Seasonal Recurrence of Linear Darier’s Disease
-A Case Report

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Darier’s disease is an uncommon autosomal dominant genodermatosis. About 10% Darier’s diseases present a mosaic form with linear distribution following Blaschko’s lines. This unusual forms were named localized, linear, unilateral, segmental or zosteriform Darier’s disease. We reported a case of linear Darier’s disease in a 52-year-old female. She had recurrent keratotic yellow-brown papules over her right lower extremity every summer for thirty years and the skin lesions resolved spontaneously without any treatment. The family history was negative. Neither nail change nor mucosal involvement was noted. The biopsy specimen taken from the thigh showed characteristic acantholysis and dyskeratosis. The clinical and histological differential diagnoses are presented and discussed. (Dermatol Sinica 26: 236-241, 2008)

Key words: Linear Darier’ s disease, ATP2A2, Mosaicism

INTRODUCTION
Darier’s disease was first described by Darier and White in 1889. It is an uncommon autosomal dominant genodermatosis. The skin eruptions usually appear in patients between the age of 6 and 20 years. The disease is characterized by suprabasal acantholysis and dyskeratosis. Clinically there are keratotic papules or plaques in the seborrheic areas with occasionally nail and mucosa involvement. Sun exposure, heat and perspiration may exacerbate the condition.1 Darier’s disease in a localized pattern was first reported in 1906.2 Since then, many localized variants had been discovered and were also described by terms of localized, unilateral, linear, segmental or zosteriform Darier’s disease. We report here an unusual case of linear Darier’s disease which recurred every summer for thirty years and resolved spontaneously without any treatment.

CASE REPORT
A 52-year-old female presented with recurrent pruritic papules over her right lower leg since adolescence. She stated that the skin eruptions appeared in the summer and resolved one to two months later spontaneously with mild hyperpigmentation left. Her family history was unremarkable. The lesions were mildly pruritic and aggravated after sun exposure. In recent two years, the same skin lesions developed on her right thigh rather than the lower leg. It seems that the lesions migrated gradually along Blaschko’s lines. In addition, the skin lesions did not disappear until one year later. She visited our clinic in October 2006 since the skin lesions increased
in numbers and persisted for more than one year this time.

The physical examination revealed linear grouped, yellow-brown, keratotic papules following Blaschko’s lines on her right thigh. (Fig. 1) Several pin-head sized, hyperpigmented macules over the right lower leg were noted. There was neither nail change nor mucosa involvement. A biopsy specimen from the thigh showed suprabasal splits with acantholysis and dyskeratosis including corps ronds and grains. Overlying hyperkeratosis and parakeratotic keratinocytes were noted. Each focus is small and limited to several rete ridges. The whole picture is consistent with a diagnosis of Darier’s disease. (Fig. 2)

Topical steroid was used after skin biopsy. The skin lesions disappeared 2 months later but flared up summer of 2007.

**DISCUSSION**

About 10% of Darier’s disease presented a localized form. There are papulokeratotic lesions distributed along the Blaschko’s lines resembling epidermal nevus. The most commonly affected sites are trunk and limbs. The scalp, vulva and face involvement are occasionally seen. The histological characters of suprabasal acantholysis with typical corps ronds and grains are the clues for diagnosis. Aggravating factors are the same with Darier’s disease such as light, heat, sweating and friction. Exacerbation during pregnancy was reported in localized Darier’s disease. The family history of linear Darier’s disease is often absent and rarely other associated features of Darier’s disease (nail, palm or mucosa membrane changes) are noted. The onset of the disease is usually in the third or fourth decade of life and there is no sexual predilection.¹ Most of the lesions reported were persistent with or without response to treatment.² ³ ⁴ ⁵ However Plantin et al. reported a case of localized Darier’s disease with seasonal recurrence. They are keratotic papules following Blaschko’s lines on the chest and recurred every summer for ten years, which shared many similarities with our case.⁶

Linear Darier’s disease resembles acantholytic dyskeratotic epidermal nevus clinically and histologically. Both diseases show linear distribution and histological features of acantholytic dyskeratosis. In the past, some cases of linear Darier’s disease were reported

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**Fig. 1**

(A) Small keratotic papules in a linear arrangement on the right thigh.  
(B) Keratotic yellow-brown papules distributed following Blaschko’s lines.
as acantholytic dyskeratotic epidermal nevus. But more and more scientists held opposite opinions. Munro and Cox described a patient who had unilateral acantholytic dyskeratotic skin lesions with nail and palm changes of Darier’s disease.7 Cambiaghi et al. reported a case of acantholytic dyskeratotic epidermal nevus associated with ipsilateral nail dystrophy and palmar pits which are characteristics of Darier’s disease.7 In other literature, patients with acantholytic dyskeratotic epidermal nevus got worse after sunlight, sweating and friction which were common precipitating factors in Darier’s disease. Moreover those cases that were called acantholytic dyskeratotic epidermal nevus before had a late age of onset. Sakuntabhai et al. and Wada et al. detected ATP2A2 mutation in the involved skin of several cases of segmental Darier’s disease.9,10 More and more evidences pointed that linear Darier’s disease is the mosaicism of ATP2A2 mutation. Such mosaic forms can be explained by an early postzygotic mutation. According to Happle’s classification for cutaneous mosaicism of autosomal dominant skin disorders, segmental Darier’s disease were classified into type 1 and type 2 forms.11 The type 1 form keeps the heterozygosity of the mutation. It shows a similar severity as original Darier’s disease and the skin outside the segmental lesions is quite normal as our patient. The type 2 form loses the heterozygosity. It shows a more severe involvement. Currently, cases of type 2 segmental Darier’s disease were rarely reported.

The differential diagnosis included transient acantholytic dermatosis (Grover’s disease) and Hailey-Hailey disease. It is particularly difficult to differentiate between Grover’s disease and linear Darier’s disease. Both Grover’s disease and linear Darier’s disease may share similar morphology and histology and may both be triggered by sunlight, sweating or heat. Grover’s disease is a pruritic, papulovesicular disease with isolated lesions disseminated on the trunk or extremities. Although the term ‘transient’ has been used, most cases are persistent lesions with durations from weeks to months.12 In a review article of 72 cases of Grover’s disease, it is found that 88% were male; all patients but one had trunk involvement; 21% were bedridden; most patients had other

![Fig. 2](image_url)

(A) Biopsy specimen of the lesion on the right thigh shows hyperkeratosis with suprabasal acantholysis and dyskeratosis. (H&E, original magnification x100)

(B) High power view shows characteristic corps ronds and grains. (H&E, original magnification x400)
comorbidities except in 6 patients. The most common histology type was pemphigus vulgaris-like pattern. We favored the diagnosis of linear Darier’s disease because the grouped keratotic papules were distributed along Blaschko’s lines; moreover the presence of typical suprabasal acantholysis and dyskeratosis.

The distribution of Hailey-Hailey disease involves the intertriginous areas, especially the axilla and the groin. Histologically, acantholysis is more prominent and dyskeratosis is less marked than Darier’s disease.

The effectiveness of treatment is often not satisfactory. For mild disease, removal of exacerbating factors, using sunscreen or using emollient substances such as urea or lactic acid may have benefits. For more severe cases, the treatment includes topical and oral retinoids, topical steroid, lactic acid, salicylic acid and oral antibiotics. Tazarotene gel is the newest retinoid which has been reported to successfully treat linear Darier’s disease. O’Malley et al. reviewed 40 cases of linear Darier’s diseases. Fifteen (38%) patients showed partial or complete response to topical tretinoin. Two patients responded to systemic vitamin A therapy and four patients responded to lactic acid, salicylic acid and steroid cream. There were two patients showing spontaneous resolution. What interested us is that the skin lesions resolved spontaneously without any treatment in the past thirty years in our patient.

If medical therapy is ineffective, carbon dioxide laser and erbium:YAG laser have been used for chronic, recalcitrant cases. However the evidence of efficacy is limited.

Linear Darier’s disease is an uncommon skin disorder. Seasonal recurrence of linear Darier’s disease is even more rare. When the clinicians encounter the patients with recurrent papules following Blaschko’s lines, linear Darier’s disease should be in the differential diagnoses.

REFERENCES
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Darier’s disease 是一種罕見之遺傳性皮膚病，大約百分之十患者呈現基因鑲嵌形式，其皮膚病灶會沿著布拉許口氏線分布，這些不尋常之形式特別局限型，線型，單側型，分節型或帶狀型 Darier’s disease。我們報告一例 52 歲女性身上呈現線型 Darier’s disease，她於每年夏天反覆在下肢出現一些角化，棕黃色丘疹，持續三十年之久，這些丘疹在沒有給予任何治療下自動消失。患者無家族史，亦無指甲與粘膜病變，大腿皮膚病灶切片，病理顯示典型棘層分解與角化不全，關於臨床及病理下類似的鑑別診斷，將在本文中加以討論。（中華皮誌: 26: 236-241, 2008）