Distinguishing diffuse alopecia areata (AA) from pattern hair loss (PHL) using CD3$^+$ T cells

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Background: Distinguishing between diffuse subacute alopecia areata (AA), in which the peribulbar infiltrate is absent, and pattern hair loss is challenging, particularly in cases that lack marked follicular miniaturization and a marked catagen/telogen shift.

Objective: We sought to distinguish diffuse AA from pattern hair loss using CD3$^+$ T lymphocytes.

Methods: A total of 28 cases of subacute AA and 31 cases of pattern hair loss were selected and a 4-mm punch biopsy was performed. All the specimens were processed using the "HoVert" (horizontal and vertical) technique. In all cases, hematoxylin-eosin and immunohistochemical stains for CD3, CD4, CD8, and CD20 were performed.

Results: The presence of CD3$^+$ lymphocytes within empty follicular fibrous tracts (stela), even without a concomitant peribulbar infiltrate, is a reliable histopathological clue in supporting a diagnosis of AA (sensitivity 0.964, specificity 1, $P \leq .001$).

Limitations: Limited tissue for analysis remained in the clinical sample tissue blocks.

Conclusion: The presence of CD3$^+$ T-cells within empty follicular fibrous tracts (stela) supports a diagnosis of AA. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.12.011.)

Key words: alopecia areata; CD3; follicular fibrous tracts; pattern hair loss; stela.

Distinguishing diffuse alopecia areata (AA) and female or male pattern hair loss (PHL) may be challenging because both are characterized histopathologically by follicular miniaturization and an increased catagen/telogen shift. Clinicians are often confronted with the differential diagnosis among diffuse AA, PHL, and chronic telogen effluvium (CTE), especially when diffuse hair loss occurs over androgen-dependent areas. The frequent coexistence of PHL and CTE further complicates this distinction, because both PHL and CTE are characterized by global shedding, which is often accentuated in the frontal and mid scalp areas.

Abbreviations used:

AA:	alopecia areata
AAI:	alopecia areata incognita
CTE:	chronic telogen effluvium
PHL:	pattern hair loss
T:V:	terminal:vellus

For a histologic distinction, there are clues to specific diagnoses. CTE does not have follicular miniaturization. AA, PHL, and CTE, however, all have empty follicular fibrous tracts (so-called "empty stela" or "streamers") because of either follicular

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miniaturization or a catagen/telogen shift.[1] The miniaturized follicles are not long enough to extend down the fibrous tracts into the reticular dermis and subcutis. Similarly, the follicular epithelium of a catagen/telogen follicle resides only in the papillary dermis, with the subjacent tract being empty. In a minority of cases of AA, some lymphocytes may persist in the empty follicular fibrous tracts (stela).[2-4] Further complicating diagnostics, melanin may also be present in the fibrous tracts in AA, and even pigment casts may be identified, especially in people with dark hair.[1,5] This creates the potential for a misdiagnosis of trichotillosis (trichotillomania or traction alopecia). Fortunately, follicular miniaturization does not occur in CTE and trichotillosis.[6]

CAPSULE SUMMARY

- Without peribulbar lymphocytes, distinguishing between alopecia areata and pattern hair loss is challenging because both possess follicular miniaturization and a catagen/telogen shift.
- We describe a new tool to help overcome this diagnostic challenge.
- The presence of $CD3^+$ lymphocytes within empty follicular fibrous tracts (stela) reliably favors alopecia areata over pattern hair loss.

The presence of a peribulbar lymphocytic infiltrate, the so-called "hive of bees," sometimes admixed with eosinophils, confirms a diagnosis of AA. However, in subacute AA, where the peribulbar infiltrate is usually absent, an appropriate diagnosis of AA must be based on marked follicular miniaturization and a marked catagen/telogen shift.[3] A marked catagen/telogen shift, particularly more than 50%, and profound follicular miniaturization, with a terminal:vellus (T:V) ratio of greater than 1:7, are diagnostic of subacute AA.[2,7] However, when the T:V ratio is somewhere between 1:1 and 1:7, and the catagen/telogen shift is between 20% and 50%, a histologic distinction between AA and PHL is not possible.

The presence of a T-cell lymphocytic infiltrate in AA is well established.[4] However, the distribution and number of these T cells is not well documented in subacute AA, because the T-cell infiltrate is often sparse or absent on a simple hematoxylin-eosin examination. In this study, we characterized the inflammatory cell infiltrate in both AA and PHL in an attempt to identify reliable histopathological clues that can distinguish these entities. Here we report the use of the CD3 antigen, which is found on all mature T lymphocytes.

METHODS

Selection of cases

A total of 28 cases of subacute AA and 31 cases of PHL were selected.

The selected cases diagnosed as AA had to meet the following criteria: (1) a characteristic clinical presentation; (2) a confirmed histopathological diagnosis confirmed by 2 hair-loss dermatopathologist experts; and (3) histopathological findings with at least 1 of the following conditions: (a) the presence of a peribulbar lymphocytic infiltrate; (b) a catagen/telogen shift of more than 50%; or (c) marked follicular miniaturization with a T:V ratio of <1:7. Other findings, such as the presence of so-called "nanogen" hairs,[3] lymphocytes and melanin in empty follicular fibrous tracts (stela), eosinophils in the tracts and around follicular bulbs, and dilated follicular openings were also taken into consideration. Cases with both a T:V ratio between 1:1 and 1:7 and catagen/telogen shift between 20% and 50% were included if there was a peribulbar lymphocytic infiltrate. In cases AA2 and AA4 only vertical sections were obtained so the T:V ratio and catagen/telogen percentage could not be established, but these were included because of the presence of a peribulbar infiltrate.

The selected cases diagnosed as PHL had to meet the following criteria: (1) a characteristic clinical presentation; (2) a confirmed histopathological diagnosis by 2 hair-loss dermatopathologist experts; and (3) histopathological findings including all 3 of the following conditions: (a) a decreased T:V hair ratio between 1:1 to 1:3 for patients younger than 50 years of age, and 1.5:1 to 1:3 for patients older than 50 years (no distinction between PHL and senescence was made for patients age >50 years); and (b) an increased percentage of catagen/telogen-phase hairs between 10% to 30%; and (c) an absence of a peribulbar lymphocytic infiltrate on hematoxylin-eosin examination. An additional histopathological finding taken into consideration was increased variability of follicle diameter within the same examined section.

In all cases, a diagnosis of CTE alone was ruled out by the presence of follicular miniaturization. Trichotillomania and traction alopecia were ruled out because of clinical findings and the absence of a trichomalacia, pigment casts, and a distorted follicular architecture. In cases with a marked catagen/telogen shift, a diagnosis of syphilis was also excluded by the absence of a plasma cell-rich