

Beyond atopic eczema: filaggrin loss-of-function mutations in dry, fissured hand eczema

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The focus of previous epidemiological research on filaggrin mutations has been mainly on the association with ichthyosis vulgaris, based on the seminal findings in patients with this disease, and on atopic eczema, covering several European and Asian populations.¹ Clearly, the consideration of other disease phenotypes in which epidermal barrier impairment may play a role, such as chronic hand eczema, is a worthwhile approach.

Thyssen et al.² from Gentofte Hospital, Copenhagen University, used data from the Glostrup Allergy Study with participants of both the 1990 and 1998 examinations. Specifically, they relate self-reported 'fissures on the hands and/or fingers' and 'vesicles on the hands and/or between the fingers' (1-year prevalence 19.0% and 13.8%, respectively) to carrier status of the filaggrin gene mutations R501X or 2282del4. In an age- and sex-adjusted analysis, stratified for atopic eczema, they identified a significant positive association with the former, but not with the latter morphology. This finding was confined to the subgroup of participants without atopic eczema, while in those with atopic eczema, an inverse, negative association between loss-of-function mutations and fissured hands was found. This latter finding should, however, not be over-rated, as (i) it was not significant and (ii) due to the sampling scheme of the study, with > 50% of participants selected for presence of 'upper or lower respiratory symptoms', the proportion of patients with extrinsic atopic eczema might be over-represented in relation to the intrinsic type. This may have led to some selection bias affecting the relationship between filaggrin mutation and any disease outcome in the subgroup with atopic eczema. Thus the main, and very interesting, finding is the association of filaggrin mutation with dry, fissured skin in persons without atopic eczema (93.7% in the sample, i.e. pivotal for the observed 'overall effect').

This type of hand eczema, which is interestingly not associated with atopic eczema according to a recent clinical study,³ could be a morphologically characteristic response to chronic irritation. In filaggrin-deficient persons, with or without (extrinsic) atopic eczema, the threshold for irritation is presumably lowered, similar to the lowered threshold for allergen penetration repeatedly identified in filaggrin-deficient atopic eczema.⁴ However, as in the case of allergen penetration, such a lowered threshold seems neither a necessary nor a sufficient condition, but a 'facilitating condition' for the development of 'dry, fissured skin', in view of the fact that, for example in the present study, 120 of 139 individuals with 'dry, fissured skin' were not filaggrin deficient (at least regarding the two most common mutations in Europe).

This interesting study not only provides a new 'clinical-genetic association' which should be considered in future studies, but also points to the complexity of relationships between genotype and phenotype: not only are certain polymorphisms or loss-of-function mutations linked to certain clear-cut diseases, but also to clinical signs shared by several, otherwise apparently unrelated, disease entities.

Conflicts of interest

None declared.

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References

- 1 Akiyama M. FLG mutations in ichthyosis vulgaris and atopic eczema: spectrum of mutations and population genetics. *Br J Dermatol* 2010; **162**:472–7.
- 2 Thyssen JP, Ross-Hansen K, Johansen JD et al. Filaggrin loss-of-function mutation R501X and 2282del4 carrier status is associated with fissured skin on the hands: results from a cross-sectional population study. *Br J Dermatol* 2012; **166**:46–53.
- 3 Johansen JD, Hald M, Andersen BL et al. Classification of hand eczema: clinical and aetiological types. Based on the guideline of the Danish Contact Dermatitis Group. *Contact Dermatitis* 2011; **65**:13–21.
- 4 O'Regan GM, Irvine AD. The role of filaggrin in the atopic diathesis. *Clin Exp Allergy* 2010; **40**:965–72.

Photodynamic therapy for actinic keratoses: procedure matters?

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There is no doubt that photodynamic therapy (PDT) is effective for the treatment of nonmelanoma skin cancers, especially actinic keratoses (AK). Numerous well-designed studies have been published to date and PDT for AK is part of multiple guidelines and treatment recommendations.^{1,2} However, besides efficacy and cosmetic benefit there are some drawbacks which are linked to the procedure. In contrast to a simple application of a drug onto the target lesion for a couple of days or weeks, as for diclofenac sodium, imiquimod or 5-fluorouracil, PDT is a complex treatment modality which requires