Loss of Langerhans cells in scar lesion of lichen planopilaris is due to diminished active TGF-β caused by downregulation of integrin αvβ6 in the epidermal keratinocytes

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INTRODUCTION

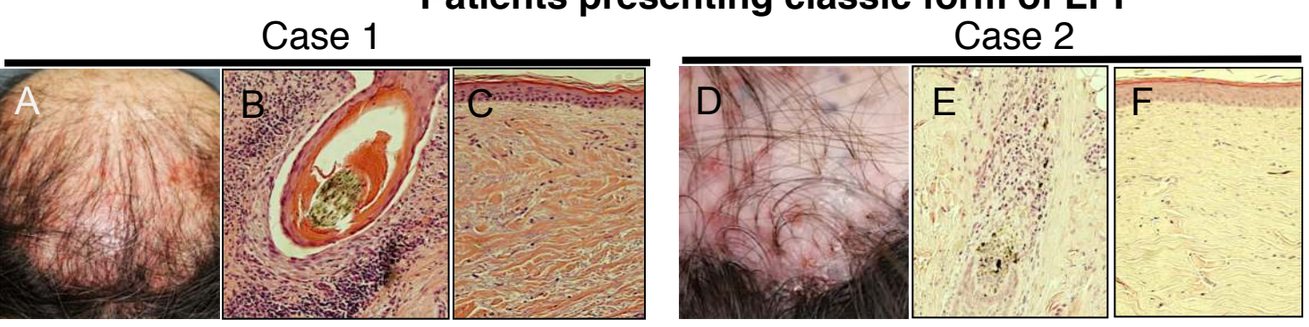
Lichen planopilaris (LPP) is one of scarring alopecias that is characterized by chronic lymphocytic inflammation around the hair follicle and subsequent hair loss and scar formation.
Past reports showed that langerhans cells (LCs) are absent in the epidermis of LPP scar[1].
However, the underlying mechanism of LC loss and the involvement of LC loss in the pathogenesis of LPP are still unknown.

HYPOTHESIS

Five proteins associated with LC development and maintenance in epidermis were previously studied in some reports, such as TGF-β[2,3], IL-34[4], Bone Morphogenetic Protein-7 (BMP-7)[5], integrin (ITG) αvβ6[6] and ITG αvβ8[6].
However, so far, there is no comprehensive investigation or report that how these all proteins distribute and express in the epidermis of normal scalp skin and moreover their hair follicles.
Thus, this study has two purposes. The first is to clarify expressions and distributions of these five proteins in normal scalp skin and hair follicles.
The second is to investigate the alteration of expression patterns of these proteins in folliculitis and scar lesion of LPP.

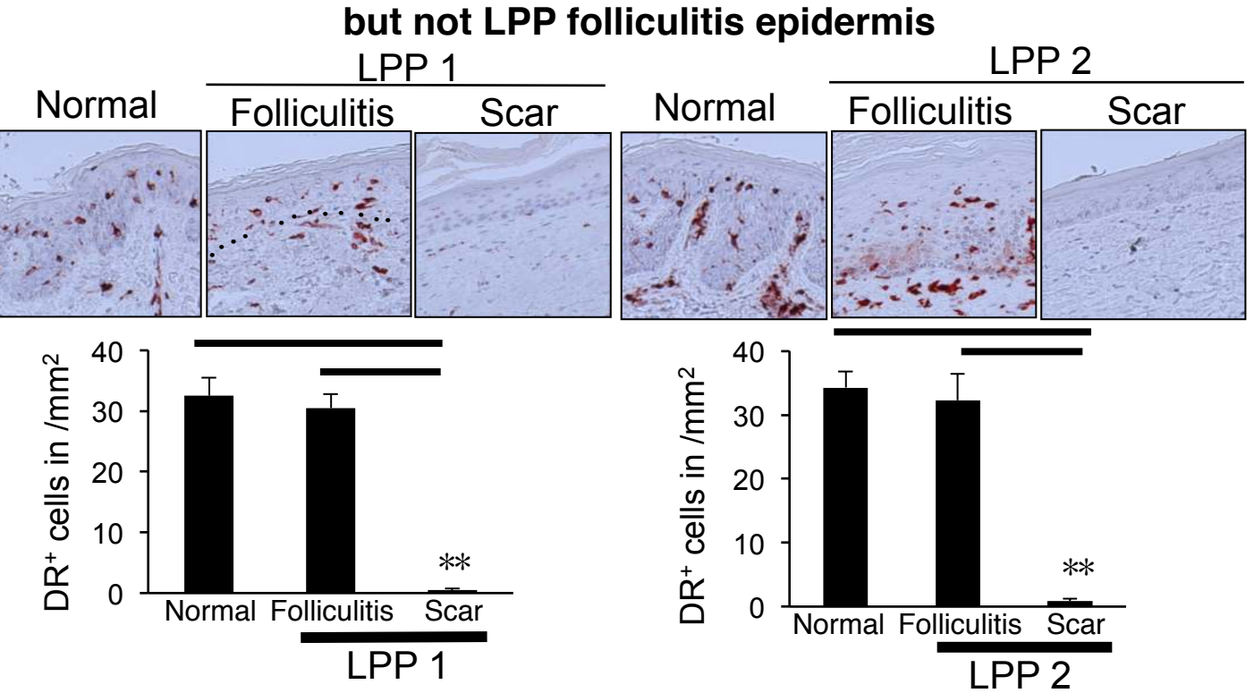
OUR CASES

Patients presenting classic form of LPP



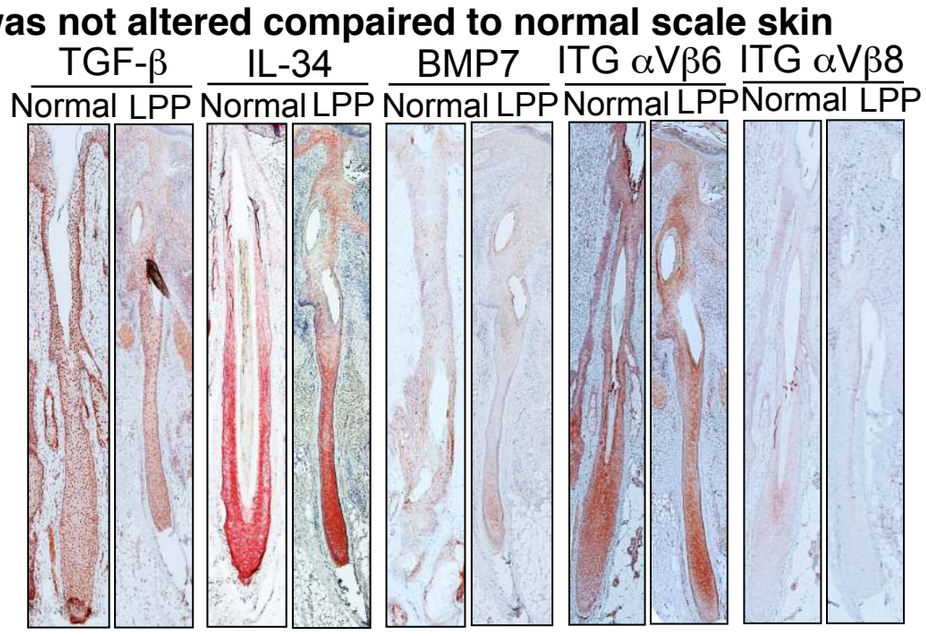
We obtained scalp biopsy specimens from both red papules around hair follicles (B, E) and scarring lesions of hair loss (C, F) from each paitient.
(B, E): In lymphocytic inflammatory phases, lymphocyte locally infiltrate at isthmus destroying the follicle germ cells.
(C, F): Advanced lesions have little inflammation, but demonstrate extensive fibrosis without hair follicles.

LCs were diminished in LPP scar epidermis, but not LPP folliculitis epidermis

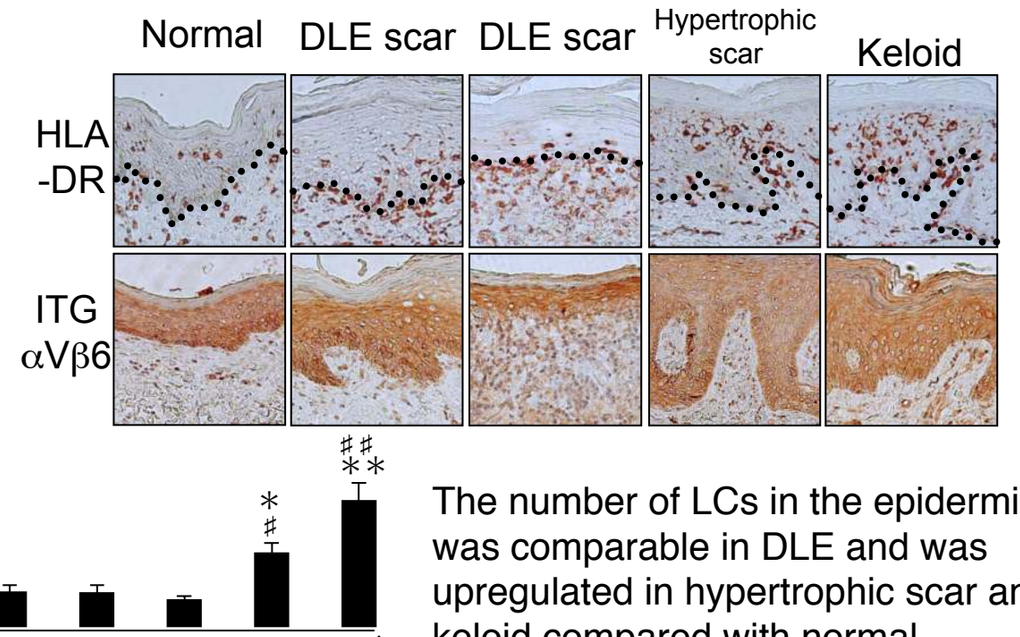


Whereas HLA-DR+ cell (LCs) were present in interfollicular epidermis (IFE) of folliculitis much the same number in normal scalp skin, these cells were dramatically decreased in scar lesion.

Expression patterns of these proteins in hair follicules of LPP was not altered compaired to normal scale skin



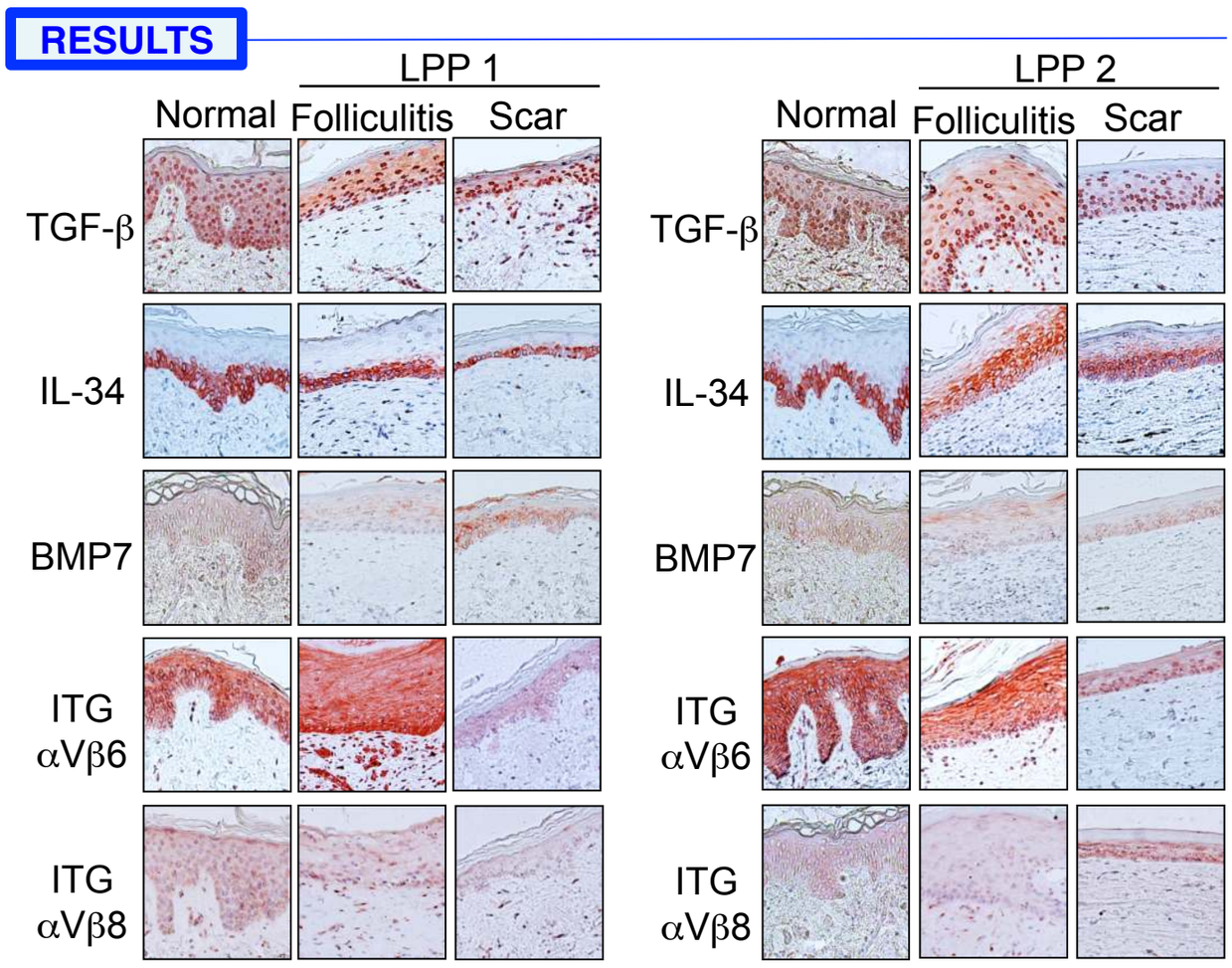
Expression of ITG αvβ6 in the epidermis was comparable in DLE, Hypertrophic scar and Keloid compared with normal epidermis



*P< 0.05 versus Normal scalp skin.
**P< 0.01 versus Normal scalp skin.
#P< 0.05 versus DLE 1 and 2.
##P< 0.01 versus DLE 1 and 2.

The number of LCs in the epidermis was comparable in DLE and was upregulated in hypertrophic scar and keloid compared with normal epidermis.

RESULTS



- Only ITG αvβ6 was apparently downregulated in LPP scar epidermis.
- ITG αvβ6 is crucial for the maintenance of epidermal LCs by facilitating the processing of inactive LAP TGF-β derived from LCs into active TGF-β.
- However, TGF-β was not downregulated in LPP scar epidermis, because this TGF-β antibody recognizes both active and inactive form of TGF-β.
- We presume that active TGF-β is also downregulated.

SUMMARY / DISCUSSION

This is the first study that comprehensively elucidated the distributions and expressions of molecules associated with LC development and maintenance in normal scalp skin and hair follicles.

	TGF-β1	IL-34	BMP7	αvβ6 integrin	αvβ8 integrin
Upper KC IFE	+	-	-	+	-
Basal KC	-	+	+		
IF	+	+	-	++	-
IM	+	+	-	-	+++
Bulge	+	+?	-	+++	-

Blue squares: previously reported (human or mice).
Red squares: newly revealed unknown expression patterns.

These data suggested that **loss of LCs is specific for LPP among scar formation diseases and the downregulation of ITG αvβ6 in scar epidermis may be one of causes of LC loss**.
The expression of ITG αvβ6 in LPP folliculitis epidermis was not downregulated compared with normal hair follicles.
Accordingly, some events occurring from folliculitis stage to scar formation seem to result in the downregulation of ITG αvβ6, followed by LC loss due to lack of active autocrine TGF-β derived from LCs.