

Alfred Blaschko



INFLAMMATORY LINEAR VERRUCOUS EPIDERMAL NAEVUS WHOSE LINE IS IT ANYWAY?

Dermatology and the manifestation of skin disease can show great diversity. The authors present an unusual podiatric lesion demonstrating a well-recognised, but rarely discussed, dermatological pattern

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CASE PRESENTATION

A mother presented her three-year-old son to the podiatry clinic with a developing skin lesion on his leg and foot. The child was in good health apart from asthma for which an inhaler was used. Previously he had had pneumonia but his development from birth was otherwise good as he had attained all the normal milestones. The pregnancy was normal, but the mother had developed gestational diabetes during the term. Her son was born three weeks premature without complications.

On examination, he presented with a linear lesion (about 1 cm in diameter) running from his groin, along the medial side of his left leg to the plantar surface of the calcaneum (Figures 1-3). The lesion was initially papular in structure but evolved, merging to form a discontinuous plaque. It had gradually developed from two months after birth and was roughened in texture and extremely pruritic. No other skin lesions were evident on the patient. Rubbing from nappies had previously caused bleeding but since toilet training this was no longer an issue.

The initial diagnosis was made by the patient's GP as lichen planus for which he was prescribed salicylic acid. This was uncomfortable and increased the soreness and so he was subsequently prescribed a moderately potent steroid. This reduced the itching, but the lesion remained.

DIAGNOSIS: INFLAMMATORY LINEAR VERRUCOUS EPIDERMAL NAEVUS (ILVEN)

A naevus is defined as an abnormal collection of normal skin cells, which most often is present at birth. An epidermal naevus denotes a lesion composed primarily of keratinocytes. The verrucous epidermal naevus is a rare sub-type (around 1:1000 children) that affects males and females equally and mostly arises a few months after birth. It develops initially as velvety linear streaks which become warty with an erythemic base as the lesion evolves. Lesions are most frequently observed on the limbs¹ (particularly the left leg²), occasionally on the trunk and rarely on the mucosal or genital areas.³ The length of the naevus is highly variable, from very short to the entire length of a limb. In such cases, nail involvement can arise and present as hyperkeratosis and inflammation.⁴

ILVEN can be eczematous or psoriatic in form, with flexural lesions that can become macerated. For most, ILVEN presents as a single line although bilateral cases do arise. It can be classified as both non-epidermolytic and epidermolytic in form. The former is the most common and is usually restricted to the skin but the epidermolytic form is associated with extra-cutaneous features. Around one-third of patients are suspected to have involvement beyond the cutaneous manifestations,

including the mucosal surfaces, dentition,⁵ the central nervous system⁶ and skeleton.⁷ No evidence of extra-cutaneous involvement was apparent in our patient, suggesting a non-epidermolytic form of the condition.

DIFFERENTIAL DIAGNOSIS

The clinical picture can give strong clues as to the cause, but biopsy can be helpful in confirming the diagnosis. The main differential diagnosis is with lichen striatus (LS), this being a similar presenting condition in children. It begins with pink or red papules in a linear arrangement, along the limb, and can be in singular or in parallel lines. In contrast to ILVEN, this occurs in older children (5-15 years of age). Moreover, the lesions associated with LS are generally asymptomatic and self-resolve within months, regardless of treatment.⁸



Figure 1



Figure 2



Figure 3

Figure 1. Medical view of the thigh
Figure 2. Medical view of the calf
Figure 3. Plantar view of the calcaneum
Figure 4. Map of Blaschko's lines.
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MANAGEMENT OF ILVEN

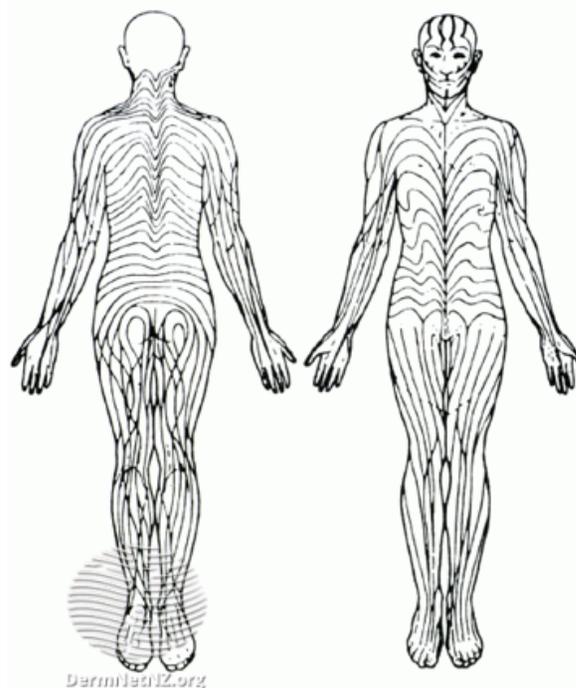
Once established the condition remains static but symptoms of itching can persist and may require topical therapies. Corticosteroids have also been used topically but with limited success. In addition, various papers have reported the use of retinoids, 5-fluorouracil and dithranol.^{3,9} Two papers have reported the successful use of calcipotriol in children with the disorder.^{10, 11} Laser ablation has also shown improvement in symptoms and appearance in treated lesions.^{4, 12}

WHY THE DISTINCT LINEAR PATTERN IN THESE DISEASES?

Podiatrists may be familiar with various anatomical lines in the body including Langer lines, dermatomes, the soleal line and even Wallace's line of the foot¹³ but, dermatologically, some inherited and acquired disorders can develop along another set of lines - the lines of Blaschko. In 1901, Alfred Blaschko¹⁴ first described a set of invisible lines occurring in the skin that did not conform to any known anatomical pathway such as nerves, blood vessels or lymphatics but that were sometimes demonstrated by the presence of certain skin diseases and naevi. It is now thought these lines represent epidermal cell migration and proliferation pathways from development of the foetus. Blaschko's lines run their unique course of whorls, lines and wave-like shapes across skin and mucosal surfaces. The pattern of the lines can be seen in Figure 4. In the lower limbs these tend to be represented by vertical straight lines.

Blaschko's lines are regarded as a manifestation of mosaicism. A mosaic is considered an artwork that is made of multiple, small coloured pieces of stone or glass. In genetics, a mosaic refers to an individual made up of two genetically distinct cell populations that are derived from a homozygous zygote.¹⁵ Mosaicism, or separate cell populations, can develop in two ways. Firstly, by spontaneous mutation in the DNA sequence so that subsequent daughter cells contain the genetically distinct material. Secondly, it can result from changes in gene expression that are passed on from one cell generation to the next but do not entail an alteration in the DNA sequence – known as epigenetic factors.¹⁵ The

Figure 4



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CONGENITAL SKIN DEFECTS	
X-linked dominant skin disorders:	Incontinentia pigmenti Focal dermal hypoplasia Congenital hemidysplasia with ichthyosiform erythroderma and limb defects (CHILD) syndrome Microphthalmia with linear skin defects (MLS) syndrome Oral facial digital syndrome Type 1 X-linked dominant chondroplasia punctate
Epithelial naevi:	Inflammatory linear verrucous epidermal naevus (ILVEN) Sebaceous naevus Non-organoid epidermal naevus
Pigmentary disorders:	Pigmentary demarcation lines Naevus achromicus (including hypomelanosis of Ito) McCune–Albright syndrome Segmental vitiligo
ACQUIRED SKIN DISORDERS	
Disorders with polygenic background:	Linear lichen planus Linear psoriasis Linear cutaneous lupus erythematosus Lichen striatus Linear morphea

stage at which the change occurred determines the extent of the phenotypic expression. If the mutation occurred early in embryonic development, the abnormal cells will likely be widely distributed and affect multiple tissues, whereas a mutation that occurred late in development will be limited in distribution and might affect only the skin, for example.

During embryological development, epidermal tissue develops in streams. If one imagines coffee and milk as the two distinct cell lines, pouring milk into coffee causes a swirling mixture, creating the observed mosaic pattern (Figure 5) akin to the appearance seen on the skin. A similar phenomenon is seen in animals, for example the brindle colouration of dogs (Figure 6) is analogous to the lines of Blaschko in humans.¹⁶

Mosaicism can occur in any tissue or organ and is rarely visualised. In human skin it can only be seen under intense UV light or as the manifestation of the pattern of certain skin diseases that follow the lines of Blaschko. There are several skin disorders that follow the lines of Blaschko (Table 1) including a rare form of linear psoriasis and lichen planus. Subsequent research has established four other cutaneous patterns that may manifest during skin disease, which may also represent mosaicism¹⁷ but are less frequently observed. ■

SUGGESTED READING: BLASCHKO'S LINES

<https://www.dermnetnz.org/topics/blaschko-lines/>



Figure 5



Figure 6

Figure 5. Visual depiction of cell streaming during embryonic development with two distinct cell lines (coffee vs milk). [Note to editor creative commons licence]

Figure 6. A dog with brindle colouration – a canine equivalent of the lines of Blaschko. [Note to editor creative commons licence]

Table 1. Skin conditions that are known to follow Blaschko's lines¹⁸

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