Hyperkeratosis lenticularis perstans (Flegel disease)

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Abstract

Hyperkeratosis lenticularis perstans (Flegel disease) is a rare, benign hyperkeratotic skin disorder which typically occurs in lower extremities of Caucasian middle-aged patients. Most cases are sporadic although familial cases with an autosomal dominant mode of inheritance have been reported.[1–5] Clinically the condition mimics many other hyperkeratotic and inflammatory disorders and the diagnosis is only confirmed on histopathological and clinical correlation.[2,5,6] The condition typically presents with asymptomatic keratotic/scaly red/brown papules which histomorphologically show lamellar hyperkeratosis with abrupt peripheral basket-weave orthokeratosis, irregular acanthosis and underlying lichenoid lymphocytic infiltrate.[1–7] The pathogenesis remains unclear and thus various topical and/or systemic treatments have shown variable success rates. Herein we describe a classical case with review of the current literature.

Keywords dermatopathology; Flegel disease; hyperkeratosis lenticularis perstans; keratin

Case report

A 44 year old female was referred to the dermatologist with a 2.5 year history of asymptomatic pinkish/light brown papules on her ankles, lower legs which had progressively spread to her thighs, arms and neck. There was no other significant past medical history. On examination, there were a number of non-tender, non-ulcerated, light brown papules ranging in size from 1 to 5 mm, some of which were scaly/keratotic on the feet, ankles, thighs, arms and neck (Figure 1). A 4 mm diameter punch biopsy of one of the lesions on the ankle was taken and sent for histopathology at the local hospital. The case was then referred to the regional dermatology grand round for specialist opinion.

Histological examination revealed skin containing a central area with abrupt compact hyperkeratosis and focal parakeratosis, epidermal thinning, interface dermatitis with occasional colloid bodies and underlying lichenoid chronic inflammation (Figure 2). There was no evidence of dysplasia or malignancy.

Discussion

Hyperkeratosis lenticularis perstans (Flegel disease) is a rare disorder of kertinisation/hyperkeratotic dermatosis which was originally described by H. Flegel in 1958.[1–5] The pathogenesis is unknown although ultraviolet light and cell-mediated cytotoxicity against epidermal cells have been implicated.[1,3,4,7] Most cases are sporadic and are more commonly seen in a middle-aged and older, Caucasian population with no gender bias. Familial cases have also been reported and previously the disease was thus typically described as an autosomal dominant disorder.[1–7] An association with endocrinopathies and cutaneous or gastrointestinal malignancies has been suggested but this is still debatable.[3,4] Nevertheless, a complete systems review, social and family history are therefore necessary. Radiological or further laboratory tests are not required unless other associations are revealed. The condition typically presents symmetrically as asymptomatic, small red/brown keratotic papules on the lower extremities which may gradually progress to involve proximal sites, including the back, arms, palms, ear pinnae and even the oral mucosa. There are isolated case reports of lesions involving the trunk, flexor creases and eyelids. The disease demonstrates a protracted clinical course lasting years to decades.[1–7] Clinically Flegel disease may resemble other hyperkeratotic and inflammatory entities. Differential diagnoses include: keratosis pilaris, Darier disease, lichen planus, lichenoid drug reaction, stucco keratosis, hyperkeratosis follicularis et parafollicularis in cutem

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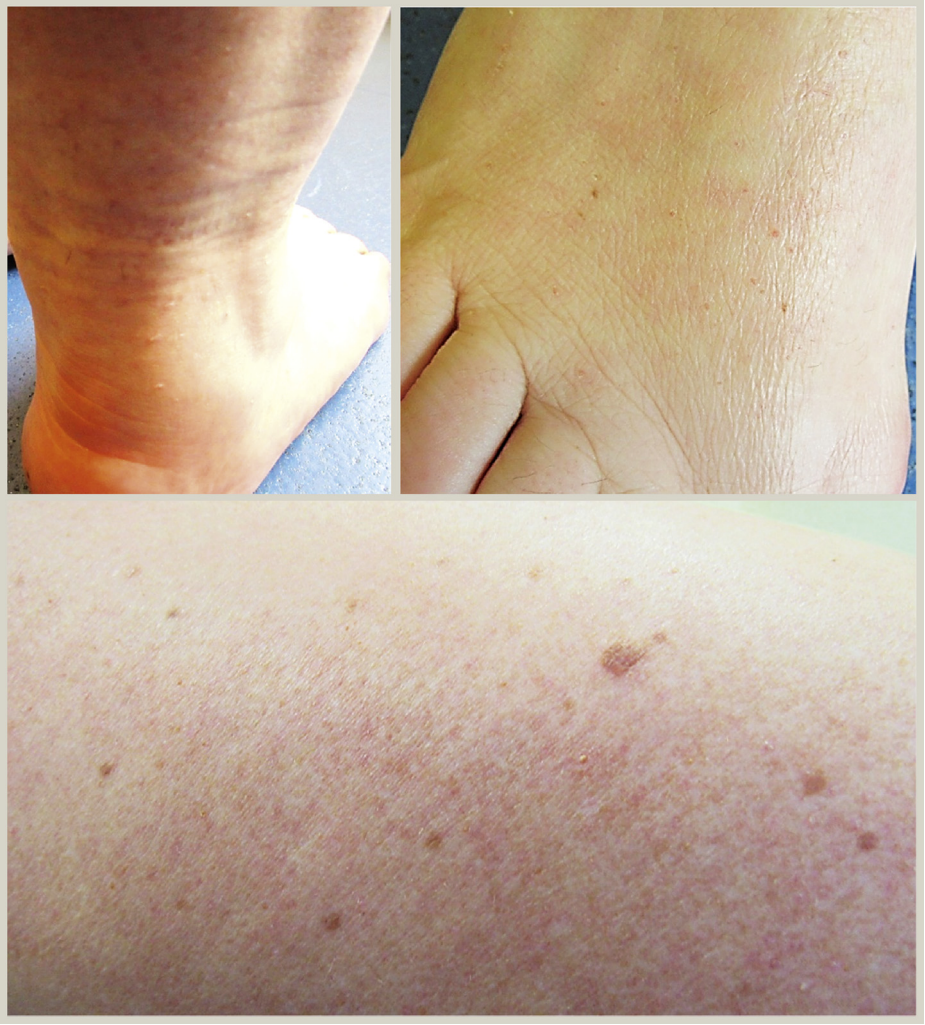

Figure 1 Clinical photographs taken of the extremities demonstrating the pinkish/light brown papules.

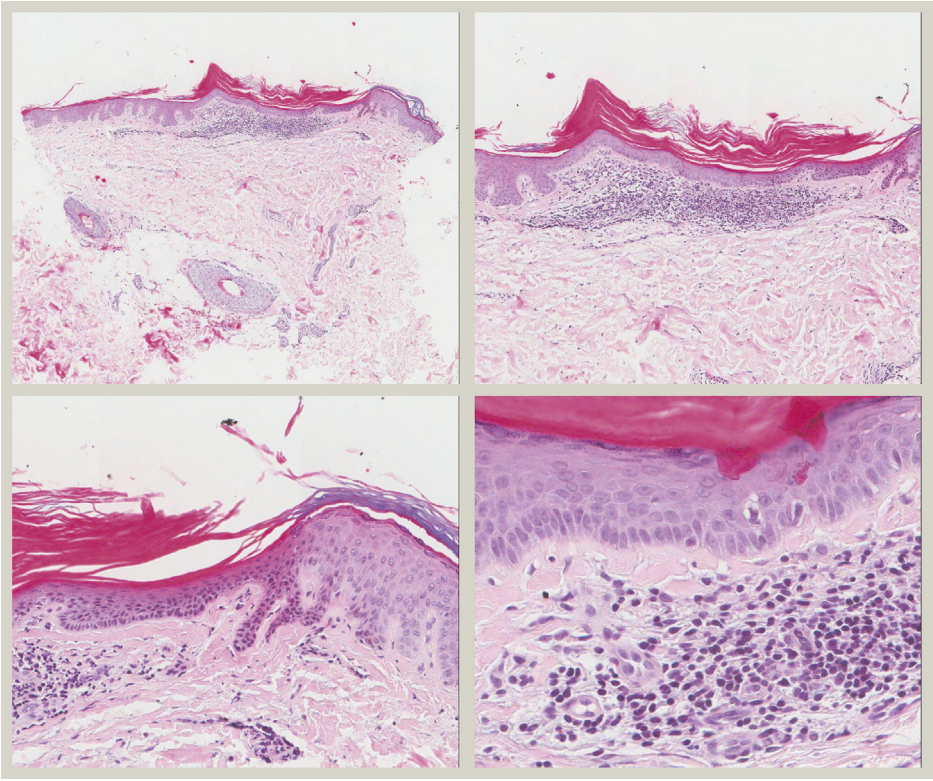

Figure 2 Skin sections showing a well-demarcated lesion with compact hyperkeratosis and abrupt orthokeratosis, focal parakeratosis, epidermal thinning with occasional colloid bodies at the epidermo-dermal junction and underlying lichenoid chronic inflammation (H&E; various magnifications).

pentetrans or Kyrle disease, superficial actinic porokeratosis and scurvy.[2,5,6] Scale removal curettage can cause pinpoint bleeding and raise confusion with psoriasis. The diagnosis is established on clinical and histopathological correlation.

Characteristic histomorphological features include: a discrete area of compact/lamellar hyperkeratosis with abrupt basket-weave orthokeratosis on either side; focal parakeratosis; thinned or absent granular cell layer; irregular acanthosis or thinning with loss of rete ridges; variable spongiosis; basal vacuolation with occasional cytoid bodies; underlying lichenoid lymphocytic infiltrate and/or perivascular chronic inflammation with oedema in the papillary dermis.[1–7] The histological differential diagnosis includes other causes of a lichenoid/interface dermatosis. The distinctive changes in the stratum corneum (discrete and abrupt area of hyperkeratosis), however, is a clue to the diagnosis. Previous investigators have also shown that CD8+-suppressor T cells predominate the dermal lymphocytic infiltrate and epidermotropic lymphocytes, indicating an autoimmune response.[3,4] Ultrastructurally, vesicular bodies in the granular layer, persistence of desmosomal discs in the stratum corneum and the absence or reduction of membrane-coating granules (Odland bodies) have been demonstrated. Odland bodies are involved in normal process of desquamation. Abnormalities in their structure and function may result in a decreased desquamation and hence the distinctive abnormal/retention hyperkeratosis seen in Flegel disease.[1,3–5]

With the pathogenesis still unknown, various treatments such as: topical 5-fluorouracil, topical and systemic retinoids, calcipotriene, topical corticosteroids, emollients and PUVA therapy, have shown ranging success rate. Ablative treatments (CO_2 laser, curettage, dermabrasion and electrocoagulation) might be useful because of the removal of defective keratinocytes but impractical for a large number or the certain locations of lesions. Importantly, however, the condition is benign and no mortality has been documented.[1–5] ◆

Practice points

- Hyperkeratosis lenticularis perstans (Flegel disease) is a rare hyperkeratotic dermatosis which presents predominantly on the lower extremities and may progressively involve proximal sites.
- Both sporadic and familial cases (autosomal dominant inheritance pattern) have been reported.
- The pathogenesis is unknown but UV light and immune mediated responses against epidermal cells have been implicated.
- Histopathology is distinctive with a characteristic pattern of discrete and abrupt hyperkeratosis with an associated lichenoid/interface inflammatory reaction.
- Lesions are benign and treated mainly for cosmesis. Various treatments have shown variable response rates.

Multiple choice questions

1. Hyperkeratosis lenticularis perstans is considered a variant of which of the following?

A. Kyrle disease
B. Stucco keratosis
C. Lichen planus
D. Keratosis pilaris
E. None of the above

Answer: E.

2. Which of the following bodies may be found in hyperkeratosis lenticularis perstans?

A. Verocay bodies
B. Russell bodies
C. Odland bodies
D. Mott bodies
E. Rushton bodies

Answer: C.

3. Which of the following changes in the stratum corneum are characteristic of hyperkeratosis lenticularis perstans?

A. Confluent parakeratosis
B. Alternating hyperkeratosis and parakeratosis
C. Discrete and abrupt hyperkeratosis
D. Perifollicular parakeratosis
E. Absent stratum corneum

Answer: C.

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