

Filaggrin Null-mutations May be Associated with a Distinct Subtype of Atopic Hand Eczema

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Null-mutations in the profilaggrin gene are associated with atopic dermatitis (AD) and palmar hyperlinearity (1). Before the filaggrin era, there were several attempts to identify the phenotype of atopic hand eczema (2–5). In 1944 Nexmand observed 100 patients with AD over a mean period of 6 months and found that 24%, 9% and 34% had dermatitis on the volar aspect of the wrists, and the dorsal aspects of the fingers and hands, respectively, whereas no patients had palmar hand eczema (3). These findings were confirmed in more recent studies: Fartasch et al. showed that palmar hyperlinearity was a phenotypic marker of atopic dermatitis in 17 (34%) of 49 patients (4), and Simpson et al. showed that among 777 consecutive patients with AD, hand dermatitis mainly affected the dorsal hand surfaces and the volar wrists, whereas vesicular lesions of the palms and sides of fingers were found in only 4.3% (5). Taken together, in a subgroup of patients with AD, hand eczema is characterized by dermatitis on the dorsal aspects of the fingers and hands, palmar hyperlinearity and, rarely, by palmar vesicles.

Most patients who have attended our tertiary referral contact dermatitis and AD clinic within the past 3 months have been genotyped for the two most prevalent filaggrin null-mutations, R501X and 2282del4. So far, approximately 200 patients have been tested. In this relatively small patient series, a striking phenotype of atopic hand eczema was observed in 8 patients. All had severe generalized AD and asthma. Their atopic hand eczema was characterized by dermatitis on the dorsal aspects of the hands and sometimes on the volar aspects of the wrists as well as palmar hyperlinearity (Fig. 1). In two patients, there were signs of mild palmar dermatitis with a few vesicular lesions. Light palmar scaling was observed in one patient. Two of the patients were related (father and son) and had identical distribution of their hand eczema. Of note, we found that all 8 patients with this specific phenotype had null-mutations in the filaggrin gene (of which 5 were heterozygotic for either mutation, and 3 were compound heterozygotic), whereas no patients with wildtype filaggrin status had a similar clinical expression. Thus, we speculate that the special phenotype of atopic hand eczema identified in previous reports may be explained consistently by null-mutations in the profilaggrin gene.

Prospective studies are clearly warranted to confirm our clinical observations. If they are confirmed, atopic hand eczema in patients with null-mutations in the profilaggrin gene represents a distinct clinical subtype that may be easy to diagnose. It is possible that patients



Fig. 1. Patients with the atopic hand eczema subtype defined by mandatory null-mutations in the profilaggrin gene typically had asthma, generalized atopic dermatitis, hand eczema on the dorsal aspects of the hands and fingers, palmar hyperlinearity, and absence of palmar hand eczema.

with filaggrin null-mutations and atopic hand eczema should be treated differently than, for example, patients with irritant hand eczema. Furthermore, this genetic subtype of atopic hand eczema could have been the leading phenotype at Nexmand's time. Today, a more varied pattern is observed, probably due to the increase in AD caused by environmental factors.

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