

CLINICAL SCIENCE

PRIMARY CICATRICIAL ALOPECIAS: A REVIEW OF HISTOPATHOLOGIC FINDINGS IN 38 PATIENTS FROM A CLINICAL UNIVERSITY HOSPITAL IN SAO PAULO, BRAZIL

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BACKGROUND: Scarring alopecias are classified into primary and secondary types according to the initial site of inflammation. In primary scarring alopecias, the hair follicle is the main target of destruction; the term secondary cicatricial alopecia implies that follicular destruction is not the primary pathologic event.

AIMS: To review the histopathologic diagnoses of cases of cicatricial alopecia in order to classify them according to the North American Hair Research Society.

PATIENTS AND METHODS: Patients with biopsy specimens diagnosed as cicatricial alopecia seen from 2000 to 2005 at the Dermatologic Department of Hospital das Clínicas, São Paulo University Medical School had hematoxylin and eosin, Periodic acid-Schiff and Weigert stained slides reevaluated and sub-typed into different primary cicatricial alopecias.

RESULTS: Thirty-eight cases of primary cicatricial alopecias were reclassified as: chronic cutaneous lupus (17), lichen planus pilaris (4), pseudopelade of Brocq (12), folliculitis decalvans (3), dissecting folliculitis (1), and non-specific scarring alopecia (1). In our cases, the methods employed allowed an accurate diagnosis in 12 of 13 cases (92.3%) previously classified as non-specific cicatricial alopecias.

CONCLUSIONS: Even in the late, pauci or non-inflammatory phases, an approach with systematic evaluation of a constellation of criteria in routine hematoxylin and eosin stain, Periodic acid-Schiff and Weigert stain allowed for a more accurate diagnosis of cicatricial alopecias.

KEYWORDS: Cutaneous lupus erythematosus; Lichen planus pilaris; Pseudopelade of Brocq; Folliculitis decalvans; Dissecting folliculitis.

INTRODUCTION

Alopecias can be broadly classified into non-scarring or non-cicatricial and scarring or cicatricial forms. Pathologically, a scar constitutes the end point of reparative fibrosis with permanent destruction of the preexisting tissue.¹

Scarring alopecias are further subdivided into primary

and secondary types. In primary scarring alopecias, the hair follicle is the primary target of destruction, which is microscopically evident as “preferential destruction of follicular epithelium and/or its associated advential dermis with relative sparing of the reticular dermis.”² This group includes the following clinical entities: chronic cutaneous lupus erythematosus (CCLE), lichen planopilaris (LPP), pseudopelade of Brocq (PB), folliculitis decalvans (FD), dissecting cellulitis/folliculitis (DF). If the follicular destruction is secondary to the scarring and occurs outside the follicular unit, e.g., the reticular dermis, epidermis, or sub cutis, it can eventually impinge upon and even eradicate the whole follicle. The term secondary scarring alopecia implies that follicular destruction is not the primary pathologic

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event. Exogenous factors, such as burns, and endogenous infiltrative and inflammatory diseases, such as sarcoidosis, pemphigus vulgaris and reticular dermal sclerosis, can result in secondary alopecias.

In 2001, a group of hair clinicians, pathologists and researchers, under the rubric of the North American Hair Research Society (NAHRS),³ issued a consensus opinion on the classification of primary cicatricial alopecias. The proposed classification subdivides primary scarring alopecias on the basis of the predominant type of inflammatory cell component, an approach that had already published^{1,4,5-7} and was further refined by the workshop. In addition to the lymphocyte- and neutrophil-associated subgroups, a mixed and nonspecific group was differentiated and newly defined (Table 1).

Table1 - Primary Scarring (Permanent) Alopecias (according to the Proposed Working Classification of Primary Cicatricial Alopecia by the North American Hair Research Society; 1999)³

Lymphocyte-associated primary scarring alopecias
Chronic cutaneous lupus erythematosus
Lichen planopilaris
Classic lichen planopilaris
Frontal fibrosing alopecia
Graham Little syndrome
Classic pseudopelade (Brocq)
Central centrifugal cicatricial alopecia
Alopecia mucinosa
Keratosis follicularis spinulosa decalvans
Neutrophil-associated primary scarring alopecias
Folliculitis decalvans
Dissecting cellulitis/folliculitis (<i>perifolliculitis abscedens et suppurativa</i>)
Mixed inflammatory primary scarring alopecias
Folliculitis (acne) keloidalis
Folliculitis (acne) necrotica
Erosive pustular dermatosis
Nonspecific primary scarring alopecias*

* Non-specific scarring primary alopecia is defined as an idiopathic scarring alopecia with inconclusive clinical and histopathologic findings and may include the end stage of a variety of inflammatory primary scarring alopecias, such as lichen planopilaris and folliculitis decalvans.

In the late phase of cicatricial alopecias, a histopathologic diagnosis is more difficult because the main criteria of classification, i.e., the type of inflammatory infiltrate, cannot always be evaluated. In these cases, additional criteria, such as the evaluation of the perifollicular elastic sheet and the fibrosis, can be useful.

The goal of this study was to review clinical and histopathologic findings of 38 patients diagnosed with late,

pauci or non-inflammatory phase of cicatricial alopecias at the Dermatologic Department of the Hospital das Clinicas, São Paulo University Medical School, over a six-year period in order to classify them by sub-types according to NAHRS and evaluate the dermal elastic system and thickness of the epidermal basement membrane, using Weigert and PAS stains, respectively.

PATIENTS AND METHODS

Biopsy specimens obtained using 5-mm punches from patients seen between 2000 and 2005 at the Dermatologic Department of Hospital das Clinicas, São Paulo University Medical School with cicatricial alopecias in the late, pauci or non-inflammatory phase were reevaluated. Essential criteria included histopathologic diagnosis of cicatricial alopecia and accessibility of the patient's clinical records. Slides stained with hematoxylin and eosin, PAS and stain for elastic tissues (Weigert with previous oxidation by peracetic acid) were reviewed, evaluating the presence or absence of criteria listed in the Table 2. This table shows the histopathologic criteria for different causes of cicatricial alopecia.

RESULTS

A total of 38 cases with a histopathologic diagnosis of cicatricial alopecia were included in the study. These cases had been previously diagnosed as follows: eight cases of CCLE, two cases of LPP, 13 cases of PB, two cases of FD, one case of scleroderma and 13 cases of non-specific cicatricial alopecia.

The cases were reclassified into primary or secondary alopecias. The ratio of primary versus secondary alopecias was 37:1. One case was classified as non-specific alopecia. Twelve of 13 cases (92.3%) that were initially classified as non-specific cicatricial alopecias could be specifically reclassified.

Chronic cutaneous lupus erythematosus was diagnosed in 17 cases, representing 43.6% of the total number of scarring alopecias. The female to male ratio was 4.7: 1 (14 females and three males). The age at onset ranged from 29 to 75 years, with a mean age of 46.5 years. Characteristic histopathologic findings of the late phase included hyperkeratosis, horn plugs, atrophy of the Malpighian layer, slight vacuolar degeneration of the basal layer, and fibrous tract replacing the follicles. A thickened basal membrane could be seen in 58.8% of the cases on PAS -stained sections, and an incomplete elastic sheet occurred around the fibrous tracts. in all cases on Weigert- stained sections. Elastolytic foci were also found in areas of fibrosis outside the perifollicular zone (Figure 1d-f).

Table 2 - Histopathologic characteristics of primary scarring alopecias

	@ LPP	* CCLE	# PB	§ FD	## DF
Hyperkeratosis extrafollicular	–	+	–	+/-	+/-
Horn plug	+	+	–	+/-	+/-
Epidermal atrophy	–	+	–	+/-	+/-
Vacuolar degeneration of epidermal basal cells	–	+	–	+/-	+/-
Neutrophilic folliculitis	–	–	–	+	+
Lichenoid Perifolliculitis	+	+	–	–	–
Dermal lymphocytic periecrine infiltrate	–	+	–	–	–
Fibrous tract replacing follicle	+ colloid bodies within	+	+	+	+
Extrafollicular extensive dermo-hipodermal fibrosis	–	+/-	–	+ dermal	+ dermo-hipodermal
Sinus tract	–	–	–	–	+
Preserved perifollicular elastic sheet	–	–	+	–	–
Thickened basement membrane (epidermal or follicular)	–	+	–	–	–

@ Lichen Planus Pilaris (LPP); * Chronic Cutaneous Lupus (CCLE); #Pseudopelade of Brocq (PB); §Folliculitis decalvans (FD); ##Dissecting folliculitis (DF)

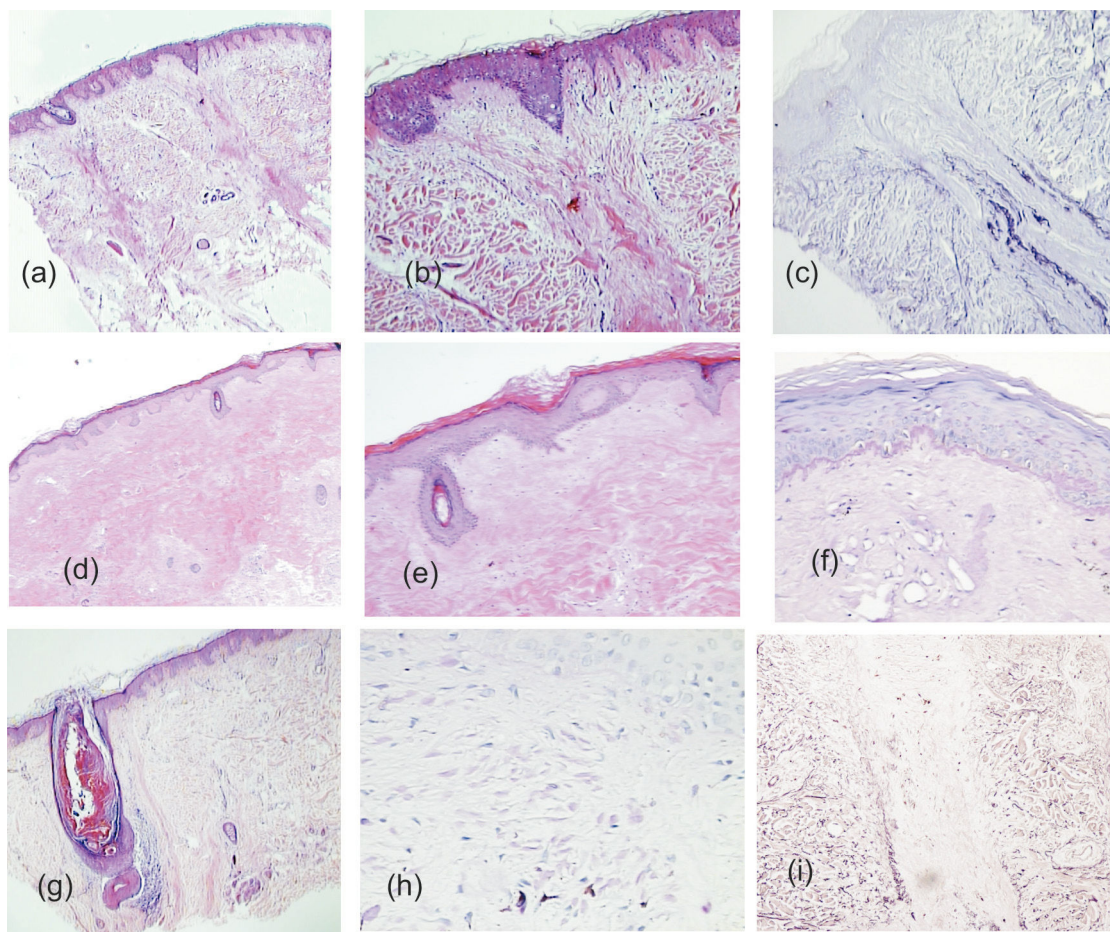


Figure 1 - Cicatricial alopecias of the lymphocytic group in the late phase: Pseudopelade of Brocq : (a) – cicatricial alopecia, HE, OM: x 40 (b) – absence of criteria for lupus erythematosus and for lichen planus, HE, OM: x 100 (c) – perifollicular elastic sheet well preserved Weigert, OM: x 100; – lupus erythematosus: (d) – cicatricial alopecia with dermal collagen sclerosis, HE, OM: x 40 (e) – hyperkeratosis with horn plugs and epidermal atrophy, HE, OM: x 100 (f) – even in this late, non-inflammatory phase, thickening of the basement membrane, PAS, OM: x 200; lichen planus: (g) – besides fibrous tracts, a lichenoid perifolliculitis and no other epidermal or dermal alterations, HE, OM: x 40; (h) – numerous colloid bodies within the fibrous tract that succeeded the lichenoid perifolliculitis, PAS, OM: x 400; (i) – perifollicular elastic sheet partially destroyed, Weigert, OM: x 100. Original magnification: OM

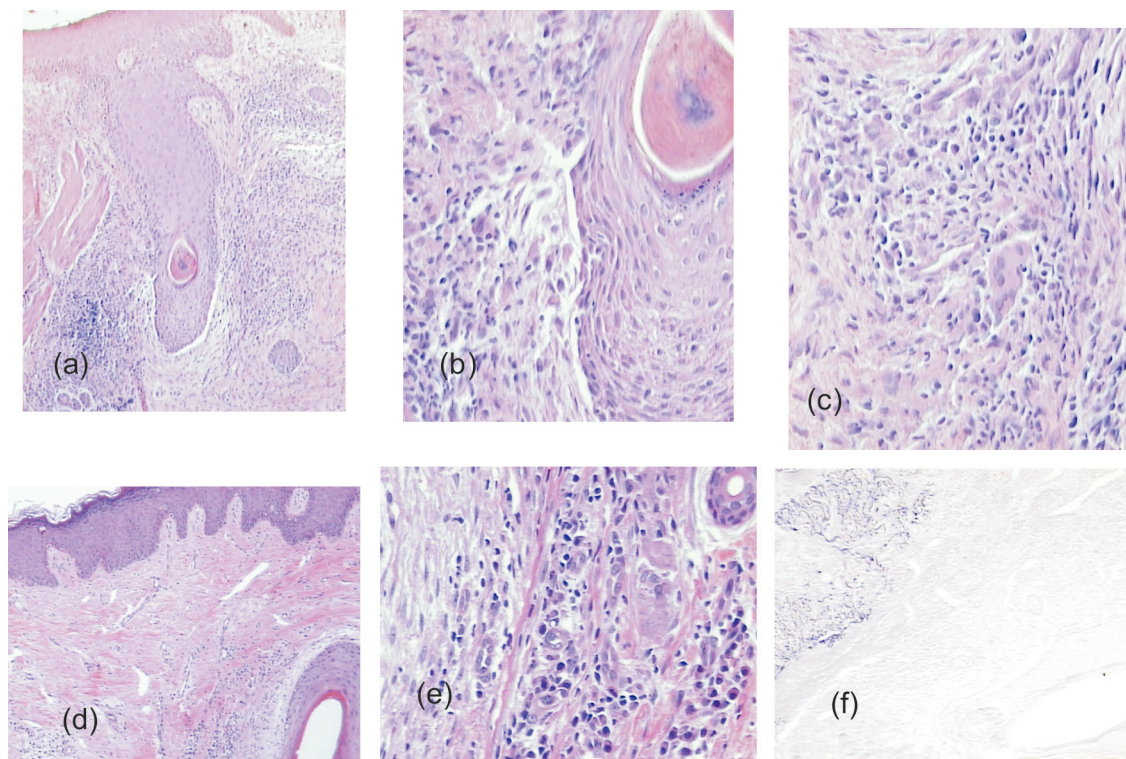


Figure 2 - Cicatricial alopecias of the neutrophic group in the late phase. Folliculitis decalvans; (a) – neutrophilic folliculitis with intense perifolliculitis, HE OM: x 100; (b) – degenerated neutrophils inside the infundibulum and mixed perifollicular inflammatory infiltrate, HE OM: x 400; (c) – some perifollicular multinucleated histiocytes and plasma cells; Dissecting folliculitis, HE OM: x 400; (d) – perifolliculitis and extensive and deeper perifollicular cicatricial fibrosis than in folliculitis decalvans, HE OM: x 40; (e) – perifollicular mixed inflammatory infiltrate, HE OM: x 400; (f) – Extensive elastolysis near and outside the follicle, Weigert OM: x 100. Original magnification: OM

Lichen planus pilaris: This category of cicatricial alopecia represented 10.2% of the total number of biopsies, totaling four cases. The genders were equally represented. The ages at onset were 21, 25, 28 and 48 years. In one case, there was a lichenoid infiltrate around the infundibuloisthmic segment of one follicle in addition to fibrous tracts replacing follicles. In all the others, absence of inflammation, absence of sebaceous epithelium, and atrophy of the bulge area occurred, resulting in hourglass figures. Fibrous tracts replacing the follicle, with or without the presence of colloid bodies, were also observed. The basal membrane was not thickened on PAS-stained sections, and the perifollicular elastic sheet was partially destroyed, as observed with the Weigert stain (Figure 1g-i).

Pseudopelade of Brocq was diagnosed in 12 cases, representing 30.8% of the total number of biopsies. The female to male ratio was 10:2. Age of onset ranged from 23 to 69 years, with a mean age of 54.4 years. Characteristic histopathologic findings were the absence of criteria seen in CCLE and LPP and preservation of the elastic sheet around the follicles (Figure 1a-c).

Folliculitis decalvans was diagnosed in three cases,

representing 7.7% of the total number of biopsies. The female to male ratio was 1:2. The age of onset was 17, 29 and 36 years.

The histopathologic hallmark was the presence of superficial suppurative folliculitis and fibrosis replacing the follicle and the perifollicular area, with elastolysis visible with the Weigert stain (Figure 2a-c).

Dissecting folliculitis: This category of cicatricial alopecia represented 2.6% of the total number of cicatrizing biopsies, totaling one case in a female 19 year-old patient. In this case, the inflammation was slight, and there was an extensive and deeper dermal fibrosis extending to the hypodermis, with elastolysis (Figure 2d-f).

Idiopathic alopecias: One case of non-specific alopecia was diagnosed due to the destruction of the follicles being the only histopathologic finding. No additional criteria pointed to a more specific diagnosis.

DISCUSSION

Considering the group of primary lymphocytic cicatricial alopecias in the inflammatory phase, a differential diagnostic

consideration for CCLE is LPP. However, the interface alteration is primarily vacuolar rather than lichenoid in CCLE. The superficial and deep perivascular and periecrine patterns of inflammation further aid in differentiating CCLE from LPP. In the late pauci or non-inflammatory phase, as observed in our cases of CCLE, interfollicular epidermis alterations were evident (hyperkeratosis and atrophy), in an area usually spared in LPP cases. Commonly, in the dermis in LPP, the only disturbance was the fibrous tract replacing the follicle, while in CCLE, there was frequent extra follicular fibrosis and elastolysis; even in this late phase, the basement membrane was thickened in 58.8% of cases. CCLE is differentiated from PB by the presence of predominately vacuolar interface changes at the level of follicular infundibulum in the former and lack of interface alterations in the latter.¹ In our cases, the perifollicular elastic sheet was preserved in PB cases, while it was partially destroyed in LPP and CCLE, confirming the previous findings of Pinkus et al.⁷

Some authors believe that PB is not a distinct clinical-pathologic entity but a variant of certain primary cicatricial alopecias or, alternatively, a form of end-stage alopecia caused by other scarring alopecias, such as CCLE, LPP and FD.⁷⁻⁹

According to Stephen (1993)¹ and other authors, with whom we agree, PB does indeed have sufficient distinct pathologic features to merit a separate classification.^{5,10-12} Klaus and Wilma (2006)¹ believe that the close clinicopathologic correlation in the histologic absence of significant follicular plugging, as well as the use of elastic fiber stain in addition to evaluation of conventional HE-stained sections, should enable the differentiation of classic PB from late stage lesions of LPP and CCLE in most cases and further justify the classification of the condition as an entity *sui generis*.

In relation to the neutrophilic cicatricial alopecias, it is remarkable that even in the late phases of this disorder, it seems that the inflammatory process persists in our cases, and a neutrophilic folliculitis can frequently be seen, which helps make the correct histopathologic diagnosis. We could also see that the fibrotic process that is secondary to this neutrophilic folliculitis was more intense and proceeded by a granulation tissue, as is expected after a suppurative process. This fibrosis is deeper in DF than in FD. Sinus tracts are the histopathologic hallmark of dissecting cellulites and are not seen in either folliculitis decalvans or acne keloidalis and were not observed in our late phase cases. Bacterial or fungal folliculitis (kerion and favus) may have to be excluded in the group of neutrophilic cicatricial alopecias, with the use of special stains. Acne keloidalis cases were not seen in our series because they are histopathologically reported in our laboratory as a superficial and deep suppurative and giant cellular granulomatous folliculitis with extensive fibrosis compatible with acne keloidalis, not as a cicatricial alopecia. Besides, the clinical aspect of this disorder is so typical that histopathologic exam is seldom required.

CONCLUSION

A scalp biopsy is mandatory in all cases of cicatricial alopecias, representing the clinically inflammatory area. If there is no evidence of inflammation, a biopsy at the border of the cicatricial zone should be performed. Multiple biopsies are sometimes required to achieve a definitive diagnosis. A precise diagnosis is possible, even in the late, pauci or non-inflammatory phase of cicatricial alopecias if a systematic evaluation of a constellation of criteria is employed, using routine HE, PAS and a stain for elastic tissue. In our cases, this method allowed a precise diagnosis in 97.4% of cases, even in those initially considered non-specific cicatricial alopecia.

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