Follicular psoriasis: a report of 5 cases and review of the literature, likely an under-recognized yet distinctive variant of psoriasis

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Abstract

Psoriasis is a common autoimmune dermatosis representing an interplay between certain genetic predisposing factors along with clonally restricted T_h1 T cells responding to epidermal keratinocyte derived antigen. A unique IL17/IL23 cytokine-rich milieu is pathogenetically significant and conducive to its salient histomorphologic features, such as epidermal hyperplasia and intraepidermal influx of neutrophils. The classic cutaneous manifestation is that of plaque psoriasis also referred to as psoriasis vulgaris with characteristic well-circumscribed erythematous plaques covered by silvery scales. Follicular psoriasis is an uncommon variant manifesting as a scaly folliculocentric hyperkeratotic eruption of the trunk and extremities, irrespective of the presence or absence of conventional lesions of psoriasis vulgaris. In this study we present 5 cases of follicular psoriasis, review the literature, and provide a proposal regarding relevant pathologic findings and potential pathogenetic mechanisms. The incidence of follicular psoriasis is unknown, emphasizing its rarity given the overall incidence of conventional psoriasis in the general population. Owing to the lack of awareness, this clinical presentation is often mistaken for other follicular dermatoses, including bacterial folliculitis, pityriasis rubra pilaris, keratosis pilaris, or follicular eczema.

Keywords: psoriasis, follicular psoriasis, folliculocentric hyperkeratotic eruption

Introduction

Psoriasis is a common dermatosis that typically first manifests in the third decade of life with a subsequent peak in the 6th decade. Psoriasis is also recognized in children. There are various subtypes including classic psoriasis vulgaris, guttate psoriasis, pustular psoriasis, inverse psoriasis, and erythrodermic psoriasis [1].

Pathogenically, psoriasis is considered an autoimmune dermatosis representing an interplay between predisposing genetic factors and clonally restricted Th1 T cells responding to antigens derived from epidermal keratinocytes. Various genetic susceptibility loci have been described including 6p21 (PSORS1) and 17q25 (PSORS2), containing three loci with one related to psoriatic arthritis, and 1q21 (PSORS4), [2].

From an immunologic perspective, T cells responding to keratinocyte antigen are pathogenetically relevant. High levels of IL17 are observed. IL17 is a proinflammatory cytokine capable of activating the innate immune response against extracellular pathogens by producing neutrophil chemoattractants and antimicrobial

peptides [3]. Tumor necrosis factor (TNF) facilitates IL23 production of dendritic cells (DCs), in turn provoking IL17 elaboration by T cells, suggesting that TNF acts as a regulator of the IL23/Th17 axis [4].

The worldwide prevalence of psoriasis is age- and location-dependent. In the United States the incidence of psoriasis is approximately 2%, with a higher frequency in the Caucasian population [5]. The classic cutaneous manifestation of plaque psoriasis, also termed psoriasis vulgaris, characteristically represents as well-circumscribed erythematous plaques covered by silvery scales that exhibit the Auspitz sign upon removal. Follicular psoriasis (FP) is an uncommon variant manifesting as scaling folliculocentric hyperkeratotic eruptions of the trunk and extremities, irrespective of co-existent conventional lesions of psoriasis vulgaris.

The precise incidence of FP is unknown with roughly 23 reported cases. Owing to the lack of awareness, this clinical presentation is often misinterpreted as other follicular dermatoses such as bacterial folliculitis, pityriasis rubra pilaris, keratosis pilaris, and follicular eczema. Herein, we present 5 cases of follicular psoriasis, review the literature, and provide a proposal regarding relevant pathologic findings and potential pathogenetic mechanisms.

Case presentation

Case 1

A 61-year-old woman presented with a sudden and self-remitting pruritic papular eruption involving bilateral forearms and bilateral lower legs of several months' duration. She denied any constitutional symptoms. The patient had no other medical history and other family members were not similarly afflicted. Physical examination revealed numerous erythematous-crusted folliculocentric papules with supervening purpuric features involving the arms and legs and extending to the superior and inferior back. Symptomatic improvement was seen with the use of pimecrolimus cream 1% (Elidel), (**Figure 1A, B)**.

Multiple shave biopsies were performed on the right superior back, right inferior back, right upper arm, and right forearm, all of which manifested the same light microscopic findings: an extensive pustular folliculocentric process with permeation of the outer root sheath epithelium by neutrophils. In addition, the ostium of the follicle was occluded by dense keratin intimately admixed with neutrophils (**Figure 1C, D)**. The background epidermis exhibited classic features of a psoriasiform diathesis, namely neutrophil-imbued parakeratosis, granular cell layer loss, and dilated dermal papillary capillaries lying in intimate apposition to the basal layer of the epidermis (**Figure 1E, F)**. Direct immunofluorescence revealed entrapment of immunoglobulin and complement within the stratum corneum along with variable granular deposition of complement

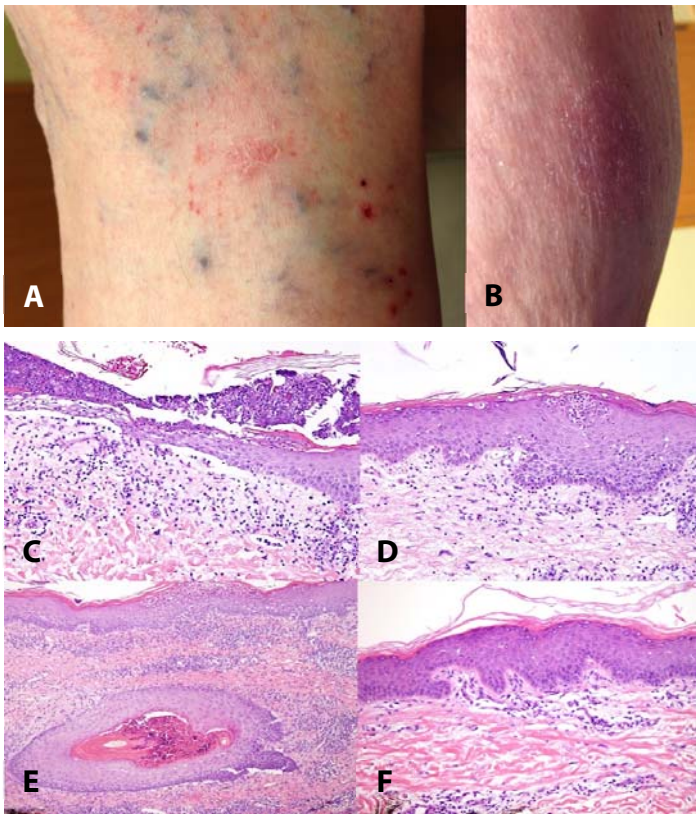

Figure 1. ***A-B)*** *Erythematous hyperkeratotic follicular papules and supervening purpuric features involving the arms and legs. The biopsy shows a pustular folliculocentric process.* ***C-D)*** *There is marked infiltration of the follicular ostium by neutrophils intimately admixed with compact keratin.* ***E)*** *The interfollicular epidermis reveals subtle features of a psoriasiform diathesis as characterized by lenticular-shaped foci of neutrophil imbued parakeratosis, and* ***F)*** *characteristic dilated capillaries lying in intimate apposition to the basal layer of the epidermis. H&E,* ***C)*** *200x,* ***D)*** *100x,* ***E)*** *200x,* ***F)*** *200x.*

along the dermal epidermal junction. A diagnosis of follicular psoriasis was made. The patient was placed on a TNF inhibitorwith clearing of the eruption. A remote history of psoriasis was subsequently established.

Case 2

A 77-year-old man presented with a widespread eruption present for several years. His past medical history was remarkable for hypertension treated with propranolol and hyperlipidemia. Clinical examination revealed typical widespread lesions of psoriasis with a micaceous scale and Auspitz sign. Recently the patient had also developed folliculocentric scaly lesions on a purpuric base, clinically suspicious for vasculitis (**Figure 2A)**. A biopsy was performed revealing a dilated hair follicle filled with keratin and many neutrophils (**Figure 2B)**. There was infiltration of the outer root sheath epithelium by neutrophils. The follicular ostium showed an absent granular cell layer with extensive infiltration of the periostial stratum corneum by neutrophils (**Figure 2C)**. The blood vessels in the adventitial dermis were dilated and demonstrated red cell extravasation with intrafollicular neutrophil entrapment (**Figure 2D)**. There was also focal infiltration of the adventitial dermis by eosinophils. A few dyskeratotic cells were noted in the follicular epithelium. The background epidermis demonstrated fully evolved changes of psoriasis, namely psoriasiform hyperplasia, granular cell layer loss, neutrophil-imbued parakeratosis, suprapapillary plate thinning, and classical psoriatic capillary changes (**Figure 2E)**. There was a superficial interstitial and perivascular lymphocytic and histiocytic infiltrate.

Case 3

The patient was a 72-year-old woman who presented with red, scaling patches and plaques over the anterior shins (**Figure 3A**, **B)** as well as a red scaling patch of the gluteal cleft. She had pitting of the right first, third, and fourth fingernails as well as the left first and fifth fingernails. The remainder of her skin examination revealed scattered verrucoid papules with horned cysts and photo-distributed tan lentigines.

The patient noted a history of a widespread rash in August 2016 that was diagnosed in November 2016 as an erythrodermic drug reaction leading to the discontinuation of citalopram and suvorexant with significant improvement. However, she continued to have involvement of the scalp, ears, and legs. The scalp and ear lesions were consistent with psoriasis (**Figure 3C**, **D)**. Patch testing performed in January 2018 revealed an allergic reaction to para-

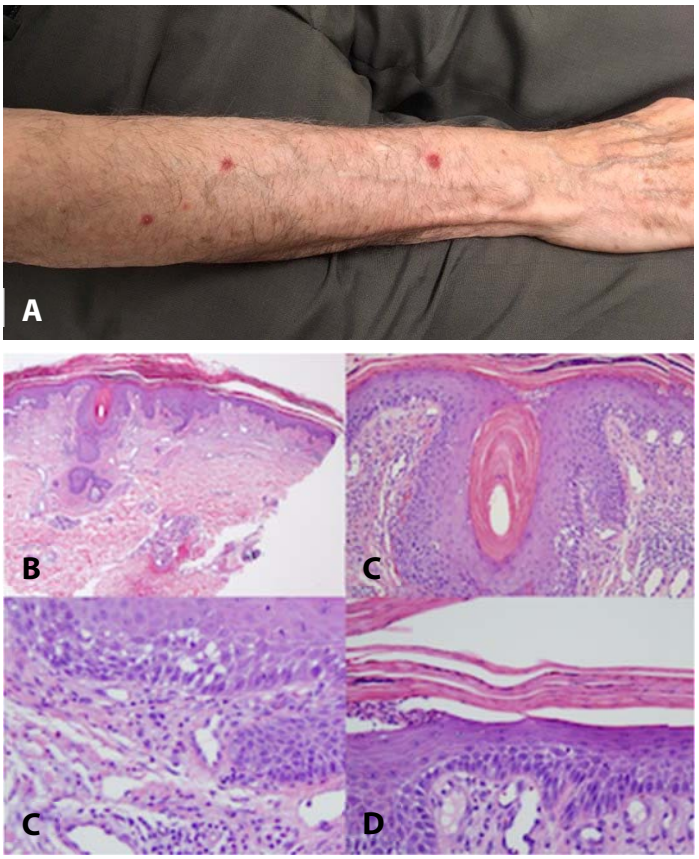

Figure 2. ***A)*** *Folliculocentric scaly lesions on a purpuric base, clinically suspicious for vasculitis.* ***B)*** *A biopsy was performed revealing a dilated hair follicle filled with keratin and many neutrophils. There was infiltration of the outer root sheath epithelium by neutrophils.* ***C)*** *The follicular ostium showed an absent granular cell layer with extensive infiltration of the periostial stratum corneum by neutrophils.* ***D)*** *The blood vessels in the adventitial dermis were dilated and demonstrated red cell extravasation with intrafollicular neutrophil entrapment. There was also focal infiltration of the adventitial dermis by eosinophils. A few dyskeratotic cells were noted in the follicular epithelium.* ***E)*** *The background epidermis demonstrated fully evolved changes of psoriasis, namely psoriasiform hyperplasia, granular cell layer loss, neutrophil-imbued parakeratosis, suprapapillary plate thinning and classical psoriatic capillary changes. There was a superficial interstitial and perivascular lymphocytic and histiocytic infiltrate. H&E,* ***B)*** *20x,* ***C)*** *200x,* ***D)*** *400x,* ***E)*** *400x.*

phenylenediamine and she subsequently discontinued dying her hair without significant improvement of the rash. More recently the patient developed a lower extremity scaly purpuric folliculocentric rash. She was treated with fluocinolone 0.01% scalp solution, tacrolimus 0.03% ointment to the face, and mometasone 0.1% ointment to the legs. She has started narrow-band ultraviolet therapy to the legs with some improvement.

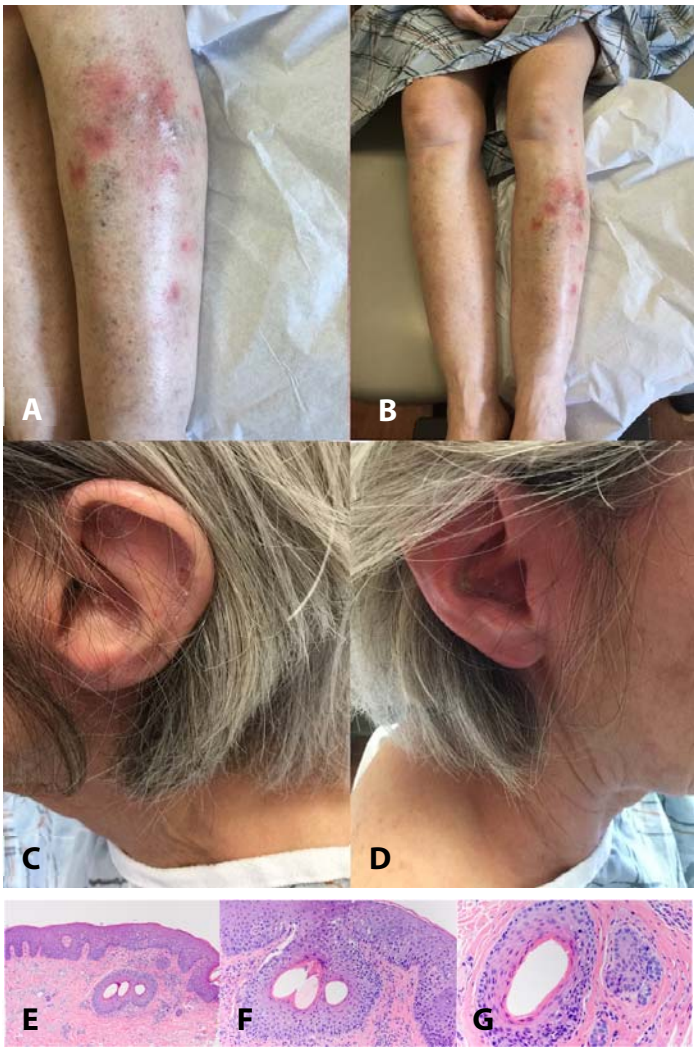

Figure 3. ***A-B****) Red, scaling patches and plaques over the anterior shins;* ***C-D****) in addition, there was involvement of scalp and ears.* ***E-G****) The epidermis exhibits a psoriasiform pattern of epidermal hyperplasia with loss of the granular cell layer and an overlying parakeratotic scale. There is an inflammatory cell infiltrate permeative of the outer root sheath epithelium of the hair follicle. There are a number of sebaceous glands which appear very atrophic. H&E,* ***E)*** *100x,* ***F)*** *400x,* ***G)*** *400x.*

A biopsy was performed of the lower extremity and showed a psoriasiform epidermal hyperplasia. The granular cell layer was diminished and the epidermis was surmounted by a parakeratotic scale. There was some infiltration of the epidermis by lymphocytes and neutrophils. The hair follicle was permeated by neutrophils. The neutrophilic reaction involved the ostium and the superficial isthmic part of the hair follicle. There was a folliculocentric mixed inflammatory cell infiltrate comprising a mixture of lymphocytes, histiocytes, and neutrophils accompanied by folliculocentric hemorrhage (**Figure 3E-G**). Overall the brunt of the inflammatory reaction was one that was folliculocentric with background psoriasiform epidermal changes. A few lymphocytes were present within the epidermis where they were localized to the basal layer of the epidermis. Some mild nuclear contour irregularity was noted but overall the lymphocytes were very well-differentiated. A very striking feature of the biopsy was the noticeable lack of sebaceous glands characteristic for the follicular involvement in the setting of psoriasis.

Case 4

The patient was a 66-year-old man who presented with a ten-year history of an intermittent eruption on his anterior calves (**Figure 4A**, **B)**. His past medical history was remarkable for hypercholesterolemia. In addition, there was a family history for psoriasis in the father. The patient complained of crusted plaques in the area that had intermittently been positive for *Staphylococcus aureus* and he had been treated with antibiotics with partial clearing. At times he had several pink patches in the axilla and inguinal folds. Patch test at that point showed a positive reaction to bacitracin and fragrance mix. The patient returned several years later with several pustules with an erythematous base on the anterior calves and again grew a positive culture for *Staphylococcus aureus*. The follicular eruption was persistent despite different oral and topical antibiotics, although the pustular component would resolve. Fungal culture was negative. The patient was then given a constellation of clindamycin, ammonium lactate lotion, and hydrocortisone lotion that appeared to control his disease. The patient again developed follicular erythema as well as a few pustules that

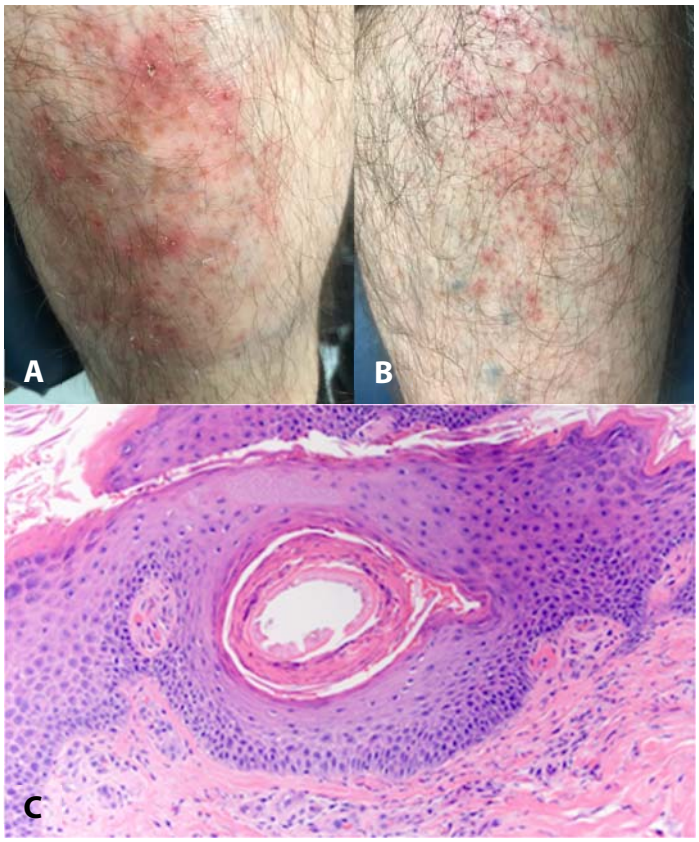

Figure 4. ***A-B)*** *Follicular eruption on his anterior calves.* ***C)*** *There is loss of the granular cell layer. The hair shaft is surrounded by keratin showing a few neutrophils. The capillaries are dilated and close to the follicular epithelium and basement membrane zone. H&E, 400x.*

grew *Staphylococcus aureus*. A complete blood count and comprehensive metabolic profile were within normal limits. The patient was given triamcinolone cream and was lost to followed up.

A biopsy of the left shin was centered around a follicle that was plugged with keratin. There was folliculocentric red cell extravasation, some component of neovascularization around the follicle, and rare eosinophils. Few neutrophils were also noted in close apposition to the hair shaft (**Figure 4C)**. The periodic acid-Schiff and Gram stains did not show pathogenic organisms.

Case 5

The patient was a 31-year-old woman with a past medical history of diabetes mellitus. Clinical examination revealed multiple red hemorrhagic appearing scaly plaques some having a silvery scale situated on her legs bilaterally (**Figure 5A-E**). Her eruption was unresponsive to topical therapy and antibiotics. A previous biopsy was compatible with folliculitis.

A repeat biopsy showed psoriasiform reaction with striking folliculocentricity and hyperplastic epithelial changes. There was infiltration of the outer root sheath epithelium by neutrophils. The follicular canal was filled with neutrophils and parakeratin. The adjacent epidermis showed classic features of a psoriatic diathesis as revealed by psoriasiform hyperplasia with granular cell layer loss and neutrophil imbued parakeratosis. The capillaries in intimate apposition to the follicle were markedly dilated, lying in intimate apposition to the peripheral layers of the outer root sheath epithelium, defining a classic folliculocentric psoriatic capillary diathesis. Owing to the concomitant red cell extravasation there was also elimination of blood into the follicular canal. Prominent lack of sebaceous glands was also noted (**Figure 5F-H**). Periodic acid-Schiff stain did not show pathogenic organisms.

Discussion

We have presented five patients with diagnostic features of FP. As expected, there was an excellent response to biologic therapy. The first paper referring to follicular psoriasis was published by Michelson in 1958; the index cases were children. Stankler and Ewen subdivided FP into two broad categories: the adult type and juvenile type [6]. The adult group comprised five women and one man, ranging in age from 18 to 69 years of age. All patients had a prior diagnosis of psoriasis and manifested bilateral follicular lesions on the thighs in a background of more conventional lesions of psoriasis vulgaris. The juvenile group comprised one girl and three boys, below the age of 10 years. A prior diagnosis of psoriasis under the age of 10 was rendered in all four patients. This group presented with asymmetric plaque-like follicular lesions on the trunk and axilla.

In the series of FP by Ploysangam and Mutasim, four women and one man ranging in age from 23 to 73 years, had clinical symptoms of erythematous

hyperkeratotic follicular papules on the trunk and extremities [7]. Only two patients had a prior history of psoriasis, both exhibiting a peculiar localization of psoriasis to the scalp. There appeared to be an association with diabetes mellitus and African ancestry.

There are several additional anecdotal case reports describing FP. In particular, Arps et al. described a 46-year-old diabetic African American woman with symptomatic pruritic folliculocentric hyperkeratotic papules on the scalp, neck, back, and extremities [8]. This patient had no previous diagnosis of psoriasis and lacked the classical findings for psoriasis vulgaris. Thomas et al. presented a case in an 18-year-old Asian male who exhibited bilateral follicular lesions involving the thighs, calves, and arms, initially misinterpreted as lichen planopilaris [9]. Patil et al. described a 13-year-old boy with symptomatic scaling and erythema of the skin that began as horny papules on the knees and elbows that evolved into erythematous scaly papules encompassing the entire body [10]. Our patients had lesions on the arms similar to the extremity distribution seen in other cases of FP. The clinical presentations and microscopic examinations in the previously described reports were similar to the findings in our cases. A summary of these 25 cases is presented in **Table 1** [6-10].

The characteristic and reproducible biopsy findings in FP include folliculocentric neutrophilia of the outer root sheath epithelium with concomitant follicular hyperkeratosis in the absence of any demonstrable pathogenetic bacteria or fungi. The acquisition of dilated tortuous psoriatic capillaries is observed within the adventitial dermis and can be associated with folliculocentric hemorrhage, which can present clinically as follicular-based purpura.

Sterile neutrophilic follicular reaction is not unique to FP and can be seen in a diverse spectrum of conditions encompassing corticosteroid acne, corticosteroid rosacea, and the sterile neutrophilic folliculitis seen in certain autoimmune and autoinflammatory conditions, including inflammatory bowel disease, Behcet disease, and folliculocentric acute generalized exanthematous pustulosis. Among the distinctive features that would suggest FP are the absence of folliculocentric vasculitic changes (although there can be folliculocentric hemorrhage), the presence of compact follicular hyperkeratosis, the intimate association of neutrophils and keratin to produce a cohesive cellular neutrophil-imbued pattern of

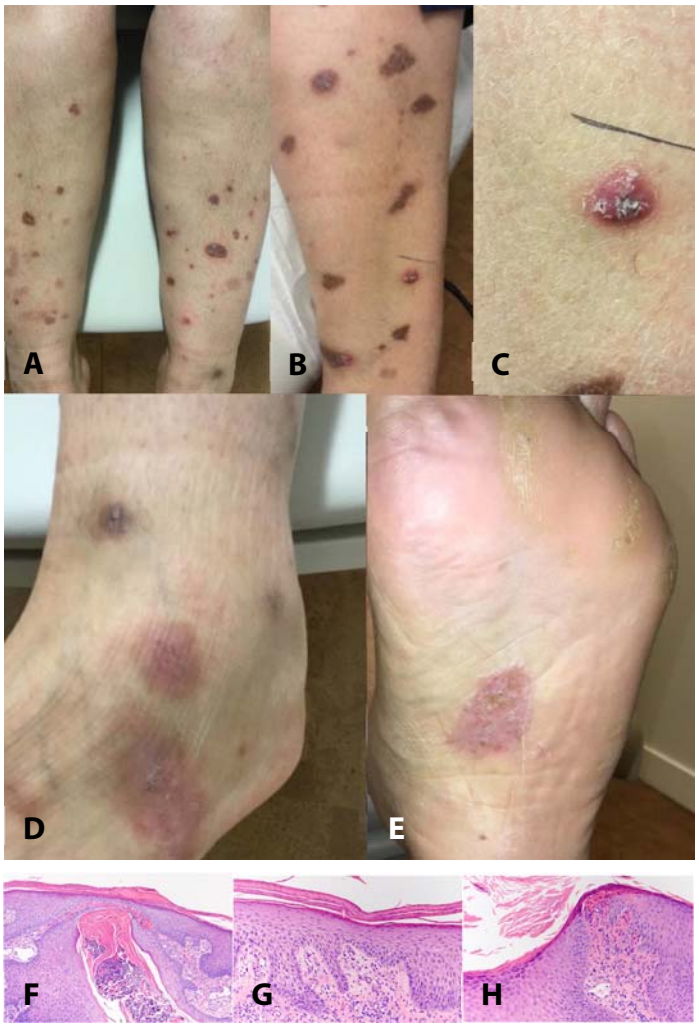

Figure 5. ***A-E****) Multiple red hemorrhagic appearing scaly plaques, some having a silvery scale situated on her legs bilaterally.* ***F-H****) The biopsy shows a neutrophilic folliculitis whereby there is infiltration of the outer root sheath epithelium by neutrophils with an adjacent perifollicular psoriatic diathesis. The granular cell layer in the superficial isthmic part of the follicle is absent; there are markedly ectatic capillaries within the adventitial dermis in close apposition to the outer root sheath epithelium; sebaceous glands are not discernible. The intervening epidermis exhibits features of a psoriasiform diathesis characterized by markedly attenuated suprapapillary plates in association with an increase in dermal papillae vascularity along with capillary dilatation. There are classic psoriasis-like features involving the interfollicular epidermis as revealed by the pattern of epidermal hyperplasia, granular cell layer loss and an overlying confluent parakeratotic scale. H&E,* ***F)*** *200x,* ***G)*** *200x,* ***H)*** *200x.*

follicular hyperkeratosis, and an absent granular cell layer in the follicular ostium and the perifollicular epidermis. Other considerations could include pityriasis rubra pilaris, inflammatory keratosis pilaris, and scurvy. In the setting of pityriasis rubra pilaris there would be a noticeable lack of folliculocentric neutrophilic infiltration and the distinctive psoriatic capillary changes would also not be present. In inflammatory keratosis pilaris the follicular hyperkeratosis is primarily a laminated one devoid of parakeratosis. In addition, the dominant infiltrate is a lymphohistiocytic one. As far as scurvy is concerned the hair shaft is coiled, resulting in follicular distortion and oblique malalignment. There is a noticeable lack of inflammation apart from a nonspecific mononuclear one.

Sebaceous gland atrophy has been emphasized as a feature unique to hair follicle involvement in the setting of psoriasis with most descriptions occurring in the context of scalp psoriasis including cases of psoriatic alopecia. This has not been emphasized in FP [11]. Since FP specifically includes an anatomic location not involving the scalp, the frequency of sebaceous gland atrophy is not known.

Although the basis for the folliculocentricity of this variant of psoriasis is unclear it is well established that many other primary autoimmune conditions that primarily target the epidermis can exhibit a follicular component. These include lupus erythematosus, lichen planus, and pityriasis rubra pilaris. The hair follicle is a site of preferential antigenic processing and is enriched in immune cells that enhance both the adaptive and innate limbs of immunity involving plasmacytoid, myeloid, dendritic, and Langerhans cells.

Conclusion

Follicular psoriasis is a rare form of psoriasis that involves the trunk and extremities and needs to be distinguished from classic psoriasis. Although it occurs most commonly in patients with a history of psoriasis there are de novo presentations. The lesions are distinctive and in fact do not resemble conventional psoriasis; they are recognizably

Table 1. *Summary of clinical presentations and microscopic examinations in the previously described reports of follicular psoriasis.*

Year	Author	Clinical Presentation	Histologic Findings
1981	Stankler et al. [6]	- Adult group: Bilateral follicular lesions on the thighs - Juvenile group: Asymmetrical follicular plaque lesions affecting the trunk and axillae	- Early lesions: Follicular plugging with a perivascular and perifollicular infiltrate of lymphocytes and mast cells - Older lesions: Follicular plugging with marked parakeratosis of the ostium; contiguous with the ostium the adjacent epidermis was mildly hyperplastic with loss of the stratus granulosum
1997	Ploysangam et al. [7]	Widespread discrete, erythematous, round hyperkeratotic papules measuring 2-4 mm in diameter on the torso and extremities	Acanthotic follicular epithelium with thinning or loss of the granular layer. Follicular hyperkeratotic plugging with parakeratosis containing neutrophils. Psoriatic acanthosis of epidermis contiguous with the ostium with sparse dermal perivascular lymphocytic infiltrate
2010	Arps et al. [8]	Asymptomatic symmetrical follicular lesions on the thighs, calves, and arms	Dilated central hair follicle with parakeratotic plugging and discrete areas of granular cell layer loss in the ostial-infundibular epidermis with a neutrophilic infiltrate
2013	Thomas et al. [9]	Pruritic follicular-based hyperkeratotic papules on the scalp, neck, back, and extremities, occurring singly or in clusters	Distended follicular infundibula with parakeratotic scale admixed with neutrophils. Mild acanthosis and hypogranulosis of infundibular epithelium
2014	Patil et al. [10]	Dark rough horny papules on the knees and elbows that became diffuse erythematous scaly papules	Follicular plugging and ostial parakeratosis with adjacent epidermis exhibiting classic changes of a psoriatic diathesis including parakeratosis, hypogranulosis, elongated rete ridges with dermal papillary hyperplasia, suprapapillary plate thinning and dermal neutrophilic infiltrates

follicular-based and show folliculocentric purpura along with hyperkeratosis. Rather than follicular psoriasis the clinical considerations encompass scurvy and vasculitis. The therapeutic interventions target the proinflammatory pathways that are pathogenetically relevant to psoriasis.

References

1. Greb JE, Goldminz AM, Elder JT, et al. *Nat Rev Dis Primers* 2016;2:16082. [PMID: 27883001].
2. Theeuwes, M, Morhenn V. Allelic instability in the mitosis model and the inheritance of psoriasis. *J Am Acad Dermatol* 1995;32:44-52. [PMID: 78228516].
3. Zheng CJ, Thomson G, Peng, YN. Allelic instability in mitosis can explain "genome imprinting" and other genetic phenomena in psoriasis. *Am J Med Genet* 1994;51:163-164. [PMID: 8092195].
4. Grine L, Dejager L, Libert C, et. al. An inflammatory triangle in psoriasis: TNF, type I IFNs and IL17. *Cytokine Growth Factor Rev* 2015;26:25-33. [PMID: 25434285].
5. Langley RG, Krueger GG, Griffiths CE. Psoriasis: epidemiology, clinical features, and quality of life. *Ann Rheum Dis* 2005;64 Suppl 2: ii18-23; discussion ii24-5. [PMID: 15708928].
6. Stankler L, Ewen SW. Follicular psoriasis. *Br J Dermatol* 1981;104:153-6. [PMID: 7213548].
7. Ploysangam T, Mutasim DF. Follicular psoriasis: an under-reported entity. *A report of five cases*. Br J Dermatol. 1997;137:988-91. [PMID: 9470921].
8. Arps DP, Chow C, Lowe L, et al. Follicular psoriasis. *J Cutan Pathol* 2013;40:860-862. [PMID: 24074364].
9. Thomas LJ, Dadzie OE, Francis N, et. al. Follicular psoriasis – a forgotten entity? *Open Dermatol J* 2010;4:95-6. [DOI: 10.2174/1874372201004010095].
10. Patil JD, Chaudhary SS, Rani N, et al. Follicular psoriasis causing erythroderma in a child: A rare presentation. *Indian Dermatol Online* J 2014;5:63-5. [PMID: 24616860].
11. Werner B, Brenner FM, Böer A. Histopathologic study of scalp psoriasis: peculiar features including sebaceous gland atrophy. *Am J Dermatopathol* 2008;30:93-100. [PMID: 18360109].