Original paper

The relationship between atopy and allergic contact dermatitis in Israeli patients

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Abstract

Introduction: Whether individuals with atopic diseases have a different risk of contact allergy compared to those who are non-atopic is controversial and data are conflicting.
Aim: To explore the association between atopy and allergic contact dermatitis (ACD).
Material and methods: This retrospective cross-sectional study included 301 patients referred to a tertiary clinic to evaluate ACD. Demographic details including personal and familial mucosal or cutaneous atopic status were recorded. Patch tests were tailored to their clinical presentations and relevant exposures.
Results: At least 1 positive patch test reaction was observed in 177 patients (59% of the study cohort), of which 52% had a history of atopic diseases, compared with 44% of patients with a negative patch test result (p = 0.2). Additionally, 147 patients had an atopic background, of which 92 (62%) had ≥ 1 positive patch test result, compared with 55% of non-atopic patients (p = 0.2). Nickel sulphate was the most common contact allergen (13.4% of the patch test reactions).
Conclusions: We identified a positive tendency for atopic diseases among individuals with ACD and vice versa. Our study supports the aggregate data from previous studies despite the non-significant differences between the study and control groups. However, further research performed in larger populations of patients is necessary to evaluate the real association between atopy and ACD on a solid basis. Our results indicate the necessity of systematic patch testing in patient setups with atopic background and chronic dermatitis.

Key words: atopy, allergic contact dermatitis, allergen, patch testing.

Introduction

Atopic patients have an inherent tendency to develop allergic reactions to environmental stimuli such as chemical, physical and biological ones. Atopic diseases are classically divided into mucosal atopic diseases that include allergic rhinoconjunctivitis and asthma, and cutaneous atopic disease, e.g. atopic dermatitis (AD). Although a clear association between atopy and increased reactivity to irritants is known [1], the association between atopy and allergic contact dermatitis (ACD) still remains controversial. Individuals with AD may be at a higher risk of contact sensitization due to a defective skin barrier caused by the well-replicated filaggrin (FLG) loss-of-function mutation and other mutations such as SPINK5, FLG-2, SPRR3, and CLDN1, leading to increased allergen penetration [2–5]. On the other hand, such patients were considered to be characterized by a clearly dominant Th2 cytokine profile, responsible for attenuated delayed hypersensitivity responses.

Aim

In this study, we aimed to explore possible association between mucosal and cutaneous atopic diseases and ACD. Although most former studies considered the

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relationship between AD and ACD, the literature regarding the whole spectrum of atopic diseases with respect to ACD is relatively sparse.

Material and methods

This retrospective case-control study included 301 patients, referred to a tertiary referral patch test clinic over a 2-year period. Patients were predominantly referred for the investigation of suspected ACD. Complete medical history was obtained including demographic data, relevant domestic and occupational exposures, personal and family history of AD, asthma, and rhinoconjunctivitis. All patients were extensively patch tested with the European baseline as well as individually composed series of contact allergens (Chemotechnique Diagnostics, Vellinge, Sweden). Readings were obtained on day (D) 4 for all patients. The patients were instructed to return on D7 if additional reactions were observed later [6]. Positive reactions were evaluated as weak (+), strong (++), and extreme (+++) according to the International Contact Dermatitis Research Group and European Society of Contact Dermatitis (ESCD) criteria [6]. Clinical relevance was defined according to the ESCD criteria [6].

Statistical analysis

Univariate analysis was used to determine the correlation between each explanatory variable and study group (atopic vs. non-atopic). Categorical variables were analysed using Pearson's χ^2-test or Fisher's exact test and were reported as relative frequencies. A p-value of 0.05 was considered significant. Statistical analysis was performed by SAS for Windows version 9.4 (SAS, NC, USA). Ethical approval was obtained from the local committee.

Results

This study included 301 patients. A hundred forty-seven (49%) had a personal or family history of atopic diseases. Within the general population study of 301 patients, 177 presented with ≤ 1 positive patch test reaction (study group A). Non-reacting patients were defined as the control group A (Figure 1). In the study group A, 117 patients (80% of the atopic group) had only mucosal presentation of atopic allergy. The MOAHLFA index for the investigated populations is shown in Table 1. Characteristics of the study and control groups A are further described in Table 2. Difference in terms of atopic background between the 2 groups mentioned above was not significant (study group – 52% and control group – 44%, $p = 0.2$).

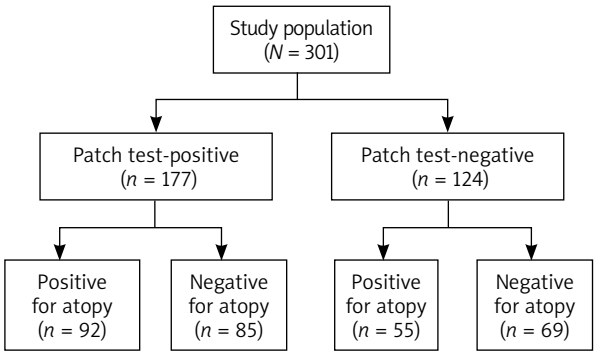

Figure 1. Study population characteristics

Occupational characteristics of the study group A and the control group A are described in Table 3. There was a significant difference in occupational distribution ($p < 0.03$) between the groups. The difference was especially observed in the proportion of teaching, housekeeping and health professionals and army personnel among the groups. Localization of dermatitis is described in Table 4. Prevalence of the most common allergens in the study group is summarized in Table 5.

All data were further categorized to study and control groups B according to the atopic background, meaning that the study group B was defined as patients with an atopic background while the control group B had no atopic background. In the population of 147 atopic patients (study group B), 62% of positive reactions were recorded in comparison to 55% of those in the control group B (Table 6). However, the difference was not significant ($p = 0.2$). The relevance rate of the positive reactions was 90% in the study group and was not significantly different from that of the control group (93%). Localizations of dermatitis and occupational parameters were also not significantly different between the study and control groups B.

Discussion

Two contradictory mechanisms determine the relationship between atopy and contact sensitization. Early experimental studies found reduced contact sensitization among patients with AD. The simplistic archaic concept theorized that contradictory unmixed Th1/Th2 immune profiles promote either atopic tendency or contact sensitization [7–9]. On a clinical level, a biased referral pattern

Table 1. MOAHLFA index for the investigated populations

Parameter	*N*	%
Men	124	41.3
Occupational dermatitis	51	16.9
Atopic dermatitis	60	19.9
Hand dermatitis	69	22.9
Leg dermatitis	29	9.6
Face dermatitis	52	17.2
Age > 40	119	40

of patients with AD for patch testing to exclude contact sensitization in patients with poorly controlled dermatitis may lead to inverse association [10]. As mentioned above, patients with atopic diseases present a genetic induced impaired skin barrier structure and function. This type of defect may potentially increase allergen penetration.

A Polish study performed by Poninska *et al.* demonstrated that filaggrin mutations increase the risk of ACD development as well as atopic asthma also in the absence of AD [11]. Possible immunological mechanisms for contact sensitization in patients with atopy are increased levels of Th2 cytokines being responsible for promotion of ACD development [12] and elevated antigen presentation and processing components [13]. In addition, patients with AD are more likely to systematically use various skin-care products and therefore significantly increase the risk of skin sensitization to allergenic ingredients [14] of the formulations.

Another possible challenge in determining a possible correlation is a lack of uniformity in defining "atopy". Spiewak [15] reviewed the literature regarding the interplay between atopy and contact dermatitis and found more than 10 different definitions of the term "atopy," some of which interchange terminology of atopy and atopic eczema, making the analysis of results highly difficult.

Past decade publications tend to support a positive correlation between atopy and ACD. Kirchhof identified that patients with a personal or familial history of atopy have an increased risk of ACD [1]. A Danish study demonstrated that contact allergy was more frequent in participants who reported AD in comparison to non-AD patients [16]. Another study in Californian paediatric patients showed a significantly different rate of contact reactivity in 89% of patients with AD, as compared with 66% rate in non-AD patients [17]. A recent single centre study performed in a population of 46,250 patients examined over a 30-year period, concluded that contact allergy to nickel sulphate, cobalt chloride, and primin was less likely to develop in the group of AD, whereas substances found in topical dermatological products were more likely to induce contact allergy in patients with AD [18]. A slightly different view regarding this issue was addressed by Scott *et al.*; the authors compared the prevalence of positive results of patch tests to allergens known to be causative for development of systemic contact dermatitis in patients with AD with and without respiratory atopic diseases. Their conclusion was that children and adolescents, although not adults, with AD and respiratory atopy, were more likely to have positive patch tests to allergens with potential to induce systemic contact allergy than age-matched patients with AD without respiratory atopy [19]. A systematic review and meta-analysis [20] of 74 publications from the last 60 years indicated a positive correlation in studies that compared patients with AD with individuals from the general population, but an inverse association when comparing with referred populations.

Table 2. Demographic and atopy data in the study group A and the control group A

Variable	Study group A (n = 177)	Control group A (n = 124)	P-value
Age [years] mean ± SD	39.32 ±15.48	36.11 ±16.91	0.75
Gender, n (%):			
Male	62 (35)	62 (50)	< 0.01
Female	115 (65)	62 (50)	< 0.01
Atopic background, n (%)†	92 (52)	55 (44)	0.2

†Atopic background was not significantly different between study and control groups.

Table 3. Occupational distribution among the study group A and the control group A*

Occupation	Study group A (%)	Control group A (%)	Ratio (A : B)§
Administration	17.51	16.93	1.034
Laboratory	3.95	3.22	1.226
Teaching	10.73	5.64	1.92
Service workers	7.34	8.87	0.82
Health professionals	8.47	5.64	1.50
Building and maintenance	3.95	3.22	1.22
Machinery and mechanics	7.91	9.6	0.82
Manufacturing	3.39	4.83	0.70
Combat soldiers	7.91	25	0.3164
Housekeeping	9.04	5.64	1.602
Unknown#	19.77	11.29	1.75

**Occupation classification is according to the Standard Occupational Classification and Coding Structure, SOC. §Distribution of the occupation among the members of the groups, was significantly different (p < 0.003). #Unknown occupation means that no data were found regarding occupation in the patient's file.*

Table 4. Dermatitis location among the study group A and the control group A

Site	Study group A (%)	Control group A (%)	Ratio (A : B)§
Head and neck	37.4	42.9	0.87
Extremities	17.0	17.5	0.97
Palms	23	16.5	1.39
Torso	9.1	12.7	0.71
Soles	9.5	8	1.22
Groins	3.9	2.4	1.62

§Distribution of the dermatitis location among the members of the groups was not significantly different (p = 0.58).

It is clearly noticeable that the results provided by different researchers are conflicting. The lack of consistency in the definition and terminology of atopy is one of

Table 5. Prevalence of the most common allergens among the study group

Allergen	Percentage (%) of tested recruits*
Nickel sulfate	13.4
MI	6.7
Cobalt chloride	6.4
Fragrance mix I	5.5
Potassium dichromate	4.3
Thiomersal	4.3
Acrylates	4.3
Colophony	4.0
Methyldibromo glutaronitrile	3.9
Myroxylon pereirae	3.6
Formaldehyde	3.6
Own products	3.3
MCI/MI	3.0
Dodecyl gallate	2.4
Quaternium 15	2.1
p-Phenylenediamine	1.8
Epoxy resin	1.8
Textile dyes	1.5
Neomycin	1.5
Thiuram mix	1.5
Paraben mix	1.5
4-tert-butylphenol formaldehyde resin	1.2
Cocamidopropyl betaine	1.2
Sorbitan sesquioleate	1.2
Benzocaine	1.2

**45% of the subjects reacted to 1 allergen, the rest reacted to 2 or more allergens.*

Table 6. Demographic and atopy data in the study group B and the control group B

Variable	Study group B (n = 147)	Control group B (n = 154)	*P*-value
Age [years] mean ± SD	36.35 ±15.54	39.57 ±16.57	< 0.09
Sex, *n* (%):			
Male	62 (43)	62 (41)	> 0.82
Female	85 (57)	92 (59)	
Positive patch test, *n* (%)†	92 (62.6)	85 (55.2)	0.2

†Prevalence of allergic contact dermatitis was not significantly different between the study and control groups (p = 0.2).

the reasons responsible for such variability. Most studies refer almost exclusively to AD. Others use inconsistent criteria for inclusion such as a family history of atopic diseases, but no personal history of AD. Other factors may include lack of uniformity in study designs, the vast number of them being retrospective. Some studies show differences in patch test techniques including differences in the haptens and concentrations used and in the interpretation of patch test reactions and relevance.

Our study is the first report from Israel to evaluate the relation between atopy and ACD. We did not find a significant difference between persons with atopy to non-atopic; however, a positive tendency for atopy among individuals with ACD and vice versa was identified.

Our cohort characteristics align with that of European reports regarding MOAHLFA index [21] except for age. It may reflect a referral bias as our centre is a tertiary referral centre for the army. It may also explain differences of occupational distribution as army personnel tend to have higher rates of irritant contact dermatitis [22]. Moreover, the relatively high atopy rate in our cohort should also be considered, given the referral bias of persons with atopy in patch test clinics and the rising atopy rate in Israel over the past decades [23, 24].

Conclusions

Our study supports a positive tendency of patients with atopy to have ACD, although not significantly. This observation aligns with that of former studies and emphasizes the need for patch testing in patients with atopy with long standing dermatitis.

Conflict of interest

The authors declare no conflict of interest.

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