

Inflammatory Linear Verrucous Epidermal Nævus with Auto-immune Thyroiditis: Coexistence of Two Auto-immune Epithelial Inflammations?

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We report a patient with an inflammatory linear verrucous epidermal nævus (ILVEN) coexisting with an auto-immune lymphocytic thyroiditis. The occurrence of two epithelial inflammatory processes could be linked and raises the question of auto-immune involvement in the inflammatory part of ILVEN. Moreover, expression of a membrane antigen, OKM5, usually assigned to antigen-presenting cells, especially macrophages, has been demonstrated on keratinocytes in some dermatological diseases including ILVEN. These data suggest that keratinocytes in ILVEN could present some antigens and perhaps auto-antigens modified by the hamartomatous process, leading to an (auto-immune?) inflammatory reaction.

mis with orthokeratotic and parakeratotic areas and a superficial, mainly perivascular, inflammatory infiltrate of the dermis (Fig. 1). Because of aesthetic discomfort, the lesions on right lower limb were surgically excised. Ophthalmological examination, renal function tests, ultrasonic examination of abdomen and kidneys were normal. Because of the lack of symptoms, no X-ray scan of the brain was performed. By contrast, hypothyroidism was still present, with a raised TSH (11 μ UI/ml) and low peripheral hormone levels ($T_3 = 1.8$ ng/l; free $T_4 = 5$ ng/l) in spite of a supplemental, but insufficient, treatment by L-thyroxine with a daily dose of 100 μ g. Furthermore, she still had antibodies to thyroid microsomal antigen with a 1/160^e titer but no antibodies to thyroglobulin; search for other auto-antibodies (to parietal cells, nucleus, DNA, soluble nuclear antigens, smooth muscle, mitochondria) was negative.

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Epidermal nævi are cutaneous, benign hamartomatous epithelial lesions, characterized by hyperplasia of the usual components of the epidermis. The inflammatory variant is often referred to as "inflammatory linear verrucous epidermal nævus" (ILVEN). We describe a young patient with an ILVEN coexisting with a lymphocytic thyroiditis, rather different from the two cases already reported with atrophy of the thyroid gland associated with an epidermal nævus. This new association raises the question of auto-immune involvement in the pathomechanisms of inflammation in ILVEN.

MATERIAL AND METHODS

A 25-year-old woman was referred to our institution for the first time in October 1991 for evaluation of linear hyperkeratotic lesions of the right lower limb. She had a medical history of isolated hypothyroidism by lymphocytic thyroiditis; the diagnosis had been established by usual histological and immunological means (presence of antibodies to thyroid microsomal antigens) when she was 11. Other endocrinological functions (i.e. corticotropin, somatotropin, gonadotropin, prolactin) were normal. Cutaneous lesions were observed, with brownish verrucous and hyperkeratotic, grossly linear lesions on the medial side of the right thigh and leg, as well as on the umbilicus. According to the patient's parents, these lesions had appeared at the age of 8 months as small red and hyperkeratotic patches on the umbilicus and right knee, with subsequent spreading of the last one. At the time of consultation in our department, a clinical diagnosis of ILVEN was made, based on the clinical pattern of the lesions and on report by the patient of inflammatory, pruritic flares of variable duration of the hyperkeratotic patches. This diagnosis was confirmed by a histological examination, with a characteristic pattern of hyperplastic and papillomatous epider-



Fig. 1. Histological features of cutaneous lesions: hyperplastic and papillomatous epidermis, orthokeratotic areas alternating with parakeratotic areas and perivascular inflammatory infiltrate of superficial dermis.

DISCUSSION

We report a case of ILVEN with clinical and histological typical features associated with an early auto-immune lymphoid thyroiditis leading to hypothyroidism.

Lymphoid thyroiditis is often described in association with other pathological states, mainly auto-immune disorders such as myasthenia gravis, diabetes mellitus, systemic lupus erythematosus (2), polymyositis and Gougerot-Sjögren's syndrome (3). It can also coexist with some dermatological diseases such as REM syndrome, ill-defined keratotic acral papules (4), bullous pemphigoides (5), erosive lichen planus (6), chronic pustular dermatosis of the scalp (7), alopecia areata and chronic urticaria (8). Only two cases of association between thyroid gland disease and epidermal nevus are reported in the dermatological literature (9, 10).

In the first one, multiple visceral malformations were present at birth with phocomelia, alopecia, ichthyotic pattern of head, neck and right side of the body, left hydronephrosis and atrophy of the right part of the skeleton. The dermatological changes were those of a verrucous nevus but no biopsy was performed. Death occurred at the 26th day of life and autopsy findings were hypoplasia of thyroid gland without further precisions regarding the presence of hypothyroidism (9). The second observation described a patient with epidermal nevus and hypothyroidism probably of hypophysial origin (10).

Our case is clearly different from the patients mentioned above because of the auto-immune pathomechanisms involved in the endocrine disorder (without any malformative pattern) and by the association with an ILVEN and not with common epidermal nevus. In this way, it seemed to us noticeable enough to be reported because of the coexistence of two unusual diseases, both involving an inflammatory process specifically directed against epithelia.

Organ-specific auto-immune pathomechanisms are almost certain in lymphoid thyroiditis. However, although suggested by our case, it is not the case for the inflammatory side of ILVEN, where no auto-immune pattern has to date been demonstrated, even partially. Nevertheless, although the association reported here could be a coincidence, it must be kept in mind that auto-immune thyroiditis is often associated with other auto-immune or partially auto-immune disorders. Furthermore, it has been demonstrated (11) that some keratinocytes of ILVEN lesions express the OKM5, but not OKM1, membrane antigen (unfortunately, such immunological studies could not be performed in our patient). Since this immunological pattern is found mainly on cells of monocyte-macrophage lineage, i.e. antigen-presenting cells, it could be assumed that the keratinocytes of ILVEN act as antigen (and perhaps autoantigen in this

condition)-presenting cells too with triggering of a subsequent inflammatory reaction. This hypothesis is obviously consistent with the involvement of auto-immune pathomechanisms in ILVEN lesions, the auto-antigen being perhaps a normal component of keratinocytes modified by the hamartomatous process. Moreover, in our peculiar case, it can be speculated that both cutaneous and thyroid epithelia share the "auto-immunity promoting" antigenic pattern.

To conclude, it appears that it could be interesting in the future: 1) to study the expression of OKM1 and OKM5 antigens on thyroid epithelium in lymphoid thyroiditis (identical pattern as keratinocytes in ILVEN?) and more systematically these antigens in ILVEN lesions when possible; and 2) to search more systematically for an associated auto-immune disorder in patients with ILVEN.

By this means, new insights would possibly be gained regarding the involvement of an auto-immune reaction in the pathomechanisms of ILVEN lesions.

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