Blaschko-linear lichen planus: Clinicopathological and genetic analysis

Dear Editor,

The lines of Blaschko represent developmental pathways of ectoderm, and several skin diseases may show Blaschko-linear manifestations, often arising as a result of postzygotic mutations. Mendelian diseases may present in this manner at birth but complex traits may also manifest like this later in life. It is feasible that the latter may provide new opportunities to further explore the pathobiology of these dermatoses.

A 34-year-old Thai woman presented with a generalized itchy brownish and violaceous rash of 4 months’ duration. She was otherwise well with no medication history and no family history of similar skin lesions. Examination revealed bilateral

Figure 1. (a) Multiple bilateral linear brownish patches on back and (b) scaly violaceous plaques on right leg along Blaschko’s lines. (c) Multiple linear scarring alopecia. (d) Dorsal pterygium of right middle fingernail. (e) Histopathology of the right leg skin biopsy showing irregular acanthosis, wedge-shaped hypergranulosis, vacuolar degeneration of the basal layer of the epidermis with necrotic keratinocytes and band-like lymphocytic infiltrate in the papillary dermis (hematoxylin–eosin [HE], original magnification ×100). (f) Scalp biopsy from scarring alopecia shows follicular epithelial atrophy, basal vacuolar change of the outer root sheet, perifollicular fibrosis, and perifollicular and perivascular inflammation (HE, ×100). (g) Histopathological findings from a brownish patch on the trunk shows compact hyperkeratosis, hyperpigmentation of the basal layer and dermal melanophages (HE, ×400).

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linear brownish patches and scaly violaceous plaques along Blaschko’s lines on the face, trunk (Fig. 1a) and all extremities, notably on the right leg (Fig. 1b). She also had multiple linear areas of scarring alopecia (Fig. 1c). Dorsal pterygium of the right middle fingernail was noted (Fig. 1d). No other manifestations were noted except mild scoliosis. Light microscopy of lesional skin from the right leg, scalp and trunk were consistent with lichen planus (LP), lichen planopilaris and LP pigmentosus, respectively (Fig. 1e-g). Bilateral Blaschko-linear LP was diagnosed. She was treated with topical steroid creams, hydroxychloroquine and acitretin with a good response.

Following ethics committee approval, we undertook whole-exome sequencing (WES) in DNA from the patient’s peripheral blood and six skin biopsies (three lesional and three from adjacent non-lesional skin; Table S1). Based on the rarity of the phenotype and likely postzygotic mutation, we filtered all protein-altering variants with a minor allele frequency (MAF) of more than 1%, and kept all variants that were present in the three affected skin sites and absent in the three unaffected skin sites and blood. This analysis highlighted a single novel mutation in \(KDELC1\) (c.662T>C; p.Leu221Ser). \(KDELC1\), now known as \(POGLUT2\), is an O-glucosyltransferase that modifies Notch signaling. However, visualization with Integrative Genomics Viewer showed that this variant was present in both lesional and non-lesional skin and therefore not of clinicopathological significance (Fig. S1).

Next, we undertook an alternative analysis of the WES data based on allele counts for each of the four bases (A, T, C, G) at every variant position. For each variant, allele count proportions in lesional and non-lesional skin samples were compared using a beta-binomial model.\(^3\) Protein-altering variants with a MAF of less than 1% and a significant difference \((P < 0.01)\) in allele proportion between lesional/non-lesional samples were kept during a stepwise filtering process (Table S2). Two potentially interesting differences were noted: (c.5920A>C; p.Thr1974Pro) in \(NOTCH3\) (Notch signaling) and (c.751A>T; p.Lys251*) in \(AIM2\) (encodes DNA sensor). However, Sanger sequencing analysis detected only wild-type alleles in all DNA samples (Fig. S2, Table S3).

Several inflammatory dermatoses have been described manifesting along the lines of Blaschko, including LP.\(^4\) Most reported cases of Blaschko-linear LP have been unilateral and therefore our case represents an unusual clinical manifestation, even if the underlying molecular pathology remains unresolved for now. Future work using whole-genome sequencing may unravel regulatory or structural variation that is not captured by WES.

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**SUPPORTING INFORMATION**

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Visualization of sequencing reads at the putative \(KDELC1\) variant (c.662T>C) with Integrative Genomics Viewer.

**Figure S2.** Sequencing chromatograms of \(NOTCH3\) and \(AIM2\) candidate variants displaying wild-type alleles in all DNA samples.

**Table S1.** Exome sequencing coverage and mapping statistics

**Table S2.** Candidate variants generated based on the beta-binomial statistical model

**Table S3.** Primer sequences used for Sanger sequencing

**CONFLICT OF INTEREST:** None declared.