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CASE REPORT

A patient with subacute cutaneous lupus erythematosus along Blaschko lines: Implications for the role of keratinocytes in lupus erythematosus

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ABSTRACT

Blaschko lines are manifestations of cutaneous mosaicism, with apparent contrast between normal cells and abnormal cells, which carry postzygotic mutations. Linear cutaneous lupus erythematosus is a rare subset of cutaneous lupus erythematosus (CLE), characterized by skin lesions along Blaschko lines. In this paper, we presented a 47-year-old female with subacute CLE lesions along Blaschko lines. Although the antinuclear antibody and anti-Ro titers were remarkably high, there were no systemic symptoms. The histopathology showed atrophic epidermis with vacuolization of basal keratinocytes and papillary edema. While no typical linear lupus band was found, the direct immunofluorescence revealed cytoid bodies with immunoglobulin G, immunoglobulin M, C3, and C4 depositions in the papillary dermis. The skin lesions completely resolved after topical tacrolimus treatment, and the clinical course was 10 months without recurrence. We reviewed the literature and summarized that CLE along Blaschko lines supports the functional role of Ro antigens and keratinocytes in the development of CLE.

Introduction

Linear cutaneous lupus erythematosus (LCLE) is a rare subset of cutaneous lupus erythematosus (CLE), characterized by skin lesions that follow Blaschko lines.[1] However, there are a variety of descriptions of lupus erythematosus (LE) lesions in these cases, including discoid LE and LE profundus among others. Although there is one case with other organ involvement that fulfilled the diagnostic criteria of systemic lupus erythematosus (SLE),[2] cutaneous lesions are the only manifestation in most of the LCLE cases. In this paper, we presented a female patient with LCLE. We discussed the origin of Blaschko lines and summarized that CLE along Blaschko lines supports the functional role of keratinocytes in the development of CLE.

Case report

A 47-year-old female presented with a 2-month history of scattered pigmented macules over her right waist. The lesions were neither pruritic nor painful. She had neither trauma history nor associated symptoms. She had no known underlying systemic disease except thalassemia. A complete blood count showed microcytic anemia, compatible with thalassemia. The antinuclear antibody (ANA) was weakly positive (1:40). One month later, however, the pigmented lesions became scaly and papular, progressing toward the right lower extremity. The lesions were arranged in arch shapes on the right waist (Figure 1A) and in linear configuration on the right lower extremity (Figure 1B). A skin biopsy was performed. The histopathology showed atrophic epidermis with vacuolization of basal keratinocytes and papillary edema. Scattered dyskeratotic cells in papillary dermis were also found. There was inflammatory lymphocytic infiltration around the vascular structure and

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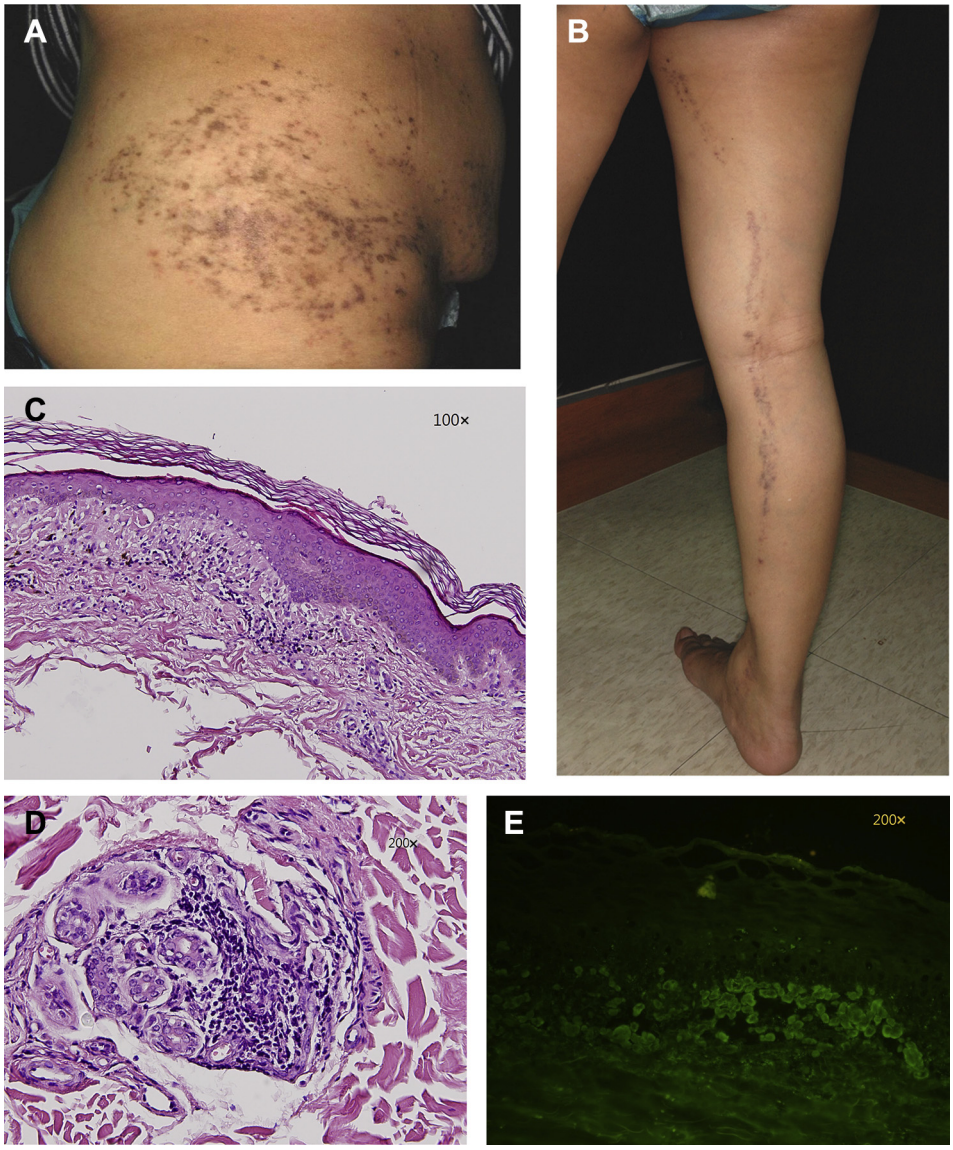

Figure 1 The pigmented papular scaly lesions on the right abdomen and right leg. (A) The figure shows lesions were arranged in arch shapes on the right side of the waist; (B) the figure shows lesions were in linear configuration on the right lower extremity; (C) the figure shows histopathology at the junction between the lesional (left side) and perilesional skin (right side). In the lesional skin, there was atrophic epidermis with vacuolization of basal keratinocytes and papillary edema. Scattered dyskeratotic cells were also found in papillary dermis; (D) the figure shows there was periadnexal lymphocytic infiltration; and (E) the figure shows cytoid bodies of immunoglobulin G in the papillary dermis in direct immunofluorescence examination.

melanophages in the upper dermis (Figure 1C). Periadnexal lymphocytic infiltration was also observed (Figure 1D). The histopathologic findings were compatible with LE.[3,4] Direct immunofluorescence revealed cytoid bodies with immunoglobulin G, immunoglobulin M, C3, and C4 depositions in the papillary dermis (Figure 1E). ANA was followed up and showed >1:1280 positive. Other autoantibody surveys showed anti-Ro positive (80.6 EliAU/mL, normal <7), anti-La negative, antiphospholipid immunoglobulin M and immunoglobulin G negative, and rheumatoid factor negative. The viral-infection survey showed negative for herpes simplex virus, varicella-zoster virus, and Epstein–Barr virus. Based on the clinical manifestation, histopathology, and autoantibody findings, subacute cutaneous lupus erythematosus (SCLE) along Blaschko lines was diagnosed. Because there were no systemic symptoms, topical treatment with 0.1% tacrolimus ointment was prescribed without oral medication. After a 5-month topical tacrolimus treatment, the skin lesions gradually resolved (Figure 2). The autoantibody survey was followed up again and showed ANA >1:1280 positive. The anti-Ro titer slightly decreased (51.3 EliAU/mL, normal <7) as compared to the previous anti-Ro titer. The topical treatment was continued, and the skin lesion resolved with complete clearance. No scaring or skin atrophy was noted. The total clinical course was 10 months.

Discussion

The first case of discoid LE with linear distribution along Blaschko lines was reported by Umbert and Winkelmann in 1978.[5] In 1998, the term LCLE was proposed by Abe et al[1] to describe discoid LE with linear configuration following Blaschko lines. From then on, several papers reported patients with LE lesions along Blaschko lines. In addition to linear discoid LE, some cases were diagnosed as linear LE profundus,[6–9] and one was diagnosed as linear tumid LE.[10] In 2006, Röckmann et al[11] reported a female with SCLE on Blaschko

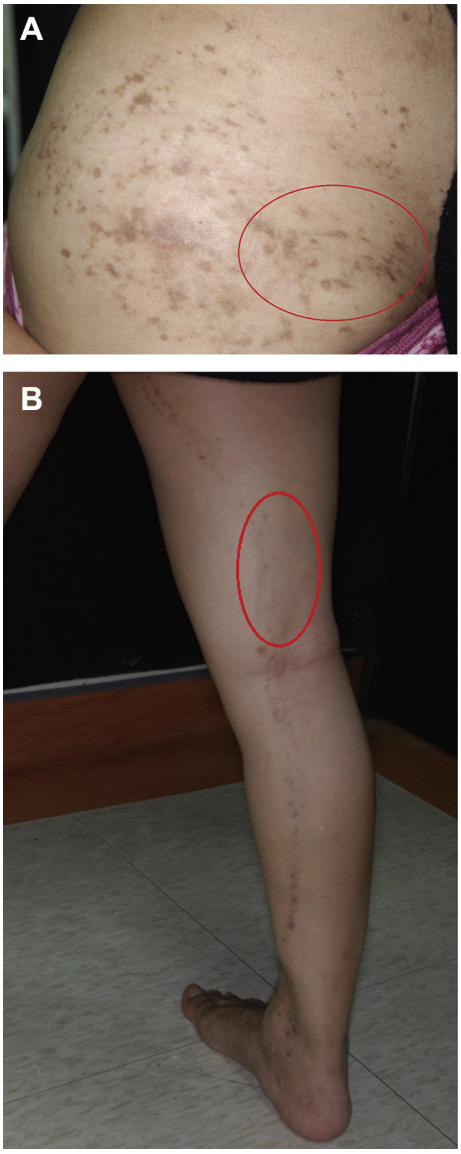

Figure 2 Clinical photos at 8 months (i.e., after topical tacrolimus treatment for 5 months). (A) The papular scaly lesions on the right abdomen and (B) the right lower extremity flattened and disappeared gradually (as shown in circles).

lines, and this is the only SCLE case with skin lesions on Blaschko lines reported to date. Because the spectrum of CLE lesions is wide and because different CLE subsets share some similarities,[12] some cases were designated as linear LE without specific subtypes.[13–15] In a report presented by Lee et al,[14] the term LCLE was used to describe LE lesions associated with Blaschko lines, regardless of their LE subtypes. In addition, linear configuration does not necessarily mean Blaschkoid distribution. For example, zosteriform distribution, which reflects dermatome, is also linear. Therefore, the term "Blaschkoid CLE" instead of linear CLE may more specifically describe the skin lesions.

ANA was positive in some of those patients with Blaschkoid CLE. Among those ANA-positive cases, two showed positive for other autoantibodies. In a female case reported by Röckmann et al,[11] ANA was 1:2560 and anti-Ro was positive. The papulosquamous lesions were distributed along Blaschko lines on the right side of her trunk to her right leg and foot without systemic symptoms. The distribution of skin lesions and pathological findings were similar to our case. After treatment with systemic corticosteroids and chloroquine, the skin lesions improved without progression to SLE.[11] In another male case presented by Heid et al,[13] ANA was 1:1280 and anti-ribonucleoprotein was positive. The unilateral skin eruption was distributed on his right chest, the axillary area, and the arm. CLE was described, but no specific subtype was indicated by the authors. The eruption lasted for 6 months and regressed spontaneously.[13] Similar to our present case, Blaschkoid lesions in these two reported cases resolved without progression to SLE or associated systemic symptoms despite the high autoantibody titers.

Blaschko lines are attributed to the clonal proliferation of genetically distinct ectodermal cells that develop from postzygotic mutation during embryogenesis.[16,17] Paller et al[18] demonstrated that Blaschko lines represent genetic mosaicism in keratinocytes. The cases of CLE along Blaschko lines highlight the functional roles of keratinocytes in the pathogenesis of LE. A growing body of literature supports that keratinocytes participate in the initiation of LE. After UV irradiation or chemical exposure, damaged keratinocytes secrete proinflammatory cytokines and chemokines, upregulate Ro antigen expression on the cell membrane, and undergo apoptosis.[19,20] Specifically, cytoplasmic Ro52 was upregulated in keratinocytes in CLE, which in turn contribute to Ro52-associated autoimmunity and keratinocyte apoptosis. It could be hypothesized that genetic mutation of *Ro52* or *Ro52* upregulation-associated gene in localized keratinocytes predisposes these mutated keratinocytes to autoimmune response, which accounts for the Blaschkoid distribution in these CLE cases. This hypothesis is supported by the direct immunofluorescence finding in our case. Cytoid bodies, which represent apoptotic keratinocytes with attached immunoglobulins and/or complements,[21] were observed in our case, while there was lack of linear lupus band at basement membrane, which is typical of SLE.[22] In addition, the only clinical manifestation of our case was Blaschkoid skin lesions in spite of high ANA and anti-Ro titers in active stage. Indeed, polymorphisms of the *Ro52* gene have been associated with SLE[23] and primary Sjögren's syndrome,[24] another autoimmune disease that shows an overlapping entity with LE.

It is noteworthy that our case responded well to topical tacrolimus. Although the role of T cells in LE remains to be elucidated, a growing body of literature indicates that T cells are involved in the pathogenesis of LE.[20] The successful treatment in our case highlights T cells as a potential therapeutic target in CLE.

In conclusion, we presented a female with CLE lesions along Blaschko lines. The histopathology, immunofluorescence, and autoantibody survey confirmed the diagnosis of SCLE. To our knowledge, this is the only reported Taiwanese case with CLE along Blaschko lines. Although the ANA and anti-Ro titers were remarkably high, there was no systemic symptom. The skin lesions responded well to topical tacrolimus. Because Blaschko lines represent genetic polymorphisms in keratinocytes, CLE lesions following Blaschko lines indicate the functional role of keratinocytes in the initiation of LE. We also suggest the new term "Blaschkoid CLE" to encompass all CLE following Blaschko lines regardless of their subtypes.

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