

Primary cicatricial alopecia associated with systemic indolent mastocytosis



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INTRODUCTION

We present a case of a 63-year-old woman diagnosed with indolent cutaneous and systemic mastocytosis (SM) who presented with hair loss due to primary cicatricial alopecia (PCA).

CASE REPORT

A 63-year-old woman with known telangiectasia macularis eruptiva perstans (TMEP) presented to our hair loss clinic with an 8-year history of alopecia of the eyebrows, eyelashes, and vertex aspect of the scalp with associated pruritus, tenderness, and burning. Clinical examination showed perifollicular erythema and scale visible throughout the vertex and bitemporal aspects of the scalp (Fig 1). She had received a diagnosis of biopsy-proven PCA 8 years prior by an outside provider and was treated with daily fluocinonide solution for 6 months, but she discontinued this therapy given the risk of skin atrophy. She was not receiving any treatment for her PCA at the time of presentation to our clinic.

Given the patient's persistent scalp symptoms and a recent diagnosis of TMEP, we ordered Giemsa and immunohistochemical stains on the original scalp biopsy specimen to assess for mast cell infiltration. The biopsy specimen showed prominent activity of spindled mast cells and mast cell degranulation in areas of scarring hair loss (Fig 2). The patient was offered topical tacrolimus and oral sodium cromolyn for treatment of her scarring alopecia. She opted for treatment with topical tacrolimus and noted complete resolution of scalp symptoms and scalp erythema after 3 months of daily use.

A review of the patient's medical chart showed a diagnosis of TMEP 13 months before her

Abbreviations used:

PCA: primary cicatricial alopecia
SM: systemic mastocytosis
TMEP: telangiectasia macularis eruptiva perstans

presentation to our hair loss clinic. At that time, the patient presented to a general dermatology clinic with a 3-year history of erythematous and pruritic maculopapules involving the anterolateral aspects of the thighs and forearms. The Darier sign was negative (Fig 3). A skin biopsy specimen of the lower extremity showed increased numbers of spindled mast cells in a perivascular and interstitial distribution consistent with TMEP. Laboratory values showed total serum tryptase level of 121 ng/mL, suggestive of underlying systemic mastocytosis.

The patient was then referred to a mastocytosis specialty clinic and reported a 1-year history of severe nausea, epigastric pain, vomiting, and diarrhea. Duodenal biopsy showed abnormal mast cell aggregation and infiltration at the villi. The patient was treated with 10 mg cetirizine and noted significant improvement in gastrointestinal symptoms. Additionally, she underwent a bone marrow biopsy, which showed CD117⁺ and CD25⁺ mast cells and the presence of mast cell tryptase. Notably, the mast cells were negative for CD2. Approximately 5% to 10% of the cellularity was composed of mast cells, including spindled forms, occurring singularly and in clusters. The patient's genomic test results were positive for *c-kit* mutation. These findings confirmed a diagnosis of systemic mastocytosis.

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Fig 1. Primary cicatricial alopecia involving the right frontal and temporal aspects of the scalp.

DISCUSSION

Mastocytosis refers to a class of disorders characterized by abnormal mast cell proliferation and infiltration into 1 or more organs, often with cutaneous involvement. According to the 2016 World Health Organization classifications, mastocytosis can be categorized into subvariants of cutaneous mastocytosis with no systemic involvement, SM, or localized mastocytotic tumors.¹ We present a case of indolent SM with cutaneous involvement in a patient with known scarring alopecia affecting the eyelashes, eyebrows, and scalp.

This patient presented to a general dermatology clinic with TMEP, a rare telangiectatic variant of urticaria pigmentosa, with perivascular distribution of mast cells confirmed by histology.² Because urticaria pigmentosa occurs in more than 90% of patients with cutaneous mastocytosis, the patient was initially diagnosed with cutaneous mastocytosis. However, given gastrointestinal concerns and an elevated tryptase level, the patient underwent duodenal and bone marrow biopsies; the latter confirmed indolent

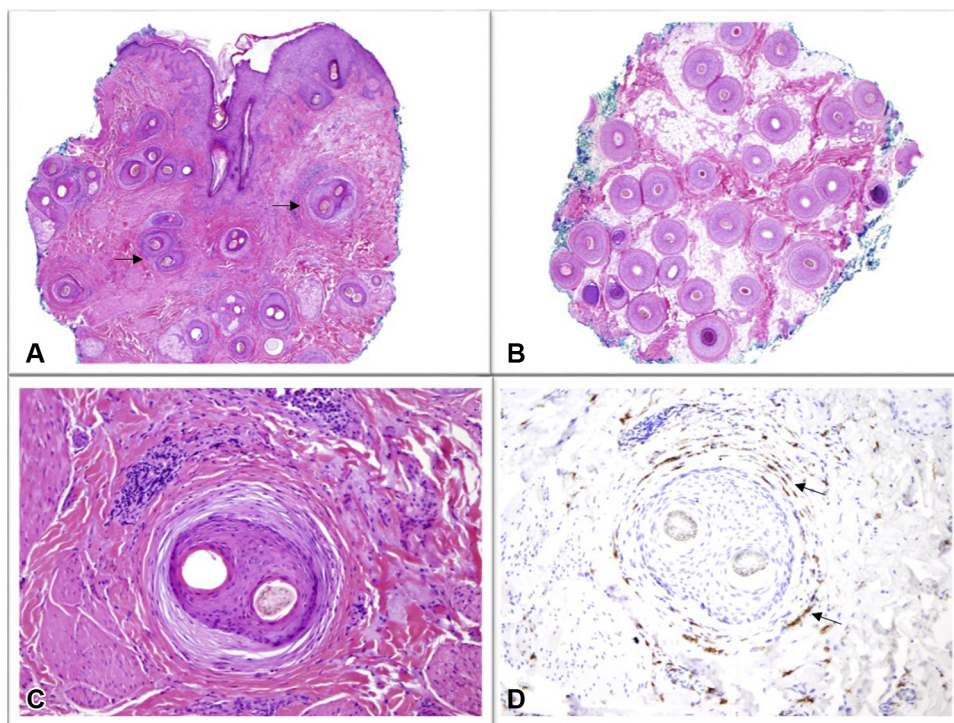


Fig 2. Scalp punch biopsy showing early scarring alopecia with features of primary cicatricial alopecia. **A**, Superficial sections of the scalp show perifollicular fibrosis and inflammation (arrows) at the level of the isthmus/infundibulum without interface changes at the dermoepidermal junction. (Hematoxylin-eosin; original magnification: $\times 4$.) **B**, Transverse sectioning shows no significant inflammation at the deep aspect of the biopsy. (Hematoxylin-eosin; original magnification: $\times 4$.) **C**, A compound follicle with perifollicular fibrosis and inflammation shown at higher power. (Hematoxylin-eosin; original magnification: $\times 20$.) **D**, Immunohistochemical staining for CD117 highlights mast cells with spindled morphology (arrows) in the area of scarring, compatible with involvement by the patient's underlying mastocytosis. (CD117 stain; original magnification: $\times 20$.)



Fig 3. Clinical presentation of telangiectasia macularis eruptiva perstans involving the anterior aspect of the left knee.

SM by all major and minor criteria used for diagnosis.¹

Reports of scarring alopecia in adult patients with systemic mastocytosis are relatively uncommon, and to our knowledge only 1 has been published to date.³ Although PCA is characterized by permanent damage to hair follicle stem cells and dermal fibrosis within the bulge region of the follicle, its exact etiology and pathogenesis have not yet been elucidated. Most studies have described the collapse of immune privilege within the hair follicle as the key to lymphocytic infiltration at the infundibuloisthmic region, with subsequent follicular destruction. However, more recent research has implicated mast cells in the primary phases of PCA pathogenesis,⁴⁻⁷ and other reports note PCA developing in the absence of lymphocytic infiltrates and presence of mast cell aggregates.^{3,4}

Hobo et al⁶ sought to identify infiltrating cells in PCA lesions and reported substantial aggregates of

mast cells expressing interleukin 17A in the presence of CD4⁺ and CD8⁺ lymphocytes. Interleukin 17 has been theorized to have a profibrotic effect on fibroblasts, most notably in systemic sclerosis. Hobo et al thus concluded that mast cells may play a significant role in PCA pathogenesis by induction of fibrosis.

The case we report here adds to the mounting evidence implicating mast cells in the pathogenesis of PCA. More research is needed to further clarify the underlying disease mechanisms of scarring alopecia, because it may identify more definitive therapies targeting specific variants of PCAs. Furthermore, patients presenting with scarring alopecia should have biopsy specimens analyzed with immunohistochemical and Giemsa stains if they also present with urticaria or other systemic symptoms. In addition, patients who show increased mast cell infiltrates on biopsy specimens should be considered for mastocytosis workup at a specialty clinic.

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