

Table 1 Cases of Hailey-Hailey Disease Treated with Photodynamic Therapy.

Reference	Age	Sex	Duration of Disease	Site Affected	Prior Treatments	Disease-Free Interval After PDT
Ruiz-Rodríguez et al., 2002 ⁷	45	♀	4 y	Axillas, groin	Topical and systemic corticosteroids, topical and systemic antibiotics, dermabrasion	Complete response, 19 mo
	51	♀	24 y	Groin, vulva	Topical and systemic corticosteroids, topical and systemic antibiotics	Complete response, 25 mo
Fernández Guarino et al., 2008 ⁸	45	♀	3 y	Axillas	Topical corticosteroids and vitamin D analogs	No response
	40	♂	2 y	Perianal	Corticosteroids, vitamin D analogs, topical immunomodulator	Partial response, 6 mo
	28	♀	8 mo	Vulva	Corticosteroids, vitamin D analogs, topical immunomodulator	Partial response
Lobato-Berezo, 2015	56	♂	30 y	Axillas, neck	Copper and zinc sulfate, topical and systemic corticosteroids, vitamin D analogs, topical tacrolimus, acitretin	Complete response, 6 mo

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Mast Cells and Scarring Alopecia: Is There a Clear Pathophysiological Relationship?☆



Mastocitos y alopecia cicatricial: ¿hay una clara relación fisiopatológica?

To the Editor:

Frontal fibrosing alopecia is a subtype of scarring (or cicatricial) alopecia that is histologically characterized by the

presence of a predominant lymphocytic infiltrate.¹ The presence of unexpectedly large numbers of mast cells is a rare finding that has been reported only infrequently in the literature. A recent case described in our unit prompted us to reflect on the pathophysiological role of mast cells in frontal fibrosing alopecia and other varieties of the disorder.

A 48-year-old woman who experienced early menopause at age 42 years consulted for asymptomatic progressive alopecia. She had not undergone any previous treatment. Physical examination revealed recession of the frontal and temporal hairline (Fig. 1, A) with no desquamation, erythema, or perilesional hyperkeratosis (Fig. 1, B). There was no variation in the length or thickness of the hair shaft, nor was there any decrease in hair follicle density in the healthy area. The skin had a parchment-like appearance, and some intact hair follicles were present in the hair-loss band. Alopecia was noted in the distal third of the

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Figure 1 A, Bilateral and symmetric recession of the frontal and temporal hairline with thinning and partial loss of eyebrow hair, especially in the distal third. B, Absence of associated erythema or hyperkeratosis.

eyebrows. Clinical suspicion prompted a pathologic examination. Hematoxylin-eosin staining revealed the presence of follicular fibrosis without epidermal involvement (Fig. 2, A). Higher magnification revealed the absence of lymphocytic infiltrate and an increase in the number of mast cells (Fig. 2, B and C). Tryptase staining revealed the presence of mast cells—up to 36 per visual field in some sections—that

had even infiltrated the hair follicles (Fig. 3, A). With toluidine blue staining, as many as 12 to 13 mast cells were visible per field (Fig. 3, B). The difference in the number of mast cells per field is explained by the greater sensitivity and specificity of tryptase compared to the metachromatic staining of toluidine blue. The patient was screened for indolent mastocytosis. Tryptase levels were normal

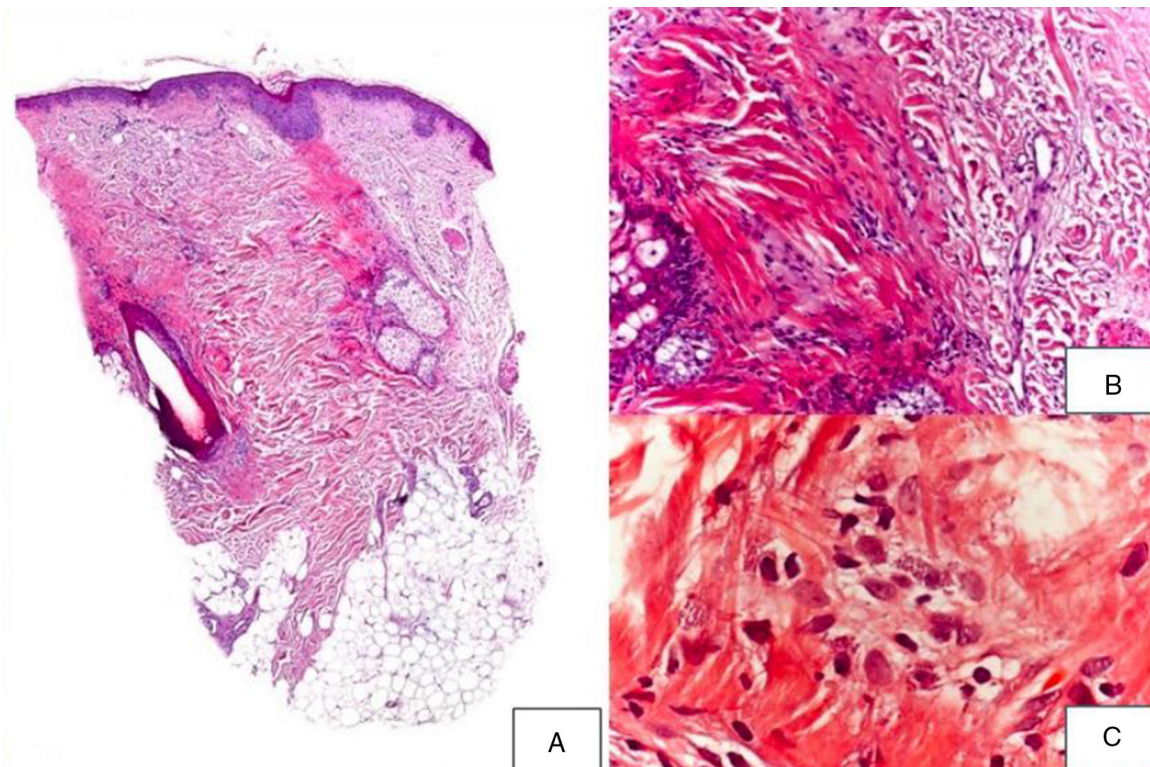


Figure 2 A, Presence of fibrosis replacing and destroying the follicle, and absence of epidermal involvement (hematoxylin-eosin, original magnification $\times 10$). B, Difference between follicular fibrosis and normal, interwoven collagen fibers (hematoxylin-eosin, original magnification $\times 40$). C, Absence of lymphocytic infiltrate. Presence of elevated numbers of mast cells (hematoxylin-eosin, original magnification $\times 200$).

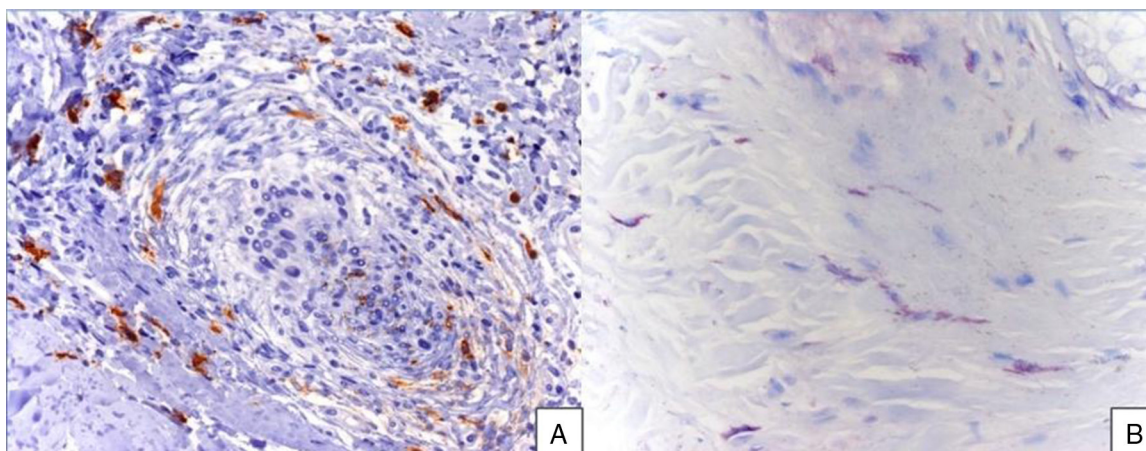


Figure 3 A, Infiltration of mast cells into the follicle (tryptase, original magnification $\times 100$). B, Elevated number of mast cells observed in the section (toluidine blue, original magnification $\times 100$).

(< 13.5 $\mu\text{g/L}$), but 24-hour urinary N-methylhistamine was 161 $\mu\text{g/L}$ (up to 61.2 $\mu\text{g/L}$ being considered normal). In view of these findings, we ordered long-bone radiography, which revealed no alterations, and bone marrow aspiration, which revealed that mast cells accounted for less than 5% of all cells.

Cicatricial alopecia refers to a group of disorders characterized by irreversible hair loss caused by various processes that culminate in the replacement of hair follicles with fibrous tissue. In primary cicatricial alopecias, the hair follicle is the main target of the inflammatory process.² In 2001, the North American Hair Research Society presented a histopathologic classification of primary cicatricial alopecias according to predominant cell type and clinical characteristics; frontal fibrosing alopecia was among the forms included in the classification.³ The differential histologic finding of an elevated number of mast cells in our patient prompted us to review the literature in order to explain the pathophysiological role of these cells. We found only 1 case with characteristics similar to those of our patient.⁴ In that case, the preponderance of mast cells was the key to a diagnosis of indolent systemic mastocytosis—an entity that was ruled out in our patient.

Mast cells are found in the skin around blood vessels, smooth muscle cells, hair follicles, and nerve endings.⁵ They can be identified with hematoxylin-eosin staining, special stains such as Giemsa and toluidine blue, and immunohistochemical techniques (c-kit).⁶

Mast cells release mediators (histamine, proteases, growth factors, prostaglandins, and cytokines) that are involved in various processes such as scar formation and tissue remodeling, thereby participating in normal wound healing, and they also participate in the pathogenesis of fibrotic diseases such as scleroderma.^{7,8} They also act as fibroblast growth factor receptors and vascular endothelial growth factor receptors, thereby promoting angiogenesis,⁸ a process involved in hair follicle development. The role of mast cells in the pathophysiology of scarring alopecia, although still undetermined, could be similar.

What happens in other forms of alopecia? On the basis of histologic evidence of perifollicular fibrosis and an increase

in mast cells—which can cause increased elastic fiber synthesis—it has been suggested that there could be a relationship between mast cells and male-pattern androgenetic alopecia.⁹ Mast cells have also been implicated in the pathogenesis of alopecia areata.¹⁰

The reason for elevated histamine metabolite excretion, despite normal tryptase levels and the absence of myeloproliferative disorder, has not been clarified. The amount of methylhistamine produced depends not only on the synthesis and release of histamine but also on the contribution of exogenous histamine from food and beverages and the activity of N-methyltransferase and diamine oxidase enzymes, which decompose histamine into urinary metabolites and can be influenced by alcohol, drugs, and genetic polymorphisms.¹¹ This could explain the high levels of urinary methylhistamine in our patient despite the absence of indolent systemic mastocytosis.

In conclusion, in light of the case described in this letter, we believe that the pathophysiological role of mast cells in the various forms of scarring and nonscarring alopecia needs to be clarified, as it could lead to the identification of new therapeutic targets. Moreover, although we were unable to demonstrate the presence of associated indolent mastocytosis in our patient, we believe that this diagnosis should be considered when the pathologic features described above are encountered.

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Dermoscopic Features of Lichen Planus Pigmentosus-Inversus[☆]



Dermatoscopia del liquen plano pigmentado inverso

To the editor:

Lichen planus pigmentosus-inversus (LPPI) is a clinical variant of lichen planus, first described by Pock in 2001. To date, 44 cases have been published in the medical literature (Table 1). It usually presents as hyperpigmented macules or plaques located in the flexion creases. Dermoscopy is a useful tool for guiding diagnosis in clinically nonspecific pigmented lesions.

The patient was a 32-year-old man, with skin phototype III, and no relevant personal or family history, who attended the clinic because of the spontaneous appearance 3 months earlier of 3 asymptomatic skin lesions on the right axilla. These lesions had been progressively spreading since onset. The patient was not taking any medications and had not been overly exposed to sunlight.

On skin examination, 3 well-defined violaceous-brown plaques were observed (Fig. 1a). Dermoscopy revealed a homogeneous white-bluish pattern with no pigmented reticulum. In several regions, blue-gray and brown-gray globules and dots were observed along with red lines, predominantly at the periphery (Fig. 1b). The lesions were biopsied, and the histologic findings were indicative of lichen planus (Fig. 2).

Serology testing for HIV and HCV was negative. Given the absence of symptoms, it was decided not to prescribe treatment. After 12 months of observation, the lesions remained unchanged and no new lesions appeared.

LPPI usually affects patients with a low phototype of Caucasian or Asian origin, with no predilection for sex. The age of presentation is usually between 25 and 84 years (mean age, 58 years). The etiology of these lesions is unknown. There is no known causal relationship with medications, exposure to sunlight, HCV infection, or malignant tumors. Pathogenesis appears to be related to the T-lymphocyte-mediated cytotoxicity affecting basal keratinocytes.¹

This clinical variant is characterized by the insidious appearance of macules or hyperpigmented plaques of a brown-violet color. The lesions are asymptomatic or mildly itchy and have variable size, well-defined borders, and a smooth surface. Wickham striae may be present. The lesions are located in intertriginous and flexion regions, mainly in the axilla (involved in 90% of the cases), groin, inframammary folds, and popliteal region. Less frequently, they can also appear on the neck and posterior auricular furrow. The condition usually involves several folds, and it is rare for it to affect a single area, as was the case in our patient. Lesions do not appear on mucosa, the scalp, skin appendages, or the palms or soles. In 10% of cases, lesions consistent with lichen planus or lichen planus pigmentosus appear simultaneously in areas outside the flexion folds, and can affect up to 10% of the body surface area.^{1,2}

Histologically, these lesions are characterized by a similar pattern to lichen planus and regression may be observed: orthokeratotic epidermal atrophy (although hyperkeratosis and minimal hypergranulosis can also appear), hydropic degeneration of the basal layer, lichenoid inflammatory infiltrate composed of lymphocytes and histiocytes in the

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