Prurigo Pigmentosa and Confluent and Reticulated Papillomatosis a Spectrum of One Disease: A New Case Report

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Abstract

Background: Prurigo Pigmentosa (PP) is a rare inflammatory dermatitis first discovered in 1971. Characterized by a sudden eruption of pruritic reticulated, pink-brown papules coalescing into plaques distributed symmetrically over shoulders, neck, chest, and back. Various triggers have been identified, including the ketogenic diet. Clinico-pathological presentation looks similar to confluent and reticulated papillomatosis (CARP) which is a rare dermatosis of unknown etiology characterized by hyperkeratotic pigmented papules & peripheral reticulation involving seborrheic areas.

Aim: To document a new case presentation of PP caused by a low-carbohydrate restricted diet and discuss the comparison with CARP clinically, pathologically, and treatment modalities.

Case report: A 15-year-old childhood male developed PP 3 weeks after self-initiating a low carbohydrate-restricted ketogenic diet for weight management. Clinically and histopathologically the lesion looks similar to CARP, treated successfully with re-introduction of high carbohydrates in his food, a short course of systemic steroids in combination with oral doxycycline capsules for the one-month duration. Conclusion: PP & CARP have been considered a spectrum of one disease, and PP is a pruritic variant from CARP caused by a low carbohydrate-restricted diet.

Keywords

Prurigo Pigmentosa, Ketogenic Diet, Inflammatory Dermatosis, Confluent and Reticulated Papillomatosis

1. Introduction

PP is considered a rare inflammatory dermatitis first described by Nagashima, et
PP most commonly presents on the back, chest, and neck. Disease progression is divided into three stages: early, fully developed, and late, each of which is distinguished by unique clinical and histologic features. Early-stage prurigo pigmentosa is characterized by pruritic urticarial papules or plaques that show a superficial perivascular neutrophilic infiltrate on pathologic examination. Patients with fully developed lesions present with crusted erythematous papules, papulovesicles, and vesicles; spongiosis and numerous necrotic keratinocytes are the histologic hallmarks of this stage. Lastly, late-stage prurigo pigmentosa is characterized by the appearance of smooth-surfaced pigmented macules. Histologic features of late-stage lesions include a predominantly lymphocytic infiltrate and melanophages in the papillary dermis. The evolution from early-stage to fully developed lesions occurs over 2-3 days. The fully developed lesions subsequently resolve within 1 week, leaving behind pigmented macules that usually persist for several months. Notably, lesions representing different stages of the disease often exist concurrently, coalescing to form a reticular pattern.

Clinical differential diagnosis of PP includes in early-stage: contact dermatitis; psoriasis Vulgaris; urticaria; in fully-developed stage: erythema multiforme; Mucha Habermann disease and in late-stage: confluent and reticulated papillomatosis; erythema dyschromium perstans; macular amyloidosis.

PP has been associated with several systemic conditions, including adult-onset Still’s disease, atopy, H. pylori infection, and Sjögren’s syndrome. In addition, prurigo pigmentosa has been reported in patients with anorexia nervosa and diabetes mellitus.

Abbass et al. hypothesized that ketosis-induced, neutrophil-mediated inflammation contributes to the development of prurigo pigmentosa. Indeed, elevated urine and/or blood ketone levels have been reported in several patients with prurigo pigmentosa. Furthermore, antibiotics that affect neutrophil chemotaxis, including minocycline and doxycycline, are usually effective in the treatment of prurigo pigmentosa. However, prurigo pigmentosa also occurs in non-ketotic patients. Therefore, although neutrophil-mediated inflammation may contribute to the development of prurigo pigmentosa, it can conceivably be induced by processes other than ketosis. Other postulated causative factors for the development of prurigo pigmentosa include mechanical stimuli, contact allergy, and climate. Oral minocycline is usually the first-line therapy for prurigo pigmentosa. Excellent results have also been achieved with doxycycline, macrolide antibiotics, and dapsone (di-aminodiphenyl sulfone). However, residual hyperpigmentation may persist even after the resolution of prurigo pigmentosa.

CARP was first described in 1972 by Gougerot and further characterized by...
Carteud [25]. It is a relatively rare dermatosis of unknown etiology characterized by persistent papules and plaques that are confluent in the center and reticulated at the periphery, typically distributed around the neck, inter-scapular region, infra-mammary area, and the abdomen [26].

The proposed diagnostic criteria by Davis et al. [25] are 1) clinical findings of scaling brown macules and patches, some reticulated and papillomatous; 2) location on the upper trunk and neck; 3) fungal staining of scale negative for spores and hyphae; 4) lack of response to antifungals; and 5) excellent response to minocycline.

The most common histopathological findings are hyperkeratosis, papillomatosis, and acanthosis. The dermis may contain perivascular lymphocytic infiltrates, mild dilatation of superficial dermal blood vessels, beading of elastic fibers, and hyper melanosis of the basal layer [27].

The disease has been considered to be an abnormal host defense, which develops against Malassezia furfur, staphylococcus, or Propionibacterium acnes. On the other hand, obesity, type 2 diabetes, hirsutism, Cushing’s syndrome, menstrual dysfunction, vitamin A deficiency, genetic predisposition, photosensitivity, cutaneous amyloidosis, and keratinization disorder have also been blamed [28] [29].

Treatment with various antibiotics especially minocycline and other macrolides have been reported to be highly effective in CARP patients [30]. The good response may be related to anti-inflammatory (Most probably attributed to inhibiting neutrophil migration and subsequent reactive oxygen species release and inhibit matrix metalloproteinase) rather than antimicrobial effects alone [26].

Insulin resistance, keratinization disorders, developing an abnormal host response against bacterial or fungal agents, such as Dietzia papillomatosis (type strain N 1280T) and Malassezia furfur, amyloid deposition, and a loss-of-function mutation in keratin 16 and genetic disorders have been suggested for the etiology and pathogenesis [31].

Ketosis is a temporary condition characterized by elevated serum ketones that are used as an alternative energy source when blood glucose is low or insulin is deficient [32] [33].

The most common causes of ketosis are the physiologic responses to fasting, prolonged exercise, or a high protein/low-carbohydrate diet, though pathologic causes include insulin-dependent diabetes mellitus, alcoholism, and salicylate overdose. In healthy individuals, blood ketone levels rarely approach 0.5 mmol/L. Prolonged fasting or restricting intake of carbohydrates to less than 40 g daily can induce mild ketosis that resolves with re-introduction of carbohydrates [33].

Ketone bodies pass from the circulating blood into tissues or remain near the blood vessels, inducing cytotoxic effects and perivascular inflammation [6] [33].

Increased ketone bodies have been shown to upregulate intercellular adhesion molecule 1 (ICAM-1) and leukocyte function-associated antigen 1 (LFA-1), a
phenomenon also seen in lesional keratinocytes of PP [34] [35].

In the present case report, we are describing a 15-year-old childhood male who developed PP 3 weeks after starting a low carbohydrate-restricted ketogenic diet. The patient was treated initially as a case of herpes zoster virus infection but without improvement. Clinically and histopathologically the lesion looks similar to CARP, treated successfully with re-introduction of high carbohydrates in his diet, a short course of systemic steroids in combination with oral doxycycline capsules for the one-month duration without any signs for relapse 2 months followed-up after stopped therapy. The written consent form was taken from his mother about the publication of his condition.

2. Case Report

An otherwise healthy 15-year-old childhood male presented to the dermatology clinic with a history of sudden onset of itchy skin eruption over his upper left chest, lower central chest, and lower back. He noticed this rash 3 weeks after self-initiating a low carbohydrate-restricted ketogenic diet for weight management. Food and dietary supplement history reflected a daily net carbohydrate of 25 gm a day, 110 gm of protein daily, and an unrestricted amount of fat.

Initially, he visited a general practitioner who prescribed a topical & systemic anti-viral as a case of herpes zoster virus without improvement.

On examination, there were multiple well-defined reticulated, pink-brown papules coalescing into plaques distributed over the left upper chest, lower central chest, and lower back covered by fine scales (Figure 1, Figure 2). A potassium hydroxide (KOH) scraping skin test was obtained and the result was negative for fungal elements.

Punch skin biopsy for histopathology was taken and differential diagnoses were PP, CARP, acute lupus erythematosus, dermatitis herpetiformis, Dowling-Degos disease, and Ashy dermatosis. Histopathology result in correlation with clinical findings goes with a diagnosis of PP, revealed undulating basket weave stratum corneum, mild papillomatosis, acanthosis, focal increased basal cell pigmentation, and perivascular lymphocytic infiltration with a sign of vasculitis (Figure 3, Figure 4). Treatment started with re-introduction of high carbohydrates into his diet, systemic prednisolone 20 mg daily for 2 weeks in combination with doxycycline 100 mg daily for 1 month. 2 weeks after starting therapy dramatic improvements in signs and symptoms started were resolved most papules and plaques revealed reticulated brownish hyperpigmentation involving the left upper chest, lower central chest, and lower back (Figure 5, Figure 6). one month after treatment, complete resolution of lesions even hyperpigmentation revealed normal skin findings. Stopped oral doxycycline and after 2 months followed-up later there were no signs of relapse (Figure 7, Figure 8).

3. Discussion

It has been suggested that both PP and CARP of Geougerot and Carteaud lie on a spectrum of one disease [36].
Figure 1. PP of a 15-year-old childhood male showed multiple well-defined reticulated, pink-brown papules coalescing into plaques covered by fine scales. (a) Left upper chest and central lower chest. (b) Left upper chest.

Figure 2. PP of a 15-year-old childhood male showed multiple well-defined reticulated, pink-brown papules coalescing into plaques covered by fine scales. (a) Central lower chest. (b) Lower back. Note dispersed pink-brown papules over the chest and abdomen.

Figure 3. Hematoxylin and Eosin (H & E) stained section showed undulating basket weave stratum corneum, mild papillomatosis, acanthosis, focal increased basal cell pigmentation and perivascular lymphocytic infiltration with sign for vasculitis. (a) Original magnification ×10. (b) Original magnification ×20.
Figure 4. Hematoxylin and Eosin (H&E) stained section showed perivascular lymphocytic infiltration with sign of vasculitis. Original magnification ×20.

(a)                                (b)

Figure 5. PP of a 15-year-old childhood male 2 weeks after therapy showed resolved most papules and plaques revealed reticulated brownish hyperpigmentation. (a) Central lower chest. (b) Left upper chest.

Figure 6. PP of a 15-year-old childhood male 2 weeks after therapy showed resolved most papules and plaques over lower back revealed reticulated brownish hyperpigmentation.
CARP is also described as a pruritic eruption of erythematous to brown plaques on the chest, back, axilla, and abdomen, which can evolve into lesions demonstrating a reticular pattern [37]. Histopathology typically demonstrates hyperkeratosis, parakeratosis, increased basal layer pigmentation, and sparse perivascular lymphohistiocytic infiltrate.

The etiology of CARP is also largely unknown, with the bacterial species Dietzia papillomatosis being identified as a possible etiologic agent [38]. However, ketosis has been suggested for the pathogenesis and etiology of both CARP and PP. Various treatment modalities such as antibiotics, antifungal agents, selenium sulfide, vitamin A derivatives, salicylic acid, and vitamin D derivatives have been
proposed. However, responses to those modalities have been unsatisfactory and inconsistent.

Recently, treatment with various antibiotics especially minocycline and other macrolides have been reported to be highly effective in CRP patients [30]. The good response may be related to anti-inflammatory (most probably attributed to inhibiting neutrophil migration and subsequent reactive oxygen species release and inhibit matrix metalloproteinases) rather than antimicrobial effects alone [26].

Dan et al. Discuss the comparison between PP & CARP where both have existed along a spectrum of the same disease. PP and CARP can both be presented with similar clinical findings, histology, and lack of clear etiologies; they both respond to similar therapies and each is listed as a differential diagnosis for the other [36]. We agree with this spectrum and we believe PP is a pruritic variant from CARP induced by a low carbohydrate-restricted ketogenic diet.

We describe a case of a 15-year-old childhood male who was diagnosed with PP 3 weeks after self-initiating a low carbohydrate-restricted ketogenic diet for weight management. Food and dietary supplement history reflected a daily net carbohydrate of 25 gm a day, 110 gm of protein daily, and an unrestricted amount of fat. Successful treatment was attained through diet modification in combination with a short course of systemic prednisolone and oral doxycycline capsules.

In our case, the resolution occurred within one month after therapy leaving normal skin findings. This indicates that early diagnosis and treatment might prevent post-inflammatory hyperpigmentation.

Recurrences are common in the course of this disease and might occur months or years after initial presentation [2]. While in our case no relapse presented 2 months followed-up after stopped treatment.

In the Arab area, PP is rarely documented despite rising new cases [39] [40]. This is probably due to misdiagnosis and under-reporting.

4. Conclusion

In conclusion, PP & CARP have been considered a spectrum of one disease, and PP is a pruritic variant from CARP caused by a low carbohydrate-restricted ketogenic diet. The importance of this report is to increase the awareness of physicians about this category especially with the differential diagnosis of sudden dermatomal eruption.

Disclosure

This study is an independent study and not funded by any of the drug companies.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.
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