Original Article

Psoriatic alopecia - fact or fiction? A clinicohistopathologic reappraisal

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ABSTRACT

Background: The incidence of psoriatic alopecia in psoriatic patients is underwhelming, given the prevalence of psoriasis in the North American population. Recently, a 60-year-old Albanian female, lacking a significant medical history for psoriasis, presented to our clinic with a 1-year history of "dandruff" associated with itch, hair thinning, and histopathologic evidence consistent with prior reports of "psoriatic alopecia." **Aims:** The absence of preceding or concomitant psoriasis suggests that the patient's alopecia is an antecedent manifestation of psoriasis, thus prompting this retrospective study to ascertain better the relationship between alopecia and psoriasis. **Methods:** We performed a retrospective review of 33 scalp biopsies on 31 patients having histopathologic diagnosis of psoriasis belonging to 31 patients seen between 2007 and 2010. **Results:** Alopecia was a presenting feature in 48% of cases with definitive clinical and/or histopathologic diagnosis of psoriasis (scale crust with neutrophils, psoriasiform epidermal hyperplasia, and hypogranulosis). The most common follicular-related changes were infundibular dilatation (87%) followed by perifollicular fibrosis (77%), perifollicular lymphocytic inflammation (68%), thinning of the follicular infundibulum (55%), and fibrous tracts (28%). Of interest, sebaceous glands were absent in 60% and atrophic in 25% of cases. **Conclusion:** While a major limitation of this study is that it is a retrospective one, given that these changes are common to varying degrees in all lymphocytic scarring alopecias, we posit that psoriatic alopecia likely represents a secondary clinical change to a primary process and is not a unique histopathologic entity. A prospective study with a control group that includes lymphocytic scarring alopecias from non-psoriatic patients is required to support our findings.

Key words: Alopecia, psoriasis, scarring

INTRODUCTION

Although psoriasis is fairly common in the North American population with an incidence of 1.5-2%,[1] a paucity of data exist regarding the characterization of psoriatic alopecia, with less than 60 cases published to date.[2-7] First described by Shuster in 1972,[2] psoriatic alopecia initially was thought to be associated exclusively with acute erythrodermic, generalized pustular psoriasis or chronic plaque psoriasis.[3,5] Conflicting data exist as to whether the alopecia in psoriasis is a scarring or non-scarring process. While some histopathologic studies indicate a scarring process (i.e., reduction in hair follicle density and presence of a peri-infundibular lymphocytic infiltrate with destruction of the follicle),[3-7] clinical reports of complete hair re-growth following topical anti-psoriatic treatments favor a non-scarring process.[4,8]

Recently, a 60-year-old Albanian female, with no current or past cutaneous manifestations of psoriasis,

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presented to our clinic with a 1-year history of "dandruff" associated with itch, hair thinning [Figure 1], and histopathologic evidence consistent with prior reports of "psoriatic alopecia" [Figure 2a-e]. The lack of preceding or concomitant cutaneous psoriasis suggests that this patient's alopecia is an antecedent manifestation of psoriasis, thus prompting this study to ascertain better the relationship between alopecia and psoriasis.

METHODS

This study was approved by Boston University School of Medicine Institutional Review Board (IRB docket No. H- 30202). Archival materials between 2007 and 2010 of biopsies from the scalp with a histopathologic diagnosis of psoriasis were retrieved from the pathology files of the Skin Pathology Laboratory, Boston University School of Medicine, Boston, MA. A total of 33 cases belonging to 31 patients were identified. Histologic sections of all cases were re-reviewed, and the diagnoses confirmed by the dermatopathologist (M.M.) in all of the cases. All patient data were de-identified.

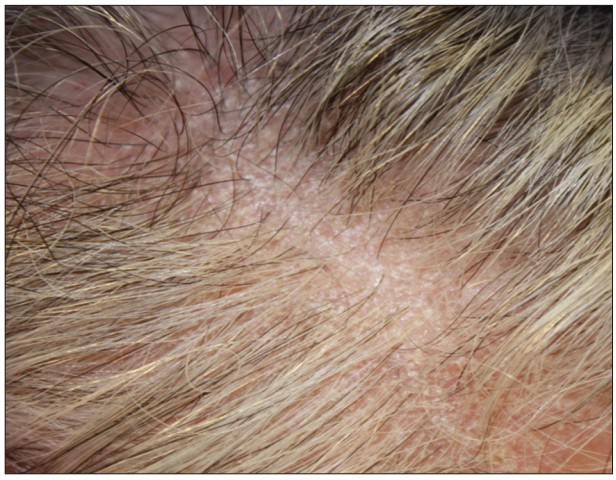

Figure 1: Mild hair loss with fine, whitish scale and surrounding erythema on frontal scalp

Statistical analysis

We performed comparisons of clinical characteristics and histopathologic findings on psoriasis patients with and without alopecia at presentation. Wilcoxon rank sums were used to compare means and standard deviations of age. Fisher exact test was used to compare the proportions of the presence of histopathologic features. These included both epidermal (scale crust with neutrophils, psoriasiform epidermal hyperplasia, and hypogranulosis) and follicular-related changes (absent or atrophic sebaceous gland, infundibular dilation, thinning of the follicular epithelium, perifollicular lymphocytic infiltrate, and fibrosis and fibrous tract formation). All statistical analyzes were performed with Statistical Analysis Software (SAS) version 9.2 (SAS Institute, Cary, NC, USA) and a *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Clinical findings

Patient demographics including indications for biopsy are summarized in Table 1. The 33 cases of psoriasis occurred in 31 patients, of whom 17 (55%) were men and 14 (45%) were women. The patient ages at time of diagnosis ranged from 10 to 68 years (mean = 39.4 years). 2 of the patients had 2 biopsies done and given that both had similar clinical and histopathologic findings, will be considered as one, bringing the total number of cases to 31. Clinical presentation data was not available for 13 cases (42%). Clinical presentations included: Scaly erythematous plaque in 11/18 (62%), scaly pruritic rash in 3/18 (17%), scaly erythematous patch in 2/18 (11%), eruptive bumps in 2/18 (11%), a weeping, painful dermatitis with scale in 1/18 (6%), and eruptive scalp scaliness in 1/18 (6%). Psoriasis was the presumptive pre-biopsy diagnosis in 16/28 (57%) cases. A presumptive pre-biopsy diagnosis was unavailable for 3 cases (10%). Remarkably, 15 patients (48%), none of whom were on systemic therapy,

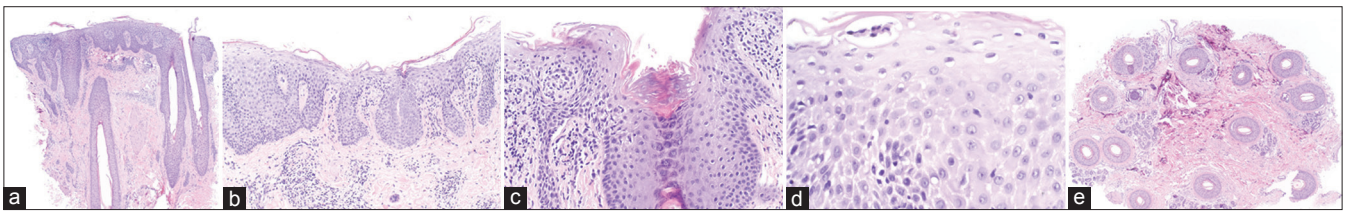

Figure 2: (a-e) H and E (a-d vertical and e horizontal sections) (H and E, ×20) (a) Scanning magnification showing loss of sebaceous glands (b) Epidermal changes of confluent hypogranulosis and psoriasiform epidermal hyperplasia (c) Infundibular dilatation (d) Aggregates of neutrophils in the stratum spinosum (reminiscent of spongiform pustule of Kogoj) (e) Decrease in density of hair follicles (total of 13 hair follicles seen, all in anagen)

Table 1: Patient demographics and clinical characteristics

Case #	Age	Sex	Clinical presentation	Presumptive clinical diagnosis	Alopecia at presentation	Alopecia at follow-up	Length of follow-up (months)
1	51	F	Scaly, erythematous patch	Lichen simplex chronicus vs. psoriasis vs. seborrheic dermatitis	Present	NA	NA
2	43	M	Scaly, erythematous plaques	Seborrheic dermatitis vs. tinea corporis	Absent	NA	NA
3	13	M	Scaly, erythematous plaques	Tinea vs. erythema chronicum migrans vs. eczema	Absent	Absent	35
4	24	M	Scaly, erythematous plaques	Psoriasis vs. seborrheic dermatitis vs. granulomatous disease	Absent	Absent	32
5	42	F	Scaly, erythematous plaques	Basal cell carcinoma, rule out psoriasis.	Absent	Present	32
6	45	F	Weeping, painful dermatitis	Pustular psoriasis, rule out autoimmune pemphigus vs. pemphigoid	Present	Absent	31
7	56	F	Itchy, scaly rash	Discoid lupus erythematosus vs. lichen plano-pilaris vs. tinea vs. CCCA†	Present	NA	NA
8	56	M	Not provided	Squamous cell carcinoma vs. seborrheic keratosis	Present	Present	27
9	61	M	Not provided	Psoriasis vs. actinic keratosis	Absent	Absent	25
10	26	F	Scaly, erythematous plaques	Contact dermatitis vs. psoriasis vs. early lichen plano-pilaris	Present	Present	20
11	67	M	Not provided	Seborrheic keratosis, irritated	Absent	Absent	23
12	64	M	Not provided	Seborrheic keratosis vs. retention hyperkeratosis vs. tinea vs. tinea capitis vs. pigmented actinic keratosis vs. pigmented basal cell carcinoma vs. other pathology	Present	Absent	23
13	49	M	Not provided	Actinic keratosis vs. squamous cell carcinoma vs. irritated seborrheic keratosis	Absent	Absent	21
14, 15	52	M	Bumps on scalp	Infiltrating disease (sarcoid) vs. T-cell or B-cell lymphoma	Absent	Absent	18
16	28	M	Scaly, erythematous plaques	Psoriasis	Absent	Absent	16
17	27	M	Scaly, erythematous plaques	Sarcoidosis vs. cutaneous T-cell lymphoma vs. granuloma annulare vs. psoriasis	Absent	Present	15
18	15	F	Not provided	Not provided	Present	NA	NA
19	15	F	Not provided	Not provided	Present	NA	NA
20	65	M	Scaly, erythematous plaques	Psoriasis	Present	Present	15
21	47	F	Scaly, erythematous plaques	Psoriasis, rule out lupus erythematosus vs. cutaneous T-cell lymphoma vs. sarcoid vs. psoriasis	Present	NA	NA
22	23	M	Itchy, scaly rash	Not provided	Present	NA	NA
23	26	F	Eruptive scalp scaliness	Psoriasis vs. tinea capitis vs. seborrheic dermatitis	Absent	Absent	11
24	68	F	Scaly, erythematous patch	Lichen plano-pilaris vs. lupus erythematosus (systemic lupus erythematosus) vs. pityriasis rubra pilaris	Present	NA	NA
25, 26	21	M	Not provided	Rule out basal cell carcinomas vs. squamous cell carcinomas	Absent	Absent	10
27	10	F	Scaly, erythematous plaques	Psoriasis (likely)	Absent	Absent	8
28	38	F	Itchy, scaly rash	Psoriasis vs. dermatitis	Present	Absent	7
29	35	F	Not provided	Rule out seborrheic dermatitis vs. sebopsoriasis	Present	Present	4
30	44	M	Not provided	Wart vs. psoriasis vs. squamous cell carcinoma	Absent	Absent	3
31	46	M	Not provided	Irritated seborrheic keratosis	Absent	Absent	2
32	60	F	Scaly, erythematous plaques	Cicatricial alopecia (discoid lupus erythematosus vs. lichen plano-pilaris vs. other pathology)	Present	Present	2
33	31	F	Not provided	Psoriasis	Absent	Absent	1

*Index patient highlighted; ^NA- not available, †CCCA: Central centrifugal cicatricial alopecia

had alopecia as a presenting symptom. None of the patients in the study were on anti-TNF-α therapy and, to the best of our knowledge, no extraneous factors were involved in patients presenting with or in those who had alopecia.

Histopathologic findings

Histopathologic findings are summarized in Table 2. Overall, we observed epidermal changes consistent with psoriasis (scale crust with neutrophils, hypogranulosis, and psoriasiform epidermal hyperplasia) in all 31 (100%) cases.

Notable follicular-related changes included: infundibular dilatation in 26/30 (87%) cases, thinning of the follicular infundibulum (FI) in 17/31 (55%) cases, perifollicular lymphocytic inflammation (PFLI) in 21/31 (68%) cases, perifollicular fibrosis (PF) in 24/31 (77%) cases, and fibrous tracts in 10/28 (28%) cases. None of the cases demonstrated naked hair shafts or granulomas.

Sebaceous gland-related changes included: Complete absence in 12/20 (60%) cases and atrophy in 5/20 (25%) cases, while a normal size and number were observed in 3/20 (15%) cases. In 11/31 (35%) cases, no sebaceous glands were seen as a consequence of the biopsy type (i.e., shave biopsies).

Histopathologic findings in the follicle were limited by the type of biopsy done (i.e. shave biopsies).

Summary of statistical analyzes

Overall, no statistically significant differences were observed on histopathologic features between scalp biopsies from psoriasis patients presenting with and without alopecia [Table 3]. All specimens exhibited epidermal changes (scale crust with neutrophils (SCN), psoriasiform epidermal hyperplasia (PSEH), and hypogranulosis (HOG)) consistent with the diagnosis of psoriasis. None of the biopsy specimens demonstrated naked hair shafts or had granulomas. A significantly larger proportion of patients presenting with alopecia were female (73% vs. 25%, $P = 0.01$). There were trends for an older age at biopsy (44.3 vs. 36.5 years, $P = 0.23$), more sebaceous gland abnormalities (92% vs. 63%, $P = 0.25$), perifollicular lymphocytic infiltrate (PFLI) (80% vs. 56%, $P = 0.25$), and presence fibrous tract (21% vs. 50%, $P = 0.24$), but these comparisons did not reach statistical significance. These associations remained even after correction for patients that developed alopecia on follow-up (12%, N = 2).

DISCUSSION

Shuster first described psoriatic alopecia in 1972.[2] In this seminal article, all study patients (although not enumerated) presented concomitantly with alopecia and various types of cutaneous psoriasis. Of interest, he excluded patients with the erythrodermic and pustular forms of psoriasis, as alopecia in these 2 is well accepted. Shuster derived his data from clinical examination of hair roots plucked in bunches of 50 or more hairs. Based on his observations, he concluded that scalp psoriasis results in 3 distinct types of alopecia: 1) hair loss confined to lesional skin as confirmed by hair pluck revealing dystrophic bulbs (most common); 2) acute hair fall with a predominance of telogen hairs; and 3) "destructive or scarring alopecia" associated with decreased hair density and "perifollicular inflammation with destructional folliculitis and fibrous tissue replacement" (least common).[2] A paucity of studies on psoriatic alopecia exists (n = 7), particularly given the frequency of psoriasis in the Caucasian population.[2-8] The histopathologic findings in our index case encompass the spectrum of changes described in psoriatic alopecia and include epidermal changes consistent with psoriasis, decreased hair density (totaling 13 hair follicles, predominantly in anagen), and loss of sebaceous glands. In contrast to prior studies in which patients with a known history of psoriasis presented with alopecia,[2-8] our index case presented with alopecia without a definitive history of psoriasis. In our retrospective review, alopecia was a presenting feature in 45% (14 of 31) of patients identified by definitive clinical and/or histopathologic diagnosis of psoriasis. Observed histopathologic changes included traditional epidermal changes of psoriasis and follicular-related changes (infundibular dilatation, perifollicular inflammation and fibrosis, thinned follicular epithelium, and fibrous tracts).

First, we questioned whether there is difference in the clinical and histopathologic findings of those patients who presented with alopecia from those who did not have alopecia at presentation. A significantly larger proportion of patients with alopecia were female ($P = 0.01$). No statistically significant differences were observed from the scalp biopsies between the 2 groups although a trend was observed for an older age at biopsy (44.3 vs. 36.5 years, $P = 0.23$), more sebaceous gland abnormalities (92% vs. 63%,$P = 0.25$), perifollicular infiltrates (80% vs. 56%, $P = 0.25$), and less fibrosis tract formation (21% vs. 50%, $P = 0.24$), but these comparisons did not reach statistical significance.

Table 2: Histopathologic diagnosis and features of cases studied

Case	Sign-out histopathologic diagnosis	Histopathologic Features												
		Epidermal changes			Follicular-related changes									
		SCN	PSEH	HOG	Infundibular dilation	Sebaceous gland			Hair follicle number	Thinning of FI	Naked hair shafts/ granulomas	PFLI	PF fibrosis	Fibrous tract
						Absent	Atrophy	Normal						
1[S]	S/o psoriasis, D/dx sebopsoriasis	P	P	P	CNBE	CNBE			CNBE	A	A	P	P	A
2[PV]	Non-diagnostic; S/o chronic spongiotic dermatitis	P	P	P	P			P	5	P	A	P	P	A
3[S]	Psoriasiform dermatitis, D/dx partially-treated psoriasis	P	P	P	A	CNBE			3	A	A	A	A	P
4[PV]	Psoriasis	P	P	P	P			P	2	A	A	A	P	P
5[S]	Psoriasiform dermatitis, D/dx partially-treated psoriasis	P	P	P	A	CNBE			CNBE	A	A	A	A	A
6[PV]	Psoriasis	P	P	P	P	P			7/8	P	A	P	P	P
7[PV]	Scarring alopecia, +/-associated seborrheic dermatitis	P	P	P, I	P	P			2/3	P	A	P	P	A
8[S]	S/o psoriasis	P	P	P	CNBE	CNBE			3	P	A	A	A	A
9[S]	Seborrheic dermatitis, D/dx sebopsoriasis.	P	P	P	P	CNBE			2	P	A	P	P	P
10[PV]	Psoriasiform dermatitis s/o partially-treated psoriasis	P	P	P, I	P	P			4	P	A	P	P	A
11[S]	S/o psoriasis	P	P	P	P	CNBE			1	P	A	A	CNBE	A
12[S]	Partially-treated psoriasis, D/dx pityriasis rubra pilaris or chronic superficial dermatitis	P	P	P	P		P		3	A	A	A	P	A
13[S]	Psoriasiform dermatitis, D/dx subacute to chronic spongiotic dermatitis, partially-treated psoriasis	P	P	P	P	CNBE			2	A	A	P	P	P
14, 15[PV]	Psoriasis	P	P	P	P		P		2	P	A	P	P	P
16[PV]	Psoriasis	P	P	P	P		P		2	P	A	P	P	A
17[PV]	Psoriasis	P	P	P	P		P		3	P	A	A	P	A
18[S]	S/o psoriasis	P	P	P	P	P			2	P	A	P	A	CNBE
19[PV]	Female pattern hair loss with superimposed psoriasis	P	P	P	A	P			7	P	A	A	P	P
20S	Psoriasiform dermatitis, D/dx psoriasis	P	P	P, I	P	P			2	A	A	P	P	A
21PV	Psoriasis, loss of sebaceous glands is concerning for scarring alopecia	P	P	P	P	P			4	A	A	P	P	A
22PT	Psoriasis, D/dx erosive pustular dermatitis	P	P	P	P		P		30	A	A	P	P	A
23PV	Psoriasiform dermatitis, D/dx partially-treated psoriasis	P	P	P	P	P			4	A	A	P	P	A
24 A] PV B] PT	Psoriasis, D/dx seborrheic dermatitis in combination with alopecia areata or psoriatic alopecia	P	P	P	P	P			15	P	A	P	P	A

Contd...

Table 2: Contd...

Case	Sign-out histopathologic diagnosis	Histopathologic Features													
		Epidermal changes			Follicular-related changes										
		SCN	PSEH	HOG	Infundibular dilation	Sebaceous gland			Hair follicle number	Thinning of FI	Naked hair shafts/ granulomas	PFLI	PF fibrosis	Fibrous tract
						Absent	Atrophy	Normal						
25, 26S	S/o psoriasis	P	P	P	P	CNBE			2	P	A	P	A	CNBE
27S	Psoriasis	P	P	P	P	CNBE			2	P	A	A	P, mild	P
28PV	Psoriasis	P	P	P	P			P	5	A	A	P	P, mild	P
29PV	Psoriasis	P	P	P	P	P			4	A	A	P	P	A
30S	Inflamed verruca vulgaris, D/dx verrucous psoriasis	P	P	P	P	CNBE			2	P	A	A	P	P
31S	S/o psoriasis	P	P	P	P	P			2	P	A	P	P	CNBE
32 PV, PT	S/o psoriatic alopecia	P	P	P	P	P			14	A	A	P	A	A
33S	Psoriasis	P	P	P	P	CNBE			4	A	A	P	P	A

*Index patient highlighted; A- Ab˙sent; P- Present; CNBE- Could not be evaluated; I- Intermittent; S/o- suggestive of; In superscript: S- Shave biopsy; PV -punch biopsy, vertical; PT - punch biopsy, transverse

These associations remain even after correcting for patients that developed alopecia on follow-up (12%, N = 2). Of interest, and a clinical trend that was statistically significant was that, females tend to present earlier than males – a feature that can perhaps be attributed to increased concern and sensitivity to hair loss in females compared to males.

Next, we questioned whether psoriatic alopecia has specific histologic changes or if similar findings are present in other lymphocytic scarring alopecias, like central centrifugal cicatricial alopecia (CCCA), lichen planopilaris (LPP) or frontal fibrosing alopecia (FFA) and lupus. Histopathologic features seen in these entities include: Decreased or absent follicular units, a perifollicular lymphocytic infiltrate, distention of follicular ostia (lupus), infundibular hyperkeratosis (LPP/ FFA), fibrous tracts, and naked hair shafts.[9] While the frequency of these changes varies with both the diagnosis and the stage of disease at which the biopsy is performed, the follicular changes noted in our study are not unique to psoriatic alopecia and are often present in other lymphocytic scarring.

Of interest, 87% of patients with alopecia at time of presentation had complete absence or atrophy of sebaceous glands. In a recent series, comparing 19 patients with scalp psoriasis (no clinical information on the presence, absence, or degree of alopecia mentioned) with 26 normal controls, atrophy of sebaceous glands was the only statistically significant histopathologic finding present in the psoriatic group.[10] Although this led the authors to conclude a feature "peculiar to scalp psoriasis was sebaceous gland atrophy", a retrospective review of the literature indicates that "sebaceous glands are often atrophic or absent in other lymphocytic scarring alopecias such as LPP/ FFA,[9,11-17] CCCA,[12,17-20] and DLE[9,12,16,21] [Table 4]. In those that were original articles, the prevalence of sebaceous gland atrophy or absence in lymphocytic scarring alopecias varied from 28 to 100%, often being observed as an early event in all 3 entities.

Why does sebaceous gland atrophy/loss occur in psoriasis? One possible explanation is that psoriasis has an extremely complex cytokine milieu. The psoriatic plaque is characterized by the predominance of cytokines produced by T_{H1} cells.[22] Briefly, these include IFN-γ, IL-2, and TNF-α.[22] It is not unreasonable to hypothesize that the interactions of cytokines and chemokines produced in lesional epidermis could cause sebaceous glands to atrophy in an autocrine

Table 3: Summary of statistical analyses

Clinical characteristics and histopathologic features	No alopecia N = 16	Alopecia N = 15	*P* value
Age, years (mean ± SD, range)	36.5 ± 16.5, 10-67	44.3 ± 18.1, 15-68	0.23
Gender, % female (N)	25% (4)	73% (11)	0.01
Epidermal changes	100%	100%	
Absent/ atrophic sebaceous gland changes, % (N/Total)	63% (5/8)	92% (12/13)	0.25
Infundibular dilatation, % (N/Total)	88% (14/16)	92% (12/13)	1
Thinning of follicular epithelium, % (N/Total)	62% (10/16)	46.7% (7/15)	0.48
Naked hair shafts / granulomas, % (N/Total)	0%	0%	
Perifollicular lymphocytic infiltrate, % (N/Total)	56% (9/16)	80% (12/15)	0.25
Perifollicular fibrosis, % (N/Total)	80% (12/15)	80% (12/15)	1
Fibrous tract, % (N/Total)	50% (7/14)	21% (3/14)	0.24
Alopecia on follow-up, % (N/Total)		12% (2/16)	

Table 4: Sebaceous glands findings in lymphocytic scarring alopecias

Reference	Article type	Findings	Conclusions
Wilson, *et al* (1992)[21]	Original Article	10/10 (100%) patients with scarring alopecia and DLE had significantly reduced number and size of sebaceous glands in involved scalp	Sebaceous gland atrophy or loss is an early sign of DLE
Nayar, *et al* (1993)[11]	Original Article	10 patients with scarring alopecia (7 with LPP and 3 with pseudopelade), 6/7 with LPP (86%) had atrophy or loss of sebaceous glands	
Headington (1996)[14]	Review		Sebaceous glands are lost in early lesions of LPP and DLE
Annessi, *et al* (1999)[15]	Original Article	118 patients with scarring alopecia (68 with LPP, 25 with DLE and 25 with pseudopelade), sebaceous gland atrophy detected in 19/68 (28%) cases	
Whiting (2001)[12]	Original Article	95 patients with lymphocytic scarring alopecia (36 with LPP, 31 with DLE and 28 with CCCA)	All 3 entities with loss or destruction of sebaceous glands in early lesions
Ross, Tan and Shapiro (2005)[9]	Review		Loss/ atrophy of sebaceous gland in DLE and LPP
Mirmirani, *et al* (2005)[17]	Original Article	12 patients with lymphocytic scarring alopecia (4 with LPP, 2 with FFA, 4 with pseudopelade and 2 with CCCA), loss/ atrophy of sebaceous gland in all entities	
Tandon, *et al* (2008)[13]	Original Article	27 patients with LPP, 8/27 (30%) had reduced sebaceous glands and 19/27 (70%) had absent sebaceous gland	
Moure, *et al* (2008)	Original Article	33 patients with lymphocytic scarring alopecia (17 with DLE, 12 with pseudopelade and 4 with LPP), absence of sebaceous epithelium in LPP (4/4 or 100%)	
Somani and Bergfeld (2008)[16]	Review		Destruction of sebaceous glands early in both DLE and LPP
Whiting and Olsen (2008)[18]	Review		Sebaceous glands are lost early in CCCA
Gathers and Lim (2009)[19]	Review		Loss of sebaceous epithelium in CCCA
Stefanato (2010)[20]	Review		Loss of sebaceous gland in CCCA

and paracrine manner akin to the role of IGFBP7 (a secreted protein produced by normal melanocytes) in *BRAFV600E* mutated nevi.[23] In *BRAFV600E*-positive nevi, constitutive activation of the *BRAF-MEK- ERK* pathway increases expression and secretion of IGFBP7, resulting in high levels of IGFBP7 that inhibit *BRAF-MEK-ERK* signaling and activate senescence.[23] Extending this analogy to psoriasis and lending credence to our hypothesis, Kristensen *et al*, showed that TNF-α and its receptor are expressed in basal layers of epidermis and sebaceous glands in normal skin, but are confined solely to the epidermis in psoriatic skin.[24] In addition,

prior research indicates that TNF-α is present in normal sebaceous glands and murine skin,[25] is implicated in the induction of psoriatic skin lesions on the scalp including alopecia, and is reported secondary to anti-TNF-α therapy.[26-28] Of note, none of the patients in the current study were on anti-TNF-α therapy.

An alternate explanation for sebaceous gland atrophy/loss relates to the perifollicular inflammation of the upper "permanent" portion of the hair follicle present in psoriatic alopecia which is also common to all scarring alopecias.[3] Near this site (particularly where the arrector pili attaches), the bulge contains stem cells that give rise to multipotent matrix cells.[29-31] It is thought that these multipotent cells give rise to the hair shaft, as well as the sebaceous gland and adjacent epidermis.[31] Thus, damage to this region compromises the sebaceous gland. Using antibodies to stem cell markers nestin, CK15 and CD34, we previously demonstrated that the bulge region is involved in "active" stages of scarring alopecias.[32] Could alopecia be secondary response to sebaceous gland loss? Asebia mouse mutants, having markedly hypoplastic sebaceous glands, experience progressive hair loss and striking scarring alopecia.[33]

From a clinical perspective, 4 of the 7 published articles refer to psoriatic alopecia as a scarring form of alopecia,[3,5-7] one categorizes it as a non-scarring alopecia[8] and two had features of both,[2,4] favoring a non-cicatricial process is the presence of hair re-growth. In the largest study to date (n = 47), 7 patients experienced permanent hair loss while 34 patients had re-growth.[4] Similarly, multiple patients in our study experienced hair re-growth (4 of 7 patients with follow-up), albeit obvious limitations in the numbers of patients with follow-up (averaging 18.1 months).

While a major limitation of this study is that it is a retrospective one, given that these changes are common to varying degrees in all lymphocytic scarring alopecias, we posit that psoriatic alopecia likely represents a secondary clinical change to a primary process and is not a unique histopathologic entity. A prospective study with a control group that includes lymphocytic scarring alopecias from non-psoriasis patients is required to support our findings.

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