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Clinical characteristics and genetic variation in atopic dermatitis patients with and without allergic contact dermatitis

Background: In patients with atopic dermatitis (AD), the risk of contact sensitization may be higher as the disrupted skin barrier may increase the penetration of contact allergens. Therefore, it is necessary to screen for concurrent allergic contact dermatitis (ACD) in AD patients. *Objectives:* To identify the clinical characteristics and genetic variation in AD patients with concurrent ACD. *Materials & Methods:* In total, 281 AD subjects who underwent patch testing were included. Subjects with a positive result were classified as "AD with ACD", while the others were classified as "AD only". Clinical characteristics and prevalence of genetic variants (*FLG* 3321delA, *FLG* K4022X, *KLK7*, *SPINK5*, *DEFB1*, *KDR*, *IL5RA*, *IL9*, and *IL12RB1*) were compared between the two groups. *Results:* Seventy-one subjects (25.3%) were found to have AD and ACD. Female sex, older age, late onset, self-reported personal or family history of ACD, and presence of prurigo nodularis were associated with concurrent ACD in AD patients. Age was useful for predicting concurrent ACD based on the receiver operating characteristic curve. However, no differences in the frequency of genetic variants were identified between the two groups. *Conclusion:* A personal or family history of ACD, late onset, and prurigo nodularis support a suspicion of concurrent ACD, although these correlations were less apparent after correcting for age and sex. Patch testing for AD in males >20 years and females >14 years may aid diagnosis of concurrent ACD with high sensitivity and specificity.

Key words: allergic contact dermatitis, atopic dermatitis, comorbidity, contact sensitization, genetic difference, skin barrier

Atopic dermatitis (AD) is a chronic and recurrent inflammatory skin disorder characterized by an impaired skin barrier, dry skin, pruritus and eczema with a characteristic distribution [1]. Various genetic and environmental factors contribute to the development of AD. Dysfunction of the skin barrier and the innate immune response has recently been suggested to play a key role in the development of recurrent skin infection and sensitization to foreign allergens [2].

Allergic contact dermatitis (ACD) is a type IV hypersensitivity reaction caused by exposure to cutaneous contact allergen in sensitized individuals [3]. ACD is diagnosed by patch testing, a process involving the application of contact allergens under occlusion and examining the skin reaction. Although AD and ACD are recognized as diseases with independent pathogeneses, recent studies suggest that they have a dynamic and complex relationship or similar pathomechanisms [4]. It remains controversial whether patients with AD have a higher prevalence or increased risk of contact sensitization compared to controls. Many patients with AD also have concurrent ACD, as observed in clinical practice. Some studies report that increased contact sensitization in AD results from an impaired skin barrier [5-7]. Previous studies also suggest that increased contact sensitization occurs in subjects with an *FLG* null mutation compared to healthy populations [5, 8, 9]. In contrast, other studies report that the prevalence of ACD in AD patients or subjects with an *FLG* null mutation is the same as, or lower than that in healthy populations [10-12]. Moreover, a recent systematic review revealed an inconsistent relationship between AD and increased contact sensitization [13]. Patients with AD and concurrent ACD require not only management for eczema, but also confirmation of sensitized-contact allergens and education in order to avoid aggravating factors related to ACD. Therefore, accurate diagnosis is necessary. Regarding the genetic aspects of AD, we recently identified several genetic differences in the genes for Kallikrein 7 (*KLK7*), serine protease inhibitor Kazal-type 5 (*SPINK5*), filaggrin (*FLG*), β-defensin 1 (*DEFB1*), kinase insert domain receptor (*KDR*), and interleukin (IL)-5 receptor alpha (*IL5RA*), IL-9 (*IL9*), and IL-12 receptor beta-1 subunit *(IL12RB1)* between AD and non-AD patients [14]. We hypothesized that some clinical features and genetic variants of the above genes may differ between AD patients with and without ACD. Therefore, the goal of this study was to compare clinical characteristics and genetic variants

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between AD subjects with and without ACD, and establish an indication for patch testing in patients with AD. These results will aid physicians predict concurrent ACD in AD patients more effectively, leading to more appropriate management and education.

Methods and materials

Study approval and ethics statement

This study was approved by the Yonsei University Wonju Campus Institutional Review Board (CR316120) and was performed in accordance with their guidelines. Informed consent was obtained from all subjects enrolled in this study.

Subjects

The study subjects consisted of 281 AD patients who had visited the outpatient clinic of the Department of Dermatology, Wonju Severance Christian Hospital from May 2015 to August 2017. Patients had no prior history of ear or body piercing in order to exclude sensitization to contact allergens by direct penetration. All AD patients were diagnosed by a dermatologist and had undergone patch testing (TRUE Test [SmartPratice, Phoenix, AZ, USA]) for diagnosis of concurrent ACD. Reactions designated as +, ++, or +++ after 48 hours were classified as positive (allergic). AD patients with a positive result according to the patch test were classified as AD with ACD while the others were classified as AD only.

Clinical characteristics

Basic information such as age, sex, age at onset of AD, disease duration of AD, self-reported personal or family history of atopic diseases (AD, allergic rhinitis, and asthma) and ACD were collected. Recalcitrant AD patients were defined as subjects whose disease had been controlled only by immunomodulators such as cyclosporine, methotrexate, or azathioprine over one month. Associated skin findings included the presence of impetigo, prurigo nodularis, nummular eczema, and eczema herpeticum. History was obtained and physical examination for the above items was carried out for all subjects. Serum total IgE levels and allergen-specific IgE level for *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* were evaluated.

Genetic variants

Based on previous studies on the relationship between AD and single-nucleotide polymorphisms highly related to AD in Asian populations, single-nucleotide polymorphisms related to skin barrier (*KLK7*, *SPINK5*, and *FLG*) and immune response (*DEFB1*, *KDR*, *IL5RA*, *IL9*, and *IL12RB1*) were analysed [15-27]. These genes were selected because they showed significant differences between AD and non-AD subjects in our previous study [14].

Specific primer sequences for *KLK7*, *SPINK5*, *FLG*, *DEFB1*, *KDR*, *IL5RA*, *IL9*, and *IL12RB1* were obtained using data from the GenBank database of the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov). Using these primers, polymerase chain reaction (PCR) was performed on genomic DNA extracted from blood samples of the subjects using the QIAamp DNA Mini Kit (Qiagen GmbH, Hilden, Germany). The amplification mixture for *KLK7*, *SPINK5*, *FLG*, *DEFB1*, *KDR*, *IL5RA*, *IL9* and *IL12RB1* contained 1x primer-mix, 2x PCR premix (Genetbio, Daejeon, Korea), 2 mM $MgCl_2$, 250 μM dNTPs and 10 ng of genomic DNA in a final volume of 50 μL. Multiplex PCR was performed using this amplification mixture, followed by direct sequencing of both strands of the PCR products using the ABI 3100 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA) at COSMO Genetech Co., Ltd. (Seoul, Korea). Subsequent sequence alignment was performed using multiple sequence alignment programs (http://bioinfo.genopole-toulouse.prd.fr).

Reverse blot hybridization assay (REBA)

The genus-specific oligonucleotide probes for *KLK7*, *SPINK5*, *FLG*, *DEFB1*, *KDR*, *IL5RA*, *IL9*, and *IL12RB1* were designed using sequence data from the NCBI database, followed by a BLAST search (National Center for Biotechnology Information of the National Library of Medicine website) to confirm the sequence homology of each probe. Thereafter, a REBA membrane capable of detecting a total of 26 probes, including 13 wild-type (WT) and 13 mutant-type (MT) probes, was designed to examine *KLK7*, *SPINK5*, *FLG*, *DEFB1*, *KDR*, *IL5RA*, *IL9*, and *IL12RB1* and one control probe using colourimetric signal detection. The REBA was performed as follows. First, 20 μL of each PCR product was mixed with an equal volume of denaturation solution (0.2 N NaOH and 0.2 mM EDTA) and incubated at room temperature for 5 minutes. Next, the denatured PCR products were diluted with 960 μL of 2x SSPE/0.1% SDS. The REBA membrane strips were then placed on a Minitray (Bio-Rad, Hercules, CA, USA) and incubated with 2x SSPE/0.1% SDS for 5 minutes. After residual fluid in the slot was removed, the slots were filled with denatured single-stranded PCR products. The PCR products were incubated at 55°C for 30 minutes, washed twice with 2x SSPE/0.5% SDS at 62°C for 10 min, and incubated in 1:2,000 diluted streptavidin-conjugated alkaline phosphatase (Roche Diagnostics, Mannheim, Germany) with 2x SSPE/0.5% SDS for 30 minutes at room temperature. The hybridized amplicons were detected colourimetrically by incubating the strip in 1:50 diluted nitro blue tetrazolium chloride/5-bromo-4-chloro-3-indolyl phosphate, toluidine salt (NBT/BCIP) (Roche Diagnostics, Basel, Switzerland) in 67% DMSO (v/v) with TBS (pH 9.5) for 5-10 minutes. The presence of the MT and WT probes was confirmed by analysing the band pattern. All experimental procedures were performed in duplicate.

Statistical analysis

Differences in clinical characteristics and genetic variation (*FLG* 3321delA, *FLG* K4022X, *KLK7*, *SPINK5*, *DEFB1*, *KDR*, *IL5RA*, *IL9*, and *IL12RB1*) were identified using the Chi-square test or Fisher's exact test with Yates' continuity correction. Univariate and multivariate logistic regression analyses were performed to calculate the odds ratio (OR)

and 95% confidence interval (CI). For statistical analysis, R 3.2.0 software (Foundation for Statistical Computing, Vienna, Austria) was used. *P* value less than 0.05 was considered statistically significant.

Results

Clinical characteristics

Among the 281 subjects, 71 (25.3%) showed at least one positive reaction in the patch test and were classified as AD with ACD. The most commonly sensitized allergen was cobalt followed by nickel, thimerosal, mercury, and p-phenylenediamine. No subjects who showed a positive reaction to nickel on patch testing had a history of ear piercing.

A comparison of the clinical characteristics of subjects is presented in *table 1*. Females with AD showed a greater probability of having concurrent ACD than males (OR: 2.51; 95% CI: 1.46-4.38; $p < 0.001$). A large OR was also determined for older age (OR: 1.05/year; 95% CI: 1.03-1.07; $p < 0.001$) and later onset of disease (OR: 1.05/year; 95% CI: 1.03-1.07; $p < 0.001$). Significantly larger ORs were determined for subjects' self-reported personal history of ACD (OR: 4.60; 95% CI: 2.36-9.03; $p < 0.001$) and family history of ACD (OR: 4.51; 95% CI: 2.27-9.08; $p < 0.001$). Based on skin examination, large ORs were determined for the presence of prurigo nodularis (OR: 2.69; 95% CI: 1.27-5.63; $p = 0.009$).

However, because the prevalence of ACD varies greatly depending on patient sex and age, an additional analysis was conducted to exclude these effects. Based on logistic regression analysis with age and sex as covariates, only subjects' self-reported family history of ACD showed significantly much larger ORs for concurrent ACD (OR: 7.09; 95% CI: 3.15-16.25; $p < 0.001$).

Genetic variation

A comparison of the genetic variation of subjects is presented in *tables 2, 3*. A heterozygous mutation in *IL12RB1b* showed lower ORs for developing concurrent ACD in AD patients based on crude analysis (OR: 0.47; 95% CI: 0.25-0.87; $p = 0.019$). However, the difference decreased after adjusting for age and sex. Overall, there was no genetic difference between AD only and AD with ACD for skin barrier-related genes (*KLK7*, *SPINK5*, and *FLG*) and immune response-related genes (*DEFB1*, *KDR*, *IL5RA*, *IL9*, and *IL12RB1*).

Determination of optimal cut-off age to screen for concurrent ACD in AD patients without a self-reported family history of ACD

To predict concurrent ACD in AD patients without a self-reported family history of ACD, an optimal cut-off value for age was set for receiver operating characteristic (ROC) analysis (*figure 1*). In males, a cut-off value for age greater than 20 years showed 79.2% sensitivity and 73.4% specificity for predicting concurrent ACD with AD, with area under the curve (AUC) of 0.820 (95% CI: 0.73-0.908). In females, a cut-off value for age greater than 14 years showed 84.0% sensitivity and 70.1% specificity, with AUC of 0.814 (95% CI: 0.721-0.906).

Discussion

Based on a systematic review by Thyssen *et al.* [13], the prevalence of contact sensitization was found to be 28.6% in AD subjects and 22.5% in non-AD subjects in the general population ($n = 6,161$). In this study, 25.3% of AD subjects had concurrent ACD, and the composition of the study population was consistent with that of previous studies. However, because this study did not include non-AD subjects, we could not directly compare the prevalence of ACD between AD subjects and the general population (non-AD subjects).

The prevalence of AD with ACD was higher in women (OR: 2.51) and older subjects (OR 1.05/year) than in the AD only group. This is consistent with the epidemiology of ACD in the general population. In addition, later onset of AD (OR: 1.05/year) was associated with an increased prevalence of AD with ACD. However, there was no significant relationship between concurrent ACD and the presence of self-reported personal and/or family history of atopic diseases (AD, allergic rhinitis, and asthma). In contrast, the presence of a self-reported personal history (OR: 4.60) and family history (OR: 4.51) of ACD was significantly associated with concurrent AD. In particular, the presence of a self-reported family history of ACD was found to be an independent factor for concurrent ACD, with an OR of 7.90 after adjusting for patient age and sex. This suggests that genetic factors or environmental factors related to the family's lifestyle significantly impact the development of concurrent ACD in AD patients. Because the entire study population underwent patch testing and the personal or family history of ACD were taken, the effect of selection bias was not likely to have been significant. Based on skin examination, the presence of prurigo nodularis (OR: 2.69) was also associated with concurrent ACD. However, although we predicted that patients with AD and ACD would show a more intractable and refractory disease course (recalcitrant AD) compared to AD only, there was no difference between the two groups.

In our previous study [14], we demonstrated a difference in the prevalence of genetic variants between non-AD and AD subjects. In this study, additional analyses were conducted to identify genetic differences associated with contact sensitization in AD subjects. However, no difference was identified between the two groups regarding genetic variants of *KLK7*, *SPINK5*, *FLG*, *DEFB1*, *KDR*, *IL5RA*, *IL9* and *IL12RB1*. Many previous studies have reported an association between an *FLG* null mutation and increased contact sensitization with varying results [8-11]. The results of this study suggest that no association exists between increased contact sensitization and *FLG* null mutation. However, this may be because few *FLG* null mutation carriers are found in the Asian population (less than 10% of Koreans) compared to Western countries (up to 50% of Caucasians) [28, 29]. Few studies have evaluated the genetic factors associated with, or affecting increased contact sensitization in patients

Table 1. Comparison of clinical characteristics between the "AD only" and "AD with ACD" groups.

	AD only ($n = 210$)	AD with ACD ($n = 71$)	OR (95 % CI)	p	Adjusted OR (95 % CI)*	Adjusted p*
Sex						
– Male	136 (64.8%)	30 (42.3%)	Reference	-	-	-
– Female	74 (35.2%)	41 (57.7%)	2.51 (1.46-4.38)	<0.001	-	-
Age (years)	13.6 ± 13.9	27.4 ± 18.2	1.05 (1.03-1.07)	<0.001	-	-
Onset (years)	7.7 ± 13.0	20.4 ± 19.4	1.05 (1.03-1.07)	<0.001	1.01 (0.97-1.05)	0.774
Duration (months)	70.1 ± 83.1	82.7 ± 100.0		0.338		
Type of atopic dermatitis						
– Intrinsic	45 (21.4%)	7 (9.9%)	Reference	-	Reference	-
– Extrinsic	165 (78.6%)	64 (90.1%)	2.49 (1.13-6.31)	0.046	1.53 (0.64-4.15)	0.365
Self-reported history of atopic diseases	109 (51.9%)	38 (53.5%)	1.07 (0.62-1.84)	0.922	1.22 (0.67-2.25)	0.521
Self-reported family history of atopic diseases	164 (78.1%)	46 (64.8%)	0.52 (0.29-0.93)	0.038	0.91 (0.44-1.95)	0.808
Self-reported history of ACD	21 (10.0%)	24 (33.8%)	4.60 (2.36-9.03)	<0.001	1.76 (0.80-3.79)	0.153
Self-reported family history of ACD	19 (9.0 %)	22 (31.0 %)	4.51 (2.27-9.08)	<0.001	7.09 (3.15-16.25)	<0.001
Recalcitrant atopic dermatitis	37 (17.6%)	14 (19.7%)	1.15 (0.56-2.24)	0.400	0.53 (0.22-1.19)	0.137
Associated skin findings						
– Impetigo	20 (9.5%)	6 (8.5%)	0.88 (0.31-2.16)	0.788	1.13 (0.35-3.18)	0.832
– Prurigo nodularis	19 (9.0%)	15 (21.1%)	2.69 (1.27-5.63)	0.009	1.67 (0.70-3.87)	0.235
– Nummular eczema	25 (11.9%)	14 (19.7%)	1.82 (0.87-3.69)	0.103	1.02 (0.42-2.35)	0.970
– Eczema herpeticum	12 (5.7%)	3 (4.2%)	0.73 (0.16-2.37)	0.631	0.41 (0.08-1.53)	0.221
Serum IgE level (IU/mL)						
– Total IgE	624.6 ± 876.2	687.3 ± 847.5	1.00 (1.00-1.00)	0.579	1.00 (1.00-1.00)	0.534
– Allergen-specific IgE for *D. farinae*	30.4 ± 82.4	210.9 ± 1182.5	1.00 (1.00-1.00)	0.977	1.00 (1.00-1.00)	0.927
– Allergen-specific IgE for *D. pteronyssinus*	19.2 ± 39.5	95.7 ± 498.0	1.00 (1.00-1.00)	0.505	1.00 (1.00-1.00)	0.417

**Adjusted by age and sex. AD: atopic dermatitis; ACD: allergic contact dermatitis; OR: odds ratio; CI: confidential interval; D: Dermatophagoides.*

Table 2. Comparison of skin barrier-related genetic variants between "AD only" and "AD with ACD" groups.

	AD only ($n = 210$)	AD with ACD ($n = 71$)	OR (95 % CI)	p	Adjusted OR (95% CI)*	Adjusted p*
KLK7						
– WT	72 (34.3%)	27 (38.0%)	Reference	-	Reference	-
– Heterozygous MT	113 (53.8 %)	35 (49.3 %)	0.83 (0.46-1.49)	0.520	0.75 (0.39-1.44)	0.381
– Homozygous MT	25 (11.9%)	9 (12.7%)	0.96 (0.38-2.26)	0.928	0.89 (0.32-2.32)	0.820
SPINK5 G1156A						
– WT	121 (57.6 %)	41 (57.7%)	Reference	-	Reference	-
– Heterozygous MT	81 (38.6 %)	28 (39.4 %)	1.02 (0.58-1.77)	0.944	1.00 (0.53-1.86)	0.992
– Homozygous MT	8 (3.8 %)	2 (2.8 %)	0.74 (0.11-3.09)	0.708	1.09 (0.13-5.98)	0.925
SPINK5 C1188T						
– WT	61 (29.0%)	23 (32.4%)	Reference	-	Reference	-
– Heterozygous MT	102 (48.6 %)	33 (46.5 %)	0.86 (0.46-1.61)	0.628	0.70 (0.35-1.41)	0.316
– Homozygous MT	47 (22.4 %)	15 (21.1 %)	0.85 (0.39-1.79)	0.665	0.51 (0.19-1.25)	0.151
SPINK5 G2475T						
– WT	104 (49.5%)	33 (46.5%)	Reference	-	Reference	-
– Heterozygous MT	78 (37.1%)	31 (43.7%)	1.25 (0.71-2.22)	0.440	1.56 (0.82-2.99)	0.178
– Homozygous MT	28 (13.3%)	7 (9.9%)	0.79 (0.29-1.89)	0.610	1.09 (0.38-2.84)	0.868
FLG 3321delA						
– WT	196 (93.3%)	64 (90.1%)	Reference	-	Reference	-
– Heterozygous MT	14 (6.7%)	7 (9.9%)	1.53 (0.56–3.85)	0.379	1.78 (0.61-4.81)	0.269
FLG K4022X						
– WT	195 (92.9 %)	67 (94.4%)	Reference	-	Reference	-
– Heterozygous MT	15 (7.1%)	4 (5.6%)	0.76 (0.21-2.19)	0.643	0.79 (0.19-2.68)	0.723

**Adjusted by age and sex. AD: atopic dermatitis; ACD: allergic contact dermatitis; OR: odds ratio; CI: confidential interval; WT: wild-type; MT: mutant type.*

Table 3. Comparison of immune response-related genetic variants between "AD only" and "AD with ACD" groups.

	AD only ($n = 210$)	AD with ACD ($n = 71$)	OR (95 % CI)	p	Adjusted OR (95% CI)*	Adjusted p*
DFB1 C2266T						
– WT	50 (23.8 %)	14 (19.7%)	Reference	-	Reference	-
– Heterozygous MT	121 (57.6 %)	45 (63.4 %)	1.33 (0.68-2.71)	0.416	1.55 (0.73-3.48)	0.270
– Homogenous MT	39 (18.6 %)	12 (16.9 %)	1.10 (0.45-2.65)	0.833	11.98 (0.61-6.01)	0.212
KDR						
– WT	164 (78.1 %)	56 (78.9%)	Reference	-	Reference	-
– Heterozygous MT	46 (21.9%)	15 (21.1%)	0.95 (0.48-1.81)	0.891	0.99 (0.47-2.01)	0.970
IL5RA						
– WT	89 (42.4%)	37 (52.1%)	Reference	-	Reference	-
– Heterozygous MT	121 (57.6 %)	34 (47.9 %)	0.68 (0.39-1.16)	0.155	0.73 (0.40-1.33)	0.306
IL9						
– WT	147 (70.0%)	44 (62.0%)	Reference	-	Reference	-
– Heterozygous MT	62 (29.5 %)	26 (36.6 %)	1.40 (0.79-2.46)	0.245	1.66 (0.88-3.15)	0.117
– Homozygous MT	1 (0.5 %)	1 (1.4 %)	3.34 (0.13-85.65)	0.400	5.38 (0.17-174.84)	0.294
IL12RB1 a						
– WT	105 (50.0 %)	38 (53.5%)	Reference	-	Reference	-
– Heterozygous MT	105 (50.0 %)	33 (46.5 %)	0.87 (0.50-1.49)	0.608	1.17 (0.64-2.17)	0.610
IL12RB1 b						
– WT	124 (59.0 %)	52 (73.2%)	Reference	-	Reference	-
– Heterozygous MT	81 (38.6 %)	16 (22.5%)	0.47 (0.25-0.87)	0.019	0.60 (0.29-1.17)	0.141
– Homozygous MT	5 (2.4%)	3 (4.2%)	1.43 (0.29-6.05)	0.480	1.78 (0.33-8.19)	0.464

**Adjusted by age and sex. AD: atopic dermatitis; ACD: allergic contact dermatitis; OR: odds ratio; CI: confidential interval; WT: wild-type; MT: mutant type.*

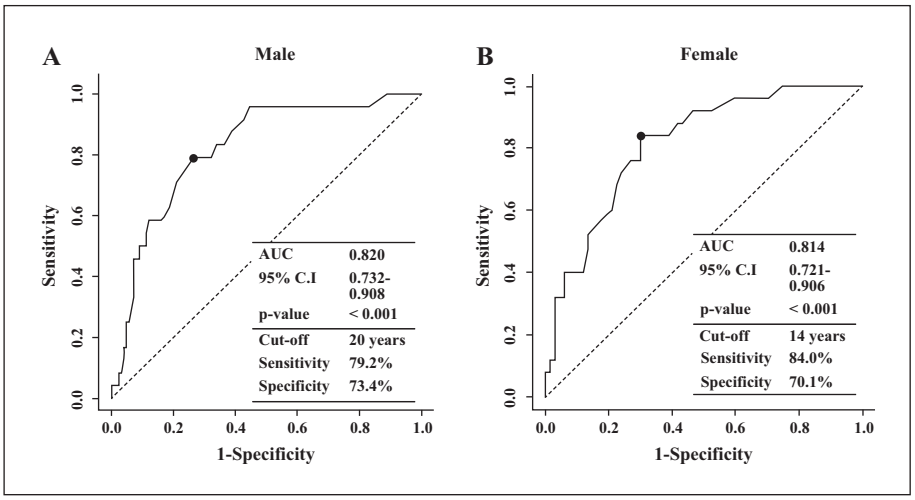

Figure 1. Association between patient age and concurrent ACD in AD patients without a family history of ACD. The optimal cut-off age for screening concurrent ACD was calculated from the maximum of the Youden index: (**A**) males; (**B**) females. ACD: allergic contact dermatitis; AD: atopic dermatitis; AUC: area under the curve.

with AD. However, the presence of a family history of ACD was strongly associated with concurrent ACD in patients with AD in this study. Thus, further studies are needed to confirm the genetic impact on increased contact sensitization in patients with AD.

An increase in the prevalence of contact sensitization and ACD has been suggested to be due to various factors such as skin barrier abnormality, altered bacterial colonization, and increased topical allergen exposure to emollients or topical corticosteroids [7, 13, 30]. Thus, a significant proportion of patients with AD are likely to have concurrent ACD. However, these disorders are not always detected and physicians do not always provide appropriate treatment and education for ACD. AD patients with ACD should be informed of any sensitization to antigens using patch testing, and appropriate patient education should be given to avoid exacerbating their condition. However, patch testing is not commonly performed for many patients because of the complexity of application, cost, and time-related burdens. In particular, for patients with AD, a suspicion of ACD and patch testing is often lacking.

In *table 4*, we provide a list of indications for suspecting concurrent ACD and performing patch testing in patients with AD with remarkable clinical features. Patch testing should be performed in AD patients with a self-reported family history of ACD; this was found to be the most significant independent factor associated with AD and ACD. In AD patients without a family history of ACD, patient age was found to be a very useful variable for predicting concurrent ACD in these patients (AUC of 0.820 in male subjects and 0.814 in female subjects). Patch testing of male AD patients over 20 years and female AD patients over 14 years may allow concurrent ACD to be diagnosed with high sensitivity and specificity (79.2% and 73.4%, and 84.0% and 70.1%, respectively). In addition, the presence of a personal history of ACD, late onset (adolescent or adult-onset), and presence of prurigo nodularis support a suspicion of concurrent ACD (although these correlations decreased after correcting for age and sex), and a patch test might be considered in AD patients with these clinical features.

Table 4. Indications for patch testing in patients with AD.

Patch testing – highly recommended
– Presence of family history of allergic contact dermatitis
– Male aged over 20 years
– Female aged over 14 years
– Presence of typical skin lesions consistent with ACD
Patch testing – to be considered
– Presence of personal history of ACD
– Late onset (adolescent or adult-onset disease)
– Presence of prurigo nodularis

AD: atopic dermatitis; ACD: allergic contact dermatitis.

A limitation of this study is that non-AD subjects were not included, and thus the prevalence of ACD between the AD and non-AD population could not be compared. In addition, the study population consisted of only one group (Korean) and was too small to exclude genetic variation within the population. ■

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