Factors associated with combined hand and foot eczema
Associations between foot and hand eczema

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Abstract

Background

As for hand eczema, the etiology of foot eczema is multifactorial, and not very well understood. The aim of the present study was to identify factors associated with foot eczema in a cohort of hand eczema patients being classified into different subgroups.

Methods

Associations between foot and hand eczema was studied in a cross sectional design in a cohort of hand eczema patients. Consecutive patients were recruited from 9 different European Centres during the period October 2011 – September 2012. Data on demographic factors, presence of foot eczema, hand eczema duration and severity, and whether the hand eczema was work-related or not were available, as well as patch-test results.

Results

Of a total of 427 hand eczema patients identified, information on foot eczema was available in 419 patients who were included in the present study. 125 patients (29.8 %) had concomitant foot and hand eczema. It was found more often in association with hyperkeratotic hand eczema ($p=0.007$), and was less often associated with irritant hand eczema ($p<0.001$). However, foot eczema was nevertheless found in 18% of patient with irritant hand eczema and in 25% of patients with occupational hand eczema. Combined foot and hand eczema was associated with more severe and long standing hand eczema ($p< 0.001$ and $p=0.004$, respectively). Contact allergy was found in 51.8 % with no difference between patients with combined foot and hand-eczema and patients with hand eczema only.

Conclusion

Occurrence of combined foot and hand eczema is a common finding and not restricted to endogenous hand eczema.

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Background

Foot eczema may affect children as well as adults, and due to the localization of the disease it may often cause severe problems, compromise physical activity and sometimes be debilitating. Foot eczema may be a localized single skin problem, or may present with concomitant hand eczema. Recently Brans et al (1) evaluated the prevalence of foot eczema in patients with occupational hand eczema and found concomitant foot eczema in 27.8%.
As for hand eczema, the etiology of foot eczema is multifactorial, and not very well understood.
Genetic disposition as well as environmental exposures and, to a lesser degree, life style factors, have been thought to influence the development and severity of foot eczema. As for hand eczema, etiological factors are not necessarily reflected in the phenotypic expression of the disease (2-4). Foot eczema has been reported to be associated with filaggrin mutations, however, the increased prevalence was found in patients with atopic dermatitis only (5). Children with atopic dermatitis affecting hand and/or feet have been shown to have an increased prevalence of contact allergy as compared to children with atopic dermatitis but without hand or foot eczema (6)..

Allergic contact dermatitis affecting the feet is frequently due to shoes or socks, and the most common allergens reported to cause shoe dermatitis are chromate (in leather), rubber chemicals, adhesives and textile dyes (7,8). Allergic contact dermatitis with onset on the hands may occasionally spread to the feet and vice versa. Sometimes, hands and feet are exposed to the same allergens causing allergic contact dermatitis on both sites, e.g. due to leather shoes and leather gloves, or rubber chemicals in shoes and gloves.
. For irritant contact dermatitis and endogenous eczema the concomitant presence of foot and

hand eczema is less well explained. Factors, such as atopy, male sex and tobacco smoking have been reported to be associated with increased prevalence of foot eczema in patients with hand eczema, and interestingly, identical morphology on hands and feet has been reported in 71.1% of patients (1). The aim of the present study was to identify factors associated with foot eczema in a cohort of hand eczema patients in which eczema had been classified into different subgroups.

Material and study design

Associations between foot and hand eczema was studied in a cross sectional design in a cohort of hand eczema patients. Consecutive patients with hand eczema were recruited from 9 different centres all over Europe during the period October 2011 – September 2012. The centres were tertiary referral centres, and all patients underwent detailed examination including patch test. Foot eczema, current or previous, was recorded. Data on gender, age, duration of hand eczema and previous skin diseases (with emphasis on atopic eczema and psoriasis) was registered. Previous or current atopic skin disease was defined according to the UK-criteria (9). Information as to whether the eczema was work-related was obtained. Relevance for positive patch tests was assessed as recommended in the ESCD guidelines (10). Patients were classified into one of **7** sub-classifications with respect to hand eczema: irritant contact dermatitis, allergic contact dermatitis, atopic hand eczema, hyperkeratotic eczema, vesicular eczema, and protein contact dermatitis/contact urticarial and unclassifiedThis data has previously been published (2). Eczema which did not fit into any of the subgroups mentioned above was diagnosed as “unclassified”. Cases in which more than one main-diagnosis had been used are referred to as multiple diagnosis. Severity of hand eczema was assessed by HECSI score (11).

Statistics

For statistical analysis the Chi-square test was used to test possible differences between patients with concomitant hand and foot eczema and hand eczema only. For sub-groups of hand eczema, the Fisher exact test was calculated for each subgroup versus the other groups. To avoid mass significance Bonferroni`s correction was applied, and for these data only p-values < 0.008 should be considered statistically significant.

Differences in means were calculated using a T-test. P-values < 0.05 were considered statistically significant.

Results

A total of 427 HE patients from the 9 participating European centres were identified (2) , and information on foot eczema was available in 419 patients who were included in the present study. 125 patients (29.8%) had concomitant foot and hand eczema. Demographic data, as well as data on hand eczema sub-diagnosis, occupational hand eczema, duration and severity, stratified with respect to concomitant foot and hand eczema or hand eczema only is given in Table 1.

Concomitant foot and hand eczema was not significantly associated with age or gender, although there was a trend towards greater frequency in men (Table 1). The prevalence of foot eczema was significantly lower in patients with irritant contact dermatitis ($p<0.001$) and significantly higher in patients with hyperkeratotic hand eczema ($p=0.007$) than in other subgroups. (Table 1). Foot eczema was found in 24.6 % of all patients with occupational hand eczema, which is lower than in patients with non-occupational hand eczema (34.2%), although not significantly different ($p=0.051$). Long duration of hand eczema was significantly

associated with concomitant eczema on the feet (p=0.004). With respect to severity of hand eczema, patients with concomitant foot and hand eczema had significantly higher HECSI score than patients with hand eczema only (p<0.001).

Information on localisation of eczema at onset was available from 83 patients with foot eczema. In 12% the eczema had started on the feet, in 71% on the hands, and in 17% the eczema had started elsewhere on the body.

A total of 217 patients (51.8 %) had a positive patch test, with no significant difference between patients with concomitant foot and hand eczema (67; 53.6 %) and with hand eczema only (150; 51.3 %). Data on more frequent contact allergens in both groups are given in Table 2. The prevalence percentages of contact allergy to chromate, mercaptobenzothiazole, mercapto mix, p-tert.-butyphenol formaldehyde resin and epoxy resin were higher in patients with foot eczema than in those without.

Discussion

Main findings in the present study are that concomitant foot eczema in patients with hand eczema is significantly linked to certain subgroups of hand eczema, being decreased in patients with irritant hand eczema and increased in patients with hyperkeratotic hand eczema. There was a trend that the prevalence of foot eczema was lower in patients with occupational hand eczema, and that foot eczema was strongly positively associated with longer duration and increased severity of hand eczema.

Concomitant foot and hand eczema is highly prevalent, in this study 29.8 %, however the contextual significance of this is not very well understood or elucidated in other studies. The prevalence of foot eczema in a cohort of patients with occupational hand eczema was found to be 27.8% by Brans et al (1), which is in line with our findings of 25% (Table 1). With respect to gender differences we found a trend for foot eczema to be more common in males, which

supports the findings of Brans et al (1), who also found a significant association with atopic hand eczema , which could not be confirmed in our study, neither regarding personal history of atopic eczema nor atopic hand eczema. A possible explanation for this is the slightly different definition of atopy used in the two studies, Erlangen criteria (12) versus UK-criteria (9). Another explanation may be that in the study of Brans et al. (12) a combined diagnosis was possible, whereas in the present study an atopic hand eczema was excluded if relevant irritant or allergic exposures were documented.

Although the prevalence of foot eczema was slightly lower for occupational hand eczema than for non-occupational, it is still interesting that 25% of patients with occupational hand eczema also have eczema problems on the feet, and that the prevalence of foot eczema in patients with irritant contact dermatitis on the hands is as high as 18%. One explanation for the high prevalence of foot eczema in patient with occupational irritant contact dermatitis on the hands may be that wearing of safety shoes may lead to increased plantar sweating and promote eczema. Patients with irritant hand eczema may be particularly at risk for this, although this aspect has not been studied.. In more than 70% of all cases, concomitant eczema on the feet has onset in hands. This data indicates that more factors than allergic contact sensitization, and inherited aspects, are involved. Occupational hand eczema may sometimes be an aggravation of a previous, sometimes subclinical, hand eczema, or it may be understood the other way round, i.e. that hand eczema in may lead to an eczema on the feet. Our data shows that concomitant foot eczema is associated with longer duration and more severe hand eczema. To our knowledge this has not previously been reported. However, our data indicates that endogenous eczema is more severe than other subdiagnosis of hand eczema, and the fact foot eczema was found to be associated with longer duration and more severe hand eczema is

possibly explained by the association between foot eczema and hyperkeratotic and vesicular hand eczema. Palmar and plantar skin have similar morphologic features, namely similar keratin pairs and type of eccrine sweat gland, which in case of any endogenous/genetic effect may affect both areas of the skin equally.

With respect to contact allergies in patients with concomitant foot and hand eczema our findings overall confirm previous findings, that chromate, rubber chemicals (mercaptobenzothiazole and mercapto mix) and adhesives are important allergens in relation to eczema on feet (7,8,13). The finding that also epoxy resin allergy was double as high in patients with foot eczema was based on only few patients. Presence of cobalt in leather shoes has been reported (14), however, the frequency of cobalt allergy did not differ much between patients with combined foot and hand eczema as compared to patients with hand eczema only.

The advantage of the present study is that data comprises information on foot eczema in a cohort of 419 hand eczema patients from 9 different European countries. A limitation of the study is that we have focused on patients with hand eczema and concomitant eczema on the feet, and that a precise diagnosis for the foot eczema was not always obtained, and it cannot be excluded that in some cases the cause of the eczema on the feet and hands could be completely different.

Conclusion

Data from the present study helps to shed light on a poorly understood subject. Our main findings are that concomitant foot and hand eczema is found in particular when the hand eczema is severe and long standing, and that the onset of foot eczema in most cases was preceeded by eczema on other body parts, mainly on the hands. Foot eczema is more prevalent in patients with endogenous hyperkeratotic hand eczema and less in patients with irritant contact dermatitis on the hands. However, concomitant foot eczema cannot in all cases be explained by endogenous, genetic causes or simultaneous exposure to identical contact allergens on feet and hands – also in cases with occupational and/or irritant contact dermatitis on the hands, foot eczema may be a complication. The prevalence of foot eczema in patients with hand eczema is high, and exploring for foot eczema in hand eczema will improve our clinical management of the patients.

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Table 1

Demographic data, as well as data on hand eczema sub-diagnosis, occupational hand eczema, duration and severity, stratified with respect to concomitant foot and hand eczema or hand eczema only. Percentage are calculated as percentage of total number of patients with combined foot and hand eczema and patients with hand eczema only, respectively.

	Combined foot and hand eczema	**Hand eczema only**	**Total**	**p-value**
Total	125 (29.8%)	294 (70.2%)	419	
Age (years) mean and sd	42.8 (sd=14.6)	39.5 (sd=14.7)	40.4 (sd=14.7)	P=0.96
Gender				0.088
men	61 (48.8%)	11739.8%)	178	
women	64 (51.2%)	177 (60.2%)	241	
Previous history of atopic dermatitis*	30 (24.5%)	74 (25.8%)	104	0.7853
Previous history of psoriasis*	9 (7.3%)	13 (4.6%)	22	0.2665
Hand eczema diagnosis*				
ICD	26 (20.8%)	115 (39.1%)	141	**P<0.001***
ACD	33 (26.4%)	68 (23.1%)	101	P=0.532
A HE	17 (13.6%)	33 (11.2%)	50	P=0.511
Hyperkeratotic	20 (16.0%)	21 (7.1%)	41	**P=0.007***
Vesicular	13 (10.3%)	13 (4.4%)	26	P=0.026

PCD/CU	3 (2.4%)	9 (3.2%)	12	1.0000
Unclassified	8 (6.5%)	8 (2.7%)	16	0.0932
Multiple diagnosis	5 (4.0%)	27 (9.2%)	32	0.0727
Reported as occupational HE* 370 (108)	48 (44.4%)	147 (56.1%)	195	0.041
Duration (years) mean and sd	7.7 (sd=10.4)	5.3 (sd= 8.0)	6.1 (sd=8.9)	**P=0.004**
HECSI (N=417. 2 missing)	48.2 (sd=43.9)	28.1 (sd=24.9)	34.2 (sd=33.1)	**P<0.001**

p-values considered statistically significant are marked with bold letters.
*Fisher's exact test was calculated for each subgroup of hand eczema versus the other groups. To avoid mass significance Bonferroni's correction was applied, and for these data only p-values < 0.008 should be considered statistically significant. * =Missing data for questions about psoriasis:10, missing data for question about atopic dermatitis:11, missing data for question about reported occupational eczema:49.ICD, irritant contact dermatitis; ACD, allergic contact dermatitis; AHE, atopic hand eczema (HE); PCD/CU, protein contact dermatitis/contact urticaria; Vesicular, vesicular endogenous HE; Hyperkeratotic, hyperkeratotic endogenous HE; Multiple diagnoses, patients with more than one main diagnosis; Unclassified, patients which could not be classified.

Table 2.

Contact allergies in patients with combined foot and hand eczema and in patients with hand eczema only. Only allergens to which 3 or more patients with concomitant foot- and hand eczema had reacted are included.

	Patient with combined foot- and hand eczema N = 125 *(125 are 100 %)*	Patients with hand eczema only N= 294 *(294 are 100%)*
Positive patch test	**67 (53.6%)**	**150 (51.3%)**
Nickel	23 (18.4 %)	57 (38.0 %)
Cobalt	17 (13.6 %)	19 (12.6 %)
Chromate	19 (15.2 %)	5 (3.3 %)
Fragrance mix I	8 (6.4 %)	22 (14.6 %)
Fragrance mix II	4 (3.2 %)	7 (4.6 %)
MCI	6 (4.8 %)	22 (8.8 %)
MI	3 (2.4 %)	9 (6.0 %)

PPD	5 (4.0 %)	17 (11.3 %)
Thiuram mix	8 (6.4 %)	11 (7.3 %)
Carba mix	3 (2.4 %)	4 (2.6 %)
Mercapto mix	4 (3.2 %)	0 (0 %)
Mercaptobenzothiazol	3 (2.4 %)	0 (0 %)
Peru balsam (Myroxylon pereirae)	5 (4.0 %)	12 (8.0 %)
Tixocortol pivalate	4 (3.2 %)	2 (1.3 %)
Epoxy resin	5 (4.0 %)	2 (1.3 %)
p-tert.-butyphenol formaldehyde resin	4 (3.2 %)	1 (0.6 %)
Colophony	5 (4.0 %)	11 (7.3 %)