Progressive Eyelash Loss and Scale of the Right Eyelid

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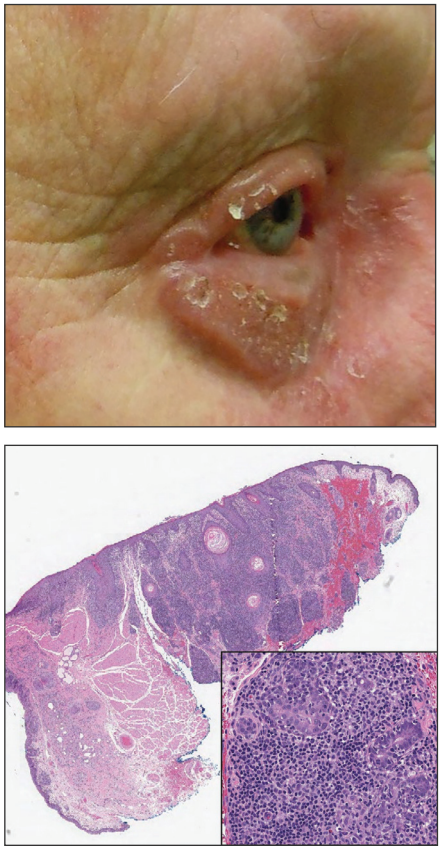

H&E, original magnification ×10; inset: original magnification ×200.

An 88-year-old man presented with progressive eyelash loss and scale involving the right eyelids (top). Dermatopathologic examination was performed (bottom).

THE BEST **DIAGNOSIS IS:**

a. alopecia areata
b. alopecia mucinosa
c. folliculotropic mycosis fungoides
d. psoriatic alopecia
e. seborrheic dermatitis

PLEASE TURN TO PAGE 27 FOR THE DIAGNOSIS

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THE **DIAGNOSIS:** Folliculotropic Mycosis Fungoides

Folliculotropic mycosis fungoides (FMF) is a variant of mycosis fungoides (MF) characterized by folliculotropism and follicular-based lesions. The clinical manifestation of FMF can vary and includes patches, plaques, or tumors resembling nonfolliculotropic MF; acneform lesions including comedones and pustules; or areas of alopecia. Lesions commonly involve the head and neck but also can be seen on the trunk or extremities. Folliculotropic mycosis fungoides can be accompanied by pruritus or superimposed secondary infection.

Histologic features of FMF include follicular (perifollicular or intrafollicular) infiltration by atypical T cells showing cerebriform nuclei.[1] In early lesions, there may be only mild superficial perivascular inflammation without notable lymphocyte atypia, making diagnosis challenging.[2,3] Mucinous degeneration of the follicles—termed *follicular mucinosis*—is a common histologic finding in FMF.[1,2] Follicular mucinosis is not exclusive to FMF; it can be primary/idiopathic or secondary to underlying inflammatory or neoplastic disorders such as FMF. On immunohistochemistry, FMF most commonly demonstrates a helper T cell phenotype that is positive for CD3 and CD4 and negative for CD8, with aberrant loss of CD7 and variably CD5, which is similar to classic MF. Occasionally, larger $CD30^+$ cells also can be present in the dermis. T-cell gene rearrangement studies will demonstrate T-cell receptor clonality in most cases.[2]

Many large retrospective cohort studies have suggested that patients with FMF have a worse prognosis than classic MF, with a 5-year survival rate of 62% to 87% for early-stage FMF vs more than 90% for classic patch- and plaque-stage MF.[4-7] However, a 2016 study suggested histologic evaluation may be able to further differentiate clinically identical cases into indolent and aggressive forms of FMF with considerably different outcomes based on the density of the perifollicular infiltrate.[5] The presence of follicular mucinosis has no impact on prognosis compared to cases without follicular mucinosis.[1,2]

Alopecia mucinosa is characterized by infiltrating, erythematous, scaling plaques localized to the head and neck.[8] It is diagnosed clinically, and histopathology shows follicular mucinosis. The terms *alopecia mucinosa* and *follicular mucinosis* often are used interchangeably. Over the past few decades, 3 variants have been categorized: primary acute, primary chronic, and secondary. The primary acute form manifests in children and young adults as solitary lesions, which often resolve spontaneously. In contrast, the primary chronic form manifests in older adults as multiple disseminated lesions with a chronic relapsing course.[8,9] The secondary form can occur in the setting of other disorders, including lupus erythematosus, hypertrophic lichen planus, alopecia areata, and neoplasms such as MF or Hodgkin lymphoma.[9] The histopathologic findings are similar for all types of alopecia mucinosa, with cystic pools of mucin deposition in the sebaceous glands and external root sheath of the follicles as well as associated inflammation composed of lymphocytes and eosinophils (Figure 1).[9,10] The inflammatory infiltrate rarely extends into the epidermis or upper portion of the hair follicle. Although histopathology alone cannot reliably distinguish between primary and secondary forms of alopecia mucinosa, MF (including follicular MF) or another underlying cutaneous T-cell lymphoma should be considered if inflammation extends into the upper dermis, epidermis, or follicles or is in a dense bandlike distribution.[11] On immunohistochemistry, lymphocytes should show positivity for CD3, CD4, and CD8. The CD4:CD8 ratio often is 1:1 in alopecia mucinosa, while in FMF it is approximately 3:1.[10] CD7 commonly is negative but can be present in a small percentage of cases.[12] T-cell receptor gene rearrangement studies have detected clonality in both primary and secondary alopecia mucinosa and thus cannot be used alone to distinguish between the two.[10] Given the overlap in histopathologic and immunohistochemical features of primary and secondary alopecia mucinosa, definitive diagnosis cannot be made with any single modality and should be based on correlating clinical presentation, histopathology, immunohistochemistry, and molecular analyses.

Inflammatory dermatoses including seborrheic dermatitis also are in the differential diagnosis for FMF. Seborrheic dermatitis is a common chronic inflammatory skin disorder affecting 1% to 3% of the general population.[13] Patients usually present with scaly and greasy plaques and papules localized to areas with increased

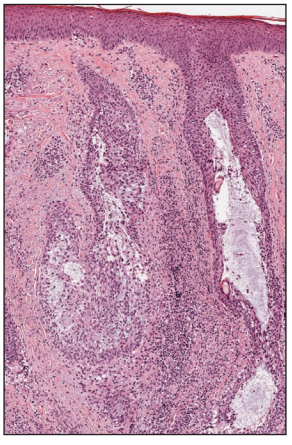

FIGURE 1. Alopecia mucinosa demonstrates cystic pools of mucin deposition in sebaceous glands and follicles (H&E, original magnification ×50).

sebaceous glands and high sebum production such as the face, scalp, and intertriginous regions. The distribution often is symmetrical, and the severity of disease can vary substantially.[13] Sebopsoriasis is an entity with overlapping features of seborrheic dermatitis and psoriasis, including thicker, more erythematous plaques that are more elevated. Histopathology of seborrheic dermatitis reveals spongiotic inflammation in the epidermis characterized by rounding of the keratinocytes, widening of the intercellular spaces, and accumulation of intracellular edema, causing the formation of clear spaces in the epidermis (Figure 2). Focal parakeratosis, usually in the follicular ostia, and mounds of scaly crust often are present.[14] A periodic acid–Schiff stain should be performed to rule out infectious dermatophytes, which can show similar clinical and histologic features. More chronic cases of seborrheic dermatitis often can take on histologic features of psoriasis, namely epidermal hyperplasia with thinning over dermal papillae, though the hyperplasia in psoriasis is more regular.

Alopecia areata is an immune-mediated disorder characterized by nonscarring hair loss; it affects approximately 0.1% to 0.2% of the general population.[15] The pathogenesis involves the premature transition of hair follicles in the anagen (growth) phase to the catagen (nonproliferative/involution) and telogen (resting) phases, resulting in sudden hair shedding and decreased regrowth. Clinically, it is characterized by asymptomatic hair loss that occurs most frequently on the scalp and other areas of the head, including eyelashes, eyebrows, and facial hair, but also can occur on the extremities. There are several variants; the most common is patchy alopecia, which features smooth circular areas of hair loss that progress over several weeks. Some patients can progress to loss of all scalp hairs (alopecia totalis) or all hairs throughout the body (alopecia universalis).[15] Patients typically will have spontaneous regrowth of hair, with up to 50% of those with limited hair loss recovering within a year.[16] The disease has a chronic/relapsing course, and patients often will have multiple episodes of hair loss. Histopathologic features can vary depending on the stage of disease. In acute cases, a peribulbar lymphocytic infiltrate preferentially involving anagen-stage hair follicles is seen, with associated necrosis, edema, and pigment incontinence (Figure 3).[16] In chronic alopecia areata, the inflammation may be less brisk, and follicular miniaturization often is seen. Additionally, increased proportions of catagen- or telogen-stage follicles are present.[16,17] On immunohistochemistry, lymphocytes express both CD4 and CD8, with a slightly increased CD4:CD8 ratio in active disease.[18]

Psoriatic alopecia describes hair loss that occurs in patients with psoriasis. Patients present with scaly, erythematous, psoriasiform plaques or patches, as well as decreased hair density, finer hairs, and increased dystrophic hair bulbs within the psoriatic plaques.[19] It often is nonscarring and resolves with therapy, though scarring may occur with secondary infection. Psoriatic alopecia may occur in the setting of classic psoriasis and also may occur in psoriasiform drug eruptions, including those caused by tumor necrosis factor inhibitors.[20,21] Histologic features include atrophy of sebaceous glands, epidermal changes with hypogranulosis and psoriasiform hyperplasia, decreased hair follicle density, and neutrophils in the stratum spinosum (Figure 4). There often is associated perifollicular lymphocytic inflammation with small lymphocytes that do not have notable morphologic abnormalities.

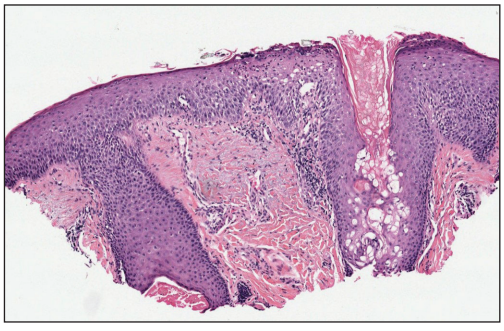

FIGURE 2. Seborrheic dermatitis demonstrates spongiosis of the epidermis and follicular ostia (H&E, original magnification ×20).

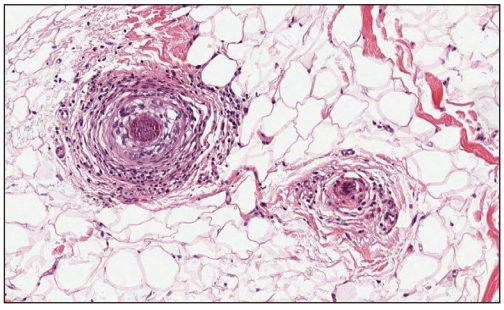

FIGURE 3. Alopecia areata demonstrates peribulbar lymphocytic inflammation (H&E, original magnification ×100).

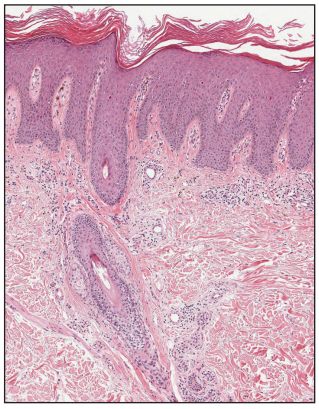

FIGURE 4. Psoriatic alopecia demonstrates psoriasiform hyperplasia with hypogranulosis, mild sebaceous gland atrophy, and decreased hair follicle density (H&E, original magnification ×50).

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