Prurigo Pigmentosa after a Strict Ketogenic Diet

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Abstract: Prurigo pigmentosa (PP) is a rare inflammatory dermatosis of unknown cause characterized by a predominantly truncal eruption of pruritic erythematous papules in a reticular pattern, resolving with hyperpigmentation. PP is twice as common in girls and women, and the mean age at onset is 25 years. Diagnosis of PP is challenging and is aided by characteristic histopathologic findings. We report a case of PP in a 17-year-old white boy. The eruption arose during strict adherence to a ketogenic diet.

A previously healthy 17-year-old white boy presented with a 2-week history of a mildly pruritic rash on the chest, upper back, and abdomen accompanied by acute onset of arthralgias and arthritis of the knees, elbows, wrists, and ankles. Before transferring to our institution, the boy was evaluated at an outside hospital and was believed to have dermatomyositis, which prompted treatment with a single 1.5-mg/kg dose of intravenous methylprednisolone. This treatment dramatically improved his joint condition within 72 hours, but his rash persisted.

On clinical examination, countless poorly marginated, 3- to 4-mm scaly pink papules were present on the central middle and upper back and coalesced into a larger reticulated plaque (Fig. 1). Superficial erosions were observed throughout the larger plaque and at its periphery. Biopsy specimens were obtained from representative lesions of the upper back.

Histopathologic examination revealed intraepidermal vesicles underlying a basket-woven stratum corneum (Fig. 2). Neutrophils and eosinophils filled the vesicles and infiltrated the epidermis as single cells (Fig. 3). Apoptotic keratinocytes were scattered throughout the lower levels of the epidermis (Fig. 4). The dermis contained a superficial and deep infiltrate of neutrophils, eosinophils, and lymphocytes. Direct immunofluorescence was negative for autoimmune blistering disorders.

Laboratory studies including complete blood cell count, comprehensive metabolic panel, immunofixation electrophoresis, erythrocyte sedimentation rate, and C-reactive protein, creatine kinase, lactate dehydrogenase, and aldolase levels completed during hospitalization were within reference limits. Serologic testing was negative for Epstein-Barr virus, cytomegalovirus, parvovirus B19, hepatitis B and C.
mycoplasma pneumonia, anti-DNAse B, antistreptolysin O, Coccidioides spp., and syphilis through rapid plasma reagin. An autoimmune evaluation, including antinuclear antibody, C3, C4, antiproteinase-3 antibody, and antomyeloperoxidase antibody, revealed no abnormalities.

The patient was monitored closely for several months, during which time his rash waxed and waned in severity. It was learned at a follow-up appointment that he had consumed a diet almost completely devoid of carbohydrates for the past year. He was referred to a dietitian, who instituted a balanced diet including carbohydrates. He concurrently started 2 months of treatment with doxycycline at a dose of 100 mg twice daily.

Within a week his rash improved significantly (Fig. 5) and has not recurred during 15 months of follow-up, during which time he has maintained his carbohydrate-replete diet. The arthritis observed on presentation never recurred and ultimately was attributed to a viral origin, although no specific viral etiology was found. Taken together, the clinical, histopathologic, and laboratory examinations and his response to diet modification and tetracycline-class antibiotic therapy support the diagnosis of prurigo pigmentosa (PP).

**DISCUSSION**

More than 250 cases of PP have been reported since Nagashima et al (1) first described it in 1971, largely in the Japanese population (2–4). PP is observed at least twice as commonly in girls and women as in boys and men, and it typically presents at a mean age of 25 years, with no family history of the disease (2–5).
Prurigo pigmentosa is a pruritic dermatosis characterized by recurrent erythematous papules distributed on the back, chest, and neck and converging into a reticular pattern. Vesicular variants have been reported and in most cases the eruption resolves with mottled hyperpigmentation (2,3,6).

Although the etiologic factors of PP are unclear, it has been associated with several exogenous factors, including physical trauma, friction from clothing, and acupuncture (7). The long-term relapsing nature of PP has led to conjecture of a viral pathogenesis, but association with herpes simplex virus 1, herpes simplex virus 2, and human herpesvirus 6 has been disproven (8). Of particular interest in our case, PP has been associated with metabolic derangements, including those observed in ketosis (diet-induced or diabetes mellitus–associated ketosis), anorexia nervosa, and rapid weight loss (9–12). As in previous reports, upon diet modification, our patient had rapid resolution of his PP without subsequent recurrence (12). Our patient had evidence of reference blood glucose levels. Ketone levels were not obtained during his examination.

The histopathologic characteristics of PP are distinctive and have been described as rapidly evolving through three phases (2). The initial phase shows a superficial, perivascular infiltration of neutrophils, followed by neutrophil collections in the papillary dermis and epidermis. The second phase shows neutrophilic spongiosis, microabscesses, and balloonning degeneration of keratinocytes. The third and final phase shows a lichenoid infiltrate composed of eosinophils and lymphocytes and basal layer vacuolization. Later lesions show parakeratosis and melanophages scattered throughout the papillary dermis.

The inflammation of PP is believed to be largely attributable to neutrophilic infiltrate—a notion that the histopathologic findings and the disease response to dapsone and tetracycline-class antibiotics bolster. Minocycline and dapsone inhibit neutrophil chemotaxis, downregulate matrix metalloprotease activity, decrease proinflammatory cytokine production (e.g., tumor necrosis factor-α, interleukin-1β), and inhibit neutrophil myeloperoxidase, leading to impairment of the respiratory burst. Doxycycline has recently replaced minocycline because it has fewer adverse effects and offers similar therapeutic benefit (8,13).

Additional treatments with reported benefit include macrolides, potassium iodide, and isotretinoin (8). Antihistamines and corticosteroids have consistently proved ineffective in the treatment of PP (8).

Despite the characteristic clinical and histopathologic presentation, the diagnosis of PP can be difficult because of the lack of experience with these findings of Western physicians with this disease; only six cases of PP have been described in the United States (14–16).

Our case illustrates the prudence of a careful review of dietary habits and nascent diabetes in the examination of a recurrent reticulated, pruritic rash of the trunk. The association between PP and ketosis has been reported extensively, with most cases improve upon correction of the metabolic derangement (3,9–12). The mechanism for the role of ketosis in PP remains elusive.

In conclusion, our patient was a 17-year-old boy diagnosed with PP that was temporally associated with strict adherence to a ketogenic diet and improved markedly with diet modification and doxycycline therapy.

REFERENCES