Pattern hair loss: Assessment of microinflammation in miniaturized and terminal hair follicles through horizontal histologic sections

To the Editor: Pattern hair loss (PHL) evolves from progressive hair follicle miniaturization and the premature termination of the hair anagen phase. Its etiopathogenesis goes beyond the local activity of dihydrotestosterone, especially in women, in which the evidence of an androgen-dependent entity relies on scarce data.[1]

The microinflammation process, especially in the upper segment of the hair follicle, has been described as a possible element in the pathogenesis of PHL.[2,3] Therefore, we read with great interest the publication by Valdebran et al[4] reporting the evaluation of 37 scalp samples from patients with PHL and 45 control individuals, where they did not find a difference in inflammation and fibrosis between the 2 groups. We praise the authors for adding a new perspective on this issue. However, we would like to bring some other elements to this relevant discussion.

First, the authors mentioned the age difference between the groups. Moreover, an important imbalance existed regarding sex: 16% men versus 71% men in the alopecia and control groups, respectively.[4] Although male PHL and female PHL are histologically similar, probably the main etiologic element differs because of the less preponderant participation of androgens in female PHL. The consequences of age imbalance regarding fibrosis and inflammation are less predictable. Thus, we believe that a sex-matched or, even better, a sex-stratified analysis is fundamental for substantiating these conclusions.

Furthermore, the association of microinflammation and follicle miniaturization was not assessed, probably because of the lack of horizontal sections in all of the samples. In a previous report, we evaluated microinflammation and apoptosis in the histologic samples of 17 women with PHL and 5 control women through horizontal sections. Inflammation was also not different between the follicles from patients with PHL and control women ($P = .3$). Nevertheless, it was more intense in the miniaturized follicles compared with the terminal ones ($P = .02$). Additionally, microinflammation was correlated with the follicle apoptosis index (rho: 0.68).[5]

Recently, we evaluated the pattern of microinflammation in skin biopsy specimens from the frontal and occipital areas of 10 patients with female PHL. We did not evaluate healthy control individuals, but assuming that microinflammation has an important role in PHL, we would expect more intense infiltration in the affected region. No difference was found in $CD4^+$ or $CD8^+$ lymphocyte infiltration between the areas. Interestingly, $CD4^+$ lymphocyte infiltration was also more intense around miniaturized follicles compared with terminal ones in the frontal samples (Fig 1 and Table I).

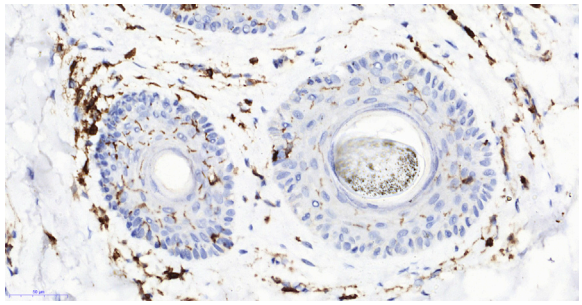

Fig 1. Female pattern hair loss. Horizontal sections (isthmus) from frontal scalp immunomarked for $CD4^+$ showing lymphocyte infiltration into and around hair follicles. There is a clear predominance of microinflammation in the miniaturized follicle.

Despite the fact that a long time has passed since the first description of microinflammation as a possible etiologic element in PHL, the data that support this hypothesis are still limited. Further studies with age- and sex-matched control individuals, preferably evaluated with horizontal sections comparing terminal and miniaturized follicles, are essential.

Maira Renata Merlotto, MD, Paulo Müller Ramos, MD, PhD, and Hélio Amante Miot, MD, PhD

From the Dermatology Department, São Paulo State University - UNESP, Brazil.

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Correspondence to: Paulo Müller Ramos, MD, PhD, Av; Prof. Mário Rubens Guimarães Montenegro, sn, UNESP – São Paulo State University – Campus Botucatu, 18618687 – Botucatu – SP, Brazil

E-mail: dermato.paulo@gmail.com

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Table I. Median (IQR) scores of lymphocyte infiltration ($CD4^+$ or $CD8^+$) in hair follicles (frontal and occipital) from 10 patients with female pattern hair loss

	Frontal			Occipital			
Lymphocyte infiltration	**Terminal**	**Miniaturized**	***P* value***	**Terminal**	**Miniaturized**	***P* value***	***P* value†**
$CD4^+$	2.2 (1.7-2.5)	2.6 (2.3-3.3)	.043	2.8 (2.5-3.0)	2.6 (1.8-2.8)	.173	.840
$CD8^+$	0.6 (0.5-1.0)	0.6 (0.5-0.8)	.796	0.9 (0.5-1.2)	0.8 (0.5-1.3)	.804	.300

IQR, Interquartile range.
*Terminal versus miniaturized, generalized mixed model (post hoc Šidák correction).
†Frontal versus occipital, generalized mixed model (post hoc Šidák correction).

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