

Tacrolimus-responsive lichen striatus

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Introduction

Lichen striatus (LS) is a relatively uncommon, self-limited, linear dermatosis of unknown etiology that primarily affects children [1]. A linear eruption consisting of clustered, flat, pink-brown papules along Blaschko lines is its characteristic clinical feature. Histologic evaluation of skin biopsies suggest a T-lymphocyte mediated immune reaction against keratinocytes. Diagnosis is established on the distinctive clinical appearance and distribution pattern of the cutaneous lesions. Due to the self-limited nature of the disease, treatment is not mandatory, unless there is significant pruritus or psychological discomfort. Various therapeutic approaches have been tried for the treatment of LS. Rapid healing without cutaneous sequela like atrophy or hypopigmentation was observed in the patient treated with tacrolimus.

Case Report

Case 1

A 6-year old girl with a 1-month history of linear, erythematous rash extending from her right shoulder (**Figure 1a**) to the dorsum of proximal phalanges of her third and fourth fingers on her right hand (**Figure 2a**) presented to our clinic. Physical examination revealed clustered, skin-colored papules in a linear arrangement. She had no relevant medical history and except the rash, she was in good general health. In histologic sections, focal keratosis and spongiosis in epidermis and a dermal lymphocytic infiltrate in perivascular and periadnexal regions and at the dermoepidermal junction was observed (**Figure 1c**). She was diagnosed with LS on the basis of clinical and histological findings and 0.03% tacrolimus ointment twice daily was started. After 12 weeks, all the cutaneous lesions were cleared (**Figure 1b**) and with the disappearance of cutaneous lesions, topical tacrolimus was stopped by the parents of the patient. But 15-months later, the patient presented with evident longitudinal ridging and onycholysis on the radial halves of the fingernails of her right middle and ring fingers (on the distal end of the affected Blaschko line) (**Figure 2b**).

Case 2

A 17-year old girl with 2-month history of linear, asymptomatic, erythematous papules extending from her left gluteal sulcus to

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the popliteal fossa presented our clinic (**Figure 3a and 3b**). Her medical history was noncontributory. LS was diagnosed on the basis of clinical and histopathological features (**Figure 3e**). 0.03% tacrolimus ointment was prescribed. This patient, then was lost to our follow-up. At her second visit 16 weeks later, she had dropped tacrolimus and instead, used mometasone furoate 0.1% ointment for 12 weeks. Active lesions among atrophic areas were observed (**Figure 3c and 3d**).

Discussion

Lichen striatus (LS) is a benign skin disease with a self-limited course. LS usually manifests as erythematous or skin-colored millimetric papules following a Blaschko line. Skin biopsies usually show a lichenoid interface dermatitis, characterized by a dense inflammatory infiltrate (consisting predominantly of CD3⁺ lymphocytes) obscuring portions of dermoepidermal junction.

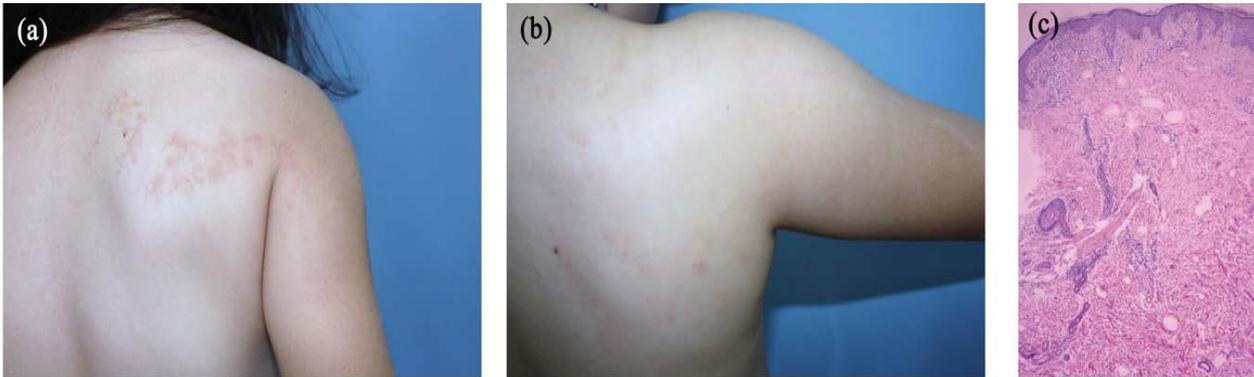


Figure 1 (a) Clustered, flat papules on the scapular area of a 6-year old girl extending to her arm along Blaschko line (b) Complete clearance of lesions after treatment with topical tacrolimus for 12 weeks (c) Histological evaluation of skin biopsy reveals lichenoid infiltrate more prominent around adnexia (H&E x40).

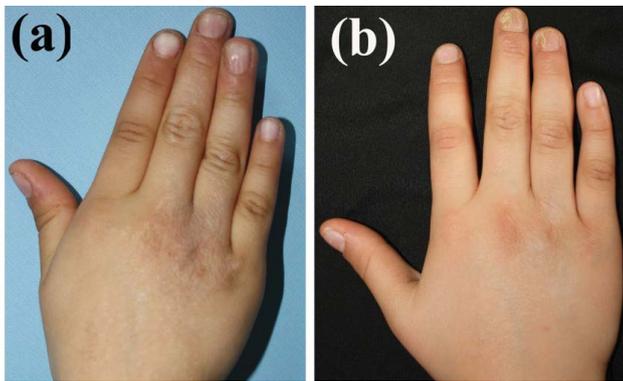


Figure 2 (a) Mild lichenification on the dorsum of the right hand of the patient (12 weeks later after the start of the treatment) (b) longitudinal ridging, onycholysis of the fingernails of her right index and middle fingers (15 months later).

CD8⁺ T-lymphocytes surrounding the necrotic keratinocytes and intraepidermal grouped Langerhans cells can be observed in the inflammatory infiltrate [2]. Although not pathognomonic, observation of lymphocytes surrounding the follicular epithelium and eccrine coils is a distinguishing feature for LS and may assist in differential diagnosis. Histo-pathological features may also mimic other inflammatory or neoplastic dermatoses, including mycosis fungoides [3]. The classic pattern of cutaneous lesions and histopathological features suggest a T-cell-mediated autoimmune response directed against a keratinocyte cell line with somatic mutation (somatic mosaicism) [1,2,4]. According to this theory, a possible causative factor like a viral infection [5,6] or cutaneous injury may disturb the immune tolerance to this divergent cell clone and trigger an autoimmune reaction, which may destroy the aberrant cell line and probably prevent the following relapses [1], but still, neither the mutations nor the exact trigger factors are identified. In 1990, a clinical entity with similar skin lesions, "Blaschkitis", was described [7]. Since then, there has been much debate over whether "Lichen striatus" and "Blaschkitis" were separate entities or not. Some reports define blaschkitis as a

distinct disease emphasizing its truncal localization and more eczema-like histologic features [7,8] but other authors contradict this notion due to the similarity between the clinical features and clinical progress of LS and blaschkitis [9]. Other diseases, which should be included in the differential diagnosis are; inflammatory linear verrucous epidermal nevus (ILVEN), linear lichen planus, linear psoriasis and incontinentia pigmenti [10] (**Table 1**).

Mean duration time for LS is reported to be about 9,5 months [4], but LS cases with active phases over 2-years have been described [11]. This protracted course may cause emotional distress, particularly when the disease manifests on the face or a visible part of the body, such as nails and these patients and their families may benefit from a therapeutic intervention. Due to the rarity of the disease, no established treatment guidelines are available, but there are anecdotal reports of successful treatments with topical calcineurin inhibitors (CI) [12-14], systemic corticosteroids [15] and photodynamic therapy [16]. Considering the previous reports [12-14], we prescribed topical tacrolimus twice daily for our patients and observed dramatical and rapid improvement in case 1. Cutaneous lesions were cleared in 12 weeks, a considerably short healing time when compared to reported mean duration time. Also, there weren't any skin atrophy or hypopigmentation in this patient. The only negative outcome was the dystrophic nail changes. Nail damage was attributed to premature discontinuation of the treatment. The outcome with case 2 was worse. This non-compliant patient had still active lesions and also cutaneous atrophy due to prolonged use of topical steroids after 12 weeks, indicating the risk of inappropriate choice (and probably inappropriate use) of topical drugs for the treatment of LS.

Conclusion

No definitive conclusion can be reached with our two-case experience but, since LS is an uncommon disease, large case series to evaluate the treatment options are practically unavailable. Therefore case reports are the only references for the physicians treating LS patients. Although LS is a benign, self-limited disease, it may cause emotional stress in patients and parents, causing

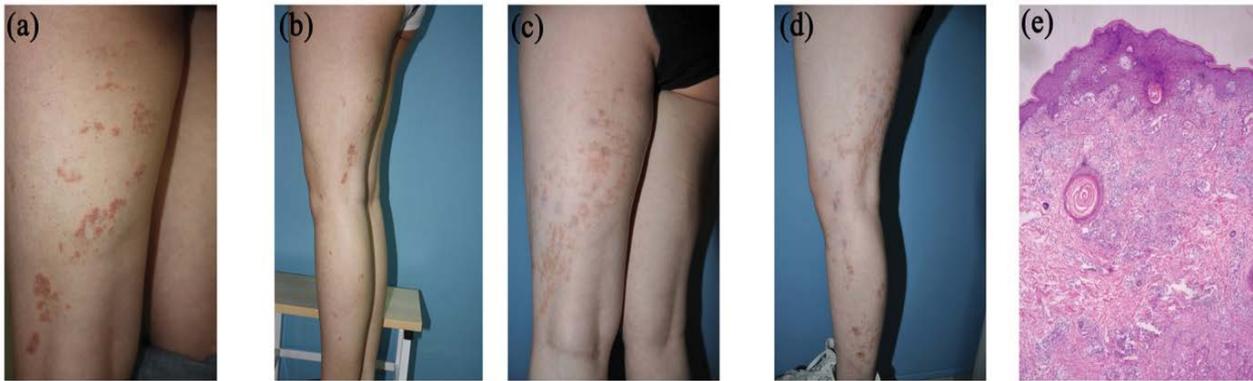


Figure 3 (a), (b) Grouped, flat papules arranged in a linear fashion on the leg of a 17-year-old girl (c), (d) Progression of lesions to lower leg and skin atrophy 12 weeks later after application of topical corticosteroid (e) Histological section at the start of therapy showing lymphocytic infiltration in dermis (H&E × 40).

Table 1 Differential diagnosis for Lichen Striatus.

Differential Diagnosis for Lichen Striatus		
Disease	Clinical Presentation	Biopsy
Lichen Striatus	<ul style="list-style-type: none"> Flat, scaly clustered papules following Blaschko lines 	<ul style="list-style-type: none"> Interphase dermatitis Sometimes psoriasiform pattern, mild acanthosis, perivascular, perifollicular lymphocytic infiltration
Blaschkitis	<ul style="list-style-type: none"> Continuous or interrupted papulovesicular eruption along the Blaschko lines. Frequently observed on trunk. 	<ul style="list-style-type: none"> Spongiotic pattern
Linear Lichen Planus	<ul style="list-style-type: none"> Rare variant of lichen planus. Frequently seen in children. Pruritic, flat, violaceous, milimetric papules following a Blaschko line (not dermatomal) 	<ul style="list-style-type: none"> Classic lichen planus histopathology. A band of lymphocytic infiltrate along the dermoepidermal junction. Epidermal acanthosis and hypergranulosis (wedge pattern) Necrotic keratinocytes (colloid bodies) in the epidermis and papillary dermis
Linear Psoriasis	<ul style="list-style-type: none"> Rare variant of psoriasis Unilateral erythematous flat papules or plaques with white scales following a Blaschko line 	<ul style="list-style-type: none"> Classic psoriasiform pattern Epidermal hyperplasia, elongated retes Parakeratosis, hypogranulosis Neutrophils in the dermis (Munro's microabscesses)
Incontinentia Pigmenti (Bloch-Sulzberger Syndrome)	<ul style="list-style-type: none"> an X-linked dominant neurocutaneous syndrome mutation in NF-κB essential modulator (NEMO) gene in chromosome Xq28 lethal for males Early stages(in utero and infancy): Skin covered with bullous lesions (later verrucous lesions) distributed in a Blaschkoid pattern on trunk and extremities Late stages (three to six months of age): Hyperpigmentation Second – third decade: hypopigmentation, atrophy Also observed; wooly hair, dental anomalies (conical teeth deformities), abnormalities of retinal vessels (ischemic optic neuropathy), seizures 	<ul style="list-style-type: none"> Vesiculo-bullous stage: eosinophilic spongiosis. Apoptotic keratinocytes and eosinophil containing vesicles in epidermis, eosinophils in dermis Verrucous stage: Epidermal acanthosis, hyperkeratosis, papillomatosis. Apoptotic keratinocytes in epidermis. Dermal perivascular lymphocytes. Scarce dermal eosinophils. Melanin incontinence Hyperpigmentation stage: Melanin incontinence, melanophages in dermis. Lack of epidermal hyperplasia Hypopigmentation stage: Epidermal atrophy, reduced number of melanocytes. Lack of melanin incontinence and other inflammatory cells (10).
Inflammatory linear verrucous epidermal nevus (ILVEN)	<ul style="list-style-type: none"> Rare variant of epidermal nevus Usually occurs in early childhood Unilateral, pruritic, erythematous, hyperkeratotic papules along the lines of Blaschko 	<ul style="list-style-type: none"> Psoriasiform epidermal hyperplasia Alternating bands of para- and orthokeratosis Chronic inflammatory infiltrate in dermis

them to self-medicate, which, in turn, can have worse side-effects than LS. Also, LS can affect nails and cause permanent dystrophic changes, due to partial destruction of nail matrix.

Tacrolimus is an established immunosuppressant, which works by inhibiting calcineurin and preventing T cell activation, which is a constant feature of LS histopathology. Tacrolimus has also been found out to be as effective as potent topical corticosteroids and

more potent than mild topical steroids in atopic dermatitis, in which activated cutaneous lymphocytes also play an important role [17]. Inhibitory effects of tacrolimus on lymphocytes and various case reports, including ours, [12-14] suggest that tacrolimus and probably the other CI may be a good therapeutic

option for LS. Without the side-effects of topical steroids, topical CI seem to be also the safer choice. We also suggest that topical CI should applied on the periungual areas (under occlusion if possible) of the nails, which are on the affected Blaschko line to prevent a permanent nail damage.

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