Update on Cicatricial Alopecia

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Cicatricial alopecia is an enigmatic group of hair disorders linked by the potential permanent loss of scalp hair follicles in involved areas. Progress in our understanding and treatment of these disorders has been stymied by the lack of clear diagnostic criteria for the current terms used to describe the various hair loss entities. Since all of these conditions evolve as the hair is destroyed or replaced, diagnosis is further made difficult by a lack of clinical and pathologic "snapshots" over the evolution of each disorder. Without some acceptance of general clinical and histological presentations in the early, mid and late stage of these disorders, one cannot begin to explore ways to make the diagnosis at a very early stage before significant follicular destraction has occurred (making the clinical diagnosis obvious) and when the damage is potentially repairable or progression preventable. ***Key words: Cicatrical alopecia. JID Symposium Proceedings 8:18–19, 2003***

A workshop on cicatricial alopecia was held February 10–11, 2001 at Duke University Medical Center. The purpose of this North American Hair Research Society sponsored conference was to provide a forum to discuss the problems in clinical and pathologic correlation, current terminology and potential areas for fruitful research on cicatricial alopecia. One of the most important outcomes of this conference was the agreement on a preliminary system for classifying the various entities of cicatricial alopecia. (**Table I**) Since a scalp biopsy is critical to establishing both the existence of obliteration of the follicle and the diagnostic category of the condition, pathologic criteria was the primary factor in the proposed classification. This pathologic classification requires a scalp biopsy from a clinically active area of the scalp: to standardize the interpretation and to facilitate assessment of potential pathologic parameters as diagnostic criteria, horizontal sections of at least one 4-mm biopsy is recommended. There are clearly cases of cicatricial alopecia that do not fit with the current pathologic descriptions and thus are identified as "Nonspecific" at this time. Also, the final common stage of cicatricial alopecia, total obliteration of the follicle with a lack of inflammatory infiltrate, is shared by most, if not all, subtypes of cicatricial alopecia, making a specific diagnosis impossible at that point; hence the term "Nonspecific" cicatricial alopecia is also used here.

Fortunately, mouse studies have given us some insight into the pathogenesis of primary follicular scarring processes. For example, when cells in the stem cell region of the hair follicle are destroyed, the follicles themselves are destroyed (Cotsarelis G, personal observation). This suggests that ablation of this cell population will lead to the cicatricial process. As in graft-vs.-host disease, in which the earliest inflammatory infiltrate attacks stem cell rich areas in the skin and gastrointestinal tract (Sale, 1996 and Sale *et al*, 1994), the inflammation in early cicatricial alopecias also involves the stem cell rich bulge area. Likewise, inflammation in alopecia areata—the prototypical noncicatricial

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Table I. Proposed Working Classification of Primary Cicatricial Alopecia[‡]

Lymphocytic
Chronic cutaneous lupus erythematosus[12]
Lichen planopilaris (LPP)[5]
Classic LPP
Frontal fibrosing alopecia[4]
Graham-Little Syndrome[12]
Classic pseudopelade (Brocq)[*] [1,6]
Central centrifugal cicatricial alopecia[**] [10]
Alopecia mucinosa
Keratosis follicularis spinulosa decalvans[7]
Neutrophilic
Folliculitis decalvans[12]
Dissecting cellulitis/folliculitis[12] *(perifolliculitis abscedens et suffodiens)*
Mixed
Folliculitis (acne) keloidalis[7]
Folliculitis (acne) necrotica[12]
Erosive pustular dermatosis[2]
Nonspecific[+]

[‡](Olsen *et al*, 2003).

[*]Clinically discrete, smooth, flesh-tone or white areas of alopecia without follicular hyperkeratosis or perifollicular inflammation.

[**]Cicatricial alopecia starting in the central scalp and progressing centrifugally. This entity has previously been referred to by other terms (ie follicular degeneration syndrome, pseudopelade in African-Americans, central ellipitical pseudopelade in Caucasians) but we are suggesting this more descriptive term which embraces all previous entities.

[+]Nonspecific cicatricial alopecia is defined as an idiopathic scarring alopecia with inconclusive clinical and histopathological findings. This category may include the end stage of a variety of inflammatory cicatricial alopecias such as lichen planopilaris and folliculitis decalvans.

alopecia—typically targets the bulb area of the follicle and spares the bulge, thus suggesting that the integrity of the upper follicle, including the stem-cell rich bulge area, is critical for preservation of the follicle (Cotsarelis and Millar, 2001). This suggests that ablation of this cell population will lead to the cicatricial process.

In other studies, the sebaceous gland pathology is implicated in the pathogenesis of cicatricial alopecia. Early studies showed that the sebaceous gland is needed for normal hair shaft/internal root sheath dissociation (Williams and Stenn, 1994). In the asebia mouse, which lacks one gene responsible for normal sebum production, the hair follicle is destroyed because the shaft cannot get out of the follicle properly; this mouse develops cicatricial alopecia (Zheng *et al*, 1999). Moreover, cicatricial alopecia develops in other mouse and dog models with defective sebaceous glands (Sundberg, 1994). The mouse observations implicating the upper portion of the follicle, including sebaceous glands and bulge cells, in cicatricial alopecia are supported by the histopathology of the human primary scarring alopecias, which show pathology in these areas in the earliest stages. Thus, there is direct evidence in the mouse and indirect evidence in the human that compromising the integrity of the sebaceous gland and/or bulge is important for the development of the scarring process in the primary cicatricial alopecias. In particular, the sebaceous gland as the potential primary diseased structure must be given greater attention in our diagnostic and therapeutic approaches to these very refractory conditions.

In summary, the Cicatricial Alopecia Workshop produced a working classification for cicatricial alopecia based on the type of inflammatory infiltrate in a scalp biopsy of active disease. Clinical and pathologic features need to be evaluated prospectively and correlation obtained. Bench research in any one of several different areas may provide insight into the cascade of events ending either in the permanent destruction of the follicle seen in the cicatricial alopecias or the interruption or delay of the hair cycle that occurs with the more common noncicatricial alopecias.

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