RESEARCH LETTERS

Loss of cytokeratin-15 (CK15) expression is not specific for lichen planopilaris (LPP)

To the Editor: Within the hair follicle, the stem cell compartment is composed of 2 spatially distinct epithelial populations, which represent 2 functionally different pools: the bulge and the hair germ. The activated hair germ cells respond to environmental stimuli to engage in new growth, whereas the quiescent bulge stem cells maintain a long-term stem cell pool.[1] Cicatricial (primary scarring) alopecia results from the destruction of the follicular and sebaceous epithelium and subsequently the bulge stem cell pool.

Lichen planopilaris (LPP) is characterized by localized infundibuloisthmic lymphocytic inflammation targeting the bulge stem cell region and destroying the cytokeratin 15 $(CK15)^+$ stem cells. Stem cells have been incriminated to be the autoimmune target in LPP and absence of CK15 immunoreactivity has been reported in active lesions.[2] Thus, we studied whether loss of CK15 immunoreactivity is found in other cicatricial alopecias, particularly in frontal fibrosing alopecia (FFA) and lupus erythematosus (LE).

A total of 19 LPP cases, 9 FFA cases, and 7 alopecic LE cases (Fig 1) were compared for CK15 expression within the infundibulum of affected follicles and unaffected follicles. In all cases a 4-mm punch biopsy was performed and all the specimens were processed using the horizontal and vertical technique.[3] Statistical results are shown in Table I. Significant χ^2 values within each row show a strong association between affected or unaffected follicles and, respectively, loss or preservation of CK15 expression in each disorder. The high *P* value for the entire table indicates that there has not been any significant difference in the loss of CK15 among these disorders.

FFA, a variant of LPP, preferentially affects vellus follicles in the frontotemporal area of the scalp. Unlike LPP, it shows limited perifollicular fibrosis. Lichenoid involvement in LE, in contrast to LPP, may be seen in the deep portion of the follicles and the interfollicular epidermis. However, the lymphocytic infiltrate in LE usually extends to the infundibuloisthmic level.[4] It is, therefore, not surprising that CK15 expression would be lost not only in LPP, but also in FFA and in LE. Sperling et al[5] also reported that CK15 expression disappears once the internal root sheath "desquamates" in central centrifugal cicatricial alopecia.

An interesting finding in LPP is the decrease or near absence of catagen/telogen hair, because damaged follicles that have lost their CK15 stem cells disappear when they enter catagen phase. Thus, the only viable remaining follicles are terminal hairs.[2] It

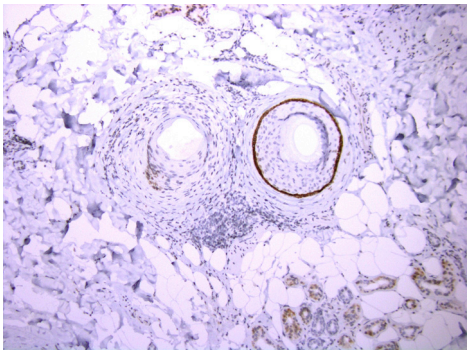

Fig 1. Alopecic lupus erythematosus. Preservation of cytokeratin 15 (CK15) expression in an unaffected follicle (*right*) and loss of CK15 expression in an affected follicle (*left*). Loss of CK15 expression was defined as complete absence of immunoreactivity.

Table I. Cytokeratin 15 expression in lichen planopilaris, frontal fibrosing alopecia, and alopecic lupus erythematosus

	Affected follicles		Unaffected follicles		No. of cases/ row	χ^2 for *P*/N × U/A within each diagnosis
Diagnosis	$CK15^+$	$CK15^-$	$CK15^+$	$CK15^-$		
LPP	2	17	18	1	19	$\chi^2 = 23.750$, $P < .0001$
FFA	1	8	9	0	9	$\chi^2 = 11.02$, $P < .001$
LE	0	7	7	0	7	$\chi^2 = 10.28$, $P < .0013$
Total	3	32	34	1	35	Combined table $\chi^2 = .837$, $P < .991$

The significant χ^2 values within each row show the strong association between affected status and CK15 expression (loss in involved follicles and preservation in unaffected follicles). The high *P* value for the entire table indicates that there has not been any significant difference in the loss of CK15 among these disorders.
A, Affected follicles; *CK15*, cytokeratin 15; *FFA*, frontal fibrosing alopecia; *LE*, lupus erythematosus; *LPP*, lichen planopilaris; *U*, unaffected follicles.

is not clear why catagen/telogen-phase follicles are preserved in other cicatricial alopecias, because destruction of the bulge zone is a common final outcome.

In conclusion, loss of CK15 expression is not a unique feature of LPP, being also present in LE and FFA. Loss of CK15 expression reflects a nonspecific destruction of the bulge area even in diseases not specifically targeting the follicular bulge stem cells and should not be used as a diagnostic clue in favor of LPP. It would be interesting to further explore CK15 expression in other scarring alopecias affecting the superficial portion of follicles, such as central centrifugal cicatricial alopecia and folliculitis decalvans.

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Brown globules in lentigo maligna (LM): A useful dermoscopic clue

To the Editor: Lentigo maligna (LM) is a slow-growing in situ melanoma commonly located on chronically sun-exposed skin. Females are more frequently affected than males, with a peak of incidence at the seventh and eighth decade of life. Clinically, LM appears as a solitary, asymmetric patch or plaque with irregular borders and variegated colors. Clinical differential diagnoses include mainly solar lentigo, pigmented actinic keratosis, and lichen planus–like keratosis. Several dermoscopic features characterize these lesions, however some overlapping dermoscopic criteria make the diagnosis of LM in its initial phase very challenging.[1-4] In equivocal cases, biopsy and histopathologic examination remain the gold standard for the diagnosis.

We describe 6 cases of facial LM characterized by brown dots/globules as the main melanocytic dermoscopic feature included in a series of 122 LM/lentigo maligna melanoma (LMM) collected from 2005 through 2010. Six LM lesions of 6 patients, 4 female and 2 male, aged 54 to 66 years (mean 60 years), were located on the ear (n = 3), neck (n = 1), cheek (n = 1), and temporal region (n = 1). In all lesions, dermoscopic examination showed light- to dark-brown irregular dots/globules and a light-brown structureless background pigmentation as the predominant features (Fig 1, *A*). Few annular-granular structures were observed in 1 of 6 cases and blue-gray granules in another case. Histopathologic examination showed in all cases a proliferation of single atypical melanocytes along the basal layer of the epidermis and down the adnexa combined with the presence of junctional nests. In 2 cases, junctional nests were prevalent over the lentiginous pattern (Fig 1, *B*).

Dermoscopy of LM was initially described by Schiffner et al[1] who proposed a progression model from the early phase of LM, characterized by dots aggregated around follicles, asymmetric pigmented follicular openings, and streaks, to an intermediate phase displaying annular-granular structures and rhomboidal structures until the invasive LM showing homogeneous areas and obliterated hair follicles. Recently, 4 new dermoscopic criteria to diagnose LM have been described: darkening at dermoscopy, increase of vascular density, red rhomboidal structures, and targetlike pattern.[2] Only the presence of homogeneous areas with obliterated hair follicles is considered highly specific of invasive LM, whereas the other criteria (asymmetric pigmented follicular openings, annular-granular pattern, and rhomboidal structures) can be also found in pigmented actinic keratosis, lichen planus–like keratosis, and solar lentigos.[3-5]