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Review

Old lines tell new tales: Blaschko linear lupus erythematosis

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ABSTRACT

Patients with lupus erythematosus (LE) specific cutaneous manifestations distributed along the lines of Blaschko are seldom encountered in clinic. In this paper, we reported 5 new cases and perform a systematic review of all the published cases in the English and Chinese literature. We provide a comprehensive summary of the clinical manifestations and explore potential etiology and pathogenesis. Sixty-eight published papers (53 English and 15 Chinese) and 93 cases (including 5 cases reported by us) were included in the analysis. In contrast to classical cutaneous LE, these cases have a series of distinctive clinical features and also have a potentially unique pathogenesis. The pathogenesis of this condition may involve the presence of mosaic abnormal skin cells, possessing crucial pathogenic gene(s)/epigenetic modification(s), located along the lines of Blaschko during embryogenesis. A comparison of the mosaic cells and surrounding "wild-type" cells and in-depth exploration of the interaction between susceptive gene(s)/epigenetic modification(s) and the immune system may potentially bring to light the secrets hidden in LE. Thus, we consider this condition to be a distinct subtype of LE and "Blaschko-linear lupus erythematosus" would be a more appropriate designation. The clues provided in the study of the pathogenesis of this form of LE may potentially unlock the mysteries of the various forms of LE as a whole.

Contents

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1. Background

The lines of Blaschko (Fig. 1) were described in 1901 by Alfred Blaschko, who carefully recorded the skin lesion distribution patterns of more than 140 patients with nevoid and acquired linear skin diseases. A composite diagram was made and has subsequently been referred to as the lines of Blaschko (B lines). These lines do not correspond to other patterns such as Langer's lines of cleavage, Voigt's lines (borders between areas of innervations by peripheral cutaneous nerves), embryonic clefts, pigmentary demarcation lines, or the lines of lymphatic drainage or blood supply [1]. The original B lines are less well defined on the head and neck. Later, Bolognia et al. [1], Restano et al. [2] and Happle et al. [3] gradually revealed the detailed appearance of B lines on the head and neck.

Patients with lupus erythematosus (LE) specific cutaneous manifestations [4] distributed along the B lines (Blaschko-linear LE) are seldom encountered in the clinical setting. Since the first case reported by Umbert et al. [5] in 1978, hundreds of new cases have been reported worldwide. Related clinicopathological diagnosis nearly covers every subtype of cutaneous lupus erythematosus (CLE), such as discoid lupus erythematosus (DLE) [6–23], subacute cutaneous lupus erythematosus (SCLE) [24,25], lupus erythematosus panniculitis (LEP) [26–43], lupus erythematosus tumid (LET) [44,45] or bullous lupus erythematosus (BLE) in systemic lupus erythematosus (SLE) patients [46]. Others may also present with features of both CLE and morphea in the same lesion [47–52].

It is believed that B lines correspond to the direction of migration and clonal expansion of ectodermal cells during cutaneous embryogenesis. The pathogenesis of polygenic Blaschko-linear inflammatory diseases (e.g. LE) might involve mosaic abnormal skin cells (such as keratinocytes, fibroblasts, or vascular endothelial cells) located along the B lines during embryogenesis. These mosaic cells originate from postzygotic somatic mutation or other mechanisms which predispose them to developing unique pathological changes under certain triggering factors [53]. The existence of mosaic cells makes it possible to compare two populations of cells exposed to the same environment and sharing the same genetic background except for the mosaic pathogenic gene, gene groups or epigenetic modifications directly responsible for the clinical expression [54]. In-depth study of the interaction between susceptive mosaic gene(s)/epigenetic modification(s) and the immune system may potentially bring to light secrets hidden in LE. Thus, it is likely that Blaschko-linear LE opens a window for us to explore the whole scene of LE.

Here, we report five new Blaschko-linear LE patients and perform a systematic review of all the published Blaschko-linear LE cases in the English and Chinese literature.

2. Case series

Case 1: A 12-year-old boy presented with 3-year history of asymptomatic linear erythema on his forehead, left check and preauricular region (Fig. 2a). The lesions first appeared on his forehead and gradually extended downwards. Old lesions were slightly atrophic without hardening. The patient did not report a history of photosensitivity nor was there a family history of such lesions. Laboratory workup including blood and urine analysis, liver and kidney functions, complement, erythrocyte sedimentation rate (ESR) and autoantibodies were all within normal range. His first skin biopsy (of a newly developed preauricular lesion) showed slightly hyperkeratosis, sporadic vacuolar alteration of basal cells, sparse superficial perivascular and periappendageal lymphocytic infiltrates, indicating the possibility of CLE. The patient received intermittent treatment with topical desonide cream for 2 months without significant improvement. A second skin biopsy of the fully developed forehead lesion revealed classical DLE histopathological features (Fig. 2b). Direct immunofluorescence (DIF) showed linear and granular deposition of IgG, IgA, IgM and C3 along the dermal-epidermal junction. He was treated with hydroxychloroquine (200 mg/day) and topical 0.03% tacrolimus ointment, and 4 months later reported partial improvement.

Case 2: A 20-year-old female presented with a linear mild atrophic erythematous lesion along her nasal bridge for 9 months (Fig. 3a). The lesion was asymptomatic and not photosensitive. She was otherwise healthy and reported no pertinent family history. Her laboratory results were all within normal range except for leucopenia (WBC 2.14×10^9/L), positive anti-nuclear antibodies (1:320) and

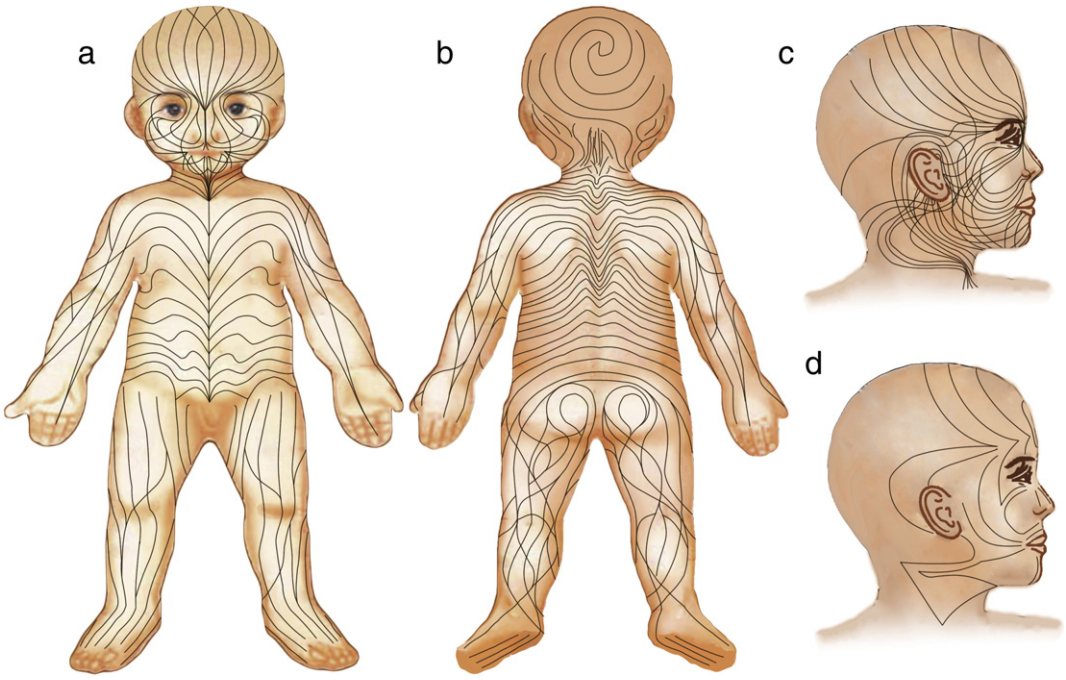

Fig. 1. Whole body appearance of lines of Blaschko. a) Anterior view (Modified from Bolognia et al., 1994 [1] and Happle et al., 2001 [3]). b) Dorsal view (Modified from Bolognia et al., 1994 [1] and Happle et al., 2001 [3]). c) Lateral view (Modified from Happle et al., 2001 [3]). d) Lateral view (Modified from Restano et al. 1998 [2]).