Treatment of Prurigo Pigmentosa with Diet Modification: A Medical Case Study

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Abstract

Prurigo pigmentosa is a rare inflammatory dermatitis first described in 1971. While the etiology of Prurigo pigmentosa is yet unknown, conditions associated with ketosis often accompany this rash. Prurigo pigmentosa is successfully treated with antibiotics and by resolution of ketosis. However, there is no dietary treatment option to successfully treat the rash without sacrificing ketosis. We report two cases successfully treated with increase of dietary carbohydrate intake. The second case suggests that cessation of ketosis may not be necessary to resolve Prurigo pigmentosa.

Keywords

Ketogenic Diet, Prurigo Pigmentosa, Epilepsy

Introduction

Prurigo pigmentosa (PP) is considered a rare inflammatory dermatitis first described by Nagashima, et al, in 1971.[1] It typically occurs in Asian women of child-bearing age but has also been documented in individuals in other regions and ethnicities, as well as in men.[2-9] Certain systemic conditions, including adult–onset Still's disease,[10] atopy,[11] *H. pylori* infection,[12] and Sjögren's syndrome[13] have been associated with PP. It has also been strongly associated with conditions that commonly produce ketosis, such as restrictive dieting, fasting, and uncontrolled diabetes mellitus.[2,14-18] Nutrition–related PP has not been reported in the pre-pubescent population.[2] It is rarely reported in the United States, although this may be due to the unfamiliarity of practitioners with this condition.[7]

PP has been characterized into three stages based on appearance and pathology. Early-stage lesions present as pruritic urticarial plaques or papules that are characterized pathologically by superficial perivascular neutrophilic infiltrates. Fully developed PP lesions manifest as crusted erythematous papules, papulovesicles with histology showing spongiosis and necrotic keratinocytes. Late-stage lesions evolve into smooth-surfaced pigmented macules with histological features of lymphocytic infiltrate and melanophages in the papillary dermis.[2,14,19] The morphology of the lesions is diverse, therefore differential diagnoses includes contact dermatitis, urticaria, erythema multiforme, and medication-induced responses. PP is distinguished from other skin lesions by its unique reticular pattern, present in any of the three stages.[2] A similar dermatosis, confluent and reticulated papillomatosis, appears in characteristic regions of the trunk, back and neck, but it is rarely accompanied by the intense pruritis that is characteristic of PP.[2]

In cases presenting with ketosis, administration of insulin or carbohydrates to correct ketosis resolves PP,[15,20,21] but antibiotics such as minocycline, doxycycline, and dapsone have also been used with success.[7,22] The ketogenic diet (KD) is a very low carbohydrate, moderate protein and high fat diet designed to induce hepatic production of ketone bodies as an alternative fuel source.[23-26] Ketogenic diets metabolically mimic starvation and were developed for use in humans to treat epilepsy based on an ancient practice of fasting to reduce seizures.[27,28] In recent years, applications for the KD has expanded.[24,29-31] As such, there is an increase in the number of people who experiment with the KD diet, many of whom initiate the diet on their own without medical supervision. This is reflected in the increased number of internet searches,[32] websites, blogs, and books that have emerged on variations of the KD.[33,34] With the growing popularity of the KD, reports of PP have emerged. There is a dermatologic phenomenon popularly coined "keto-rash" in internet blogs and discussions, suggesting that it may be more common in adult patients (with higher representation in the Asian population) on the KD than what is currently represented in the literature. Many clinicians remain unaware of the association of the KD with PP, suggesting there is a need for further education and knowledge.

The following two case reports detail the presentation and onset of PP in two Asian adults on the KD.

Case Report #1

An otherwise healthy 43-year-old Chinese-American woman presented with the symptoms of PP approximately 3 weeks after self-initiating the KD for weight management. Food and dietary supplement history reflected a daily net carbohydrates of 20 gm a day, 105 gm of protein daily and an unrestricted amount of fat. Her diet consisted of eggs, sausages, coffee with cream and medium-chain triglycerides (MCT) for breakfast; avocado, turkey, beef, vegetables, eggs prepared in coconut or avocado oil for lunch and dinner; nuts (macadamia, almond, coconut), sugar free ice cream and small amounts of berries as snacks. She developed lesions that evolved into erythematous papules (Figure 1). The rash improved after one week but promptly recurred and continued in a relapsing-remitting pattern. The rash was exacerbated by exercise and long hot showers. She took oral diphenhydramine and loratadine and applied topical steroids, and eliminated possible allergens such as her shampoo and nuts. All of these interventions were unsuccessful. The rash spontaneously resolved following resumption of a higher carbohydrate diet (self-initiated) and has not recurred in the 12 months since she resumed higher carbohydrate diet.

Case Report #2

An 18 year-old Japanese man was started on a classic KD at a 2:1 fat to carbohydrate and protein ratio to treat intractable

seizures. Other medical diagnoses include Dandy-Walker malformation (a rare congenital malformation of the cerebellum and 4th ventricle[35]), cerebral palsy, and intellectual disability. He was on Clobazam and Lamotrigine to treat seizures prior to initiation of the diet, and these medications remain unchanged with KD initiation. The patient was admitted to the hospital for three days to initiate the KD. Nutrition assessment done prior to admission by the RDN reflected a well-nourished male without any signs or risk factors for malnutrition, and no contraindications to initiation of the diet. The KD consisted of a Ketocal® (Nutricia North America, Gaithersburg, MD[36]) smoothie in the morning; eggs, fish, beef, vegetables, avocado, avocado oil, sesame oil, heavy whipping cream, and butter for lunch and dinner choices. All of his meals were pre-calculated by the RDN. The patient's seizures ceased on day 2 of the diet while in the hospital, which coincided with moderate ketosis (evidenced by urine ketones at 80 mg/dL on day 2). He was discharged on day 3 of the diet in ketosis (urine ketones were 160 mg/dL, serum beta-hydroxybutyrate levels were 1.28 mmol/L). Approximately 9 days after diet initiation he developed a pruritic rash characteristic of PP (Figure 2). Specimens drawn included a complete blood count with differential, C-reactive protein, and a urinalysis. Lab results were unremarkable. The potential side effects of the standard antibiotic treatments were concerning, so the Ketogenic diet team discussed discontinuing the diet with the patient's mother. The mother stated that the seizure cessation on the KD was of greater value than the discomfort of the rash, so it was decided to continue the diet. By day 14 the rash had worsened, with increased redness around the lesions. Therefore meals were modified to decrease his diet ratio to 1:1. This increased his carbohydrate total allotment from 16 gm per day to 51 gm per day. Protein intake was increased from 70 gm per day to 95 gm per day. Fat intake decreased from 173 gm per day to 146 gm per day. Despite the decrease in his KD ratio, his urine ketones remained consistently at 160 mg/dL. On day 17 the KD ratio was decreased to 0.75:1 with the addition of apple juice to each meal. To achieve this ratio his carbohydrate allotment was increased to 90 gm per day. Protein remained consistent at 95 gm/d. This resulted in decreased urine ketones of 80 mg/dL, with an occasional decrease to 40 mg/dL, and resulted in a significant improvement in pruritus and erythema the following day. Dairy sources (Ketocal®, cream, butter) were not eliminated, although Ketocal® consumption decreased as a result of patient preference. Seizure freedom was maintained throughout this time. Medications remained unchanged. At his 3-month visit, the patient's mother reported only one very mild seizure since initiation of the KD. This was a significant improvement compared to his previous baseline seizure frequency of 10-20 seizures daily. The patient's rash has been in remission for the past 8 months.

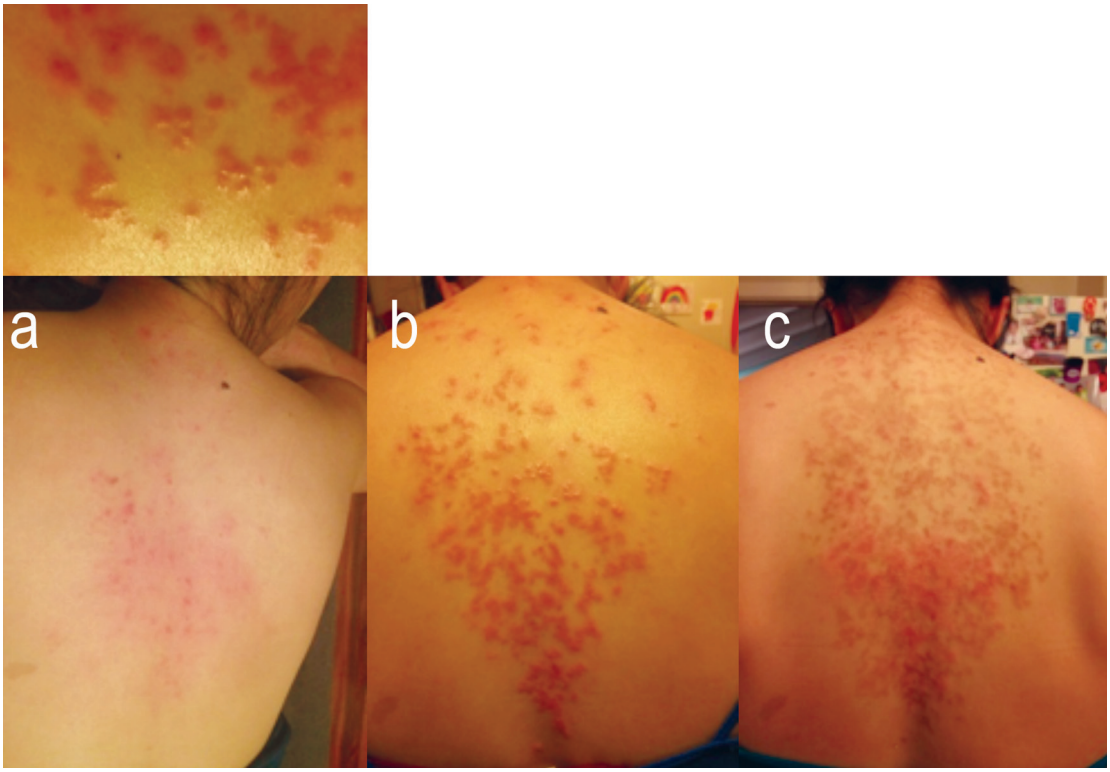

Figure 1. A 43-year old woman. Progression of prurigo pigmentosa lesions following initiation of a modified ketogenic diet.
(a) Day 22 on the KD. Erythematous papules and plaques characteristic of early lesions on the central portion of the back.
(b) Day 26 on the KD. Fully developed lesions with predominant papulovesicles distributed symmetrically in a V-shaped distribution over the upper and lower back.
(c Day 40 on the KD. Erythematous late stage lesions associated with reticular post-inflammatory hyperpigmentation in symmetrical pattern.

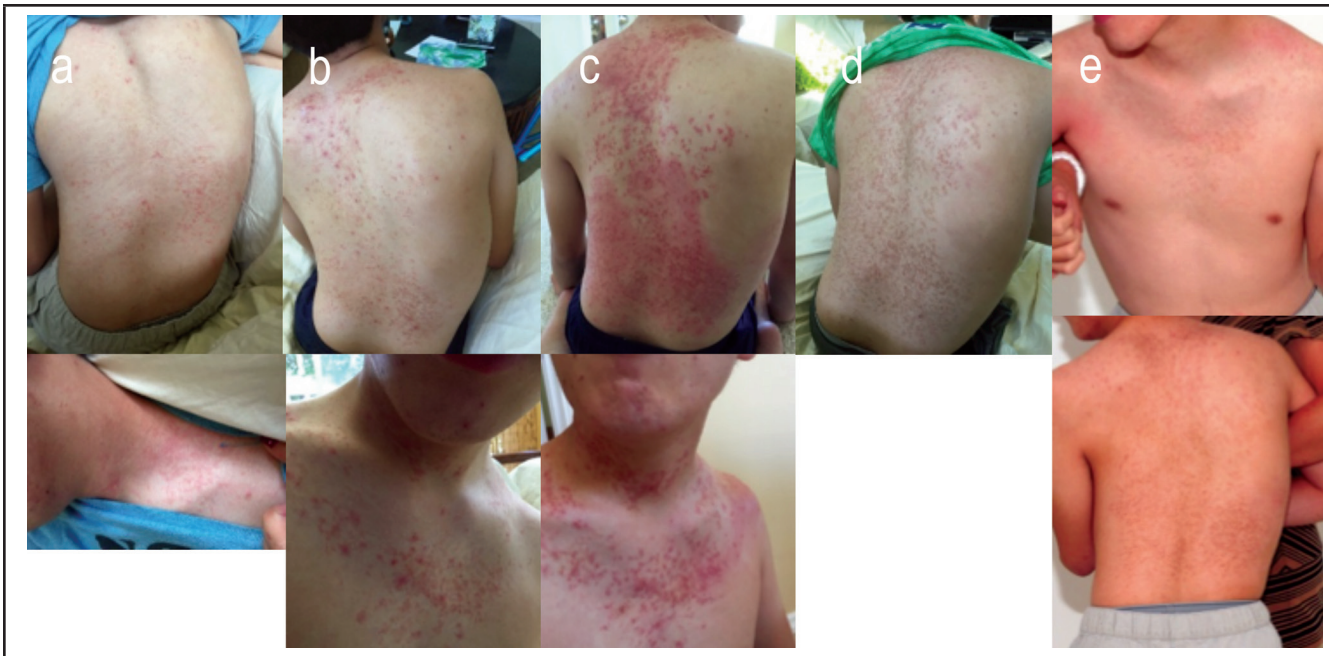

Figure 2. An 18-year old man. Progression of prurigo pigmentosa following initiation of a classic KD.
(a) Day 9 on KD @ 2:1. Eruption of erythematousd papules over the back and neck characteristic of early lesions.
(b) Day 12 on KD @ 2:1. Papulovesicle formation extending to the chest in reticular pattern.
(c) Day 14 on KD @ 2:1. Recurrent papulovesical lesions associated with post-inflammatory reticulated hyperpigmented lesions.
(d) Day 18 on KD 1 day after ratio decrease to 0.75:1. Resolving lesions, predominantly reticulated hyperpigmented macules.
(e) Day 20 on KD @ 0.75:1. Resolution of erythematous papules with remaining reticular hyperpigmentation.

Discussion

In both cases, the rash resolved with an increase in dietary carbohydrate intake. The etiology of PP is unknown[2,14]. A growing body of evidence demonstrates a connection between the gut microbiome and host immunity. Gut dysbiosis, as a result of nutritional and other environmental factors, may play a role in the pathogenesis of PP, and altering the profile of the gut microbiota through the use of antibiotics or diet would theoretically modify immune response. The effectiveness of dapsone and minocycline in treating PP speaks to this. To our knowledge, we are the first to demonstrate that complete resolution of ketosis may not be necessary to successfully treat the rash, which is of particular importance in cases where the KD is therapeutically valuable as a successful treatment modality for medical conditions. A systematic review of adverse effects of lamotrigine suggested rash was the most common adverse reaction and the most common reason for treatment discontinuation. Single maculopapular rashes are the most common type of rash reported. Rash was reported in 7.3% of the patients, and Stevens-Johnson syndrome was reported in 0.09 per 100 patients.[37] The Asian association is more commonly noted with carbamazepine. The potential underlying relationship between lamotrigine and the ketogenic diet is unknown.

Ketogenic diet centers across the US predominantly use the KD to treat intractable pediatric seizure disorders, which may help explain the uncommon incidence of PP. In addition, PP is more prevalent in Asian ethnicities, and less likely to surface in regions with smaller Asian demographics. However, as the KD is increasingly used for a number of disorders beyond pediatric epilepsy such as adult epilepsy, Alzheimer's Dementia,[38,39] Parkinson's disease,[40,41] brain and other cancers,[24] obesity,[42] Autism Spectrum Disorder,[43,44] and endurance athletics,[29,45] practitioners should be aware of the association of this dermatologic presentation with conditions that produce ketosis. Current treatment options include cessation of the KD or use of antibiotic therapy. RDNs who are trained in ketogenic therapies provide a level of expertise that may allow patients a third option for treatment of PP by helping to correctly identify the rash in its potential connection to the KD, and judiciously modifying the KD with carefully prescribed carbohydrate dosing in the diet without sacrificing ketogenesis.

Conflict of Interest

None of the authors identify a conflict of interest.

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