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Cover Quizlet

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Figures 1 and 2 are depicted on the journal cover.

Figure 3.

Figure 4.

Figure 5.

Figure 6.

Your diagnosis?

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Figure 7.

Figure 8.

Figure 9.

Your diagnosis?

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Prurigo Pigmentosa: An under-recognized inflammatory dermatosis characterized by an evolution of distinctive clinicopathological features

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Dr Satter, Rozelle and Sperling had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drafting of the manuscript and critical revision of the manuscript for important intellectual content was performed by Dr Satter, Rozelle and Sperling. Study concept, design and statistical analysis: N/A case report Interpretation of data: Dr Satter, Rozelle and Sperling. No administrative, technical, or material support was provided. No funding was obtained and the authors have no financial disclosures or conflicts of interest to report.

Prurigo pigmentosa (PP) was originally described 45 years ago, yet because of its variable histopathological manifestations it remains an under-recognized inflammatory dermatosis clinically characterized by recurrent pruritic, erythematous macules, urticarial papules and papulovesicles that eventuate in symmetric reticulated pigmentation.¹ Although the majority of cases have been reported in women of Asian descent, it also has been described in various ethnicities worldwide. Of the approximately 400 reported cases of PP, fewer than 10 have been reported from the United States.^{1–7}

Due to the relative rarity of this condition, we present two cases from the United States to illustrate the clinicopathological spectrum of PP. Both patients were healthy young women who presented with recurrent episodes of pruritic erythematous macules and subsequently developed urticarial plaques, papules and/or papulovesicles which eventuated in reticulated

pigmentation. The clinical and histological findings for these patients are summarized in Table 1.

Clinically PP presents as a recurrent intensely pruritic, symmetrically distributed eruption located on the neck, chest, upper back, lumbosacral region and abdomen, and more rarely, the forehead or arms. To date, there are no reports of mucous membrane involvement.^{5,7} The lesions tend to progress through several stages of development, initially starting as erythematous macules which then evolve to urticarial papules and papulovesicles. Subsequently the lesions become crusted or scaly and within a few weeks spontaneously resolve, leaving behind reticulated pigmentation. Due to the recurrent nature of the eruption, patients often have multiple lesions at various stages of development.¹ The clinical differential diagnosis is broad, but the distribution of the lesions and the reticulated pattern helps narrow the possibilities.

Cover Quizlet

Table 1. Clinicohistopathological presentations of patients 1 and 2

	Patient 1	Patient 2
Clinical Findings		
Ethnicity	Palestinian descent	Mexican descent
Duration	24-36 months	29-months
Anatomic location	Chest (Figs. 1 and 3)	Central chest and breast (Fig. 6), flank, sacrum, buttock (Fig. 7) and focally on left elbow
Exacerbating factors	Pregnancy	Heat and exercise
Serological findings	None	Elevated WBC with left shift
Treatments	Minocycline-improvement	Topical steroids-minimal benefit. Minocycline-resolution
Histopathological findings		
Evolving lesion:	Mild spongiosis, sparse perivascular infiltrate and dermal edema. (Fig. 4)	
Early lesions:	Superficial dermal mixed inflammatory infiltrate associated with neutrophilic spongiosis. (Fig. 2)	Epidermal spongiosis associated with a perivascular lymphocytic infiltrate and focal vacuolar degeneration.
Fully developed lesions	Dense mixed dermal infiltrate associate with combined balloon degeneration and spongiosis, and clusters of necrotic keratinocytes. (Fig. 5)	Brisk vacuolar degeneration with numerous apoptotic keratinocytes often concentrated near acrosyringium. Superficial perivascular lymphocytic infiltrate with increased eosinophils. (Fig. 8)
Resolving/late lesions	Mild spongiosis and a sparse perivascular lymphocytic infiltrate.	Parakeratosis, focal apoptotic keratinocytes, and a superficial perivascular lymphocytic infiltrate containing melanophages. (Fig. 9)

Although the histopathological findings were originally felt to be nonspecific, distinctive histological features have now been identified for each clinical stage.^{1,8–11,13,17} Early lesions present as pruritic erythematous macules or urticarial papules, and a biopsy from lesions at this stage shows a sparse, perivascular and interstitial, predominantly neutrophilic infiltrate involving the superficial dermis with focal epidermal exocytosis and variable papillary dermal edema. Fully developed lesions manifest as excoriated papules, vesicles, and papulovesicles which corresponds histologically to varying degrees of spongiosis accompanied by ballooning associated with epidermal necrosis and focal collections of neutrophils. The dermal inflammatory infiltrate at this stage is denser, and often mixed, with increased numbers of lymphocytes, neutrophils and scattered eosinophils. In late lesions, there is slight epidermal spongiosis and focal parakeratosis associated with a mild superficial perivascular lymphocytic infiltrate and variable vacuolar degeneration. Often scattered apoptotic keratinocytes and melanophages are readily found. Therefore, the findings in any given biopsy are reflective of the clinical stage of the lesion, and represent only a single point on an evolving continuum of clinical and histologic features.

Depending on the stage of development, the histopathological differential diagnosis includes dermatitis herpetiformis, irritant contact dermatitis, linear IgA disease, neutrophilic dermatoses, erythema multiforme, adult onset Still's disease, as well as various spongiotic and interface dermatitides.^{1,3,6} Although the reticulated pigmentation can be clinically impressive, histologically it is non-distinctive, showing only a superficial perivascular lymphocytic infiltrates associated pigment-laden macrophages, which is indistinguishable from other inflammatory dermatoses resulting in postinflammatory hyperpigmentation.¹ Therefore, accurate diagnosis requires detailed clinicopathological correlation with attention to the dynamic clinical and histopathological course of the disease.

The etiopathogenesis is unknown, but various hypothesizes have been postulated and include friction, contact allergens, photosensitivity, infectious agents, and metabolic disorders such as diabetes mellitus, fasting, anorexia and ketosis.^{1,3,5,9,11,14} To date, none have shown a consistent causal relationship; however, symptoms are often exacerbated by hot weather and/or sweating.^{1,5,13} There have been a few case reports of PP associated with other diseases, including autoimmune conditions, adult-onset Still's disease, atopy and pregnancy; however,

Fig. 1. Erythematous, raised clustered and reticulated papules on the chest of Patient 1.

Fig. 2. Biopsy specimen from a relatively “early” lesion of Patient 1 showing diffuse epidermal spongiosis, lymphocytic exocytosis, and subcorneal collections of neutrophils. The upper dermal infiltrate is comprised of lymphocytes, neutrophils, and a few eosinophils.

these associations may merely be coincidental rather than causative.^{1,5,12–15} Ilkovitch and Patton recently posited PP might represent an inflammatory variant of confluent and reticulated papillomatosis,¹⁶ but that hypothesis is not supported histologically and those conditions are quite distinct.

Most patients with PP experience spontaneous resolution, followed by recurrent episodes of exacerbations that can last months to years.^{1,9,11} The condition responds well to minocycline, doxycycline and dapsone, presumably due to the anti-inflammatory properties of these medications, as well as inhibition of the migration and function of neutrophils.^{1,5,9,18,19} Yet notably, the condition does not respond to treatment with

corticosteroids or anti-histamines.^{1,5} Lastly, there has been one report of 2 patients who responded well to weekly Jessner’s peels and irradiation with an 830-nm light emitting diode.²⁰

In conclusion, although PP is an uncommon inflammatory dermatoses it can be readily recognized by its distinctive clinicopathological features. Awareness of the dynamic changes that occur over the course of the eruption is essential to make an accurate diagnosis.

Fig. 3. Close-up view of Figure 1 which better demonstrates the reticulate pattern and overlying focal scaling and crusting.

Fig. 4. Biopsy of an evolving lesion from Patient 1 showing a normal basket weave stratum corneum overlying a mildly spongiotic epidermis. Within the superficial dermis there is a sparse perivascular superficial lymphocytic infiltrate associated with moderate papillary dermal edema.

Fig. 5. A fully developed lesion from Patient 1 showing a moderately dense perivascular and interstitial mixed inflammatory infiltrate composed of lymphocytes, neutrophils and rare eosinophils. The inflammatory infiltrate extends into the overlying epidermis which exhibits a combination of balloon degeneration and spongiosis associated with clusters of necrotic keratinocytes.

Fig. 6. Reticulated erythematous and hyperpigmented plaques on the chest of Patient 2.

Fig. 7. Patient 2 showing mature erythematous papules on the left flank and right lateral buttock as well as late hyperpigmented reticulated plaques on the sacrum.

Fig. 8. Biopsy from a relatively “mature” erythematous papule from the buttock of Patient 2. Massive spongiosis and lymphocytic exocytosis has progressed to reticular degeneration of the upper epidermis. The dermal infiltrate is moderately dense and composed of perivascular lymphocytes.

Fig. 9. A relatively “late” lesion from the sacrum from Patient 2. There is parakeratosis, focal necrotic keratinocytes, vacuolar interface alteration, and a predominantly lymphocytic upper dermal infiltrate. In such “late” lesions, upper dermal pigment incontinence is often found.

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