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BRIEF REPORT

Clinical Characteristics and Therapeutic Aspects of Blaschko Linear Psoriasis

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ABSTRACT

Introduction: Blaschko linear psoriasis (BLP) is characterized by the linear distribution of psoriatic skin lesions along the Blaschko lines. BLP can be divided into type I and type II, mainly on the basis of clinical manifestations. BLP can easily cause psychological burdens in patients and clinical confusion for physicians. Here, we summarize clinical cases to provide a better understanding of BLP.

Methods: The subjects included patients with BLP who visited our dermatology departments and those reported in the literature obtained from the PubMed and Wanfang databases. Quantitative data were presented as means ± SD (standard deviation), and qualitative data were represented by the frequency. Student's *t* test was employed to compare means, whereas chi-square tests were used for analyzing qualitative data.

Results: A total of 74 patients with BLP (5 our patients, 69 from literature) were included, with 61 type I and 13 type II patients. We summarize BLP's characteristics as follows: (1) More frequent in male individuals, especially in type II; (2) Earlier onset than classical psoriasis; (3) Mainly distributed unilaterally, and no preference for left or right site; (4) Asymptomatic or slight pruritus; (5) Mostly negative family history of psoriasis; (6) Possible involvement of the nails/scalp (mainly for type II); (7) Possible exogenous triggering or aggravation factors; (8) Possible concomitant classical plaque or guttate psoriasis lesions, especially in type II; (9) Conforming to histopathology features of classical psoriasis; (10) Relatively favorable response to antipsoriatic treatment, although poor for superimposed areas in type II.

Conclusion: This study analyzed the clinical characteristics and therapeutic aspects of BLP. Compared with published studies, we have new findings, such as gender bias. Besides traditional antipsoriatic treatment, a personalized selection

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of biologics may also be a promising choice. Dermatologists should recognize and understand the significance of this disease, and provide patients with appropriate psychological counseling and clinical treatments.

Keywords: Biologics; Blaschko linear psoriasis; Blaschko lines; Psoriasis; Unilateral distribution

Key Summary Points

Why carry out this study?

Blaschko linear psoriasis (BLP) can easily cause psychological burdens in patients and clinical confusion for physicians, due to unfamiliarity with its related characteristics.

The aim of this study is to summarize the clinical characteristics and therapeutic aspects of BLP.

What was learned from the study?

We have summarized ten clinical characteristics of BLP.

Besides traditional antipsoriatic treatment, a personalized selection of biologics may be also a promising choice.

INTRODUCTION

Blaschko linear psoriasis (BLP) is a rare and underdiagnosed subtype of psoriasis. It is characterized by the linear distribution of psoriatic skin lesions along the Blaschko lines (Fig. 1a, b). The pathogenesis of BLP is due to the genetic mechanism of mosaicism [1]. BLP can be the only manifestation of psoriasis (type I, or isolated type), or it can be superimposed in less severe disseminated classical lesions of psoriasis vulgaris, and unmasked when classical lesions fade away with antipsoriatic treatment (type II, or superimposed type) (Fig. 1c) [2, 3]. The term "superimposed type" was introduced in 2007 to highlight the distinction between polygenic and monogenic susceptibility backgrounds [4], which can help to elucidate the molecular basis of psoriasis.

BLP can easily cause psychological burdens in patients and clinical confusion for physicians, due to unfamiliarity with its related characteristics. Therefore, here we summarize the patients we have treated and the patients reported in the literature to provide a better understanding of BLP.

METHODS

Patients

We evaluated clinical cases of BLP who were admitted to our dermatology departments. Their diagnoses were confirmed by three independent dermatologists with the help of histopathology. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments and was approved by the Medical Ethics Committee in Guangdong Provincial People's Hospital (KY2023-154-02). Written informed consent was obtained from the clinical cases evaluated from our dermatology departments to participate and for the publication of their data.

Literature Review

Published case records of BLP were retrospectively retrieved from the PubMed (https://pubmed.ncbi.nlm.nih.gov/) and Wanfang (https://www.wanfangdata.com.cn) databases. Medical Subject Heading (MeSH) included "Blaschko" or "linear" combined with "psoriasis". Only well-documented cases of BLP were included. Psoriasis with linear manifestations related to the Köbner phenomenon caused by external provocation or nervous stimulation (e.g., herpes zoster) was excluded. The naevoid psoriasis or congenital blaschkoid psoriasis was also within the scope of our analysis. Considering that there is debate about the existence of naevoid/congenital psoriasis as a unique entity, we performed our analysis separately with or without naevoid psoriasis.

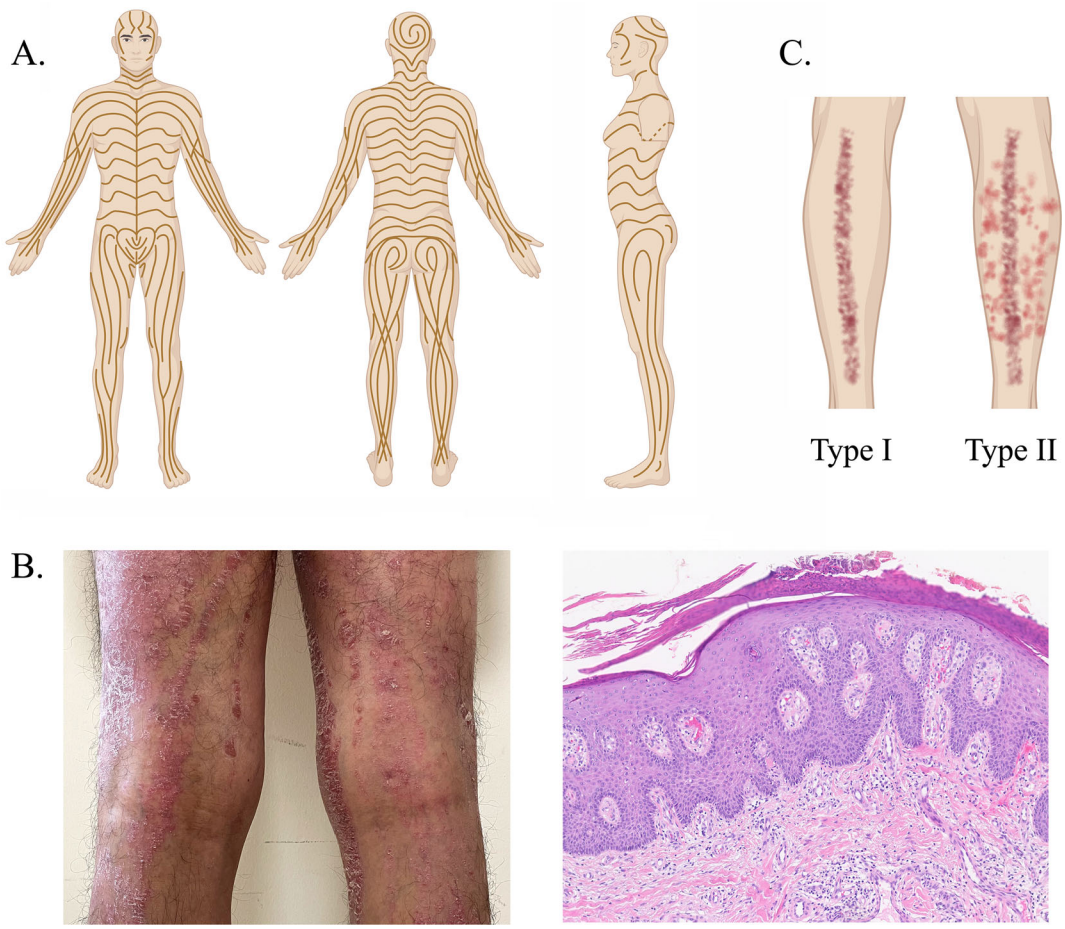

Fig. 1 Clinical interpretation of Blaschko linear psoriasis (BLP). **a** Schematic representation of Blaschko linear. **b** A case of a male patient with BLP (No. 4 in Supplementary extracted data). The left image shows the liner lesions on his legs, and the right is the corresponding histopathological image (×100). **c** Schematic representation of clinical typing of BLP

Data Analysis

The medical records of the cases were collected and reviewed. Data were extracted on demographics, age of onset, disease course, lesion distribution, subjective symptoms, family history, induced or aggravated factors, comorbidity of diseases, and medications (Supplementary extracted data). Quantitative data were presented as means ± SD (standard deviation), while qualitative data were represented by the frequency. Student's *t* test was employed to compare means, whereas chi-square tests were used for analyzing qualitative data. If the expected values in the chi-square analysis for qualitative data were less than 5, Fisher's exact test was utilized. Statistical significance was indicated by a *p* value less than 0.05. All statistical analyses were conducted using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Characteristics of Gender, Age of Onset, and Lesion Distribution

Data were extracted from the 74 patients (5 from our patients, 69 from literature, Table 1). Overall, there was a higher proportion of male patients (62%, 45/73), especially for type II

Table 1 Demographics, clinical characteristics, and treatment aspects of patients with Blaschko linear psoriasis (BLP)

Characteristics	No. (%), linear psoriasis			
	All patients	Type I	Type II	*p*
Total	74	61	13	–
Gender				
Female	28 (38)	26 (43)	2 (15)	0.113
Male	45 (62)	34 (57)	11 (85)	
Not mentioned	1	1	0	
Age of onset (years), mean ± SD	13.56 ± 15.49	12.73 ± 15.06	17.49 ± 17.49	0.318
Disease course (year), mean ± SD	9.28 ± 12.14	8.49 ± 11.68	12.97 ± 14.05	0.229
Symmetry				
Unilateral	67 (91)	56 (92)	11 (85)	0.599
Bilateral	7 (9)	5 (8)	2 (15)	
Affected sites				
Right	33 (46.5)	30 (51)	3 (25)	0.141
Left	33 (46.5)	26 (44)	7 (58)	
The whole	5 (7)	3 (5)	2 (17)	
Not mentioned	3	2	1	
Distribution				
Localized	35 (47)	31 (51)	4 (31)	0.189
Generalized	39 (53)	30 (49)	9 (69)	
Pruritus symptom				
Moderately pruritic	1 (2)	1 (2)	0	0.452
Slightly pruritic	30 (57)	28 (60)	2 (33)	
No pruritus	22 (41)	18 (38)	4 (67)	
Not mentioned	21	14	7	
Family history				
Yes	8 (12)	6 (11)	2 (25)	0.254
No	57 (88)	51 (89)	6 (75)	
Not mentioned	9	4	5	
Nail involvement				
Yes	15 (32)	10 (24)	5 (83)	0.009
No	32 (68)	31 (76)	1 (17)	
Not mentioned	27	20	7	
Scalp involvement				

Table 1 continued

Characteristics	No. (%), linear psoriasis			
	All patients	Type I	Type II	*p*
Yes	8 (21)	4 (12)	4 (80)	0.004
No	30 (79)	29 (88)	1 (20)	
Not mentioned	36	28	8	
Joint involvement				
Yes	4 (11)	3 (10)	1 (14)	1.000
No	34 (89)	28 (90)	6 (86)	
Not mentioned	36	30	6	
Exogenous triggering or aggravation factors				
Yes	13 (33)	12 (34)	1 (25)	1.000
No	26 (67)	23 (66)	3 (75)	
Not mentioned	35	26	9	
Concomitant other classical psoriasis plaques				
Yes	31 (42)	18 (30)	13 (100)	< 0.001
No	43 (58)	43 (70)	0	
Psoriatic pathological evidence				
Yes	66 (97)	56 (97)	10 (100)	1.000
Incompletely support	2 (3)	2 (3)	0	
Not mentioned	6	3	3	
Comorbidity of systemic diseases				
Yes	13 (21)	10 (18)	3 (37)	0.345
No	50 (79)	45 (82)	5 (63)	
Not mentioned	11	6	5	
Treatment regime				
Topical treatment	45 (54)	40 (60)	5 (29)	0.004
Traditional systemic treatment and light therapy	23 (27)	18 (27)	5 (29)	
Adalimumab	3 (4)	2 (3)	1 (6)	
Etanercept	3 (4)	2 (3)	1 (6)	
Infliximab	3 (4)	1 (1)	2 (12)	
Ustekinumab	2 (2)	1 (1)	1 (6)	
Ixekizumab	4 (5)	3 (4)	1 (6)	
Secukinumab	1 (1)	0	1 (6)	

Table 1 continued

Characteristics	No. (%), linear psoriasis			
	All patients	Type I	Type II	*p*
Not mentioned	4	4	0	
Outcome				
Favorable	38 (57)	36 (67)	2 (15)	< 0.001
Moderately	7 (10)	7 (13)	0	
Slight improvement	2 (3)	1 (2)	1 (8)	
Less responsive	20 (30)	10 (18)	10 (77)	
Not mentioned	7	7	0	

SD standard deviation

(85%, 11/13). After excluding congenital/nevoid psoriasis, the male proportion in type II was more predominant than that in type I (100% vs 56%, $p = 0.005$, Supplementary Table 1).

The overall age of onset was relatively young, which is clearly different from classical psoriasis, and there was no statistical difference between type I and II (Table 1, Supplementary Table 1). Skin lesions were mainly distributed unilaterally (91%, 67/74, Table 1; 91%, 57/62, Supplementary Table 1) and there was no difference between the left and right sides of the body.

Analysis of Pruritus Symptom, Triggering/Aggravation Factors, and Concomitant Conditions

The vast majority of patients complained of no or slight pruritus (98%), which is similar to classical psoriasis. Moreover, there was no significant difference in pruritus between type I and II (Table 1, Supplementary Table 1), indicating that the presence of pruritus is not the basis for distinguishing between the two subtypes.

Only 10% of patients reported a positive family history of psoriasis. Approximately 70% of patients showed no nail, scalp, or joint involvement. However, type II was mainly characterized by nail and scalp involvement (about 80%, Table 1, Supplementary Table 1). Approximately one-third of patients reported exogenous triggering or aggravation factors, including medications (e.g., lithium [5] and pembrolizumab [6]), climates (e.g., aggravated in winter, subsides in summer), and upper respiratory tract infection. Histopathologically, over 96% of patients conformed to the characteristics of classical psoriasis.

In addition to linear skin lesions, a considerable proportion of patients (about 40%) also have classical plaque or guttate psoriasis lesions, especially in type II patients (100%). A small proportion of patients (about 20%) showed comorbidity of systemic diseases including psoriatic arthritis, bipolar disorder, posttraumatic stress disorder, and depression [5] (Table 1, Supplementary Table 1).

Therapies of BLP

Overall, more than half of the patients had tried topical treatment (e.g., corticosteroids, retinoic acid, and vitamin D_3 derivatives), with approximately 20% having tried traditional systemic treatment (e.g., methotrexate, acitretin)/light therapy and biologics, respectively. The proportion of type II patients using biologics was higher than that of type I patients (42% vs 13% in Table 1; 47% vs 16% in Supplementary

Table 1). More than 50% of patients with BLP achieved favorable outcomes, especially those who used topical treatment and traditional systemic treatment/light therapy. The percentage of favorable outcomes achieved by targeting biologics was relatively low (31%, 5/16; Supplementary Tables 2, 3). However, the recurrence rate after treatment withdrawal in the biological therapy group was relatively lower (13% vs 30%, Supplementary extracted data). These findings suggest that epidermal abnormalities may be more important factors contributing to BLP occurrence.

In the regimen of targeting biologics, ixekizumab, a monoclonal antibody against interleukin-17A, performed well. All patients receiving ixekizumab (three type I and one type II, non-congenital/nevoid subtype) obtained favorable outcomes (Supplementary Tables 2, 3). Meanwhile, we also found that type II patients with BLP seemed more refractory to antipsoriatic treatment than type I patients were (favorable percentage, 15% vs 67%, overall; 18% vs 72%, excluding congenital/nevoid subtype; both $p < 0.01$). This suggests that there are still differences in the pathogenesis between type I and II.

Summary of Clinical Characteristics of BLP

Taken together, we summarize BLP's characteristics as follows:

1. More frequently in male individuals, especially in type II.
2. Earlier onset than classical psoriasis.
3. Mainly distributed unilaterally, and no preference for left or right site.
4. Asymptomatic or slight pruritus.
5. Mostly negative family history of psoriasis.
6. Possible involvement of the nails/scalp (mainly for type II).
7. Possible exogenous triggering or aggravation factors.
8. Possible concomitant classical plaque or guttate psoriasis lesions, especially in type II.
9. Conforming to histopathology features of classical psoriasis.
10. Relatively favorable response to antipsoriatic treatment, although poor for superimposed areas in type II.

DISCUSSION

Blaschko lines, described in 1901 by Alfred Blaschko, are different from other linear patterns, such as the Langer line and the innervation line of the spinal nerves. They do not follow any known neural, vascular, or lymphatic alignment in the skin [7–9]. They are V-shaped on the dorsal side, S-shaped horizontally on the front and sides of the trunk, spiral-shaped on the scalp, and parallel longitudinal directions on the limbs (Fig. 1a, b). These lines evoke the migration of embryonic cells, causing them to proliferate anterolaterally from the neural crest [10].

BLP is one of the skin diseases following Blaschko lines first described in 1951. It is even rarer than pustular psoriasis, and there is no estimated prevalence. Its pathogenesis is explained by the concept of genetic mosaicism, which means that cells harboring somatic mutation(s) linked to psoriasis migrate following the lines of Blaschko [11]. In addition, the presence of external/environmental factors is required in the occurrence of skin lesions, as linear psoriasis usually does not exist at birth and often occurs in later life. In our investigation, approximately 30% of patients with BLP reported exogenous triggering/exacerbating factors, including medications, climate change, and infection, which further supports this viewpoint.

Pembrolizumab-induced linear psoriasis has been reported in the literature [6]. Pembrolizumab is a programmed cell death protein 1 (PD-1) checkpoint inhibitor, widely applied in immunotherapy for cancers. Psoriasis de novo or exacerbation by PD-1 inhibitors in patients with cancer is one of the cutaneous immune-related adverse events (irAEs) [12]. Considering the presence of malignant neoplastic disease, the treatment of PD-1 inhibitor-related psoriasis (including BLP) is more challenging because of the concern of

immunosuppressive effects of many antipsoriasis drugs. Patients are particularly advised to avoid cyclosporine and small molecule inhibitors (e.g., JAK inhibitors) that may induce/exacerbate tumor progression [6, 13].

According to treatment responses, BLP of superimposed type (type II) can be divided into at least three situations: linear psoriasis resistant and classical plaque sensitive to treatment, both linear psoriasis and classical plaque sensitive, and treatment sensitive for linear psoriasis [14]. Our investigation shows that the first situation is the most common. This classification not only helps clinicians understand the different treatment responses between linear psoriasis and neighboring classical psoriasis but also helps to explore the relevant influencing gene(s)/genetic predictor(s) of treatment efficiency by gene sequencing of responder and non-responder region (Fig. 1c). A recent sequencing study has made a good start, in which transcriptomic analysis of BLP revealed shared and distinct signatures with classical psoriasis vulgaris (Supplementary Fig. 1, Supplementary heatmap reorder of Fig. 1) [15]. However, further research is needed to clarify the pathogenic genes of linear psoriasis. Additionally, more and more signs suggest that pathogenic genes may vary from person to person.

Currently, there are no official guidelines for the treatment of BLP. It seems logical to follow the treatment guidelines for classical psoriasis. However, the treatments are challenging, with varying reported clinical responses to traditional and biological treatments of psoriasis. It may be caused by the loss of heterozygosity in affected cells of the lesions, resulting in distinct variations in proliferation/differentiation of keratinocytes [16].

On the other hand, dysregulation of the epidermis can also cause abnormal activation of lesional inflammatory cytokine pathways. Our investigation shows that five patients responded favorably to ixekizumab (four patients) and etanercept (one patient), biologics approved for the treatment of psoriasis. Published literature also reported that a patient with linear psoriasis showed only limited response to ustekinumab; however, he responded favorably to ixekizumab [17]. This suggests that a personalized selection of biologics (different targets or even the same target) may be a promising choice for linear psoriasis.

Our research further updated the clinical characteristics of BLP. Compared with a study involving 30 patients with BLP conducted in France 6 years ago [3], we have agreements as well as new findings. The consistent aspects include earlier onset, unilateral distribution (no preference for left or right side), and triggering/aggravation factors (in about one-third of patients with BLP). New findings include more involvement of male individuals in BLP (especially in type II), a lower rate of positive psoriatic family history, and a higher favorable rate by traditional antipsoriatic treatment. More importantly, Say and colleagues showed that only ustekinumab treatment resulted in a response in BLP (2/3), while we found all patients responded favorably to ixekizumab (4/4) in our investigation. Biologics against IL-17A (ixekizumab, secukinumab) did not appear in their research, possibly as a result of their recent approval for psoriasis in Europe. Otherwise, the differences in research results may mainly be due to differences in racial susceptibility backgrounds.

A limitation of the present study is that, other than the patients we treated, the patients we reviewed were only from the PubMed and Wanfang databases. Cases of BLP not included in these two databases have not been reviewed. For the same reason, we did not analyze the differences of BLP among different races. Another point is that the standards for treatment efficiency cannot be guaranteed to be completely unified, and reporters used their own standards, but the overall trend in evaluating treatment effectiveness is consistent. Also, some patients had incomplete medical information. Although our sample size is larger than previous studies, it may not be sufficient to identify subtle differences, such as the different therapeutic responses to biologics.

CONCLUSION

This study summarized the clinical characteristics and therapeutic aspects of BLP, such as more involvement of male individuals (especially in type II); approximately one-third of patients with BLPs having triggering/exacerbating factors; a personalized selection of biologics may also be a promising choice, besides traditional antipsoriatic treatment. Dermatologists should recognize and understand the significance of this disease, and provide patients with appropriate psychological counseling and clinical treatments.

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Author Contributions. Ling Chen contributed to literature search, case collection/analysis, and drafting of the manuscript. Yufan Cheng contributed to literature search, case collection/analysis, and critical revision of the manuscript. Lu Peng contributed to literature search, figure construction, and bioinformatics analysis. Xuesong Jia contributed to literature search, and case collection/analysis. Guangren Liu contributed to literature search, and case collection/analysis. Zhu Shen contributed to conception and design of the study, literature search, case collection/analysis, and critical revision of the manuscript. All authors have approved the submitted version.

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Data Availability. All data generated or analyzed during this study are included in this published article/as supplementary information files.

Declarations

Conflict of Interest. Ling Chen, Yufan Cheng, Lu Peng, Xuesong Jia, Guangren Liu and Zhu Shen have nothing to disclose.

Ethical Approval. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments and was approved by the Medical Ethics Committee in Guangdong Provincial People's Hospital (KY2023-154-02). Written informed consent was obtained from the clinical cases evaluated from our dermatology departments to participate and for the publication of their data.

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