Lichen Planopilaris-histologic Criteria & Clues in Vertical Sections

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Abstract

We report on our histological experience in 47 patients with lichen planopilaris/frontal fibrosing alopecia. Besides presenting the spectrum of clinical appearance of the disease we emphasize the importance of vertical histologic sections of biopsies in the clinicopathological work-up of these patients and give precise histologic criteria and clues in different stages of the disease. Immunohistologically, we found a marked reduction of epithelial Ki-67 expression next to the inflammatory process especially evident in advanced stages of disease.

Keywords: Lichen planopilaris; Frontal fibrosing alopecia; Dermatopathology

To the Editor

Lichen planopilaris (LPP) is considered to represent a variant of lichen planus which predominantly affects the scalp. In LPP cutaneous lesions elsewhere on the body except the scalp have been reported in up to 50% of cases [1-4], before, concurrent as well as after the onset of LPP [1]. Mucous membranes, nails as well as hair-bearing and non-hair-bearing areas of the body have been reported to be involved, and this may sometimes be helpful when the diagnosis of LPP is in doubt or difficult from a clinical and/or dermatohistopathological point of view. Clinically, LPP presents as a multifocal, reticulated area of hairloss with periulcerated erythema sometimes accompanied by scales. Individual hairs may be preserved. In time the disease leads to follicular hyperkeratosis, follicular fusion, whitish scarring with loss of follicular orifices and mottled hyperpigmentation. The disease may also present as frontal fibrosing alopecia (FFA) [5-10] and Graham-Little-syndrome when eyebrows, axillae and/or pubic hair are involved as well combined with widespread keratotic papules on the trunk and extremities (Figure 1). While the simultaneous occurrence of LPP and FFA has been reported in up to 14% of patients [6], scalp involvement in the latter tends to be localized and not multifocal, occurs mostly in postmenopausal women and is only rarely associated with lesions of lichen planus [5-10]. However, eyebrow and especially upper limb alopecia with scarring appear to be more common in FFA than previously reported [10]. Thus, lichen planus, LPP and FFA appear to represent a spectrum of disease with clinical overlap and similar histological features. Both, LPP and FFA tend to scarring alopecia which makes the accurate diagnosis an urgent and important matter.

In contrast to lichen planus, LPP and FFA are much more commonly reported in women [1-4,8,11,12]. This is similar to lupus erythematosus and other autoimmune disorders which are much more commonly seen in (young) women. Alternatively or complementary to the above, this may be an underestimate of the true prevalence in men due to the fact that women to some degree more frequently seek medical advice because of hair loss and the simultaneous occurrence of common baldness in men, possibly in part patients with fibrosing alopecia in male pattern distribution. The difference in gender is also reflected by our study of 39 women and 8 men diagnosed to suffer from LPP/FFA at the out-patient clinic/histological laboratory of the Department of Dermatology University of Innsbruck (n=37) or sent as histologic consultation cases (n=10) between 2006 and 2013. The average age of men and women at presentation was also different with 55 (range 27-78) and 42 (range 23-67) years, respectively.

Despite advances in diagnostic procedures using microarray analysis and new insights into possible pathogenetic factors in primary cicatricial alopecia (such as loss of immune protection of stem cells, lipid metabolism dysregulation, impaired self-maintenance of hair
follicle stem cells, increased apoptosis, enhanced autoimmunity by pro-
inflammatory cytokines and environmental/genetic predisposition, 
neurogenic skin inflammation) the precise mechanisms that provoke 
the destructive reaction to the hair follicle, including LPP and FFA, 
remain to be elucidated [13,14]. Thus, at present primary cicatrical 
aloepras are best classified according to their clinical presentation and 
histopathological pattern.

While the clinical presentation of scarring alopecia may sometimes 
be non-specific and misleading, in our experience the vertical 
histological examination of biopsies taken from active lesions allows 
a precise diagnosis in the vast majority of cases (Figure 2). Diagnosis 
follows a stepwise approach from scanning to medium- and high 
power magnifications. On one hand vertical in contrast to horizontal 
technique allows to recognize on scanning magnification dermatologic 
disorders which mainly affect the interfollicular epidermis. These 
occurrences more commonly on non-hairy skin, but just by chance are 
seen in hairy areas, too or exclusively, such as eczema or psoriasis, 
to mention the most classic dermatoses. Furthermore, LPP/FFA 
is a superficial lichenoid disease and as such is best differentiated 
from lupus erythematosus and lichen sclerosus et atrophicus when 
the interfollicular epidermis is available for study. On the other 
hand identifying the level of disease with scanning magnification is 
especially helpful to evaluate deeper located inflammatory diseases 
such as alopecia areata. So, in a vertical section not only a “swarm of 
bees” around follicular papillae is diagnostic of active/full-blown stage 
of alopecia areata, but also a foreign-body granuloma to released hair-
shaft material in circumscribed subcutaneous location which may 
obscure and complicate early peracute lymphocytic periulibritis or 
some rare late stage of alopecia areata.

At intermediate magnification vertical sectioning allows to 
investigate epithelial (spongiosis, acantholysis, ballooning, interface) 
and stromal changes (granulation tissue, granulomas, scarring, mucin, 
fibrosis, sclerosis). The presence of prominent dermal mucin in lupus 
erythematosus and the location of subepidermal reduction of elastic 
fibers in lichen sclerosus et atrophicus are further helpful criteria for 
differential diagnosis.

Finally, at high power magnification the type of inflammatory 
cell involved should be investigated (lymphocytes, macrophages, 
neutrophils, plasma cells, fibrocytes, dendritic cells) in case 
supplemented by special stains for fungi, spirochetes, other 
bacteria and herpes virus to rule out infectious disease processes. 
Direct immunofluorescence and additional laboratory tests (KOH 
examination for fungi, cultures, ANA, TPHA, etc.) may be helpful to 
come to a definite diagnosis [1,2,11,15-17].

Studying vertical sections in LPP/FFA one has to be aware that not all 
criteria listed below are met in one slide. Therefore at times the method 
of horizontal sections may be a valid complement, especially in non-
scarring variants of alopecia [17-20]. They enable the histopathologist 
to investigate more follicles, which may be in different stages of disease, 
in one plane. However, good laboratory handling & practice as well as 
medical experience with these techniques are essential. Therefore, in 
our opinion, when only one biopsy in - clinically scarring - alopecia 
is available and LPP versus lupus erythematosus is the differential 
diagnosis, a vertical work-up of the biopsy should be performed.

Reviewing 47 biopsies of LPP/FFA, we found the following criteria 
and clues in vertical sectioning especially helpful for an accurate 
diagnosis of this disease, many of them confirming findings of previous 
studies [1,2,4,7,8,11,12,15-17,21,22]. Notably, most of our specimens 
represent advanced stages of disease stressing the need to establish the 
correct diagnosis as early as possible.

Early (n=5; all females)

Signs similar to classic lichen planus, such as lichenoid peri-
infundibular lymphocytic inflammation (“hugging type” [22]), reactive 
epidermal and infundibular hyperplasia (Figure 2A). The inflammatory 
infiltrate can sometimes involve the deep reticular dermis and thus 
simulate other more deeply located dermatoses especially lupus 
erythematosus. Further signs are basal cell vacuolization, necrotic 
keratocytes or apoptoses (so-called cytoid or Civatte bodies), wedge-
shaped hypergranulosis and superficial pigment incontinence.

![Figure 2: Histology of LPP in different stages of the disease (H&E).](image)

A. Early LPP. There is infundibular hyperplasia, wedge-shaped 
hypergranulosis and a dense perifollicular (“hugging type”) lichenoid infiltrate 
composed mainly of lymphocytes with little pigment incontinence and mild 
fibrosis.

B. Fully developed LPP. Infundibular hyperplasia and follicular 
plugging accompanied by a dense lichenoid infiltrate of lymphocytes, pigment 
incontinence and necrotic keratocytes/apoptoses (“cytoid or Civatte bodies”).

C. Fully developed LPP. Perifollicular fibrosis and residual inflammation 
that “backs away” from the follicle.

D. Late LPP. Infundibular hyperplasia with wedge-shaped, superficial 
perifollicular fibrosis and alopecia.

E. Late LPP. There is a residual lymphocytic inflammatory infiltrate with 
pigment incontinence, dilated capillaries (indicator of - previous - inflammatory 
process) and fibrosis in the superficial dermis.

F. Late LPP. Infundibular hyperplasia with compact orthohyperkeratosis, 
hypergranulosis and infundibular tufts (compound follicles) accompanied 
by superficial scarring, subepidermal clefts and a lymphocytic inflammatory 
infiltrate.

G. Late LPP. Beneath an unremarkable epidermis there is superficial fibrosis 
with residual lymphocytic inflammation and teleangiectasia.

H. Late LPP. Infundibular tufts (compound follicles) are evident. Note that 
the fusion occurs at the level of the infundibulum. There is mild perifollicular 
fibrosis.
Fully developed (n=30; 23 females, 7 males)

Follicular plugging, presence of a superficial perivascular lymphocytic inflammation with pigment incontinence, clefts between epithelium and dermis. Loss of sebaceous glands and stem cells (in case verified with anti-CK15 [23,24]), initial fibrosis (Figure 2B and 2C).

Late (n=11; 10 females, 1 male)

Thinning of follicular epithelium, peri-infundibular, superficial scar embracing the infundibulum accompanied by perifollicular mucin and wedge-shaped loss of elastic tissue, scant lymphocytic inflammation that “backs away” [16] from the follicle, infundibular tufts/follicular fusion (compound follicles) due to mild scarring around hair follicles and their infundibula in particular (which is in contrast to tufted folliculitis or folliculitis decalvans where a much more destructive and granulomatous scarring reaction accompanied by neutrophils is seen). Marked reduction of hairs and arrector pili muscles. Sometimes a moderate and superficial stromal foreign-body reaction to released hair shaft material (Figures 2D-2H).

‘Burnout’ (n=1; female)

Fibrous tracts in the reticular dermis mirroring the destroyed hair follicle.

In addition, we have immunohistologically investigated 38 biopsies with Mib1 (Ki-67). In contrast to normal skin and early stages of disease (n=5) we found an epithelial reduction of Ki-67 next to the inflammatory process especially in fully developed (n=6 of 22) and late stages of disease (n=9 of 11) (Figures 3A-3D). This is in part likely due to the destruction of hair follicles, especially the bulge region [12], where the follicular stem cells reside, but is similarly also observed in lichen planus without hair follicle involvement (own unpublished observations). In H&E sections of LP, LPP or FFA this is reflected by a reduction of epithelial mitoses (no more than 1 in a 4 mm punch biopsy) especially in late stages of disease. This phenomenon can only be appreciated in a vertical section and is in contrast to other lichenoid dermatoses, eczema and psoriasis (own unpublished data).

In conclusion, histopathology of scarring alopecia is a challenging...
field in dermatopathology and regularly requires clinicopathological correlation. In our opinion, a vertical section is mandatory in the investigation of scarring alopecia, especially to establish the correct diagnosis of LPP / FFA.

References