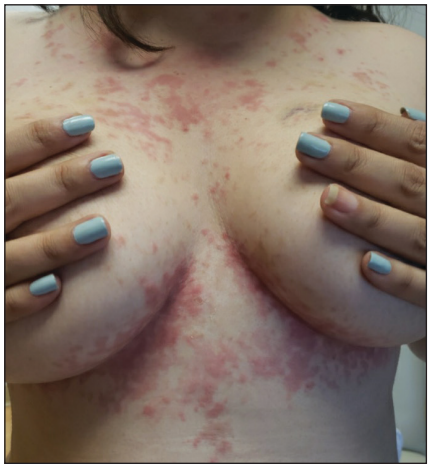
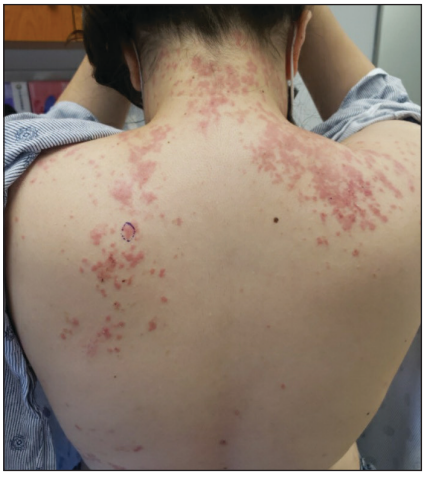
Papular Reticulated Rash

Benjamin E. Swaby, MD; Erisa Alia, MD; Michael A. Cardis, MD





An otherwise healthy 22-year-old woman presented with a painful eruption with burning and pruritus that had been slowly worsening as it spread over the last 4 weeks. The rash first appeared on the lower chest and inframammary folds (top) and spread to the upper chest, neck, back (bottom), arms, and lower face. Physical examination revealed multiple ill-defined, erythematous papules, patches, and plaques on the chest, back, neck, and upper abdomen. Individual lesions coalesced into plaques that displayed a reticular configuration. There were no lesions in the axillae. The patient had been following a low-carbohydrate diet for 4 months. A punch biopsy was performed.

WHAT'S YOUR **DIAGNOSIS?**

a. Galli-Galli disease
b. Hailey-Hailey disease
c. papular pityriasis rosea
d. prurigo pigmentosa
e. subacute cutaneous lupus erythematosus

PLEASE TURN TO PAGE E9 FOR THE DIAGNOSIS

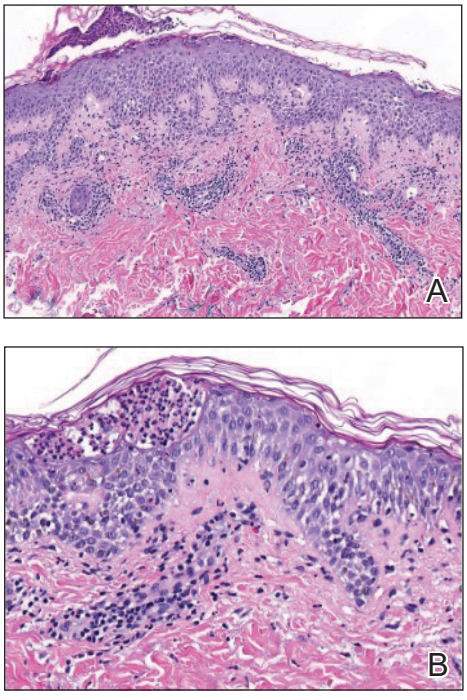
Dr. Swaby is from the Georgetown University School of Medicine, Washington, DC. Drs. Alia and Cardis are from the Department of Dermatology, MedStar Georgetown University Hospital and MedStar Washington Hospital Center, Washington, DC.
The authors report no conflict of interest.
Correspondence: Michael A. Cardis, MD, MedStar Washington Hospital Center, 110 Irving St NW, Washington, DC 20010 (Michael.A.Cardis@medstar.net).
doi:10.12788/cutis.0774

THE **DIAGNOSIS:** Prurigo Pigmentosa

Histopathology of the punch biopsy revealed subcorneal collections of neutrophils flanked by a spongiotic epidermis with neutrophil and eosinophil exocytosis. Rare dyskeratotic keratinocytes were identified at the dermoepidermal junction, and gram-positive bacterial organisms were seen in a follicular infundibulum with purulent inflammation. The dermis demonstrated a mildly dense superficial perivascular and interstitial infiltrate composed of lymphocytes, histiocytes, scattered neutrophils, and eosinophils (Figure).

Given the combination of clinical and histologic findings, a diagnosis of prurigo pigmentosa (PP) was rendered and a urinalysis was ordered, which confirmed ketonuria. The patient was started on minocycline 100 mg twice daily and was advised to reintroduce carbohydrates into her diet. Resolution of the inflammatory component of the rash was achieved at 3-week follow-up, with residual reticulated postinflammatory hyperpigmentation.

Prurigo pigmentosa is a rare, albeit globally underrecognized, inflammatory dermatosis characterized by pruritic, symmetric, erythematous papules and plaques on the chest, back, neck, and rarely the arms and forehead that subsequently involute, leaving reticular postinflammatory hyperpigmentation.[1]



A and B, Histopathology revealed subcorneal neutrophils, a spongiotic epidermis, and dermal infiltrates with a mildly dense superficial perivascular and interstitial infiltrate (H&E, original magnifications ×10 and ×20).

Prurigo pigmentosa is predominant in females (2.6:1 ratio). The mean age at presentation is 24.4 years, and it most commonly has been documented among populations in Asian countries, though it is unclear if a genetic predilection exists, as reports of PP are increasing globally with improved clinical awareness.[1,2]

The etiology of PP remains unknown; however, associations are well documented between PP and a ketogenic state secondary to uncontrolled diabetes, a low-carbohydrate diet, anorexia nervosa, or bariatric surgery.[3] It is theorized that high serum ketones lead to perivascular ketone deposition, which induces neutrophil migration and chemotaxis,[4] as substantiated by evidence of rash resolution with correction of the ketogenic state and improvement after administration of tetracyclines, a drug class known for neutrophil chemotaxis inhibition.[5] Improvement of PP via these treatment mechanisms suggests that ketone bodies may play a role in the pathogenesis of PP.

Interestingly, Kafle et al[6] reported that patients with PP commonly have bacterial colonies and associated inflammatory sequelae at the level of the hair follicles, which suggests that follicular involvement plays a role in the pathogenesis of PP. These findings are consistent with our patient's histopathology consisting of gram-positive organisms and purulent inflammation at the infundibulum. The histopathologic features of PP are stage specific.[1] Early stages are characterized by a superficial perivascular infiltrate of neutrophils that then spread to dermal papillae. Neutrophils then quickly sweep through the epidermis, causing spongiosis, ballooning, necrotic keratocytes, and consequent surface epithelium abscess formation. Over time, the dermal infiltrate assumes a lichenoid pattern as eosinophils and lymphocytes invade and predominate over neutrophils. Eventually, melanophages appear in the dermis as the epidermis undergoes hyperplasia, parakeratosis, and hyperpigmentation.[1] The histologic differential diagnosis for PP is broad and varies based on the stage-specific progression of clinical and histopathologic findings.

Similar to PP, subacute cutaneous lupus erythematosus has a female predominance and resolves with subsequent dyspigmentation; however, it initially is characterized by annular plaques with central clearing or papulosquamous lesions restricted to sun-exposed skin. Photosensitivity is a prominent feature, and roughly 50% of patients meet diagnostic criteria for systemic lupus erythematosus.[7] Histopathology shows interface changes with increased dermal mucin and a perivascular lymphoplasmacytic inflammatory infiltrate.

Papular pityriasis rosea can present as a pruritic papular rash on the back and chest; however, it most

commonly is associated with a herald patch and typically follows a flulike prodrome.[8] Biopsy reveals mounds of parakeratosis with mild spongiosis, perivascular inflammation, and extravasated erythrocytes.

Galli-Galli disease can present as a pruritic rash with follicular papules under the breasts and other flexural areas but histopathologically shows elongated rete ridges with dermal melanosis and acantholysis.[9]

Hailey-Hailey disease commonly presents in the third decade of life and can manifest as painful, pruritic, vesicular lesions on erythematous skin distributed on the back, neck, and inframammary region, as seen in our case; however, it is histopathologically associated with widespread epidermal acantholysis unlike the findings seen in our patient.[10]

First-line treatment of PP includes antibiotics such as minocycline, doxycycline, and dapsone due to their anti-inflammatory properties and ability to inhibit neutrophil chemotaxis. In patients with nutritional deficiencies or ketosis, reintroduction of carbohydrates alone has been effective.[5,11]

Prurigo pigmentosa is an underrecognized inflammatory dermatosis with a complex stage-dependent clinicopathologic presentation. Clinicians should be aware of the etiologic and histopathologic patterns of this unique dermatosis. Rash presentation in the context of a low-carbohydrate diet should prompt biopsy as well as treatment with antibiotics and dietary reintroduction of carbohydrates.

REFERENCES

1. Böer A, Misago N, Wolter M, et al. Prurigo pigmentosa: a distinctive inflammatory disease of the skin. *Am J Dermatopathol*. 2003;25:117-129. doi:10.1097/00000372-200304000-00005
2. de Sousa Vargas TJ, Abreu Raposo CM, Lima RB, et al. Prurigo pigmentosa: report of 3 cases from Brazil and literature review. *Am J Dermatopathol*. 2017;39:267-274. doi:10.1097/DAD.0000000000000643
3. Mufti A, Mirali S, Abduelmula A, et al. Clinical manifestations and treatment outcomes in prurigo pigmentosa (Nagashima disease): a systematic review of the literature. *JAAD Int*. 2021;3:79. doi:10.1016/J.JDIN.2021.03.003
4. Beutler BD, Cohen PR, Lee RA. Prurigo pigmentosa: literature review. *Am J Clin Dermatol*. 2015;16:533-543. doi:10.1007/S40257-015-0154-4
5. Chiam LYT, Goh BK, Lim KS, et al. Prurigo pigmentosa: a report of two cases that responded to minocycline. *Clin Exp Dermatol*. 2009;34. doi:10.1111/J.1365-2230.2009.03253.X
6. Kafle SU, Swe SM, Hsiao PF, et al. Folliculitis in prurigo pigmentosa: a proposed pathogenesis based on clinical and pathological observation. *J Cutan Pathol*. 2017;44:20-27. doi:10.1111/CUP.12829
7. Sontheimer RD. Subacute cutaneous lupus erythematosus: 25-year evolution of a prototypic subset (subphenotype) of lupus erythematosus defined by characteristic cutaneous, pathological, immunological, and genetic findings. *Autoimmun Rev*. 2005;4:253-263. doi:10.1016/J.AUTREV.2004.10.00
8. Leung AKC, Lam JM, Leong KF, et al. Pityriasis rosea: an updated review. *Curr Pediatr Rev*. 2021;17:201-211. doi:10.2174/1573396316666200923161330
9. Sprecher E, Indelman M, Khamaysi Z, et al. Galli-Galli disease is an acantholytic variant of Dowling-Degos disease. *Br J Dermatol*. 2007;156:572-574. doi:10.1111/J.1365-2133.2006.07703.X
10. Burge SM. Hailey-Hailey disease: the clinical features, response to treatment and prognosis. *Br J Dermatol*. 1992;126:275-282. doi:10.1111/J.1365-2133.1992.TB00658
11. Lu L-Y, Chen C-B. Keto rash: ketoacidosis-induced prurigo pigmentosa. *Mayo Clin Proc*. 2022;97:20-21. doi:10.1016/j.mayocp.2021.11.019