# Prurigo Pigmentosa with Positive Direct Immunoflurescence: A Rare Case Report in Thailand

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**ABSTRACT:**
Prurigo pigmentosa is a rare inflammatory dermatosis characterized by recurrent symmetrical erythematous papules that coalesce into reticulate hyperpigmentation. The lesions occur symmetrically on the back, trunk, and neck, which had profound pruritus. It is commonly reported in young women, especially in East Asia. Clinical and histopathological assessments are used to make the diagnosis that vary from early to late lesions. Most patients do not show positive direct immunofluorescence, except for only one case report. We report a 24-year-old Thai woman with an ill-defined erythematous plaque on her back and chest wall with pruritus for 3 weeks which direct immunofluorescence showed positive immunoglobulin M at superficial blood vessels and complement 3 with focal granular pattern at dermo-epidermal junction.
**Key words:** Prurigo pigmentosa, Direct immunofluorescence, Keto rash

## Introduction

Prurigo pigmentosa, also known as Nagashima disease, is an uncommon inflammatory skin condition of unknown cause. It mostly affects adolescents and young females. The lesions are characterized by symmetrical pruritic erythematous papules that converge to form a reticulate pattern, typically on the neck, central chest, upper back, and abdomen[1]. The etiology is not clearly understood; several factors have been proposed, including ketogenic diet, friction, diabetes mellitus, and pregnancy[2].

## Case report

A 24-year-old Thai female came with ill-defined erythematous plaques on her back and chest wall with pruritus for 3 weeks following exposure to a penicillin solution. She complained itchy only at the sites of lesions. She denied a history of ketogenic diet, fasting, or diabetes, and she was neither menstruating nor pregnant at that time. There were no similar skin lesions among her family members. Physical examination revealed confluent ill-defined erythematous to brownish reticulated

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patches, plaques, and some pustules with scales on her back, chest wall, and abdomen (Figure 1). There was no oral ulcer. Skin scraping for potassium hydroxide and wright stain were unremarkable. She had been treated with prednisolone 20 mg/day and topical corticosteroid for 1 week, but lesions still progressed. A skin biopsy from her abdomen showed mixed spongiosis and interface dermatitis. There was superficial perivascular infiltration by small lymphocytes, eosinophils, and neutrophils (Figure 2). Direct immunofluorescence (DIF) revealed positive immunoglobulin M at superficial blood vessels (intensity 2+) and complement 3 (C3) with focal granular pattern at dermo-epidermal junction (DEJ) (intensity 1+) (Figure 3). Additionally, the antinuclear antibody test was negative. Other laboratory examinations, including complete blood count, liver function test, creatinine level, and chest X-ray, were normal. The patient was diagnosed with prurigo pigmentosa and treated with oral doxycycline 200 mg/day, oral fexofenadine (180 mg) 2 tablets/day, and topical corticosteroids. The rash was resolved after 1 month of treatment, leaving only reticulated hyperpigmented patches on her chest wall and back.

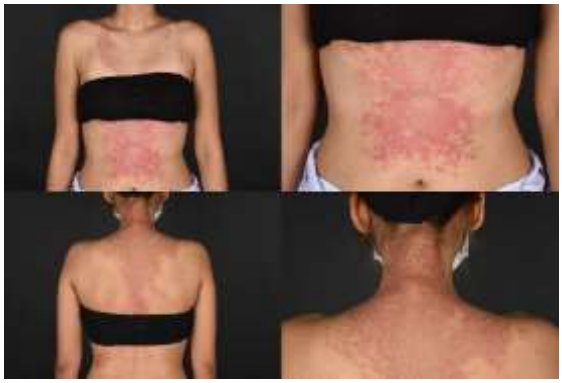

**Figure 1** A 24-year-old Thai female presented with confluent ill-defined erythematous to brownish reticulated patches and plaques with scale and some pustules on back, chest wall and abdomen

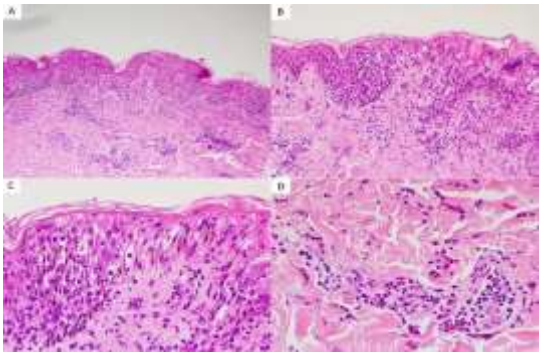

**Figure 2** The histopathology showed mixed spongiotic and interface dermatitis with superficial perivascular infiltration by lymphocytes, neutrophils, and eosinophils. The epidermis displayed spongiosis, ballooning degeneration, necrotic keratocytes, and intraepidermal vesiculation (A:X40, B:X200, and C-D:X400 magnifications, respectively)

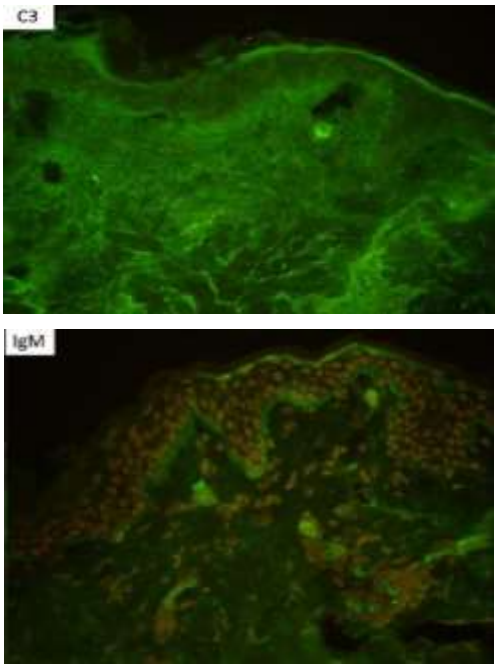


**Figure 3** Direct immunofluorescence showed positive for immunoglobulin M at superficial blood vessel (intensity 2+), complement 3 at dermo-epidermal junction with focal granular (intensity 1+) suspected immune complex-mediated blood vessel disease pattern (X400 magnification)

**Discussion**

Prurigo pigmentosa presents with itchy erythematous macules, papules, and plaques resolving in reticulate hyperpigmentation. Pustular and bullous lesions have been reported, which can mimic autoimmune bullous diseases[3]. Recurrences typically occur at the previous lesional site. The lesions are distributed symmetrically on the trunk, back, chest, and neck. Histopathological features are nonspecific and vary from early to late stage[4]. In the early stage, superficial perivascular neutrophilic infiltration with spongiosis is found, followed by patchy lichenoid infiltration with lymphocyte predominate and some eosinophils. Late lesions show sparse lymphocytic infiltration with an increased number of melanophages in the dermis[5].

The previous DIF results of prurigo pigmentosa usually were negative, except for only one case report. Dijkstra JW *et al*. reported granular deposition of C3 at the DEJ in a case presented by vesicular lesion[6]. Corresponding to our case, the DIF study revealed positive C3 at the DEJ and IgM at superficial blood vessels. Both cases presented with vesicular lesions. These findings support the potential role of basement membrane zone (BMZ) antigen exposure in the pathogenesis of prurigo pigmentosa, triggered by severe inflammation. However, the DIF was reported to have a negative result in another case with vesicular lesions[3]. Therefore, more cases are required for further study to confirm these special findings.

Special immunohistochemistry has demonstrated positive intercellular adhesion molecule-1 (ICAM-1) in erythematous and residual pigmented lesions. This finding suggests a possible mechanism for the recurrent rash at the same site, similar to findings in fixed-drug eruptions[7]. However, Sung KH *et al.* reported no or weak expression of ICAM-1 in pigmented lesions[8]. Therefore, the role of ICAM-1 in prurigo pigmentosa may be controversial.

The etiology of prurigo pigmentosa remains unclear, with both endogenous and exogenous factors implicated. Ketosis, associated with conditions like the ketogenic diet, fasting, bariatric surgery, or poorly controlled diabetes, may lead to elevated blood ketone levels. The accumulation of ketone bodies around blood vessels may lead to neutrophilic perivascular infiltration in the dermis.[1] Other reported triggers include menstruation, pregnancy, infections such as *Helicobacter pylori* or *Borrelia* spirochetes, as well as factors like sweating, friction, and contact allergens. Genetic predisposition has also been suggested, with reports of prurigo pigmentosa in monozygotic twins[9].

Treatment with tetracycline, especially minocycline and doxycycline, was reported in most cases with complete resolution in about half of the patients[1]. The anti-inflammatory effects of these drugs, which inhibit neutrophil migration and chemotaxis, may cause improvement. Additional treatments include dapsone, sulfamethoxazole, isotretinoin, and potassium iodide, although dietary modifications have shown limited effectiveness[10]. In cases of prurigo pigmentosa with blisters, the combination of oral doxycycline and topical tacrolimus has shown clinical improvement[3]. Topical or systemic corticosteroids are ineffective and can help in differentiating prurigo pigmentosa from eczema or contact dermatitis. Confluent and reticulated papillomatosis (CARP) may be confused with prurigo pigmentosa. More pruritus, hyperpigmentation, and neutrophilic exocytosis in histopathological findings can help distinguish prurigo pigmentosa from CARP[1, 4].

Our patient developed symmetrical pruritic erythematous plaques and papules on her back and chest wall for 3 weeks. The lesions did not improve with topical corticosteroids. She denied having a history of a ketogenic diet. Histopathological findings showed superficial perivascular infiltration by lymphocytes,

eosinophils, and neutrophils, which corresponds to previous studies. However, direct immunofluorescence showed positive C3 at DEJ, which is not commonly seen in prurigo pigmentosa. Exposure to BMZ antigens due to severe inflammation in prurigo pigmentosa has been proposed[3]. Improvement occurred within 1 month of doxycycline, resulting in reticulated brownish hyperpigmented patches. Because of the recurrent nature of the disease, long-term follow-up is necessary for this patient.

## Conclusion

Prurigo pigmentosa is a rare recurrent pruritic dermatosis characterized by symmetrical erythematous papules or bullous lesions that result in reticulated hyperpigmentation. Recurrent lesions commonly occur in most patients. The etiology is still unclear, although ketosis is commonly reported. Most cases do not show positive DIF but positive findings can be found. Our case was a rare case of prurigo pigmentosa that showed a positive DIF. The severe inflammation in prurigo pigmentosa may cause exposure to BMZ antigens, which could explain the positive DIF. Due to the limited number of studies, more data collection is required for further study.

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