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CASE STUDY

Linear childhood discoid lupus erythematosus along a Blaschko's line of the arm

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Abstract

Linear childhood discoid lupus erythematosus (DLE) is a rare variant of DLE with a linear distribution that preferentially occurs on the face and scalp of children. We report a rare case of linear childhood DLE on the Blaschko's line of his left upper arm of a 7-year-old Japanese boy with 4-year history of the disease. He was positive for anti-single-stranded DNA antibodies, but still showed no systemic symptoms during the 3-year follow-up period. We reviewed previous reports on linear childhood DLE and found that patients with nonfacial/nonscalp skin lesions are significantly more likely to be positive for autoantibodies.

KEYWORDS
autoantibodies, Blaschko's line, childhood, discoid lupus erythematosus, linear, systemic lupus erythematosus

1 | INTRODUCTION

Linear childhood discoid lupus erythematosus (DLE) is a rare variant of DLE with a linear distribution that preferentially occurs on the face and scalp of children. It progresses to systemic lupus erythematosus less frequently than other types of DLE. We report a rare case of this entity distributed on the left arm and discuss differences between reported cases with DLE on the face and those with limb and trunk involvement.

2 | CASE PRESENTATION

A 7-year-old Japanese boy visited our hospital because of a 4-year history of linearly distributed skin lesions on his left arm. There were no related symptoms. A history of preceding trauma and excessive ultraviolet exposure were not elicited from the medical interview. His mother was suspected to have undifferentiated connective tissue disease. On examination, several bean-to-thumb-sized brownish scaly and/or atrophic erythematous patches were located linearly from the left shoulder to the left forearm, following a Blaschko's line (Figure 1A,B). Laboratory tests showed a slight elevation in aminotransferases. The serum level of anti-single-stranded DNA (ssDNA) antibodies was slightly elevated at 12.2 U/ml (cut-off level, 7 U/ml), while other lupus-related autoantibodies were all negative. After written informed consent was obtained, skin biopsy was performed from the edge of the skin lesion. Histopathological examination revealed liquefaction degeneration with apoptotic keratinocytes in the epidermal basal layer, follicular keratotic plugs in the epidermis, perivascular and periadnexal infiltration of lymphocytes, and mucin deposition over the whole dermis (Figure 1C-E). Direct and indirect immunofluorescence tests yielded negative results. The patient was diagnosed with linear childhood DLE and treated with topical corticosteroids and tacrolimus. During the 3-year follow-up period, his lesions remained stable, and he showed no systemic symptoms. The serum levels of aminotransferases and anti-ssDNA antibody decreased to normal.

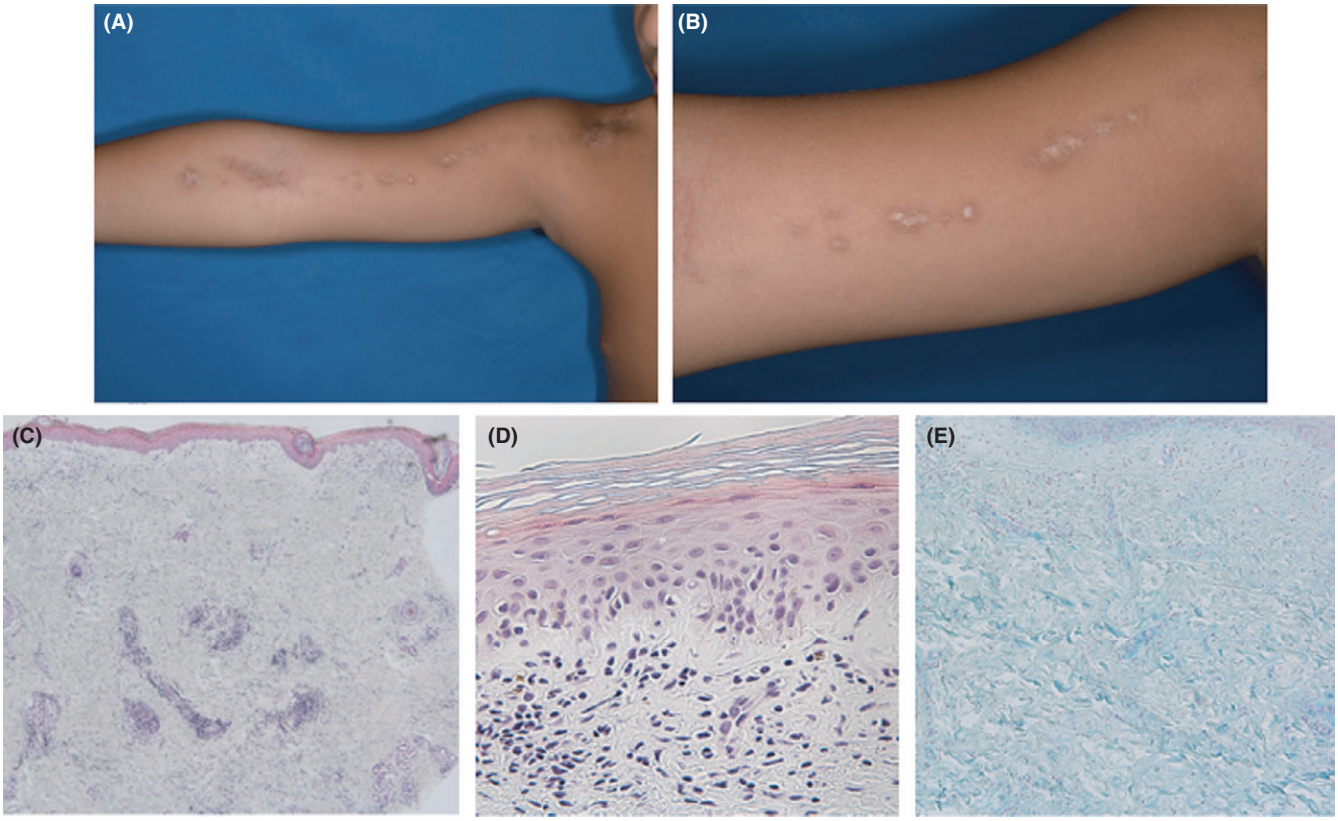

FIGURE 1 Clinical features and histopathological findings. (A) Several small brownish erythema located linearly along Blaschko's line, on the internal side of his left upper arm. (B) Each skin lesion had fine scales on the surface with central atrophy. (C) Moderate atrophy with some follicular plugging in the epidermis. Perivascular and periadnexal lymphocytes infiltration in the superficial to deep dermis (hematoxylin and eosin [H&E] staining, original magnification ×40). (D) Liquefaction degeneration with apoptotic keratinocytes and incontinentia pigmenti histologica in the epidermal basal layer (HE staining, original magnification ×200). (E) Mucin deposition in the dermis (Alcian blue staining, original magnification ×200)

3 | DISCUSSION

Based on linear distribution along Blaschko's line, lichen striatus (LS), linear lichen planus (LLP), and linear morphea should be considered as differential diagnoses.

Specific histological characteristics of DLE include vacuolar changes in the basal layer, slight hyperkeratosis, and a thickened basement membrane in the epidermis. Lymphocytic infiltration can be observed in the perivascular and periadnexal areas in the superficial to deep dermis. Mucin deposition in the dermis is also a characteristic of DLE. In some cases, a positive direct immunofluorescence (DIF) test may help diagnosis; however, it has been reported that 20% of the childhood DLE cases have a negative DIF test.[1] Although the DIF test was negative in our case, other histopathological findings and the persistent clinical course strongly supported the diagnosis of linear childhood DLE.

Lichen striatus is a self-limiting inflammatory dermatitis that occurs primarily in children. Skin lesions are characterized by 1- to 3-mm erythematous papules with fine scales on their edges, which usually appear along an extremity.[2] Histopathology of LS shows moderate acanthosis, focal spongiosis and parakeratosis, and lichenoid infiltrate of lymphocytes and histiocytes in the papillary dermis and around the sweet gland.[3] Importantly, LS lacks follicular plugging, basement membrane thickening, and dermal mucin deposition. Although it is difficult to differentiate LS from DLE, LS resolves by itself in a short period, which can be helpful in making the diagnosis.

Linear lichen planus usually affects the hair-bearing area in adults.[4] The morphology is characterized by polygonal, violaceous papules.[5] Histopathological findings in LLP are lichenoid reactions composed of dense band-like infiltration of lymphocytes just below the dermal-epidermal junction, accompanied by acanthosis with a saw-tooth appearance and wedge-shaped hypergranulosis. LLP lacks periadnexal lymphocyte infiltration, basement membrane thickening, and dermal mucin deposition.

Linear morphea is demarcated by marked fibrosis with broad collagen fibers. Given the inflammatory lymphocytic infiltration in the dermis and vacuolar change along the dermo-epidermal junction in its early stage, it occasionally results in a misdiagnosis of concomitant morphea and DLE or sclerodermiform linear cutaneous lupus erythematosus.

Blaschko's lines were firstly described by Alfred Blaschko in 1910. Blaschko's lines represent the pathways of epidermal cell migration and proliferation during fetal development. Epidermal

genetic mosaicism due to somatic mutations potentially results in an acquired blaschkitis (skin inflammation on Blaschko's lines) triggered by external stimuli. This mechanism is believed to underlie the onset and/or exacerbation of polygenic skin diseases along Blaschko's lines.

Discoid lupus erythematosus is relatively rare in children. Approximately 2% of DLE develops in children under the age of 10 years. Generally, children with DLE progress to systemic lupus erythematosus (SLE).[5] Notably, linear childhood DLE progresses to SLE less frequently than other types of childhood DLE.[1] DLE is caused by a combination of genetic and environmental factors that are partly shared with SLE. In linear childhood DLE, however, the local disease factors associated with genetic mosaicism, including altered production of cytokines, chemokines, and other molecules from affected cells, seem to contribute to DLE development even in the absence of systemic predisposition to autoimmune diseases, partly accounting for the less frequent rate of progression to SLE.

The development of DLE is presumed to be triggered by external stimuli, including trauma and sunlight exposure. Considering this, it is plausible that a higher frequency of sunlight exposure can explain the fact that the face is the main affected site of DLE, rather than the extremities and trunk, which are usually covered by clothes. The mechanism by which sunlight exposure induces DLE remains to be investigated. However, keratinocytes show enhanced cytotoxicity from ultraviolet radiation in cutaneous lupus erythematosus (LE).[6] Moreover, several inflammatory cytokines, including CXCL9, CXCL10,

TABLE 1 Literature review

	References	Age at onset (years)/gender	ANA	Specific antibodies	Direct IF	Localization	Systemic involvement
1978	Umbert P and Winkelmann RK[8]	7/female	−	−	+	Arm	−
1998	Abe M et al.[1]	3/female	+	−	+	Face	−
1998	Abe M et al.[1]	11/female	−	−	−	Face, neck	−
1999	Green JJ and Baker DJ[5]	7/male	+	−	N/A	Face, trunk	−
2001	Choi JC et al.[9]	6/female	−	−	N/A	Face	−
2001	Davies MG and Newman P[10]	10/female	−	−	N/A	Face	−
2001	Lee MW et al.[4]	4/male	−	−	+	Face	−
2002	Requena C et al.[3]	3/male	−	−	N/A	Face, neck	−
2007	Engelman DE et al.[2]	6/female	−	−	−	Trunk	−
2008	Julia M et al.[11]	13/female	−	−	−	Arm, buttock	−
2011	Daldon PEC and Lage R[12]	15/male	+	−	N/A	Arm	−
2011	Imhof L et al.[13]	15/female	−	−	+	Face	−
2011	Kawachi Y et al.[14]	4/female	−	−	+	Face, neck	−
2013	Aiyama A et al.[15]	11/male	+	−	N/A	Arm	−
2015	Frances L et al.[16]	1.5/female	−	SS-A	−	Arm	−
2015	Ma H et al.[17]	13/female	−	−	+	Face, neck	−
2016	Jin H et al.[18]	12/male	−	−	N/A	Face	−
2016	Jin H et al.[18]	12/female	−	−	N/A	Face	−
2016	Jin H et al.[18]	14/male	+	−	−	Face, thigh	Photosensitivity
2016	Marinho AK et al.[19]	9/female	+	−	N/A	Upper and lower limbs	−
2017	Campos-Munoz L et al.[20]	11/female	−	−	N/A	Face, neck	Photosensitivity
2020	Liu W et al.[21]	12/female	−	−	N/A	Face	−
2020	Liu W et al.[21]	16/male	−	−	N/A	Face, neck	−
2020	Yadav D et al.[22]	6/male	+	−	N/A	Face, limbs, trunk	−
2020	Niki M et al.[23]	12/female	+	dsDNA	N/A	Face	+
2020	Perez-Bernal J et al.[24]	15/male	−	−	N/A	Arm	−
2020	Lim D et al.[25]	12/female	−	−	N/A	Thigh	−
2020	Lim D et al.[25]	15/male	−	−	N/A	Thigh	−
2020	This report	7/male	−	ssDNA	−	Arm	−

Note: A PubMed search was conducted with "lupus AND (linear OR Blaschko) AND (discoid OR cutaneous)." Cases at the age of 20 years or over were excluded. When two and more cases were presented in one report, they are listed, respectively (N/A, not available).

and CXCL11, are up-regulated by ultraviolet stimulation.[7] These cytokines may trigger inflammation locally along Blaschko's lines containing genetic discordance, leading to skin diseases with a linear distribution.

We reviewed previous reports of linear childhood DLE. A PubMed search was conducted with "lupus AND (linear OR Blaschko) AND (discoid OR cutaneous)." Patients aged ≥20 years were excluded. There were 29 cases,[1–5,8–25] including ours. Of them, 17 patients had skin lesion on their face, while 8 patients had skin lesions on their arm, the second most common site of DLE. Among patients with DLE exclusively on their faces, only two patients were positive for autoantibodies. On the other hand, among patients with DLE even on the limbs or trunk, 8 of 14 patients were positive for autoantibodies (Tables 1 and 2). Patients with facial linear childhood DLE had a low rate of autoantibody positivity (odds ratio 0.126). Fisher's exact test showed a significant association between the location of DLE and autoantibody prevalence ($p = .0209$). This finding suggests that an external stimulus or autoimmune propensity is indispensable for the development of linear childhood DLE. The face, the body's most sun-exposed area, tends to be irritated by so many external stimuli that a weaker autoimmune predisposition, represented as a low rate of autoantibody positivity, may be required to trigger the disease.

One of the limitations of this study is that we were not able to assess differences in treatment responses according to disease location. Since there are a wide range of treatment options from topical corticosteroids to oral administration of hydroxychloroquine or other immune suppressants, it is difficult to compare treatment responses on the same condition between patients with facial skin lesion and those with nonfacial skin lesion. The second limitation is that it is not clear whether autoimmune predisposition of patients with nonfacial skin lesion more frequently results in systemic involvement or not. To answer this question, we need much longer follow-up period.

Our patient appeared to be predisposed to autoimmune disease to some extent, as represented by the family history and anti-ssDNA antibody positivity, which possibly promoted the development of linear DLE. Both local factors provided by Blaschko's lines and a systemic propensity for autoimmune diseases may cooperatively compensate for less intensive sunlight exposure. To date, we have not revealed any association between this systemic propensity for autoimmune diseases and the probability of progressing to SLE. In this perspective, wait-and-see policy can be a good option instead of resorting to systemic treatment for linear childhood DLE.

TABLE 2 Analysis of the association between autoantibody positivity and affected sites

	Autoantibodies positive	Autoantibodies negative	Sum
Face or neck	2	13	15
Other parts	8	6	14
Sum	10	19	29

Note: This table is cross-tabulation created according to Table 1. Based on the table, we conducted Fisher's exact test and found the association between the location of DLE skin lesion and autoantibody prevalence ($p = .0209$).

4 | CONCLUSIONS

In summary, we report a case of linear childhood DLE. This type of DLE has a low probability of progressing to SLE than other types of DLE. As seen in other pediatric patients with linear DLE on the limbs or trunk, our case showed mild immune abnormalities, including anti-ssDNA antibody positivity. However, the patient has not yet developed SLE. Further investigation is warranted to elucidate the underlying pathology of this condition. Although we should watch LE for signs of systemic involvement, we should refrain from overtreatment to prevent systemic progression.

DECLARATION SECTION

Approval of the research protocol: No human participant was involved in this study.

Informed consent: Written informed consent for publication was obtained from the patient's parents, using our institutional consent form.

Registry and the Registration No: N/A.

Animal studies: N/A.

CONFLICT OF INTEREST

Dr. Shinichi Sato is a member of the Journal of Cutaneous Immunology and Allergy Editorial Board. Management of the peer-review process, and all editorial decision making, for this article was undertaken by Editor-in-Chief. The other authors declare no conflict of interest.

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REFERENCES

1. Abe M, Ishikawa O, Miyachi Y. Linear cutaneous lupus erythematosus following the lines of Blaschko. Br J Dermatol. 1998;139(2):307–10.
2. Engelman DE, Kotz EA 3rd, Maize JC Sr. Linear cutaneous lupus erythematosus in the lines of Blaschko. Pediatr Dermatol. 2007;24(2):125–9.
3. Requena C, Torrelo A, de Prada I, Zambrano A. Linear childhood cutaneous lupus erythematosus following Blaschko lines. J Eur Acad Dermatol Venereol. 2002;16(6):618–20.
4. Lee MW, Choi JH, Sung KJ, Moon KC, Koh JK. Linear cutaneous lupus erythematosus in the lines of Blaschko. Pediatr Dermatol. 2001;18(5):396–9.
5. Green JJ, Baker DJ. Linear childhood discoid lupus erythematosus following the lines of Blaschko: a case report with review of the linear manifestations of lupus erythematosus. Pediatr Dermatol. 1999;16(2):128–33.
6. Furukawa F, Itoh T, Wakita H, Yagi H, Tokura Y, Norris DA, et al. Keratinocytes from patients with lupus erythematosus show enhanced cytotoxicity to ultraviolet radiation and to antibody-mediated cytotoxicity. Clin Exp Immunol. 1999;118(1):164–70.
7. Meller S, Winterberg F, Gilliet M, Muller A, Lauceviciute I, Rieker J, et al. Ultraviolet radiation-induced injury, chemokines, and leukocyte recruitment: an amplification cycle triggering cutaneous lupus erythematosus. Arthritis Rheum. 2005;52(5):1504–16.

8. Umbert P, Winkelmann RK. Concurrent localized scleroderma and discoid lupus erythematosus. Cutaneous 'mixed' or 'overlap' syndrome. Arch Dermatol. 1978;114(10):1473–8.
9. Choi JC, Chang SE, Choi JH, Sung KJ, Moon KC, Koh JK. A linear erythema on the nose of a Korean girl. J Dermatol. 2001;28(2):106–7.
10. Davies MG, Newman P. Linear cutaneous lupus erythematosus in association with ipsilateral submandibular myoepithelial sialadenitis. Clin Exp Dermatol. 2001;26(1):56–8.
11. Julia M, Mascaro JM Jr, Guilabert A, Navarra E, Ferrando J, Herrero C. Sclerodermiform linear lupus erythematosus: a distinct entity or coexistence of two autoimmune diseases? J Am Acad Dermatol. 2008;58(4):665–7.
12. Daldon PEC, Lage R. Linear chronic discoid lupus erythematosus following the lines of Blaschko. An Bras Dermatol. 2011;86(3):553–6.
13. Imhof L, Kerl K, Barysch MJ, Dummer R, French LE, Hofbauer GF. Facial blaschkitis: case and review. Dermatology. 2011;223(1):1–3.
14. Kawachi Y, Taguchi S, Fujisawa Y, Furuta J, Nakamura Y, Ishii Y, et al. Linear childhood discoid lupus erythematosus following the lines of Blaschko: successfully treated with topical tacrolimus. Pediatr Dermatol. 2011;28(2):205–7.
15. Aiyama A, Muro Y, Sugiura K, Onouchi H, Akiyama M. Extraordinarily long linear cutaneous lupus erythematosus along the lines of Blaschko. Dermatol Online J. 2013;19(7):18960.
16. Frances L, Betlloch I, Leiva-Salinas M, Marin I, Pascual JC. Subacute cutaneous lupus erythematosus starting as linear lupus erythematosus. Int J Dermatol. 2016;55(2):173–6.
17. Ma H, Liao M, Qiu S, Lu R, Lu C. Linear cutaneous lupus erythematosus with calcinosis cutis and milia. Pediatr Dermatol. 2015;32(1):e33–5.
18. Jin H, Zhang G, Zhou Y, Chang C, Lu Q. Old lines tell new tales: Blaschko linear lupus erythematosis. Autoimmun Rev. 2016;15(4):291–306.
19. Marinho AK, Ramos TB, Barbosa DM, Kozmhinsky V, Takano DM, Figueira MM. Linear cutaneous lupus erythematosus following the lines of Blaschko – case report. An Bras Dermatol. 2016;91(4):510–3.
20. Campos-Munoz L, Fueyo-Casado A, Conde-Taboada A, Carranza-Romero C, Lopez-Bran E. Clinical Images: progressive linear blaschkoid lupus erythematosus. Arthritis Rheumatol. 2017;69(11):2250.
21. Liu W, Vano-Galvan S, Liu JW, Qian YT, Fang K, Ma DL. Pigmented linear discoid lupus erythematosus following the lines of Blaschko: a retrospective study of a Chinese series. Indian J Dermatol Venereol Leprol. 2020;86(4):359–65.
22. Yadav D, Khandpur S, Mohta P. Unilateral Blaschko-linear eruption with Gottron-like papules: blaschkoid lupus erythematosus or dermatomyositis? BMJ Case Rep. 2020;13(6):e235498.
23. Niki M, Matsudate Y, Murao K, Kubo Y. A case of linear cutaneous lupus erythematosus as an initial manifestation of systemic lupus erythematosus. Int J Dermatol. 2021;60(2):e72–4.
24. Perez-Bernal J, Castellanos-Angarita A, Sanchez-Bottomley W. Linear lesions on the arm of a child: a diagnostic challenge. Dermatol Online J. 2020;26(5):1–3.
25. Lim D, Hatami A, Kokta V, Piram M. Linear cutaneous lupus erythematosus in children-report of two cases and review of the literature: a case report. SAGE Open Med Case Rep. 2020;8:2050313X20979206.

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