

## Prurigo Pigmentosa: A Clinical and Histopathologic Study of 11 Cases

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**Background:** Prurigo pigmentosa is a rare inflammatory dermatosis of unknown etiology. It is characterized by a recurrent pruritic rash and netlike pigmentation. Most of the reported cases have been from Japan; however, here we report on several cases from Taiwan.

**Methods:** This was a single hospital-based retrospective study conducted in a tertiary medical center in Southern Taiwan, recruiting 14 patients with a clinical diagnosis of prurigo pigmentosa between January 1, 2000 and December 31, 2007. Clinical information was collected and reviewed, and skin biopsies were performed for all cases.

**Results:** Of the 14 cases, 11 exhibited clinical and histopathological correlation with prurigo pigmentosa and were enrolled in our study. The age of the patients at diagnosis ranged from 16 to 30 years (mean, 22.3) with female predominance (female: male ratio, 8:3). Patient lesions were primarily distributed symmetrically over the chest and back area and they responded well to doxycycline treatment. The biopsy specimens of all patients showed nonspecific lymphocytic infiltration; folliculitis was noted in 7 specimens and both superficial and deep perivascular lymphocytic infiltration was found in 8 specimens.

**Conclusion:** Although far more prevalent in Japan, prurigo pigmentosa can be seen in Taiwan. In our study, patients were predominantly young females who had been initially diagnosed as having eczema. Therefore, young females who present with intractable eczema distributed symmetrically over the trunk should prompt physicians to consider prurigo pigmentosa.  
(*Chang Gung Med J* 2010;33:157-63)

**Key words:** prurigo pigmentosa, doxycycline, minocycline

First described by Nagashima et al. in 1971,<sup>(1)</sup> prurigo pigmentosa is a rare inflammatory dermatosis of unknown etiology rarely diagnosed outside of Japan. It is often distributed symmetrically over the trunk and presents with a recurrent pruritic rash and netlike pigmentation. In previous reports

from Japan and Taiwan, the clinical and histological characteristics of prurigo pigmentosa were rarely studied. Therefore, we retrospectively analyzed and described the clinical and pathological characteristics of prurigo pigmentosa in Taiwanese patients.

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## METHODS

We reviewed and analyzed 14 cases of prurigo pigmentosa diagnosed within an 8-year period between January 1, 2000 and December 31, 2007 in the Department of Dermatology, Chang Gung Memorial Hospital in Kaohsiung (a tertiary medical center in Southern Taiwan). Clinical data, including gender, underlying disease, age at the time of diagnosis, distribution of lesions, initial clinical diagnosis, aggravating factors, frequency of recurrence, disease duration and treatment course were collected from medical records and telephone visits. The intensity of itching was evaluated using a 10-cm visual analogue scale (VAS) with 0 cm indicating "no itch" and 10 cm indicating "worst itch imaginable."<sup>(2)</sup> We also compared the severity of itching before and after treatment. Skin biopsies of either erythematous papules or pigmented macules were performed on all enrolled patients. We reviewed the histopathology of all epidermis, dermis, appendage apparatus, and subcutis sections to exclude other inflammatory dermatitis such as lupus erythematosus, psoriasis, and pityriasis rosea. As proposed by Böer and Ackerman,<sup>(3)</sup> the criteria for diagnosis of prurigo pigmentosa include reticular skin lesions that are symmetrically distributed in the trunk area (in particular, the back, chest, and neck). Furthermore, the progression of the disease has been divided into three stages. In the early stage, the clinical presentations include itchy urticarial papules or plaques, and the histopathological findings primarily reveal a superficial and perivascular infiltrate of neutrophils, which is also accompanied by edematous papillary dermis, and spongiosis. In the fully developed stage, the clinical presentation includes itchy papulovesicles or vesicles, and the histopathological findings show patchy lichenoid lymphocytic infiltrates, and spongiosis accompanied by intraepidermal and subepidermal vesiculation. In the late stage, the clinical presentation includes pigmented macules, and the histopathological findings demonstrate a lymphocyte monopolized infiltrate and melanophages in the upper dermis.

## RESULTS

Of the 14 cases reviewed in our study, 11 cases fulfilled the diagnostic criteria of prurigo pigmentosa

as proposed by Böer and Ackerman and were enrolled in our study. The 3 cases excluded, after reviewing the clinical history and histopathology, were diagnosed as having amyloidosis, eczema, and post inflammatory hyperpigmentation. The mean age at the time of diagnosis of the 11 study patients ranged from 16 to 30 years (mean, 22.3) (Table 1), with female predominance (female: male ratio, 8:3). All patients were Taiwanese. Skin lesions were distributed symmetrically over the chest (7/11), back (7/11), lumbosacral region (4/11), abdomen (4/11), nape (3/11), and shoulders (3/11) (Fig. 1A, 2A). Acute erythematous lesions in our patients achieved complete remission within 1 day to 1 week after treatment with oral doxycycline and topical steroids.

Numerous episodes of exacerbation and recurrences were observed in all patients without evidence of underlying disease or family history. Excoriations were found in all patients. The common aggravating factors were rubbing and sweating, and summer heat. One patient mentioned that her lesions worsened during menstruation (Case 1 in Table 1). Two cases exhibited multiple tiny vesicles on the back (Fig. 1A). Frequency of recurrence varied from once per month to once to twice per year. Episodic duration varied from 6 months to 7 years. Patient skin lesions typically resolved after use of oral doxycycline, with the exception of 1 patient who required additional treatment with dapsone. The interval between each itching episode in treated patients was as short as 2 weeks and as long as 3 years. In the 11 study patients, clinical diagnosis prior to biopsy included eczema (7/11), prurigo pigmentosa (3/11), pityrosporum folliculitis (2/11), and pityriasis rosea (1/11).

Histological findings varied from case to case and showed nonspecific changes. Of the 7 specimens taken from erythematous papules, the pathological findings included superficial and deep perivascular lymphocytic infiltration (6/7), basal hyperpigmentation (6/7), eosinophil infiltration in the upper dermis (6/7), bacterial folliculitis (4/7), spongiosis (2/7), and solitary superficial perivascular lymphocytic infiltration (1/7).

Both samples obtained from vesicles on an erythematous base (Fig. 1B), showed spongiotic vesicles, vacuolar changes of the basal layer, folliculitis, neutrophils, and eosinophil infiltration in the upper dermis with superficial and deep perivascular lymphocytic infiltration.

**Table 1.** Clinical Summary of Prurigo Pigmentosa Patients in Chang Gung Memorial Hospital in Kaohsiung from 2000 to 2007

Patient	Age	Gender onset	Age diagnosis	Initial itching (cm) (before and after treatment)	Intensity of frequency (before and after treatment)	Disease attack duration years	Follow up sites	Involved	Treatment
1	22	F	19	Eczema	8-9 →2-3	1 time/mo → none	3	N	Doxycycline 200 mg/d for 8 wk
2	20	F	19	PP	10 →2-3	2 times /mo → none	0.5	N, B, L	Doxycycline 200 mg/d for 8 wk
3	21	M	16	PP	9 →2-3	>2 times/yr →1 time/yr	5	B, C	Doxycycline 200 mg/d for 8 wk
4	29	F	26	Eczema	N/A	N/A	3	B, A, L, C, S	Doxycycline 200 mg/d for 3 wk then dapsone* 100 mg/d for 1 wk
5	23	M	20	Eczema, TV	8-9 →2-3	2-3 times/yr →1 time/yr	3	B, C	Doxycycline 200 mg/d for 8 wk
6	34	F	28	Eczema, PF	8 →2-3	1 time/mo →1-2 time/yr	6	B, A, C	Doxycycline 200 mg/d for 5 wk
7	34	F	30	Eczema	N/A	N/A	4	A, L, C, S	No therapy
8	25	M	19	Eczema	7-8 →1-2	8-9 times/yr →1-2 times/yr	6	C	Doxycycline 200 mg/d for 6 wk Minocycline <sup>†</sup> 200 mg /d for 2 wk
9	28	F	21	Eczema	8 →1-2	2 times/yr → none	7	N, A, L	Doxycycline 200 mg/d for 1wk
10	21	F	21	PR	8-9 →2-3	1 time/mo → none	0.5	C,B	Doxycycline 200 mg/d for 2 wk
11	25	F	25	PP	6-7 →2-3	1 time/mo → none	0.5	B,S	Doxycycline 200 mg/d for 1 wk Minocycline <sup>†</sup> 200 mg/d for 1 wk

**Abbreviations:** PP: prurigo pigmentosa; TV: tinea versicolor; PF: pityrosporum folliculitis; PR: pityriasis rosea; N/A: not available; A: arm; B: upper back; C: chest; L: lumbosacral region; N: nape; S: shoulder; wk: week; mo: month; yr: year; \*: Case 4 initially received doxycycline for 3 weeks. The therapy response was poor, we prescribed dapsone for 1 week. Then the skin lesions improved. †: Case 8 and case 11 received minocycline in another hospital with good response.

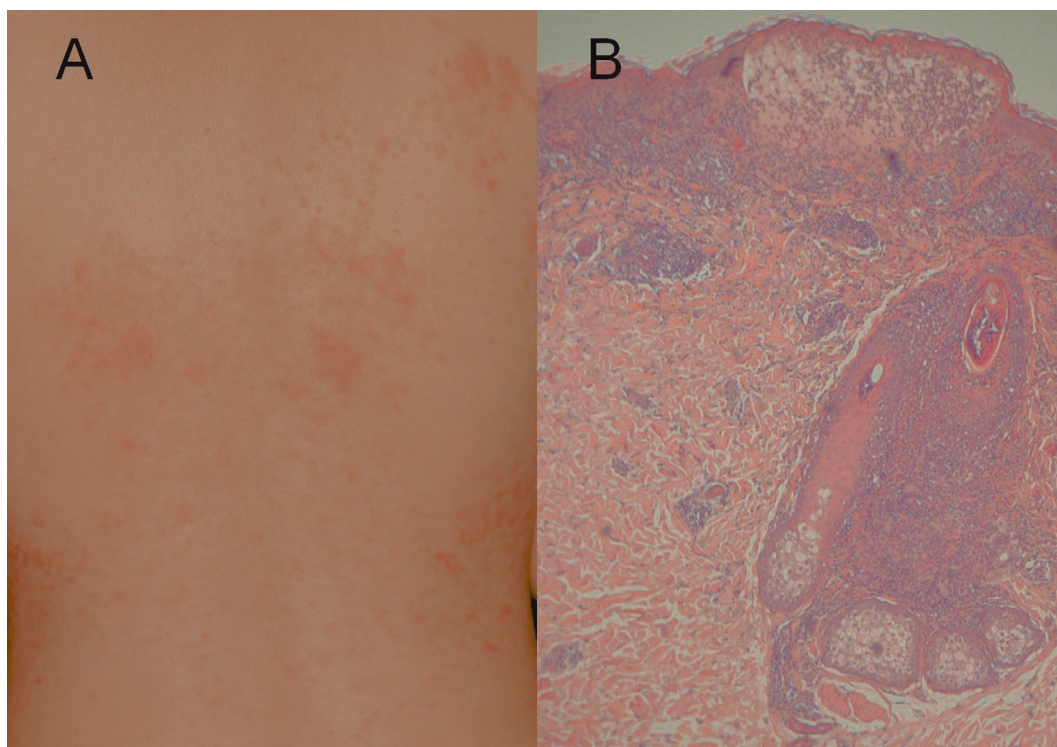
Of the 2 samples obtained from a pigmented macule (Fig. 2B), sections showed basal hyperpigmentation, melanophage, and superficial perivascular lymphocytic infiltration.

Most of our patients received oral doxycycline and topical steroid therapy. The average VAS prior to treatment was 8.3 cm (range: 6.5–10 cm), but it

decreased to an average of 2.3 cm (range: 1.5–2.5 cm) after 1 week of treatment.

## DISCUSSION

Prurigo pigmentosa was first described as “a peculiar pruriginous dermatosis with gross reticular



**Fig. 1** Case 10 A 21-year-old prurigo pigmentosa female in fully developed stage. (A) Multiple reticular pattern papulovesicles over the back. A few Hyperpigmented macules. (B) Histopathology of a papulovesicle showing intraepidermal bulla, band-like lymphocytic infiltration, superficial and deep perivascular infiltration, and folliculitis. (hematoxylin-eosin, x 40)

pigmentation” by Nagashima et al. in 1971.<sup>(1)</sup> Almost all the cases reported were from Japan.

Comparisons between the largest series reviewed by Böer et al. and the 11 cases of this study revealed several similar characteristics (Table 2).<sup>(4)</sup> These included gender distribution, absence of family history, aggravating factors, and good therapeutic response to oral doxycycline.

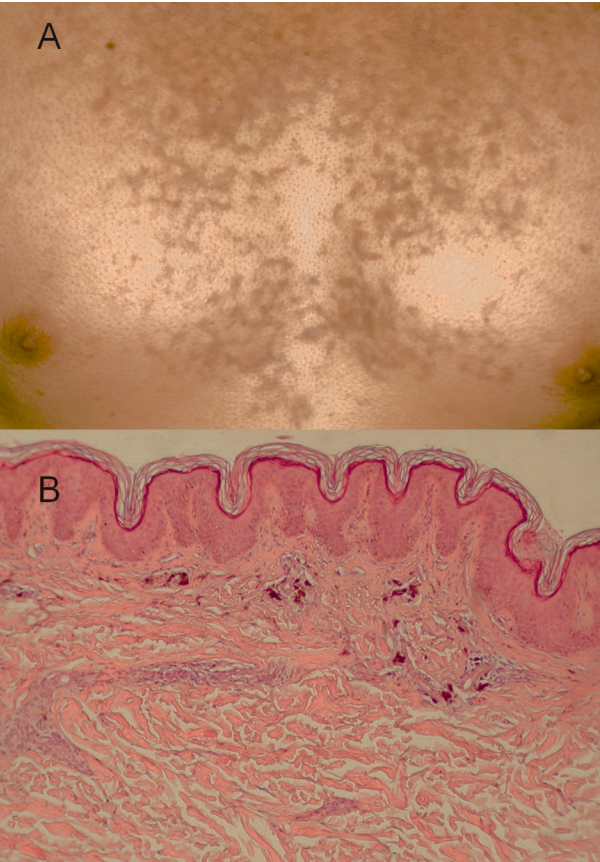
Most studies have shown that there is no underlying disease in patients with prurigo pigmentosa. However, some researchers have postulated the possibility of an association between prurigo pigmentosa and diabetic mellitus, ketonemia, fasting, dieting, or pregnancy etc.<sup>(5,6)</sup> We could not detect underlying diseases in any of our study patients. Aside from common aggravating factors such as rubbing, sweating, and summer heat, menstruation was identified as an exacerbating condition in one of the eleven patients in our study. Worsening of the manifestations of prurigo pigmentosa during the menstrual cycle and pregnancy suggests a possible correlation between

hormones and the disease, especially in young females. Hence, the role of estrogen in patients with prurigo pigmentosa warrants further investigation.

Nagashima et al. reported that, based on 14 cases of prurigo pigmentosa, the duration of the disease lasted from 6 months to 7 years.<sup>(7)</sup> Our study showed similar results, with patients experiencing attacks intermittently for several years.

According to Nagashima et al., the histopathologic findings of prurigo pigmentosa are not specific.<sup>(1)</sup> However, after reviewing 178 cases from the literature and 25 cases of their own, Böer et al. proposed that the histopathologic changes of prurigo pigmentosa may be specific and transpire rapidly.<sup>(8)</sup> Böer and Ackerman proposed initial histopathologic findings of neutrophils infiltrate over superficial perivascular, interstitial and epidermis, associated with spongiosis, ballooning, and necrotic keratocytes in the epidermis. Subsequently, eosinophils and lymphocytes predominate in the dermis. Finally, the epidermis experienced hyperplasia, parakeratosis, and





**Fig. 2** Case 3 A 16-year-old prurigo pigmentosa male in late stage. (A) Netlike hyperpigmentation with a few erythematous papules over anterior chest; (B) Histopathology of the pigmented macules showing basal hyperpigmentation, melanophages over upper dermis and superficial perivascular infiltration. (hematoxylin-eosin, x 40)

hyperpigmentation along with melanophages in the upper dermis.<sup>(3)</sup>

However, it should be noted that the changes also transpire rapidly (in most cases, within a week) and show variable histopathologic findings in cases of skin lesions similar to prurigo pigmentosa. Conversely, prurigo pigmentosa does not exhibit any pathonomic changes and a skin biopsy of prurigo pigmentosa is required to exclude other inflammatory dermatitis.

Although folliculitis related to prurigo pigmentosa has rarely been reported, 2 cases of this condition were described by Schepis et al.<sup>(9)</sup> The relationship between prurigo pigmentosa and folliculitis is

**Table 2.** Comparison between Clinical Data of Our Cases and Review by Böer et al.

	Review 172 cases of prurigo pigmentosa by Böer et al.	Our 11 cases
Female: male	2.25:1	2.67:1
Mean age of diagnosis (Female/Male)	25.0 (24/27)	22.3 (23.5/19.3)
Family history	none	none
Main skin distribution areas	back (133/172), chest (108/172), neck (69/172), lumbosacral (64/172)	back (7/11), chest (7/11), lumbosacral (4/11), abdomen (4/11)
Common aggravating factors	rubbing, sweating, hot weather	rubbing, sweating, hot weather
Therapeutic response	Good response to minocycline, dapsone, doxycycline	Most responded well to doxycycline

not well understood. We propose 2 hypotheses to explain the role of folliculitis in prurigo pigmentosa. Firstly, bacterial folliculitis may induce the formation of prurigo pigmentosa; hence, the response of prurigo pigmentosa to doxycycline may relate to both anti-inflammatory and antibacterial activity; secondly, folliculitis may be a complication from treatment with topical or even systemic steroid therapy. It is evident that the role of folliculitis in the pathogenesis of prurigo pigmentosa merits further study.

In the clinical setting, prurigo pigmentosa is easily overlooked and frequently misdiagnosed as eczema. Unfortunately, as mentioned earlier, pathological findings are nonspecific. It is necessary to combine both clinical and histopathological findings to differentiate prurigo pigmentosa from eczema or other inflammatory diseases.

Prurigo pigmentosa may also be confused with reticular pigmented papules of confluent and reticulated papillomatosis of Gougerot and Carteaud. However, keratosis is not a clinical feature of prurigo

pigmentosa.<sup>(10)</sup> Following histopathological analysis, in a comparison of confluent and reticulated papillomatosis of Gougerot and Carteaud with chronic prurigo pigmentosa, the presence of papillomatosis is not frequently noted.

Oral minocycline (100 mg), taken daily, is usually the first-line therapy for prurigo pigmentosa.<sup>(11,12)</sup> Doxycycline, dapsone, potassium iodide, and macrolide antibiotics have also been reported to be effective.<sup>(13-15)</sup> In our experience, most patients showed a good response to oral doxycycline. Comparing the severity of itching before and after treatment, the average VAS decreased from 8.3 to 2.3 cm.

In conclusion, prurigo pigmentosa is not commonly seen in Taiwan. On the basis of the findings of this study, physicians should consider a diagnosis of prurigo pigmentosa for patients presenting with reticular hyperpigmentation or intractable eczema that are symmetrically distributed over the trunk. The histopathologic findings of prurigo pigmentosa remained controversial and were nonspecific. Once prurigo pigmentosa is diagnosed, oral doxycycline can achieve a good response in most patients, and dapsone may be useful in refractory cases.

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## 色素性癢疹：11 個病例臨床和病理組織的研究

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**背景：**色素性癢疹是一個不明原因且少見的發炎性皮膚病。它的特徵是反覆性癢疹並有網狀色素沈積。大部分被報告的病例是日本人，我們報告幾個在台灣的病例。

**方法：**這是一個在南台灣醫學中心所做的回溯性研究，我們分析本院從 2000 年 1 月 1 日至 2007 年 12 月 31 日，14 位臨床診斷為色素性癢疹的病人的臨床資料和病理切片。

**結果：**其中 11 位經臨床和病理佐證的病人納入我們的研究，這些病人年齡分布從 16 至 30 歲（平均 22.3 歲），以女性居多（女：男，8:3）。皮膚病灶呈對稱性的分布在胸部和背部，而且對多西環素治療反應良好。所有病人的皮膚切片呈現非特異性的淋巴球浸潤。其中有 7 個切片呈現有毛囊炎，8 個切片同時呈現淺層和深層血管周圍淋巴球浸潤。

**結論：**色素性癢疹在臺灣並不常見。在我們的研究，大部分的病人是年輕女性，且常一開始被診斷為濕疹。所以年輕女性有難治的濕疹且對稱性的分布在軀幹時，我們應該考慮是否為色素性癢疹。

（長庚醫誌 2010;33:157-63）

**關鍵詞：**色素性癢疹，多西環素，美諾四環素

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受文日期：民國98年1月22日；接受刊載：民國98年5月6日

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