

## Skin eruption induced by dieting – an underdiagnosed skin disease in Malaysia

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### Abstract

Prurigo pigmentosa is an inflammatory dermatosis characterized by a pruritic, symmetrically distributed erythematous papular or papulo-vesicular eruption on the trunk arranged in a reticulated pattern that resolves with hyperpigmentation. It is typically non-responsive to topical or systemic steroid therapy. The exact etiology is unknown, but it is more commonly described in the Far East countries. Dietary change is one of the predisposing factors. We report on nine young adult patients with prurigo pigmentosa, among whom five were on ketogenic diets prior to the onset of the eruptions. All cases resolved with oral doxycycline with no recurrence. We hope to improve the awareness of this uncommon skin condition among general practitioners and physicians so that disfiguring hyperpigmentation due to delayed diagnosis and treatment can be avoided.

### Introduction

Prurigo pigmentosa is an inflammatory dermatosis first described by Nagashima in 14 Japanese patients in 1978.<sup>1</sup> The condition was quite rare until the last decade, when increasingly more cases were documented, and its clinical and pathological features were further defined. It is now evident that prurigo pigmentosa is not limited to patients of Far East origin, as previously thought.<sup>2</sup>

The skin lesions in prurigo pigmentosa are characterized by symmetrically distributed pruritic papules arranged in a reticulated, net-like pattern that heals with pigmentation. Lesions typically affect depressed regions of the trunk in the mid-chest and mid-back.<sup>2-5</sup> Prurigo pigmentosa does not respond to topical and systemic corticosteroid therapy. Disease recurrence is another clinical feature. Dietary changes, vigorous exercise, diabetic ketoacidosis, friction and atopic diseases have been associated with prurigo pigmentosa.<sup>3,4,6-9</sup> We present nine cases of prurigo pigmentosa to highlight dieting as a precipitating factor.

### Methods

The medical records, photographs and histopathological slides were available for nine patients diagnosed with prurigo pigmentosa at three dermatology clinics in Kuala Lumpur, Malaysia (University Kebangsaan Malaysia Medical Centre, Ting Skin Specialist Clinic and Gleneagles Kuala Lumpur) between 2015

and 2017 and were reviewed retrospectively. Consent for photography was obtained from all patients. Diagnosis of prurigo pigmentosa was based on clinicopathological findings from the adapted criteria set by Boer et al.<sup>10,11</sup> The duration of follow up ranged from 3 to 30 months.

Data from the medical records included demographics, previous medical history, disease presentation and duration, associated conditions, laboratory results, histopathological findings and treatment (duration and response).

### Results

We encountered a total of nine patients who were diagnosed with prurigo pigmentosa by dermatologists in three dermatology clinics in Kuala Lumpur, Malaysia. Eight (88.89%) of the nine patients were females, resulting in a female-to-male ratio of 8:1. The mean age was 21.4 years (range of 16-37 years). Five (55.56%) of the patients were Chinese, and the rest (44.44%) were Malays. All patients had the characteristic eruptions, except one, who presented with the bullous variant of prurigo pigmentosa. The skin lesions consisted of symmetrically distributed patches of erythematous papules in a reticulated pattern interspersed with dark brown pigmentation in the same reticulated pattern (**Figure 1**). The lesions were extensive over the anterior and posterior trunk in four patients, and two patients had lesions that were localized to the chest and upper back. The chest, abdomen and

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**Figure 1.** Distribution of prurigo pigmentosa lesions: Erythematous papular eruptions: (a) on the entire chest, (b) on the central chest, (c) with a “bra distribution” sparing the nipples and areola, (d) on the lower trunk, (e) on the upper abdomen, (f, g) scattered over the upper and mid back, (h) wedge-shaped at upper and mid-back, and (i) on the central upper and lower back

suprapubic areas were affected in two patients. One patient had reticulated bullous lesions as well as patches of reticulated erythematous papules and pigmentation. All patients reported pruritus, in particular, seven of them had mild pruritus, while two had moderate pruritus. Disease duration prior to diagnosis ranged from 2 to 24 weeks. Five (55.56%) patients were dieting for weight loss prior to the onset of eruption; three (33.33%) were on ketogenic diets, while one (11.11%) was on Atkin’s diet. Two of these patients combined dieting with vigorous exercise. Atopic diseases were reported in two (22.22%) patients. No trigger factors or concomitant diseases were found in four (44.44%) patients. Patient characteristics and clinical features are summarized in **Table 1**.

Skin biopsies were performed on two patients. Histopathological findings of spongiotic dermatitis with neutrophilic exocytosis were reported for Patient 4. Full thickness

epidermal necrosis with separation at the dermal-epidermal junction, peri-adnexal lymphocytes and neutrophils were seen in Patient 9. The histopathology findings for both patients were inconclusive for prurigo pigmentosa. Diagnosis in all patients was confirmed by the presence of the characteristic skin eruptions, recognized trigger factors (in most patients), unsatisfactory response to both topical and/or oral steroids and resolution with doxycycline. All patients had complete response to doxycycline with no relapse. Similar responses were observed with different dosages of doxycycline, i.e., 100mg daily and 100mg twice daily. Patients whose eruptions were triggered by dieting were advised to resume normal diets. There were no recurrences despite wide variation in the treatment duration, which ranged from 2 to 8 weeks. Patient 5, who received doxycycline 100mg twice daily for 2 weeks, was followed up for 1 year and remained asymptomatic. **Table 2** summarizes the treatments, treatment outcomes and recurrences for the nine patients.

**Table 1.** Demographical and clinical features of nine patients with prurigo pigmentosa

Case no.	Age (years)/ gender	Ethnicity/ Occupation	Duration of active lesions (weeks)	Distribution of skin lesions	Pruritus	Trigger factors/ association
1	26/ Female	Malay/ NA	3	Chest, abdomen, mid-back, suprapubic	mild	Atkin's diet for 10 days, exercise, friction
2	37/ Female	Chinese/ housewife	2	Anterior and posterior trunk, abdomen	mild	Eczema, ketogenic diet 2 weeks
3	19/ Female	Chinese/ Student	2	Anterior and posterior trunk	mild	Ketogenic diet 2 weeks
4	19/ Female	Malay/ Student	24	Mid upper back	moderate	nil
5	18/ Female	Chinese/ Student	4	Anterior and posterior trunk	mild	nil
6	19/ Female	Chinese/ Student	2	Chest, abdomen, suprapubic	moderate	Ketogenic diet 1 month
7	16/ Male	Chinese/ Student	6	Anterior and posterior trunk	mild	nil
8	22/ Female	Malay/ Student	24	Chest	mild	nil
9	17/ Female	Malay/ Student	3	Brassiere distribution, lumbosacral	mild	Asthma, eczema, diet, exercise

**Table 2.** Summary of treatments, treatment outcomes and recurrences

Case no.	Treatment	Time to resolution of active lesions (days)	Duration of treatment (weeks)	Duration of follow up (months)	Recurrences
1	Doxycycline 200mg/day	10	8	9	Nil
2	Doxycycline 200mg/day (2weeks), followed by 100mg/day (4weeks)	21	6	12	Nil
3	Doxycycline 100mg/day	14	6	5	Nil
4	Doxycycline 100mg/day	28	8	30	Nil
5	Doxycycline 200mg/day	14	2	12	Nil
6	Doxycycline 100mg/day	14	4	12	Nil
7	Doxycycline 200mg/day	NA	2	NA	Nil
8	Doxycycline 200mg/day	14	4	3	Nil
9	Doxycycline 200mg/day	10	8	12	Nil

### Discussion

Prurigo pigmentosa occurs mostly in young adult patients in their twenties with a strong female preponderance, as demonstrated by our group of patients. The mean age ranges from 21 to 26 years, while the male-to-female ratio is from 1:2.7 to 1:8.<sup>3-5,8</sup> Both Malays and Chinese are affected. Interestingly, none of our patients was of Indian origin. However, the number of cases in this review is too small to reflect our country's ethnic distribution of 63.1%

Malays, 24.6% Chinese and 7.3% Indians.<sup>12</sup> Although prurigo pigmentosa was initially linked to Orientals, it is now apparent that other ethnicities are affected to a certain extent.<sup>2</sup> The condition is likely to become more prevalent as dieting and vigorous exercise become more common due to either increased health awareness or social and peer pressure to achieve certain body proportions.

The term prurigo pigmentosa used for this condition can be confusing. In terms

of 'prurigo,' pruritus was mild and not a main feature in most of our patients. In the remaining patients, it was of moderate severity. This result is similar to the finding in the study by Kim *et al.* in which more than half of their patients had mild or no pruritus.<sup>3</sup> However, severe pruritus has been reported, especially in the early stages of the skin lesions.<sup>2,5</sup> The word 'pigmentosa' suggests a pigmentary disorder instead of an inflammatory disorder that resolves with post-inflammatory hyperpigmentation. The current classification of prurigo pigmentosa under hyperpigmentation disorders may require revision, as more knowledge of its pathophysiology and clinical features has emerged in recent years. In addition, prurigo pigmentosa may present with vesicles and blisters as the main clinical feature.<sup>7,13,14</sup> The clue to diagnosis lies on the arrangement of the vesicles and blisters, which follow a reticulated pattern, with reticulated pigmentation observed once the lesions heal.

Eruptions of prurigo pigmentosa can be classified into early, late or recurrent as the lesions evolve.<sup>3</sup> Early lesions consist of urticated papules or papulovesicles, whereas late lesions are reticulated hyperpigmented patches.<sup>3</sup> Early lesions exhibit mostly neutrophil infiltration of the dermis.<sup>3</sup> The majority of late and recurrent early lesions reveal predominance of lymphocytes over neutrophils.<sup>3</sup> Epidermal hyperplasia and epidermal hyperpigmentation are observed frequently in late and recurrent early lesions.<sup>3</sup> Due to the variable findings, histological confirmation of prurigo pigmentosa is difficult, as illustrated by our patients for whom a skin biopsy could not confirm the diagnosis; rather, the diagnosis was based on the classical clinical features.

Dieting was a distinctive triggering factor that induced prurigo pigmentosa among 55.6% of our patients. In the literature, dietary changes have been associated with prurigo pigmentosa in up to 50% of cases.<sup>3,8,15</sup> In addition, states of starvation, malnutrition and diabetic ketoacidosis are other predisposing factors for the disease.<sup>3,6-9,14,16,17</sup> Kim *et al.*, in their retrospective study of 50 patients in Korea, did not find demonstrable elevated blood ketones, but 33% of the urine ketones measured were positive. Urine ketone was positive in 50% of patients who were dieting and 23% of those who were not on a diet.<sup>3</sup> In about 50% of patients with prurigo pigmentosa reported by Oh *et al.*, symptoms were precipitated by dietary changes, and ketosis was demonstrated

in 75% of the cases.<sup>8</sup> The inflammatory process in the pathophysiology of prurigo pigmentosa is unclear. Overexpression of interleukin-6 (IL-6), interleukin-8 (IL-8) and monocyte chemo-attractant protein-1 (MCP-1) induced by ketosis could account for the inflammation observed on the skin.<sup>18,19</sup>

Prurigo pigmentosa could be mistaken for eczema or contact dermatitis. Another differential diagnosis to consider is confluent and reticulated papillomatosis. Eczema has similar pruritic urticarial papules vesicles and patches. Eczema also has strong association with a personal or family history of atopy. However, the distribution of the lesions in prurigo pigmentosa differs from that observed in other endogenous eczemas, such as atopic eczema or seborrheic eczema. In the context of trunk involvement, contact dermatitis related to allergens, such as fragrances, nickel, fabric dye and topical medicaments, should be considered. Lack of exposure to suspected allergens and a negative patch test would rule out allergic contact dermatitis. Endogenous eczema and allergic contact dermatitis will respond well to topical or oral corticosteroid, unlike prurigo pigmentosa. Late presentation of reticulated lesions over the trunk can be easily mistaken for post-inflammatory hyperpigmentation or confluent and reticulated papillomatosis. In confluent and reticulated papillomatosis, the patient would have hyperkeratinized papillomatous lesions in a reticular pattern, which is not observed in prurigo pigmentosa.

Doxycycline is an effective therapy for prurigo pigmentosa.<sup>4,5</sup> The dosage used ranges from 100mg to 200mg per day for 2 to 8 weeks in duration.<sup>4,5</sup> Lower doses of doxycycline and shorter treatment durations produce similar responses, but the effect on relapses is difficult to determine due to limited data. There is no data on the most effective time frame of treatment or the benefit of treatment beyond a certain duration. The effect of doxycycline is probably due to its anti-inflammatory properties rather than its antimicrobial effect, as no microbial pathogen has thus far been identified as an etiological factor in prurigo pigmentosa. Minocycline and dapson are other effective treatment options.<sup>3,8</sup> Doxycycline, minocycline and dapson are known to be effective in the prevention of the migration and function of neutrophils.<sup>3,8</sup> We prefer doxycycline due to its more favorable side effects profile. In the proportion of patients where prurigo pigmentosa is triggered by

dieting, relapse may occur when dieting is resumed.<sup>3</sup>

### Conclusion

Dieting with or without resultant ketosis seems to be an important risk factor for prurigo pigmentosa. The diagnosis should be considered in young adults who are attempting to lose weight by means of dieting and presenting with a pruritic inflammatory symmetrical truncal papular or papulo-vesicular

eruption with reticulated and confluent hyperpigmented macules. Early diagnosis and treatment may prevent disfiguring residual hyperpigmentation.

### Conflicts of interest

None

### Source of Funding

None.

### How does this paper make a difference to general practice?

- Prurigo pigmentosa is an uncommon and lesser-known skin disorder which may be a diagnostic challenge to clinicians.
- The diagnosis of prurigo pigmentosa is made clinically.
- Early diagnosis and treatment aids in minimizing the disfiguring skin pigmentation.
- Identification and elimination of dietary risk factors is crucial in preventing relapse.
- An early referral to a tertiary center is recommended, as some patients may require a skin biopsy for diagnosis.

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