Inflammatory Linear Verrucous Epidermal Naevus (ILVEN) Versus Linear Psoriasis

A Clinical, Histological and Immunohistochemical Study

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Inflammatory Linear Verrucous Epidermal Nevus (ILVEN) has been suggested to be a separate disease entity. However, the distinction from linear psoriasis has been discussed in the literature over recent decades.

The aim of the present study was to investigate, in addition to the clinical and histological criteria, the immunohistochemical aspects of inflammation, epidermal proliferation and keratinization.

From a clinical and histological point of view, ILVEN and psoriasis, according to the established criteria, have been proved to overlap. The immunohistochemical study suggests that the following procedures have an additional diagnostic impact:

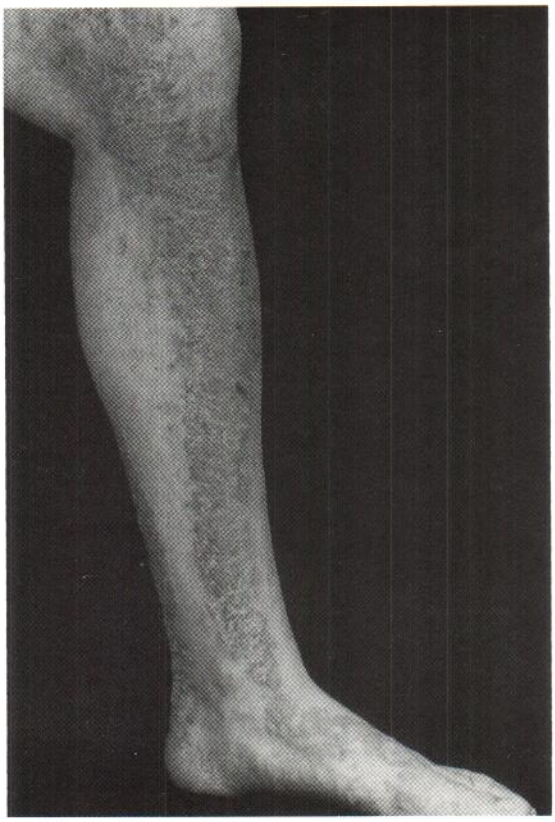

Fig. 1. Linear lesion on the left leg of patient 4.

assessment of elastase-positive cells, assessment of keratin 16 and of keratin 10. ***Key words: Inflammation; Proliferation; Immunohistochemistry.***

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Since the first description of inflammatory linear verrucous epidermal nevus (ILVEN) by Unna (1), various investigators have endeavoured to formulate both clinical and histopathological criteria with which to distinguish ILVEN from psoriasis (2, 3).

The clinical appearance of ILVEN varies from lichenoid to psoriasiform, from scaling to markedly verrucous (2, 4, 5). The nosology is rendered even more complex by the observation that linear lesions might coexist with typical psoriatic lesions (6).

At the histological level the alternation of orthokeratosis and parakeratosis has been suggested to be typical for ILVEN, although such a pattern can be seen in psoriasis as well. On the other hand, micropustules of Munro, a characteristic feature of the psoriatic lesion, can be seen in ILVEN.

In order to delineate ILVEN from linear psoriasis, we investigated a group of 4 patients suffering from linear erythematous lesions having a scaling and or a verrucous appearance.

In addition to clinical and histological description, the purpose of the present study was to assess inflammation, proliferation and keratinization by using immunohistochemical methods.

MATERIALS AND METHODS

Case 1

A 77-year-old female who had had extensive symmetrical erythematosquamous papular lesions all over her body ever since she was 5 years old. On her right arm, right upper leg and right half of the thorax, the lesions were linearly arranged. The patient suffered from severe pruritus. In some biopsies the histipathological findings were compatible with ILVEN and in other biopsies with psoriasis. Treatment with PUVA and dithranol did reduce psoriasis, but failed to influence ILVEN. Multiple excisions of linear lesions were carried out.

Case 2

A 28-year-old female with erythematous hyperkeratotic papular eruptions in the right groin and on the vulva. These lesions, which had been present since birth, caused severe itching and were both clinically and histopathologically classified as a linear verrucous nevus. Topical treatment with all-trans-retinoic acid, solutio carbonis detergens, corticosteroids, or treatment with argon laser or cryotherapy, had not afforded any positive effect.

Case 3

The third patient was a 37-year-old male with linear erythematosquamous lesions, which were diagnosed as ILVEN. The lesions appeared at the age of 24 and were localized to the left arm and axilla. Severe pruritus was experienced. Cryotherapy and several topical therapies failed to alleviate his condition. No spontaneous regression was seen. Multiple excisions reduced the extent of the lesions.

Case 4

The sixth patient was a 46-year-old male who had had slightly itching linear erythematosquamous lesions on his left leg and trunk since the age of 14 (Fig. 1). He also had signs of classical psoriasis. Histologically, both diagnoses could be confirmed. Dithranol reduced the psoriatic lesions, but the linear verrucous lesions did not respond.

Immunohistochemical investigations

In each patient a punch biopsy (3 mm) was taken from the linear lesions and snap frozen in liquid nitrogen. Staining was performed using the following antibodies in order to

characterize inflammation and proliferation. A direct or indirect peroxidase technique, or a peroxidase-anti-peroxidase technique was used on acetone-fixed slides of 7 μm.

Inflammation. Anti elastase (Serotec, Oxford, England) was used to assess elastase, a marker enzyme for polymorphonuclear leukocytes (PMN), T11 (Dakopatts, Copenhagen, Denmark) to assess T-lymphocytes (CD2), WT14 (Dept. Medicine, Div. Nephrol., University Hospital Nijmegen) to assess CD14-positive cells (monocytes and macrophages), (7), and OKT6 (Ortho Diagnostic Systems, Raritan, USA) to assess Langerhans' cells (CD1a).

Stained cells in the epidermal compartment were assessed using a scale ranging from 0 to 4 points: 0 = no expression; 1 = sporadic expression; 2 = minimal expression; 3 = moderate expression; 4 = pronounced expression. Stained cells in the dermis were expressed as a percentage of the total number of infiltrate cells: 0 = no cells stained; 1 = sporadic cell staining; 2 = 1–25%; 3 = 26–50%; 4 = 51–75%; 5 = 76–99%; 6 = 100% of the infiltrate cells stained.

Proliferation. Ki-67 (Dakopatts, Copenhagen) was used to visualize nuclei of cycling cells. The number of Ki-67 positive nuclei was counted per mm length of epidermis.

Keratinization. Ks8.12 (Sigma, St. Louis, USA), an antibody directed against keratin 13 and 16. Keratin 16 is present in hyperproliferative epidermis (8), whereas keratin 13 is absent in human adult skin (9). RKSE60 (a generous gift of Dr F. C. S. Ramaekers), directed against keratin 10, present in differentiated epidermal cells. Staining with Ks8.12 and RKSE60 was scored using the same scale as used for inflammation parameters in the epidermal compartment. Staining of suprabasal (differentiated) and basal (undifferentiated) compartments was assessed separately.

RESULTS

Staining with the monoclonal antibody Ks8.12 assessing keratin 16, showed foci of suprabasal staining coinciding with areas of parakeratosis in 3 of the 4 patients suffering from ILVEN. The number of Ki-67-positive nuclei was increased slightly to markedly in all biopsies. In contrast to the focal distribution pattern of the hyperproliferation-related keratin 16 in the suprabasal compartment, the germinative zone showed an equal distribution of Ki-67-positive nuclei. Keratin 10 was equally distributed in the suprabasal compartment; only in one biopsy of a psoriatiform lesion were distinct areas overlying dermal papillae showing less intense staining seen.

Infiltrate analysis revealed a consistent composition in all biopsies. However, in patient 4 who had a superimposed psoriasis, the occurrence of PMN in the more psoriasiform lesion was increased. The identity of the mononuclear infiltrate cells proved to be predominantly T-lymphocytes. CD14-positive cells and Langerhans cells were found in the dermal infiltrate as well as in the epidermal compartment.

DISCUSSION

Clinical criteria for the diagnosis ILVEN were described by Altman & Mehregan in 1971 (2). In a study of 25 patients they defined as diagnostic criteria: (i) early age of onset, (ii) a predominance in females (f:m = 4:1), (iii) frequent involvement of the left lower extremity, (iv) substantial pruritus, (v) persistency of the lesions, and (vi) refractoriness to treatment.

Of these criteria, nos. (ii) and (iii) have been found in larger surveys to be associated with ILVEN. In the individual patient, however, both criteria have a limited diagnostic value.

If we analyse the clinical findings of the present series using the four discriminative criteria (i, iv, v, vi), 2 out of 4 patients appeared to be 'classical cases' of ILVEN (patients 1 and 2). The 2 remaining patients (nos. 3 and 4) did show some of the criteria. Firstly a relatively late age of onset was mentioned by these 2 patients. However, relatively minor manifestations of ILVEN may have been overlooked by the patient. In patient 4, superimposed psoriasis is complicating the picture. Therefore, the partial regression mentioned, can be explained as a reduction of the psoriatic component.

Histological criteria for the diagnosis ILVEN have been defined by several authors (2, 3). Altman & Mehregan found in biopsies an inflammatory and psoriasiform appearance. Acanthosis, papillomatosis, spongiosis and exocytosis leading to spotty areas of parakeratosis were often seen. Sometimes small Munro abscesses were found. Areas of parakeratosis with loss of the granular layer, and of orthokeratosis with a prominent granular layer with a sharp demarcation were seen. A mild perivascular infiltrate consisting mainly of T-lymphocytes was present. Dupré & Christol (3) further developed these criteria. They stated that specific and non-specific lesions of ILVEN exist. Essential features of specific lesions were: alternation of hypergranulotic, depressed areas with overlying orthohyperkeratosis, and of areas of agranulosis with overlying parakeratosis. Papillomatosis, acanthosis and a lymphohistocytic infiltrate were non-specific features.

In psoriasis the criteria designated as "non-specific for ILVEN" by Dupré & Christol are usually ex-

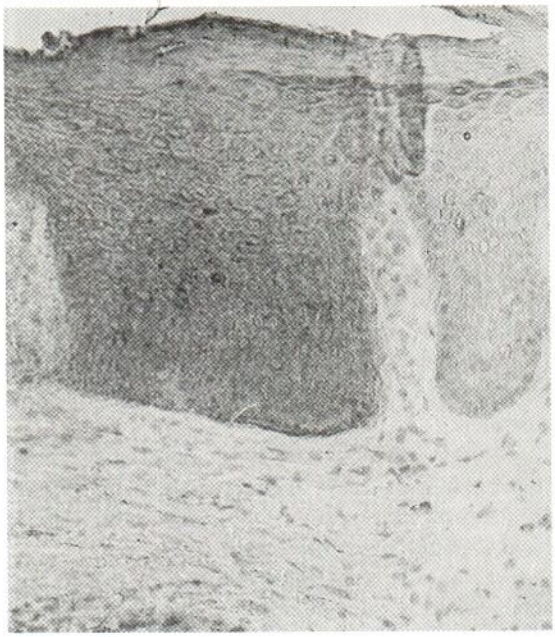

Fig. 2. Immunohistochemical staining with the antibody Ks8.12 (keratin 16) showing a focal distribution pattern (× 200).

pressed. The "specific criteria for ILVEN" can be observed occasionally in psoriasis. The micro-abscesses of Munro are believed to be a "specific criterion for psoriasis" (10). However, this feature has occasionally been reported in ILVEN. Therefore distinction between ILVEN and psoriasis is difficult on histological grounds.

In the present series, the 2 patients with classical ILVEN on clinical grounds (patients 1 and 2) showed the 'specific histological ILVEN hallmarks'. In the patients with incomplete clinical presentation of ILVEN (patients 3 and 4) again this specific picture was observed. In 2 patients with ILVEN superimposed by psoriasis, intra-epidermal PMN accumulation was seen.

The present immunohistochemical study demonstrates that abnormal keratinization and epidermal hyperproliferation are dissociated in ILVEN. No direct topographical relation was observed between the localization of the infiltrate and the epidermal changes. However, studies on incipient lesions might reveal such a relationship. The remarkable focal distribution pattern of Ks8.12 (keratin 16 expression, Fig. 2) suggests that further studies on the keratinization process in ILVEN are worthwhile.

From an immunohistochemical point of view, ILVEN and psoriasis show certain differences. In ILVEN we observed a relatively low occurrence of elastase-positive cells (PMN), a focal staining pattern of Ks8.2 (anti-keratin 16) and a homogeneous distribution of RKSE60 (anti-keratin 10). In psoriasis, the occurrence of elastase-positive cells is more substantial, Ks8.12 staining is homogeneous and RKSE60 staining shows foci of decreased staining (11). It is attractive to speculate that the relatively low occurrence of PMN in ILVEN is the cellbiological explanation for refractoriness to anti-psoriatic treatment.

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