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Case report of Inflammatory linear verrucous epidermal nevus (ILVEN): Sentence or surmountable difficulty?

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ABSTRACT

In this report, we describe a case of Inflammatory linear verrucous epidermal nevus (ILVEN) that clinically and histologically mimicked Blaschkoid (linear) lichen planus, linear psoriasis, and other linear dermatoses, for could be diagnosed by histopathologic findings. ILVEN is typically refractory to treatment, but accordingly the data of literature the various methods of cure were tried from treatment with the administration of calcipotriol, topical application of momethasone furoate 0.1%, combination therapy with topical tretinoin, 5-fluorouracil creams, crisaborole 2% ointment to invasive methods such as carbon dioxide gas laser, pulsed dye laser, UV 308-nm excimer laser. Consequently, the differential diagnosis between ILVEN and similar disorders are necessary to avoid applying an inadequate therapy.

Keywords: Inflammatory linear verrucous epidermal nevus, differential diagnosis, treatment.

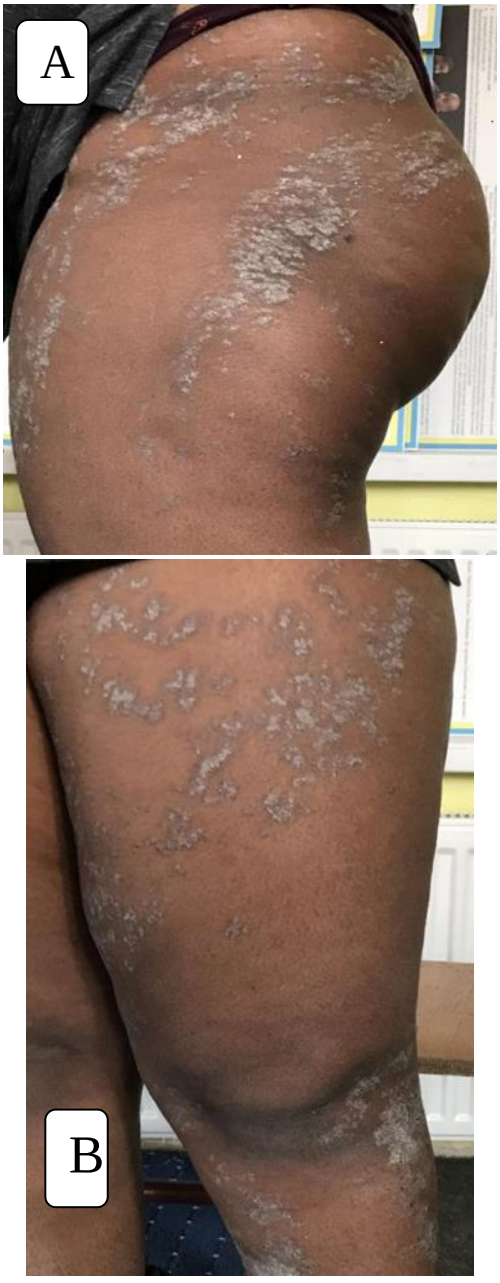
1. INTRODUCTION

Inflammatory linear verrucous epidermal nevus (ILVEN) is a version of mosaicism caused by somatic mutations (Bolognia et al., 2012). In concordance with the WHO classification, ILVEN it is classified as congenital hamartomas, thus emphasizing their embryonal ectodermal origin, as a variant of verrucous epidermal nevus, representing approximately 5% of all epidermal nevi, with predominance in females and with general therapeutic resistance (Tlish et al., 2017; Wollina et al., 2017). ILVEN is an epidermal nevus that has been confused with many diseases such aspsoriasis, lichenoid epidermal nevus, epidermal nevi, lichenoid dermatitis (Bolognia et al., 2012; Tanita et al., 2018; Wollina et al., 2017). According to report (Tanita et al., 2018), this entity clinically and histologically mimics psoriasis vulgaris. Lichen striatus, linear Darier disease, linear porokeratosis, linear lichen planus, linear psoriasis, and the verrucous stage of incontinentia pigmenti, ichthyosis hystrix, Sulzberger-Bloch syndrome may all have similar clinical presentations as the linear verrucous epidermal nevus (Bimbi et al., 2017; Ferreira et al.,2013; Grgurich et al., 2018; Tlish et al., 2017). In the dermatological community it is well known

that treatment of ILVEN is often very challenging as opposed to complete cure of the condition and lead to relief of the symptoms and not to recover.

2. CASE REPORT

A 20-year-old Indian girl visited our outpatient clinic for routine check-up. We have observed unilateral psoriasiform appearance, unilateral, giant itchy plaques for what was considered either preliminary diagnosis linear psoriasis or ILVEN. The course of disease was characterized by periodic inflammatory breakthroughs associated with increased pruritic symptoms. The initial treatment involved topical steroid, calcipotriol hydrate, emollients, with inadequate effects. She had not have significant past medical history. The age of onset was before the age of 3 years old. None of the family members had the similar type of lesions. Physical examination revealed(Figure 1A–D) brown to skin-colored, infiltrated, erythematous hyperkeratotic papules and plaques covered by mild scaling with the transition from her lower left extremity to the left buttock along the Blashko line and to the dorsal surface of the second toe causing nail alteration, such as subungual hyperkeratosis.



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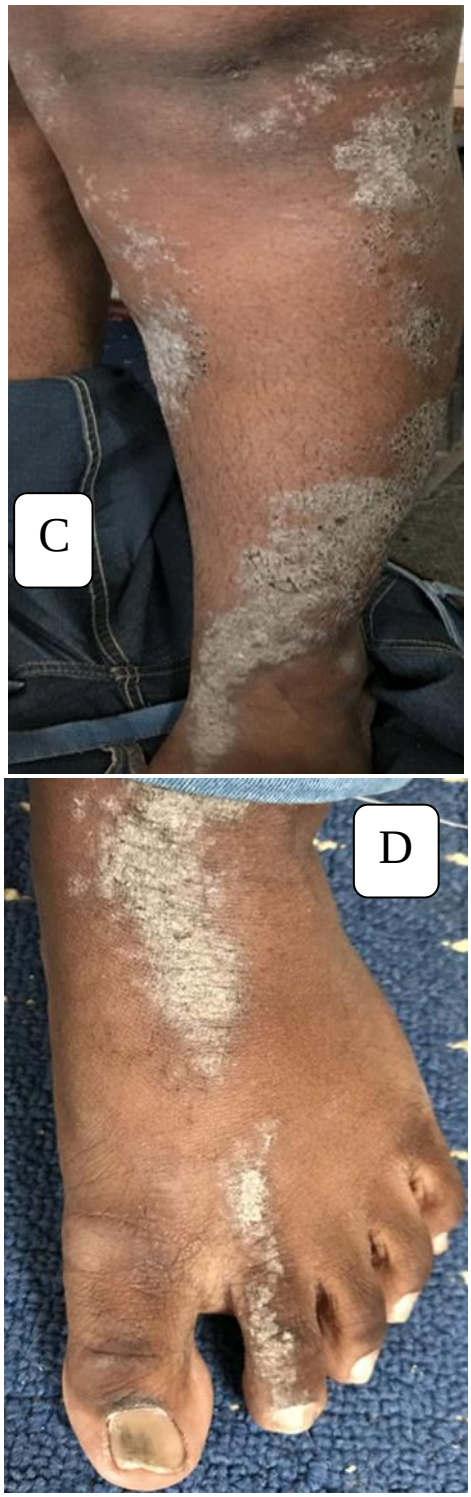

Figure 1 A-D Unilateral ILVEN in 20-year-old woman with typical clinical characteristics, including linear arrangement of thick scaly papules and plaques localized on the lateral side of her left buttoks, thigh, leg, ankle, and dorsal foot

A full blood count and biochemical profile were within normal ranges. To differentiate the preliminary diagnosis of clinically suspected linear psoriasis with ILVEN has been done an incisional biopsy. Pathologist's investigation was conducted in several labs by the means of H&E staining primarily. Obtained results prove ILVEN diagnosis for the patient. We are illustrating the H&E microspecimen (Figure 2). Histopathology report: Section of skin show acanthosis of epidermis with indulated surface having overlying hyperkeratotic and parakeratotic layer, parakeratosis is patchy in distribution the alternating with orthokeratotic areas. Granular cell layer is prominent. There is downward elongation of rete ridges with psoriasiform features. In addition, focal areas of upward projections of epidermis are seen contributing to the undulated surface. Mild hyperpigmentation is seen of the intact basal

cell layer, papillary dermis shows oedema fibrosis and perivascular lympho-histiocytic infiltration. Deeper dermis shows fibrosis with an occasional atrophic hair follicle. Sub-cutaneous fat shows no remarkable features.

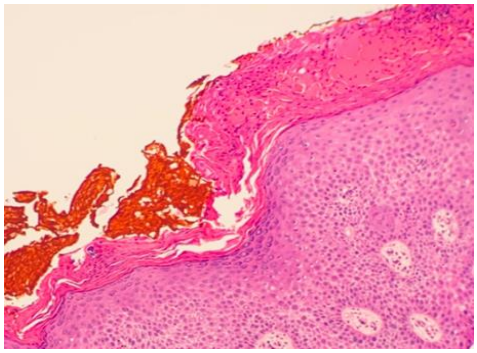

Figure 2 Microspecimen of skin biopsy. Psoriasiform acanthosis. parakeratosis. Hypergranulosis. H&E. Magnification x40.

To exclude psoriasis pathology, IHC analyses by the means of CK-10 and Ki-67 have been conducted (Tseng et al., 2021). IHC marker Cytokeratin 10 (CK 10) was used to differentiate inflammatory linear verrucous epidermal nevus from typical psoriasis, where first shows higher CK10 expression. Ki-67 market to determine level was used to estimate proliferation level of pathological process. It was positive in basal layer cells with moderate expression. From the above findings, we diagnosed ILVEN in this patient. We ruled out involvement of other sites with the thouroughly examination and skeletal X-rays, ultrasounds and abdominal CT scan. Actually, this patient did not desire to try any treatment because the most effective procedure that can guarantee a permanent outcome has not yet been established. In fact, patient was afraid of neither laser therapy nor surgical excision as they could lead to side effect, such as, disfigurement scarring (Conty et al., 2013; Wang et al., 2019). She only has agreed to use topical treatment, namely, regular emollients, keratolytics with urea 10% and from time to time potent corticosteroids (mometasone furoate 0.1%). Interestingly enough, she has refused deal with topical retinoids as they could lead to irritation. The treatments resulted in moderated improvement of the lesions and pruritus. The total follow-up period of study was two years.

3. DISCUSSION

In 1971 Altman and Mehregan defined clinical criteria for the diagnosis of ILVEN: early onset (before 5 years of age in 75% of the cases); 4:1 predominance in females; frequent involvement of the left lower extremity; pruritus; psoriasiform appearance, following the lines of Blaschko; and persistent lesions showing marked resistance to treatment (Ferreira et al., 2013). Not only in female pediatric patients ILVEN is most often observed (Böhm et al., 1999), but also in adult woman (Dickman et al., 2018; Gianfaldoni et al., 2017; Kirby et al., 2006; Tlish et al., 2017). In terms of complete epidemiology of this condition has not yet to be clearly clarified. Research has found that, ILVEN usually disappears by adolescence (Kirby et al., 2006). Furthermore, Tlish et al., (2017) described, clinical case of ILVEN in pregnant woman. He assumed the cohesion between rash onset as the pregnancy as their resolution–after abortion. Taking everything into consideration, the hormonal fluctuation might be considered as evidence of the occurrence of ILVEN and influenced the further course of ILVEN. Even with meticulous history, detailed clinical examination, including examination of other family members, in cases that do not fulfill the classic criteria for ILVEN, and close follow-up to observe the progression of the disease, differential diagnosis is sometimes difficult (Ferreira et al., 2013; Criscito et al., 2020). Therefore Ferreira et al., (2013) claimed, clinicians should use the immunohistochemical staining (IHC) of anti-involucrin to differentiate between unilateral psoriasis and ILVEN due to the specific pattern of involucrin expression in the epidermis that could give us a further clue to establish a more accurate diagnosis. On the other hand, Kirby et al., (2006) owing to characteristic histopathologic findings confirmed a suspicion of ILVEN: after performing 4mm-punch biopsy the regular alteration of parakeratotic areas of agranulosis and slightly depressed, cup-like, areas of orthokeratotic hyperkeratosis with a distinct granular layer were appreciated and elongations of the rete ridges are also noted.

In view of the fact that, Blaschko linear acquired inflammatory skin eruption (BLAISE) comprises a variety of dermatoses (Darsha et al., 2020), ILVEN has to be discerned from all of them. Firstly, we have done differential diagnosis with linear psoriasis and Blaschkoid lichen planus (BLP). To start with, ILVEN reminds clinical manifestation of the linear psoriasis (Li et al., 2012; Tanita et al., 2018) due to a number of similarities such as a distribution along Blaschko lines. The main distinguishing signs of psoriasis are its inception at any age, more freguently late onset; generally asymptomatic or only mildly pruritic and responds well to topical or systemic antipsoriatic treatment. Since the treatment for ILVEN has been vary widely from the of topical ointment for

psoriasis to invasive methods such as carbon dioxide gas laser 8, the differential diagnosis between ILVEN and psoriasis is necessary (Gianfaldoni et al., 2017; Kirby et al., 2006; Tanita et al., 2018).

As a rule BLP is rare variant, that affect 0.24% to 0.62% of all LP patients, benign and self-limited, has a unilateral distribution along the Blaschko lines, more than half of patients had complaints about pruritus demonstrating a characteristic S shape on the abdomen, V shape near the posterior midline, a linear pattern on the lower trunk and limbs, and whorls on the scalp and abdomen (Bolognia et al., 2012; Criscito et al., 2020). Remarkably, only 3 cases of bilateral multilinear LP were depicted in the database (Criscito et al., 2020). In fact, hypertrophic lesions are rare, but most cases demonstrated of polygonal violaceous papules and plaques whichheal with pigmentary alteration. Topical glucocorticoids are considered first-line therapy (Bolognia et al., 2012).

The most common of BLAISE are lichen striatus and blaschkitis (Darsha et al., 2020). Thus, clinicians should discriminate ILVEN between these ones. Regarding lichen striatus (LS) that occurs more often unilaterally along the lines of Blaschko as same as ILVEN, and rarely appearing bilaterally (Dickman et al., 2018). Three morphological variants of LS have been described. 80% of patients are presented with common signs as 2 to 4 mm, flat-topped, lichenoid papules ranging in color from red to flesh-colored. Second variant of LS is lichen striatus albus presents with hypopigmented macules and/or papules that coalesce into a patch. Third variant of LS is nail lichen striatus, which in addition to cutaneous lesions affects the nail matrix of usually a single digit. Its histopathological findings are somewhat nonspecific.

The clinical characteristics of the segmental Darier disease compared to ILVEN include multiple keratotic papules, which may coalesce in plaques, mainly in the seborrheic areas of the trunk, scalp (particularly its margins), forehead, and flexures. Some individuals experience mild involvement of the intertriginous areas and nail changes, including white and red longitudinal bands, longitudinal nail ridges, and V-shaped nick at the free margin of the nail. In addition, palmoplantar pits and whitish oral mucosal papules with a central depression (cobblestone appearance) can be detected in these patients (Alsharif et al., 2020). But only two types of Darier disease (DD) show linear distribution. The age of onset of unilateral variant DD is between the second and fourth decades with the average age being 27 years. A negative family history is typical in unilateral cases (Bimbi et al., 2017). DD is an autosomal dominant disorder. The localized types of Darier disease is treated with the use of topical retinoids, topical keratolytic agents whereas 5-fluorouracil, calcineurin inhibitors, and synthetic vitamin D3 analog are considered as treatment alternatives. For the generalized types of Darier diseasesystemic retinoids are the best option (Alsharif et al., 2020).

This article draws attention to the issue of the patient's lack of faith in the effectiveness of ILVEN treatment because of previous failure. Above all, we should persuade them to continue reseiving an up-to-date method of cure and remember about its improvement in a final visual effect of the affected areas (Gianfaldoni et al., 2017). Moreover, there was accentuated a malignant transformation, such as basal or squamous cell carcinoma and keratoacanthoma (Bolognia et al., 2012). Therefore we made a proposal for getting a laser therapy regadless the treatment of ILVEN is still challenging and often frustrating (Conti et al., 2013; Grgurich et al., 2018). We accounted for all pros and cons of contemporary methods of treatment (Conti et al., 2013), e.g. photodynamic therapy (PDT) technique, has proved to be an useful tool for treating ILVEN, although it provokes severe pain for patients who often require local anesthesia as same as surgery. Comparing surgery with the laser therapy, first one is more relevant in the case of limited lesions and itis considered as the final option (Gianfaldoni et al., 2017; Wang et al., 2019). Laser therapy is fast and generally well tolerated by all patients (Conti et al., 2013; Wang et al., 2019). Also surgery treatment is long-term, more invasive and destructive (Gianfaldoni et al., 2017; Tanita et al., 2018). Considering the area of the affected skin we convinced that patient needs to try, namely laser therapy, for its rapid re-epithelisation and the aesthetic result thanks to precise ablation and minimal damage to the surrounding tissues (Conti et al., 2013). However, Barney et al., (2019) displayed a case of ILVEN in a 5-year-old-boy, treated successfully with crisaborole 2% ointment. According to Alonso-Castro et al., (2012), just two out of five patients demonstrating a greater than 50% response rate as results of application of CO2 laser therapy and Conti et al., (2013) reported about using fractional CO2 laser treatment in a combination with CO2 laser for reducing pigment modifications and endowing a more youthful appearance to the treated areas. Whereas Wang et al., (2019) reported near resolution of ILVEN, after trialing the long-term phototherapy with 308-nm excimer laser for a woman in her 40s (regimen: 87 treatments for18 months) as well as the 20-year-old woman suffered from ILVEN was successfully treated with a UV 308-nm excimer laser and showed noticeable clinical improvement (Grgurich et al., 2018). Because of the above encouraging reports describing the successful usage of laser therapy we recommended for our patient to take a treatment with one of these regimen although the full recovering may take for month and, interestingly, Tlish et al., (2017) described, clinical case of ILVEN in pregnant woman, which illustrated the relationship of cutaneous manifestations pathological process and its further course in connection with pregnancy and with hormonal fluctuations. This is one of the isolated cases described in the literature (Gianfaldoni et al., 2017). It is unlikely that ILVEN in our patient will disappear without a trace after a future pregnancy.

4. CONCLUSION

Our case of ILVEN in a woman that had been present since her childhood highlights the patient's fear of applying modern methods of ILVEN treatment, such tretinoin, CO2 laser, 308-nm excimer laser due to concerns about the aesthetic appearance of the lesions. ILVEN is characterized by recurrent inflammatory course and the resistance to treatment. The key role in the distinction between ILVEN and psoriasis plays IHC. In particular, ILVEN has seen to be associated either with superinfection, eczema, necrosis or with a malignancy. In general, physicians should insist on getting treatment by their patients and don't wait for its spontaneous regression because it is rareness, physical discomfort and a threat to complications.

Abbreviations

ILVEN -	Inflammatory linear verrucous epidermal nevus
BLAISE -	Blaschkolinear acquired inflammatory skin eruption
BLP -	Blaschkoid lichen planus
CT-	Computed tomography
IHC -	Immunohistochemical staining
LP -	Lichen planus
LS -	Lichen Striatus

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Author Contributions

Author contributed to the research and/or preparation of the manuscript

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Conflict of Interest

The author declares that there is no conflict of interests.

Informed consent

Written & Oral informed consent was obtained from an individual participant included in the study. Additional informed consent was obtained from an individual participant for whom identifying information is included in this manuscript.

Data and materials availability

All data associated with this study are present in the paper.

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