereas the reverse was seen the CTCL group (male-to-female ratio = 2:1). Antinuclear antibody serologies were available in a subset of cases and were positive in nine of 11 CLE patients, nine of 12 LEP patients, none of three MF patients and one of two SPTCL patients. Follow-up data were available for eight CLE patients and 11 LEP patients, none of whom developed lymphoma over a mean follow-up period of 4 and 5 years, respectively.

The histopathological and immunohistochemical findings in CLE and MF are summarised in Table 1. Basal vacuolar changes and/or dyskeratotic cells were more frequently seen in CLE than in MF ($P = 0.05$) (Figure 1A,B). Pautrier microabscesses were found exclusively in MF ($P < 0.01$). Increased dermal mucin, melanin incontinence and plasma cells did not show significant differences between these groups. The mean percentage of $CD123^+$ PDCs was higher in CLE (21%; Figure 1C) than in MF (4%; Figure 1D) ($P < 0.01$). These cells more frequently comprised ≥20% of the entire infiltrate ($P < 0.01$) and formed clusters ($P < 0.01$) in CLE (Figure 1E) compared to MF (Figure 1F). Intra-epidermal $CD123^+$ PDCs were common in both groups.

The histopathological and immunohistochemical findings in LEP and SPTCL are summarised in Table 2. Plasma cells were readily identified only in LEP (Figure 2A) and not in SPTCL (Figure 2B) ($P = 0.01$). All other examined histopathological features failed to distinguish between groups (Figure 2C, D). The mean percentage of $CD123^+$ PDCs was significantly higher in LEP (17%) than in SPTCL (2%) ($P = 0.01$). Approximately half the LEP cases consisted of ≥20% $CD123^+$ PDCs (Figure 2E), while none of the SPTCL cases did (Figure 2F) ($P = 0.04$). The majority of LEP cases contained clusters of PDCs (Figure 2G), which was consistently absent in SPTCL (Figure 2H) ($P = 0.01$). Intra-epidermal $CD123^+$ cells were similarly common in both groups. Non-specific, weak and 'fluffy' CD123 staining was noted in the subcutaneous fat in both LEP and SPTCL cases with significant fat necrosis (Figure 3). Such staining appeared to be located in histiocytes and/or extracellular matrix.

Table 1. Comparison of clinical, histopathological and immunohistochemical (CD123) findings in cutaneous lupus erythematosus (CLE) and mycosis fungoides (MF)

	CLE (n = 18)	MF (n = 25)	P-value
Mean age (years)	47	70	**<0.01**
Male-to-female ratio	1:2.6	3:1	**0.04**
Basal vacuolar changes or dyskeratosis	18 (100%)	12 (48%)	**0.05**
Pautrier microabscesses	0 (0%)	12 (48%)	**<0.01**
Increased dermal mucin	13 (72%)	8 (32%)	0.06
Melanin incontinence	11 (61%)	6 (24%)	0.06
Readily identifiable plasma cells	7 (39%)	6 (24%)	0.37
Mean % $CD123^+$ cells	21%	4%	**<0.01**
≥20% $CD123^+$ cells	12 (67%)	3 (12%)	**<0.01**
Intra-epidermal $CD123^+$ cells	18 (100%)	19 (76%)	0.40
$CD123^+$ cluster(s)	17 (94%)	0 (0%)	**<0.01**

Bold type indicates statistical significance.

Additional immunohistochemical stains were performed on two CLE cases, seven LEP cases and all CTCL cases at the time of diagnosis. All examined lupus cases showed a normal T cell immunophenotype, except for one LEP case. This latter case displayed a reversed CD4:CD8 ratio (1:3) but otherwise classic histomorphological features of LEP including vacuolar interface changes, hyaline fat necrosis, increased dermal mucin and increased plasma cells. All MF and SPTCL cases revealed aberrant T cell immunophenotypes.

Results of TCR gene rearrangement studies (performed at the time of diagnosis) were available for a subset of MF, LEP and SPTCL cases. A T cell clone was identified in four of five (80%) MF cases, none of five (0%) LEP cases and four of four (100%) SPTCL cases.

Discussion

Although most cases of CLE are readily distinguishable from MF, this differential diagnosis can be

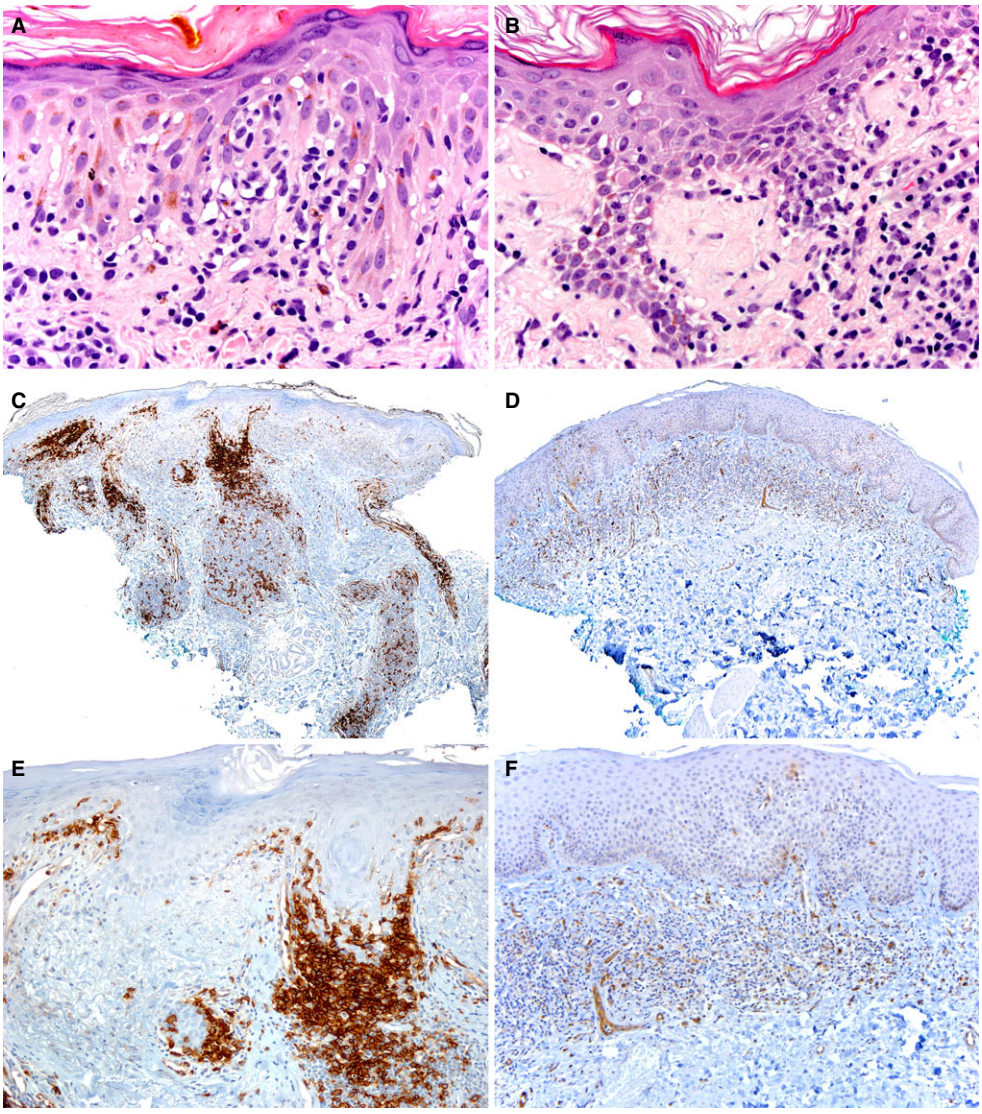

Figure 1. Selected histopathological features and CD123 immunostaining in cutaneous lupus erythematosus (CLE) and mycosis fungoides (MF). (**A**) An example of CLE shows an interface dermatitis with aggregates of lymphocytes at the dermo-epidermal junction (H&E) (**B**) An example of MF shows lymphocyte tagging and mild vacuolation of the basal layer (H&E). (**C**,**E**) This case of CLE demonstrates many $CD123^+$ plasmacytoid dendritic cells (PDCs) constituting 30% of the entire inflammatory cell infiltrate and forming prominent clusters. (**D**,**F**) This example of MF shows fewer $CD123^+$ PDCs constituting 10% of the entire infiltrate without clustering.

challenging at times. For example, mild basal vacuolar changes and occasional dyskeratotic keratinocytes in MF may raise consideration for CLE, whereas CLE with a robust lymphocytic infiltrate at the dermo-epidermal junction may simulate epidermotropism in MF. Similarly, histopathological overlap between LEP and SPTCL is well recognised,[12–14,16–19,22,23,29] and has led to a proposed spectrum of subcutaneous T cell dyscrasia encompassing both entities. As distinction between cutaneous/subcutaneous lupus erythematosus and CTCL is crucial for guiding appropriate clinical work-up and treatment, we aimed to assess the utility of the CD123 immunostain in addition to various histopathological features in differentiating these entities.

Plasmacytoid dendritic cells are a subtype of dendritic cells that produce type I interferons (alpha/beta). These cells can be highlighted by immunohistochemistry for CD123 (interleukin-3 receptor α chain) or BDCA-2/CD303. The quantity and distribution of PDCs vary in different inflammatory and neoplastic conditions. Increased number and clustering of PDCs have been described as common findings in CLE[24,26–28,30,31,34,35] and LEP,[18,29] and these cells

Table 2. Comparison of clinical, histopathological and immunohistochemical (CD123) findings in lupus erythematosus panniculitis (LEP) and subcutaneous panniculitis-like T cell lymphoma (SPTCL)

	LEP (n = 17)	SPTCL (n = 9)	P-value
Mean age (years)	43	54	0.20
Male-to-female ratio	1:2.4	1:1.3	0.65
Basal vacuolar changes or dyskeratosis	10/16 (63%)[a]	2/7 (29%)[a]	0.29
Increased dermal mucin	12 (71%)	4/7 (57%)[a]	0.70
Adipocyte rimming by lymphocytes	12 (71%)	8 (89%)	0.60
Readily identifiable plasma cells	13 (76%)	0 (0%)	**0.01**
Hyaline fat necrosis	8 (47%)	1 (11%)	0.14
Fibrinoid/ grungy necrosis	5 (29%)	3 (33%)	0.88
Mean % $CD123^+$ cells	17%	2%	**0.01**
≥20% $CD123^+$ cells	8 (47%)	0 (0%)	**0.04**
Intra-epidermal $CD123^+$ cells	4/16 (25%)a	2/7 (29%)a	0.86
$CD123^+$ cluster(s) in any location	12 (71%)	0 (0%)	**0.01**
$CD123^+$ cluster(s) in fat	7 (41%)	0 (0%)	0.06

Bold type indicates statistical significance.
[a]Absence of epidermis and/or dermis precluded evaluation of these features in some cases.

are thought to play an important role in the pathogenesis of lupus erythematosus.[26]

Only two previous studies have assessed the quantity and distribution of PDCs in MF, neither of which has compared their results with CLE or other inflammatory dermatoses.[28,39] Schwingshackl *et al.* noted an increased number of single and loosely aggregated PDCs in MF compared with normal skin, and concluded that their number was dependent on the intensity of the infiltrate.[38] Pileri *et al.* also observed rare loose aggregates of PDCs in MF, and that their number was significantly higher in stage IIB compared to stage IA/B disease.[39] While these results offered insight into the microenvironment of MF, the utility of $CD123^+$ PDCs in distinguishing MF from CLE remained to be investigated.

Of all histopathological parameters compared between CLE and MF, basal vacuolar changes and dyskeratotic cells were of particular interest given their potential to masquerade MF as an interface dermatitis.[6,8,9] In our cohort, although these changes were more frequently seen in CLE, the difference barely reached statistical significance (P = 0.05). The specificity of these changes was poor (52%), as almost half of our MF cases showed these features. Other series have reported interface changes in 59–76% of MF cases.[2,3] These findings should caution pathologists against using basal vacuolation and dyskeratotic keratinocytes alone to exclude a diagnosis of MF. Although the presence of Pautrier microabscesses was highly specific (100%) for MF, its sensitivity was low (48%). This is in keeping with previous reports of Pautrier microabscesses in fewer than half of MF cases.[2,3,7,40] Plasma cells are commonly present in connective tissue diseases, including lupus erythematosus. Although less well described in MF, plasma cells have been reported in 9% of MF/Sezary syndrome cases.[41] We found a modest amount of plasma cells in 24% of our MF cases, where they were readily identified and failed to distinguish between CLE and MF. Lastly, both increased dermal mucin and melanin incontinence (a common consequence of interface dermatitis) were slightly more common in CLE, but the associations fell short of statistical significance (P = 0.06). Together, these findings indicate that histopathological distinction between CLE and MF has its limitations, and ancillary tools are needed in challenging cases.

The percentage of PDCs and their tendency to form clusters in our CLE cases was similar to that reported previously.[28,30,31,35] We found that a cut-off of 20% PDCs separated CLE and MF reasonably well. Furthermore, presence of PDC cluster(s) was both highly sensitive (94%) and specific (100%) for the diagnosis of CLE when compared with MF, rendering CD123 a superior diagnostic tool in distinguishing these conditions. The percentage of CLE cases with intra-epidermal $CD123^+$ cells (100%) was higher than reported previously,[35] yet this feature was also common in MF and thus was not helpful.

With regard to the comparison between LEP and SPTCL, the only reliable discriminative histopathological feature in our study was the presence of readily identifiable plasma cells, seen exclusively in LEP. Other histopathological features deemed helpful in previous studies failed to show significant differences in ours. Hyaline fat necrosis was more common in LEP, but was observed in fewer than half these cases. Fibrinoid/grungy necrosis, previously reported to be supportive of SPTCL,[29] was seen at almost equal frequency in both groups. Adipocyte rimming by

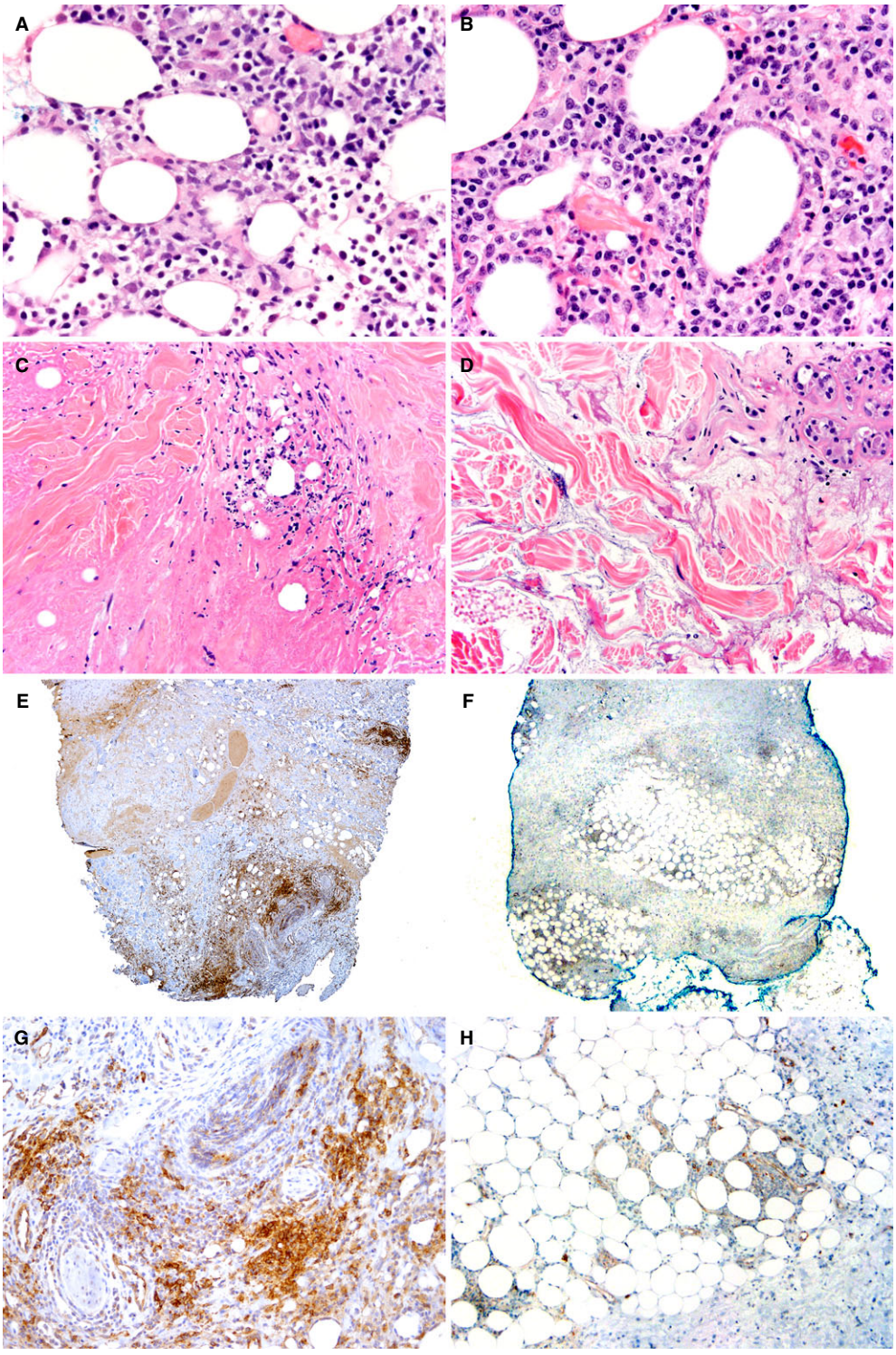

Figure 2. Selected histopathological features and CD123 immunostaining in lupus erythematosus panniculitis (LEP) and subcutaneous panniculitis-like T cell lymphoma (SPTCL). (**A**) Plasma cells and adipocyte rimming by lymphocytes in a case of LEP. (**B**) A subcutaneous lymphoid infiltrate in SPTCL lacks plasma cells. (C) Fibrinoid/grungy necrosis in LEP. (**D**) Increased dermal mucin in a case of SPTCL. (**E,G**) An example of LEP contains 40% $CD123^+$ plasmacytoid dendritic cells (PDCs) with formation of several clusters, including some in the subcutaneous fat. (**F,H**) This case of SPTCL shows a few scattered $CD123^+$ PDCs constituting less than 10% of the infiltrate, without formation of clusters.

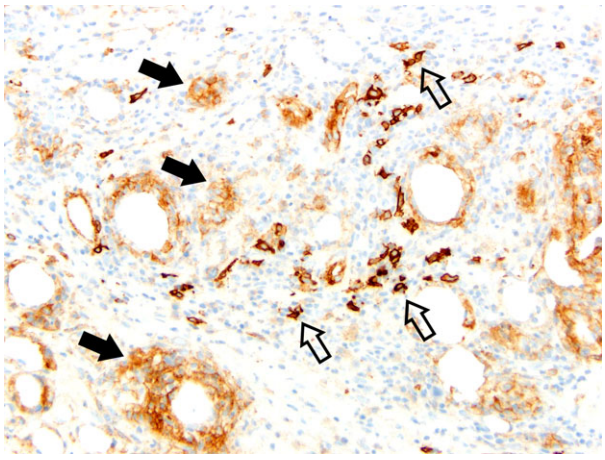

Figure 3. Non-specific CD123 immunostaining. An example of subcutaneous panniculitis-like T cell lymphoma with prominent fat necrosis demonstrates weak and 'fluffy' CD123 staining in the subcutaneous fat, mostly within histiocytes (solid arrows). This type of non-specific staining contrasts with the strong and crisp staining of the small ovoid plasmacytoid dendritic cells (empty arrows).

atypical lymphocytes was another useful feature according to previous reports.[18,29] In our experience, however, evaluation for lymphocytic atypia tends to be subjective, as it was not uncommon to find slightly hyperchromatic and irregular lymphocytes in LEP. We therefore assessed for adipocyte rimming by lymphocytes regardless of the degree of atypia, and found no association with either group. While the limited utility of histopathological features in this differential diagnosis may be attributable, in part, to the small sample size of SPTCL in this cohort, our findings again highlight a significant need for additional tools to help distinguish these conditions.

The presence of PDCs has been examined in SPTCL in comparison with LEP in three previous studies. All these studies found that PDC clusters were more common in LEP, but were also present in a smaller subset of SPTCL cases.[18,29,37] This feature must therefore be interpreted in the context of clinical, histopathological, immunophenotypical and molecular findings. As none of our SPTCL cases showed ≥20% PDCs or PDC clusters, we consider these findings highly specific for a diagnosis of LEP. Of note, we observed that cases with fat necrosis tended to show weak, 'fluffy' CD123 staining of histiocytes and/or extracellular matrix in the subcutis. Such non-specific staining could lead to overinterpretation of PDC clusters. Recognition of the strong and crisp staining of true PDCs, which are typically small and round to oval in shape, would avoid this pitfall. Also, a strict requirement of ≥15 touching $CD123^+$ PDCs in a PDC cluster will probably improve the specificity of this finding.

Interestingly, one LEP case demonstrated a reversed CD4:CD8 ratio. While this case was classified as LEP based on a history of systemic lupus erythematosus and classic histopathological features, $CD123^+$ PDCs were notably absent. We therefore speculate that the loss of PDCs could represent an early sign of progression on the LEP-SPTCL spectrum. Unfortunately, this patient was lost to follow-up a year after the biopsy, precluding further assessment.

A major limitation of this study is the small sample size, especially of the SPTCL group, due to relative rarity of this condition and over-representation of consult cases from outside facilities (hence limited access to tissue blocks). Another limitation is that only a small subset of cases has been studied by TCR gene rearrangement at the time of diagnosis; however, lack of evidence of progression to lymphoma in patients diagnosed with CLE and LEP provided additional support for their diagnoses.

In conclusion, our study confirms that the CD123 immunostain is a useful ancillary tool in differentiating CLE from MF and LEP from SPTCL. In particular, $CD123^+$ PDC clusters are highly specific for CLE and LEP in these contexts. Although CD123 immunohistochemistry shows superior sensitivity and specificity compared to most histopathological features examined in this study, it should be interpreted in conjunction with clinical history, histopathological examination, other immunohistochemical findings and gene rearrangement studies (when necessary) to ensure accurate diagnosis.

Conflicts of interest

The authors report no conflicts of interest.

References

1. Everett MA. Early diagnosis of mycosis fungoides: vacuolar interface dermatitis. *J. Cutan. Pathol.* 1985; **12**; 271–278.
2. Naraghi ZS, Seirafi H, Valikhani M, Farnaghi F, Kavusi S, Dowlati Y. Assessment of histologic criteria in the diagnosis of mycosis fungoides. *Int. J. Dermatol.* 2003; **42**; 45–52.
3. Massone C, Kodama K, Kerl H, Cerroni L. Histopathologic features of early (patch) lesions of mycosis fungoides: a morphologic study on 745 biopsy specimens from 427 patients. *Am. J. Surg. Pathol.* 2005; **29**; 550–560.
4. Reddy K, Bhawan J. Histologic mimickers of mycosis fungoides: a review. *J. Cutan. Pathol.* 2007; **34**; 519–525.
5. Kaudewitz P, Soldner R, Burg G *et al.* Reactivity of monoclonal antibody BE 2 in different stages of mycosis fungoides and in

benign dermal infiltrates. *Arch. Dermatol. Res.* 1986; **279**; 83–88.
6. Friss AB, Cohen PR, Bruce S, Duvic M. Chronic cutaneous lupus erythematosus mimicking mycosis fungoides. *J. Am. Acad. Dermatol.* 1995; **33**; 891–895.
7. Nickoloff BJ. Light-microscopic assessment of 100 patients with patch/plaque-stage mycosis fungoides. *Am. J. Dermatopathol.* 1988; **10**; 469–477.
8. Guitart J, Peduto M, Caro WA, Roenigk HH. Lichenoid changes in mycosis fungoides. *J. Am. Acad. Dermatol.* 1997; **36**; 417–422.
9. Veysey EC, Wilkinson JD. Mycosis fungoides masquerading as cutaneous lupus erythematosus and associated with antiphospholipid syndrome. *Clin. Exp. Dermatol.* 2008; **33**; 26–29.
10. Pereira A, Ferrara G, Calamaro P *et al.* The histopathological spectrum of pseudolymphomatous infiltrates in cutaneous lupus erythematosus. *Am. J. Dermatopathol.* 2018; **40**; 247–253.
11. Magro CM, Crowson AN, Harrist TJ. Atypical lymphoid infiltrates arising in cutaneous lesions of connective tissue disease. *Am. J. Dermatopathol.* 1997; **19**; 446–455.
12. Magro CM, Crowson AN, Kovatich AJ, Burns F. Lupus profundus, indeterminate lymphocytic lobular panniculitis and subcutaneous T-cell lymphoma: a spectrum of subcuticular T-cell lymphoid dyscrasia. *J. Cutan. Pathol.* 2001; **28**; 235–247.
13. Ma L, Bandarchi B, Glusac EJ. Fatal subcutaneous panniculitis-like T-cell lymphoma with interface change and dermal mucin, a dead ringer for lupus erythematosus. *J. Cutan. Pathol.* 2005; **32**; 360–365.
14. Gonzalez EG, Selvi E, Lorenzini S *et al.* Subcutaneous panniculitis-like T-cell lymphoma misdiagnosed as lupus erythematosus panniculitis. *Clin. Rheumatol.* 2007; **26**; 244–246.
15. Willemze R, Jansen PM, Cerroni L *et al.* Subcutaneous panniculitis-like T-cell lymphoma: definition, classification, and prognostic factors: an EORTC Cutaneous Lymphoma Group Study of 83 cases. *Blood* 2008; **111**; 838–845.
16. Bosisio F, Boi S, Caputo V *et al.* Lobular panniculitic infiltrates with overlapping histopathologic features of lupus panniculitis (lupus profundus) and subcutaneous T-cell lymphoma: a conceptual and practical dilemma. *Am. J. Surg. Pathol.* 2015; **39**; 206–211.
17. Shiau CJ, Abi Daoud MS, Wong SM, Crawford RI. Lymphocytic panniculitis: an algorithmic approach to lymphocytes in subcutaneous tissue. *J. Clin. Pathol.* 2015; **68**; 954–962.
18. LeBlanc RE, Tavallaee M, Kim YH, Kim J. Useful parameters for distinguishing subcutaneous panniculitis-like T cell lymphoma from lupus erythematosus panniculitis. *Am. J. Surg. Pathol.* 2016; **40**; 745–754.
19. Willemze R. Cutaneous lymphomas with a panniculitic presentation. *Semin. Diagn. Pathol.* 2017; **34**; 36–43.
20. Cho KH, Oh JK, Kim CW, Heo DS, Kim ST. Peripheral T-cell lymphoma involving subcutaneous tissue. *Br. J. Dermatol.* 1995; **132**; 290–295.
21. Weenig RH, Ng CS, Perniciaro C. Subcutaneous panniculitis-like T-cell lymphoma: an elusive case presenting as lipomembranous panniculitis and a review of 72 cases in the literature. *Am. J. Dermatopathol.* 2001; **23**; 206–215.
22. Cassis TB, Fearneyhough PK, Callen JP. Subcutaneous panniculitis-like T-cell lymphoma with vacuolar interface dermatitis resembling lupus erythematosus panniculitis. *J. Am. Acad. Dermatol.* 2004; **50**; 465–469.
23. Pincus LB, LeBoit PE, McCalmont TH *et al.* Subcutaneous panniculitis-like T-cell lymphoma with overlapping clinicopathologic features of lupus erythematosus: coexistence of 2 entities? *Am. J. Dermatopathol.* 2009; **31**; 520–526.
24. Farkas L, Beiske K, Lund-Johansen F, Brandtzaeg P, Jahnsen FL. Plasmacytoid dendritic cells (natural interferon-alpha/beta-producing cells) accumulate in cutaneous lupus erythematosus lesions. *Am. J. Pathol.* 2001; **159**; 237–243.
25. Ebner S, Ehammer Z, Holzmann S *et al.* Expression of C-type lectin receptors by subsets of dendritic cells in human skin. *Int. Immunol.* 2004; **16**; 877–887.
26. Vermi W, Lonardi S, Morassi M *et al.* Cutaneous distribution of plasmacytoid dendritic cells in lupus erythematosus. Selective tropism at the site of epithelial apoptotic damage. *Immunobiology* 2009; **214**; 877–886.
27. Magro CM, Segal JP, Crowson AN, Chadwick P. The phenotypic profile of dermatomyositis and lupus erythematosus: a comparative analysis. *J. Cutan. Pathol.* 2010; **37**; 659–671.
28. Tomasini D, Mentzel T, Hantschke M *et al.* Plasmacytoid dendritic cells: an overview of their presence and distribution in different inflammatory skin diseases, with special emphasis on Jessner's lymphocytic infiltrate of the skin and cutaneous lupus erythematosus. *J. Cutan. Pathol.* 2010; **37**; 1132–1139.
29. Liau JY, Chuang SS, Chu CY, Ku WH, Tsai JH, Shih TF. The presence of clusters of plasmacytoid dendritic cells is a helpful feature for differentiating lupus panniculitis from subcutaneous panniculitis-like T cell lymphoma. *Histopathology* 2013; **62**; 1057–1066.
30. Brown TT, Choi EY, Thomas DG, Hristov AC, Chan MP. Comparative analysis of rosacea and cutaneous lupus erythematosus: histopathologic features, T-cell subsets, and plasmacytoid dendritic cells. *J. Am. Acad. Dermatol.* 2014; **71**; 100–107.
31. Walsh NM, Lai J, Hanly JG *et al.* Plasmacytoid dendritic cells in hypertrophic discoid lupus erythematosus: an objective evaluation of their diagnostic value. *J. Cutan. Pathol.* 2015; **42**; 32–38.
32. Cinotti E, Merlo V, Kempf W *et al.* Reticular erythematous mucinosis: histopathological and immunohistochemical features of 25 patients compared with 25 cases of lupus erythematosus tumidus. *J. Eur. Acad. Dermatol. Venereol.* 2015; **29**; 689–697.
33. Fening K, Parekh V, McKay K. CD123 immunohistochemistry for plasmacytoid dendritic cells is useful in the diagnosis of scarring alopecia. *J. Cutan. Pathol.* 2016; **43**; 643–648.
34. Ko CJ, Srivastava B, Braverman I, Antaya RJ, McNiff JM. Hypertrophic lupus erythematosus: the diagnostic utility of CD123 staining. *J. Cutan. Pathol.* 2011; **38**; 889–892.
35. McNiff JM, Kaplan DH. Plasmacytoid dendritic cells are present in cutaneous dermatomyositis lesions in a pattern distinct from lupus erythematosus. *J. Cutan. Pathol.* 2008; **35**; 452–456.
36. Wenzel J, Proelss J, Wiechert A, Zahn S, Bieber T, Tuting T. CXCR3-mediated recruitment of cytotoxic lymphocytes in lupus erythematosus profundus. *J. Am. Acad. Dermatol.* 2007; **56**; 648–650.
37. Sitthinamsuwan P, Pattanaprichakul P, Treetipsatit J *et al.* Subcutaneous panniculitis-like T-cell lymphoma versus lupus erythematosus panniculitis: distinction by means of the Peri-adipocytic Cell Proliferation Index. *Am. J. Dermatopathol.* 2018; **40**; 567–574.
38. Schwingshackl P, Obermoser G, Nguyen VA, Fritsch P, Sepp N, Romani N. Distribution and maturation of skin dendritic cell subsets in two forms of cutaneous T-cell lymphoma: mycosis

fungoides and Sezary syndrome. *Acta Derm. Venereol.* 2012; **92**; 269–275.
39. Pileri A, Agostinelli C, Sessa M *et al.* Langerhans, plasmacytoid dendritic and myeloid-derived suppressor cell levels in mycosis fungoides vary according to the stage of the disease. *Virchows Arch.* 2017; **470**; 575–582.
40. Smoller BR, Bishop K, Glusac E, Kim YH, Hendrickson M. Reassessment of histologic parameters in the diagnosis of mycosis fungoides. *Am. J. Surg. Pathol.* 1995; **19**; 1423–1430.
41. Shapiro PE, Pinto FJ. The histologic spectrum of mycosis fungoides/Sezary syndrome (cutaneous T-cell lymphoma). A review of 222 biopsies, including newly described patterns and the earliest pathologic changes. *Am. J. Surg. Pathol.* 1994; **18**; 645–667.