Clinical Letter

A case of localized, unilateral hyperkeratosis lenticularis perstans on a woman's breast

DOI: 10.1111/ddg.12776

Dear Editors,

A 75-year-old woman presented with a 5-year history of asymptomatic lesions confined to the right breast, which caused her discomfort when wearing a bra. The patient denied any injury or trauma to the affected area. Clinical inspection showed three plaques, each of them formed by several yellowish keratotic adherent papules. The individual papules measured 1 to 2 mm in diameter, and consisted of isolated or contiguous monomorphic elements, ranging from 50 to 60 per plaque. Some of these elements were more elevated than others or showed a slight depression at their center (Figure 1).

A biopsy taken from one of the plaques revealed a laminar orthokeratotic and hyperkeratotic lesion, strongly eosinophilic at its center, thus representing a contrast to the normal basket-weave stratum corneum on both sides. The epidermis below the lesion showed a loss of the rete ridges. Towards the edges of the lesion, the epidermis formed papillomatous elevations similar to a church spire. In the dermis, there was a slight perivascular lymphohistiocytic inflammatory infiltrate (Figure 2). Topical treatments including calcipotriene and urea were unsuccessful. Eventually, the lesions were removed using electrocautery and curettage. There was no recurrence.

Also known by its eponym (Flegel's disease), hyperkeratosis lenticularis perstans (HLP) is a rare disorder of keratinization described by Flegel in 1958. Most cases are sporadic in origin, although it is typically described as an autosomal dominant disorder. In some series, the minority of cases was familial [1, 2]. It characteristically affects middle-aged or older men, with bilateral lesions mainly found on the back of the feet and the anterior aspects of the legs. More rarely, the disorder has been described on the upper extremities and, as an exception, also in other locations. Clinically, it is characterized by multiple red-brown papules almost symmetrically located on the dorsum of the feet and legs. The typical HLP lesion is a well-defined red to yellow-brown papule, about 2 to 5 mm in diameter, with a keratotic adherent scale. Occasionally, it has been described involving the upper extremities [1], hands [3], back [4], ears [1], palms [5], and oral mucosa. More rarely, lesions in the axillary folds, antecubital and popliteal fossae, and on the eyelids have been reported, in addition to the more common involvement of legs and hands [6]. A case with unilateral lesions on the lower extremity – existing since puberty – has also been described [7].

Histopathologic findings characteristically show an orthokeratotic and hyperkeratotic epidermis of decreased thickness. The dermis exhibits a lymphocytic infiltrate of

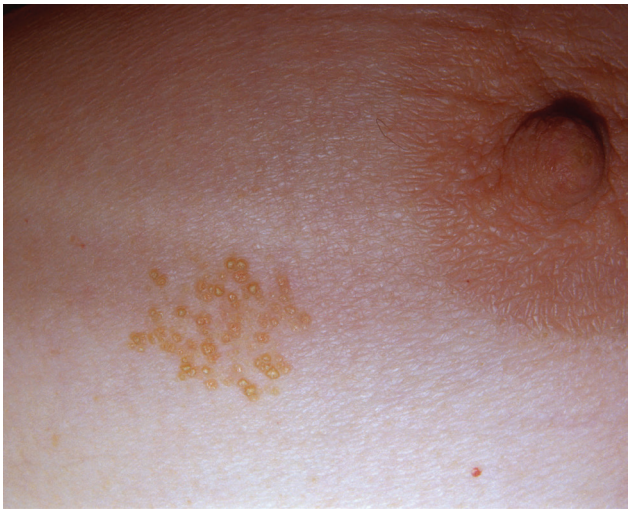

Figure 1 Grouped yellow keratotic papules forming a plaque on the breast. Individual lesions measured 1 to 2 mm in diameter. Some lesions were more elevated than others or showed a slight depression at their center.

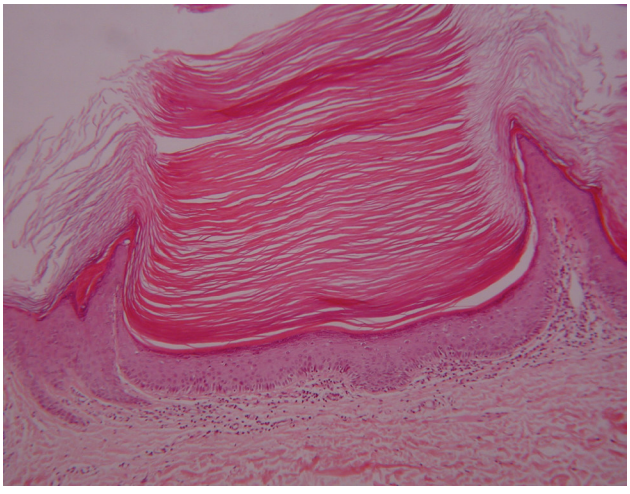

Figure 2 Hyperkeratosis, strongly eosinophilic at the center, contrasting with the normal basket-weave stratum corneum on both sides. The epidermis below showed a loss of the rete ridges. At the edges of the lesion, there were papillomatous elevations similar to a church spire. The dermis revealed a slight perivascular lymphohistiocytic inflammatory infiltrate.

varying extent. The intense eosinophilic staining of the compact stratum corneum of the lesion marks a stark contrast to the normal basket-weave layer on both sides, which is less compact and less intensely stained [7]. There may be some degree of vacuolization of the basal layer. The histopathologic appearance changes with the age of the lesions: in more recent lesions, the inflammatory infiltrate is prominent and the epidermis appears to be atrophic [8]. The histopathology of the present case corresponds to a typical older HLP lesion, without a marked inflammatory infiltrate but with diminished rete ridges [8].

On electron microscopy, the most characteristic feature is an absence or reduction of Odland bodies, which, however, is not always present [7], but potentially explains the origin of this keratinization defect. The fact that Odland bodies are not always present may be due to the individual age of the lesions. It has been noted that, in early lesions, there are no Odland bodies, whereas they are present in older lesions. Odland bodies are rich in lipids and have an impact on the extent of semi-permeability of the stratum corneum; lack of semi-permeability induces compact hyperkeratosis, as seen in early lesions, while its presence in older lesions helps reestablish the functionality of the stratum corneum, which may lead to an eventual recovery by shedding [8].

Regarding the differential diagnosis, HLP can clinically resemble stucco keratosis, Kyrle's disease, and superficial actinic porokeratosis. Scale removal curettage can cause slight bleeding and raise confusion with psoriasis; on the other hand, stucco keratoses do not bleed.

Because the pathogenesis of HLP is unknown, the response to various treatments used has been variable. Some cases responded well to topical corticosteroids [9], which is concordant with the inflammatory infiltrate observed in new lesions; by contrast, in older lesions, it seems difficult to expect a satisfactory result with topical corticosteroids due to the scarcity of the inflammatory infiltrate.

Other cases have shown a good response to topical 5-fluorouracil [2], calcipotriene [10], PUVA as well as topical and systemic retinoids [1, 6, 7]. Excisional biopsy in one case resulted in complete resolution of lesions without recurrence. It has been postulated that ablative treatments (CO_2 laser, curettage, and electrocoagulation) might be useful because of the removal of defective keratinocytes [11]. In our patient, whose histopathology showed a scarce inflammatory infiltrate, treatment with urea and calcipotriene showed no effect. Only the removal of lesions by curettage and electrocoagulation led to a satisfactory therapeutic result.

In Flegel's disease, involvement of areas other than the lower extremities is rare, and even more infrequent is its unilateral presentation in a woman. To our knowledge, HLP has not been described in the breast region.

Conflict of interest
None.

Francisco Urbina[1], Emilio Sudy[1], Carlos Misad[2]

(1) Dermatologist in Private Practice, Santiago de Chile
(2) Servicio de Anatomía Patológica, Hospital San Juan de Dios, Santiago de Chile

Correspondence to

Francisco Urbina
Algeciras 583, Las Condes
Santiago de Chile, Chile

E-mail: fcourbina@hotmail.com

References

1 Price ML, Jones EW, MacDonald DM. A clinicopathological study of Flegel's disease (hyperkeratosis lenticularis perstans). Br J Dermatol 1987; 116(5): 681–91.
2 DeArgila D, Revenga F, Rodríguez JL et al. Hiperqueratosis lenticularis perstans (enfermedad de Flegel): estudio clínico-patológico de 10 casos. Actas Dermosifiliogr 1994; 85: 309–15.
3 Massone L, Pestarino A, Gambini C, Isola V. Hyperkeratosis lenticularis perstans. A clinical case and review of the literature. G Ital Dermatol Venereol 1990; 125(6): 281–4.
4 Gutiérrez MC, Hasson A, Arias MD et al. Localized hyperkeratosis lenticularis perstans (Flegel's disease). Cutis 1991; 48(3): 201–4.
5 Fernández-Crehuet P, Rodríguez-Rey E, Ríos-Martín JJ, Camacho FM. Hiperqueratosis lenticularis perstans (enfermedad de Flegel) con afectación palmo-plantar. Actas Dermosifiliogr 2009; 100: 157–9.
6 Krishnan A, Kar S. Hyperkeratosis lenticularis perstans (Flegel's disease) with unusual clinical presentation. Response to isotretinoin therapy. J Dermatol Case Rep 2012; 6(3): 93–5.
7 Miranda-Romero A, Sánchez Sambucety P, Bajo del Pozo C et al. Unilateral hyperkeratosis lenticularis perstans (Flegel's disease). J Am Acad Dermatol 1998; 39: 655–7.
8 Ando K, Hattori H, Yamauchi Y. Histopathological differences between early and old lesions of hyperkeratosis lenticularis perstans (Flegel's disease). Am J Dermatopathol 2006; 28: 122–6.
9 Sterneberg-Vos H, vanMarion AM, Frank J, Poblete-Gutierrez P. Hyperkeratosis lenticularis perstans (Flegel's disease) – successful treatment with topical corticosteroids. Int J Dermatol 2008; 47(Supl 1): 38–41.
10 Bayramgürler D, Apaydin R, Dökmeci S et al. Flegel's disease: treatment with topical calcipotriol. Clin Exp Dermatol 2002; 27: 161–2.
11 Rheingantz da Cunha Filho R, Larangeira de Almeida Jr H. Hyperkeratosis lenticularis perstans. An Bras Dermatol 2011; 86(4 Suppl 1): S76–7.

