Title
Keratolysis exfoliativa

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Case presentation

Keratolysis exfoliativa

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Abstract

Keratolysis exfoliativa (KE) is a palmoplantar eruption of air-filled bullae on an erythematous base, which results in lamellar peeling with hallmark superficial collarettes of scale. It is distinct from other diseases of volar skin, such as dyshidrosis, contact dermatitis, tinea, epidermolysis bullosa, and acral skin peeling. We present a 55-year-old woman with extensive disease on the hands and feet, who failed to respond to standard topical therapy but showed a marked dose-response improvement with the use of oral acitretin. Recent histopathologic and molecular studies have linked KE to premature corneo-desmosomal disruption. Acitretin has previously been used to treat diseases of abnormal corneocyte desquamation, for example Netherton's disease. To the best of our knowledge, this report is the first that documents the efficacy of the use of systemic acitretin in KE.

Case synopsis

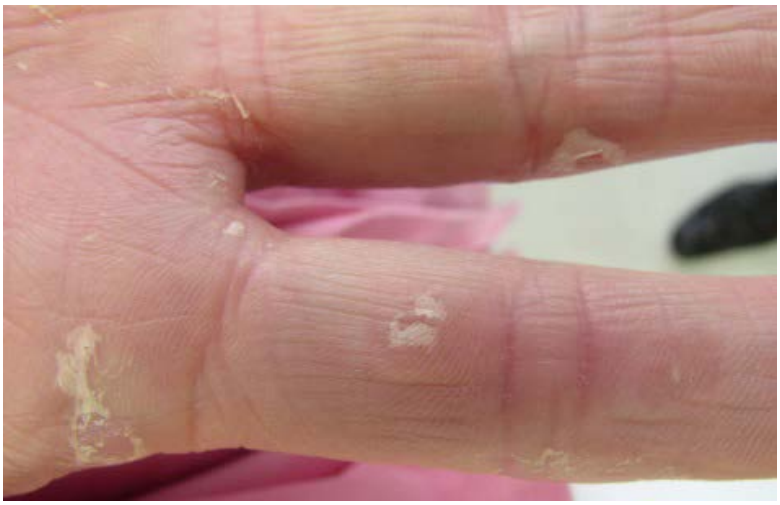
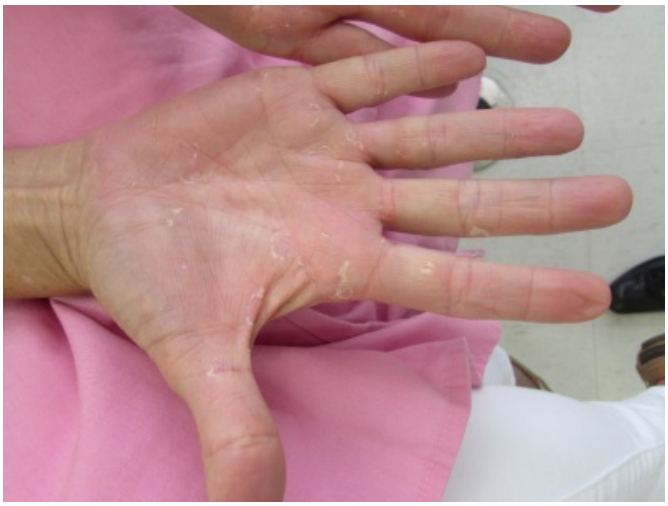
History: A 55-year-old postmenopausal woman presented to Dermatologic Associates with an over 20-year history of mildly pruritic bilateral, palmoplantar peeling that was worse distally but never formed deep-seated vesicles. Although topical glucocorticoids were somewhat helpful, no therapy had provided enduring relief. She had no unusual environmental exposures and did not routinely perform wet work or participate in any unusual occupations or hobbies aside from golfing in her spare time. Owing to a suspicion for possible allergic contact dermatitis and the patient's concern that her environment might be exacerbating this condition, she was tested with the NYU-enhanced North American Contact Dermatitis Group (NACDG) Standard Series. All patches were negative, so the patient was started on acitretin 10 mg twice weekly plus tazarotene 0.05% cream and Epicerum® barrier cream daily to the affected areas. She reported 40% improvement at a follow-up appointment one month later and her acitretin dose was increased to 10 mg three times weekly for one month then four times weekly for two months. At this dose, the patient noted attenuated signs and symptoms but had started to develop dry lips and other mucosal side effects. These symptoms worsened on daily dosing. She discontinued acitretin in early 2015. Within one month, her hands and feet returned to baseline with continuous peeling.

Past medical history included ductal carcinoma *in situ* for which the patient had undergone lumpectomy plus radiation followed by five years of tamoxifen. She took cetirizine as needed, had no allergies to medications, and was unaware of any contributing family history, which included of psoriasis, eczema, or atopy. Comprehensive review of systems was negative.

Physical examination: Annular scale with scant erythema was present on the palmoplantar aspects of the hands and feet. There was minimal scale on the elbows.

Laboratory data: A complete blood count, comprehensive metabolic panel, and lipid panel were normal, with the exception of an elevated total cholesterol of 219 mg/dL prior to starting therapy that subsequently decreased to normal.

Histopathology: None

Figures 1,2. Palmar peeling with collarettes of scale

Discussion

Diagnosis: Keratolysis exfoliativa

Comment: Keratolysis exfoliativa (KE) is an eczematous eruption of the volar aspects of the hands and feet that is characterized by annular erythema with air-filled bullae that rupture with lamellar peeling and leave a hallmark superficial collarette of scale. Extensive disease may involve the entire palmoplantar surface and present with burning or pruritus. Often misclassified as a subtype of dyshidrotic eczema, the lesions of KE are non-inflammatory and do not contain fluid.

The condition is thought to be quite common, but few publications document its epidemiology, course, and management. First described as desquamation estivale en aires des mains in 1903[1], the term keratolysis exfoliativa was coined in 1919 [2]. Since that time, the condition has been referred to as dyshidrosis lamellosa sicca, lamellar dyshidrosis, and recurrent focal palmar peeling in a handful of articles [3-5] and it was not until 2012 that the term keratolysis exfoliativa regained popularity in order to differentiate it from inflammatory processes, such as dyshidrotic eczema [6].

Clinically, there are several features that help distinguish this condition from other palmoplantar diseases, all of which are demonstrated in the present case. First, pruritus, although at times present, is mild compared to contact dermatitis and does not respond well to topical glucocorticoids, antifungal agents, or keratolytic preparations. Second, environmental and occupational exposures may exacerbate but are typically independent of the development and/or resolution of symptoms. Desquamation often predates known exposures and continues even after behavioral modification. Third, most patients have no history of atopy. And finally, fluid containing vesiculation, lichenification, and fissures are absent; the lack of these features is a strong clinical clue that points to this diagnosis [5, 6]

Recent histopathologic and molecular analyses have demonstrated that KE involves pauci-inflammatory cleavage of the stratum corneum with premature disruption of corneo-desmosomes. Electron microscopy of seven cases of KE showed that degradation of corneo-desmosomes occurs in the mid stratum corneum adjacent to the plane of cleavage rather than in the upper corneum as occurs in normal skin shedding. All corneo-desmosomal components were present on immunofluorescence study, which suggests a functional rather than structural defect in the pathogenesis of KE. It has been hypothesized that an imbalance in proteolytic enzyme activity may drive desquamation in the absence of inflammation [6].

To date, treatment of KE has been largely ineffective [5, 6]. We present a novel therapeutic approach with the use of acitretin, which has been beneficial in other conditions with abnormal or early corneocyte desquamation, for example Netherton's syndrome [6-9], but to the best of our knowledge has not been reported previously in the treatment of KE. Unlike isotretinoin, which accumulates in sebaceous units, acitretin achieves higher concentrations in the palms and soles, as demonstrated by its efficacy in palmoplantar forms of psoriasis, keratodermas, and hyperkeratotic hand dermatitis [10-15]. Our patient achieved a dose-response improvement in her skin peeling after starting acitretin then flared upon discontinuation, which is a good basis for inferring potential causality and an incentive for future trials.

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