

# Use of minocycline for the treatment of prurigo pigmentosa with intraepidermal vesiculation: a case report

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[journals.sagepub.com/home/imr](https://journals.sagepub.com/home/imr)**Jie Yang<sup>1,\*</sup> , Shicheng Jiao<sup>2,\*</sup> and Min Zhang<sup>1</sup>**

## Abstract

Pruritus pigmentosa is a skin disease mainly characterized by pruritus, inflammatory rash and reticular and macular pigmentation. The disease more commonly affects young women and may persist for several years. In this article, we report a case of a 20-year-old female patient who presented with erythema and blisters on the neck and trunk with pruritus for 20 days. Dermatological examination revealed a reticular distribution of erythema on the chest and abdomen and some areas of erythema covered with crusts. Additionally, blisters and bullae with clear fluid and negative Nikolsky's sign were noted. On the neck and back, erythema was also in a reticular distribution, and erythema secondary to erosion and/or crusts was present. In addition, histopathological analysis of the lesions showed hyperkeratosis and intraepidermal multilocular vesiculation and confirmed increased migration of inflammatory cells into the epidermis and infiltration of inflammatory cells, including lymphocytes, histiocytes and eosinophils, in the superficial dermis. The expression levels of IgG, IgM, IgA and C3 were all negative. This patient was diagnosed with prurigo pigmentosa, and the condition improved after treatment with minocycline.

## Keywords

Prurigo pigmentosa, blister, minocycline, inflammatory cell infiltration, Nagashima disease, pruritus

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## Introduction

Prurigo pigmentosa (PP) is a skin disease characterized by pruritus, inflammatory rash and reticular and macular pigmentation.<sup>1</sup> Young women are more commonly

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affected, and the disease may persist for several years.<sup>2</sup> Environmental factors and genetic factors are possible causes, but the etiology and pathogenesis remain unclear.<sup>3</sup> A diagnosis is usually made by observation and pathological examination. There are systemic and local treatments for the disease. However, the use of systemic therapy with antihistamines and corticosteroids is associated with adverse effects. It has been reported that dapsone or sulfamethoxazole has a certain curative effect, but patients often relapse and experience toxic side effects.<sup>4</sup> In a previous study, the papules and pruritus in some patients subsided rapidly after treatment with minocycline, and there was no recurrence about one year after the discontinuation of treatment.<sup>5,6</sup> This case presents a 20-year-old female patient with PP treated with oral minocycline. PP is a rare disease, and this case report demonstrates an effective treatment that can provide first-hand clinical data for clinicians.

## **Case presentation**

A 20-year-old female patient presented with erythema and blisters on the neck and trunk with pruritus for 20 days. On 5 July 2020, without an obvious cause, the patient developed edematous erythema with pruritus at the hairline of the posterior neck and then purchased a natural Chinese herbal remedy (Pifuyihao Cream, Jimingtang Biotechnology Co., Ltd, Jangxi, China) for topical application. After application, the edema was relieved, but erythema and secondary pigmentation were still present. About 1 week later, the patient developed erythema and blisters with pruritus on the chest and back, and no significant effect of the continuous application of "PIFUYIHAO" was observed. The lesions continued to expand, and erythema and blisters with severe pruritus also appeared on the waist and abdomen. On 26 July 2020, the patient visited our clinic. The patient was

unmarried and nulliparous, previously healthy, had stable weight before onset, denied food, drug and contact allergies and denied a family history of allergic, metabolic and endocrine system diseases.

Physical examination showed a good general condition, no palpable enlargement of systemic superficial lymph nodes and no abnormalities on systemic examination. Dermatological examination revealed a reticular distribution of dark red patches under the patient's breast with adherent scales. On the abdomen, multiple blisters of different sizes with clear blister fluid and negative Nikolsky's sign were noted, and some blisters were present on areas of erythema. On the neck and back, there was a large area of erythema with a reticular distribution, a few scales and scattered scratches and crusts (Figure 1a and Figure 1b). The patient was finally diagnosed with PP and administered 100 mg oral minocycline once daily. After 10 days of treatment, the primary rash subsided, and pruritus was relieved, leaving pigmented patches (Figure 1c and Figure 1d). The medication was then stopped with subsequent observation for 6 months, and no side effects have been observed.

In addition, laboratory and auxiliary examinations showed the following results: anti-extractable nuclear antigen antibody (-), antinuclear antibody (-), anti-double stranded DNA antibody (-), anti-desmoglein 1 (Dsg1) (-), anti-Dsg3 (-) and bullous pemphigoid antigen 180 (-). The results of urine and stool routine tests and biochemical tests revealed no abnormalities. Furthermore, the treponema pallidum particle agglutination, anti-human immunodeficiency virus antibody, hepatitis B antibody and hepatitis C antibody assays were also normal. In addition, histopathological analysis of the lesions showed hyperkeratosis and intraepidermal multilocular vesiculation and confirmed increased inflammatory cell migration into the epidermis and infiltration of inflammatory cells, including lymphocytes,

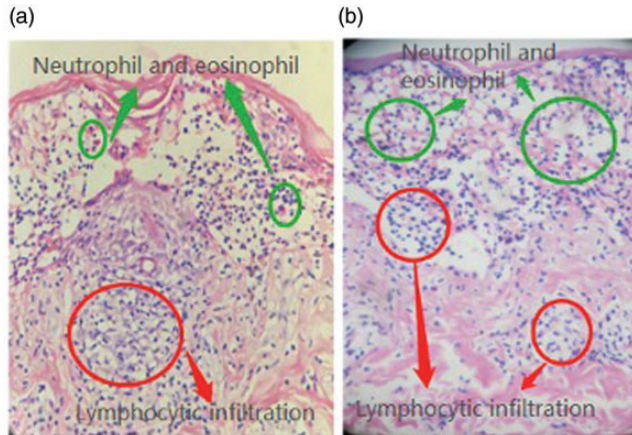


**Figure 1.** Dermatological examination of the 20-year-old female patient with pruritus pigmentosa reported in this case. (a) The distribution of blisters and pigmentation spots in the chest and abdomen before treatment. (b) Distribution of blisters and pigmentation spots on the back of the patient before treatment. (c) The distribution of blisters and pigmented spots on the chest and abdomen after 10 days of treatment with 100 mg oral minocycline once a day. (d) The distribution of blisters and pigmented spots on the back after 10 days of treatment with 100 mg oral minocycline once a day.

histiocytes and eosinophils, in the superficial dermis (Figure 2a and Figure 2b). The expression levels of IgG, IgM, IgA and C3 were all negative, and the results of the direct immunofluorescence assay were negative.

## Discussion

PP, also known as Nagashima disease, is a rare inflammatory skin disease of an unknown etiology. This disease mainly



**Figure 2.** Histopathological analysis of the patient's lesions. (a) Hematoxylin and eosin staining of the lesion before treatment (400 $\times$ ). (b) Hematoxylin and eosin staining of skin lesions after 10 days of treatment with 100 mg oral minocycline once daily. The red circles indicate lymphocytes, and the green circles indicate neutrophils and eosinophils (100 $\times$ ).

occurs in adolescents and young adults and is more common in women. The mean age of onset is 24.4 years, with 84.3% of cases occurring between 11 and 30 years old. It predominately affects the back, chest, neck and face. PP tends to recur in spring and summer and is mainly limited to the original pigmented area.<sup>7</sup>

The clinical symptoms of this disease occur in stages.<sup>8</sup> The early symptoms include sudden onset of erythema with pruritus and edema, maculopapular rashes and papules. The symptoms in the mature stage include erythema, papules, blisters and crust formation. The main symptom in the late stage is a reticular and patchy pigmented rash with a smooth surface. The changes in the histopathology of this disease are also staged.<sup>9</sup> In the early stage, the histopathology shows hyperkeratosis, interspinous spongiosis, a small number of necrotic keratinocytes, papillary dermal edema and neutrophil infiltration around superficial vessels. Neutrophils may form microabscesses in the epidermis, typically in the upper part of the basal layer of the epidermis, and adhere to edematous or

necrotic keratinocytes in a clumped or single-cell manner. This feature is highly specific for PP. In the mature stage, lymphocytes predominate in dermal infiltrates and may be accompanied by neutrophils and eosinophils. Additionally, more obvious spongiosis is observed in the epidermis, leading to intraepidermal or subepidermal vesiculation and even overall necrosis. The late stage is characterized by hyperkeratosis, sparse perivascular lymphocyte infiltration around the vessels and pigment incontinence and melanophages in the papillary dermis. A single rash varies in duration from 2 days to several weeks, ranges in reticular distribution from local to enlarged and causes reticular post-inflammatory hyperpigmentation.<sup>10</sup> Lesions at different stages often coexist and combine to form a reticular configuration.<sup>11,12</sup> The analysis of clinical symptoms and histopathology is required for the diagnosis of PP. In this case, the patient was a young woman with clinical manifestations of erythema, blisters and reticular pigmentation after relapse, consistent with the manifestations and histopathology of PP. Her clinical

manifestations were erythema and blisters on the chest and back. Pathological analysis revealed multilocular blisters in the epidermis. Neutrophils, eosinophils and lymphocytes had infiltrated the blisters. The diagnosis was consistent with bullous PP.

Because of the diversity of rash morphologies, the differential diagnosis of PP is extensive.<sup>13</sup> It needs to be differentiated from contact dermatitis, psoriasis vulgaris and urticaria in the early stage; erythema multiforme and pityriasis lichenoides et varioliformis acuta in the mature stage; and confluent and reticulated papillomatosis (CARP) and poikiloderma vasculare atrophicum in the late stage. In particular, owing to a similar reticulated configuration, it is often difficult to differentiate between PP and CARP. CARP is also a rare skin disease with an unknown etiology, more commonly occurring in adolescents and women.<sup>14</sup> Similar to PP, the lesions of CARP often begin in the intermammary and mid-dorsal regions and may involve the back, neck and trunk. However, in contrast to PP, CARP usually has no subjective symptoms, with occasional pruritus and slow disease development.<sup>15</sup> CARP is clinically characterized by the accumulation of squamous or verrucous papules that are confluent in the center and reticulated at the periphery. In this case, patients present with clinically obvious intraepidermal blisters, but this condition also needs to be differentiated from pemphigus and other intraepidermal bullous diseases. Both can present as intraepidermal blisters, but the latter occurs in middle-aged and elderly patients, often involving the skin and mucosa.<sup>16</sup> Histopathological analysis shows the loss of adhesion between keratinocytes (acantholysis), immunopathological findings in skin lesions and blood circulation of IgG antibodies. Hyperkeratosis, papillomatous hyperplasia, acanthosis, increased basal pigmentation, dermal edema and perivascular inflammatory cell infiltration are also

observed. Minocycline, imidazoles or retinoids are effective in some CARP cases.<sup>17</sup>

The pathogenesis of PP is unknown but may involve neutrophil-mediated inflammation.<sup>18</sup> In addition, mechanical irritation or contact allergies to nickel, chromium and/or climate may also contribute to the development of PP.<sup>11</sup> PP has been demonstrated to be associated with several systemic diseases, including adult Still's disease,<sup>19</sup> atopic dermatitis,<sup>20</sup> *Helicobacter pylori* infection<sup>21,22</sup> and Sjögren's syndrome.<sup>23</sup> PP has also been reported in patients with less food intake because of fasting and diet,<sup>24,25</sup> anorexia,<sup>26</sup> type 2 diabetes,<sup>27</sup> bariatric surgery,<sup>28,29</sup> gastric surgery<sup>30</sup> and early pregnancy.<sup>31</sup> Researchers<sup>29,32</sup> have speculated that dietary factors lead to the involvement of ketone-induced neutrophil-mediated inflammation in the occurrence of PP and confirmed increased ketone levels in the urine and/or blood in some patients.

PP usually improves after treatment with oral minocycline, doxycycline or dapsone, which is considered to be related to anti-inflammatory and immunomodulatory effects, such as the inhibition of neutrophil chemotaxis.<sup>12</sup> However, hyperpigmentation tends to persist even after regression of the rash.

### Author contributions

JY admitted the patient and provided her treatment plans, SJ treated the patient, and MZ performed the pathological tests.

### Ethics statement

This study was approved by the Human Ethics Committee of The Fifth People's Hospital of HaiNan Province, China (approval no.: 165). Written informed consent was obtained from the patient for their anonymized information to be published in this study.

### Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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