Prevalence and clinical characteristics of adult-onset atopic dermatitis with positive skin prick testing to mites

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Summary

Background **The clinical role of house dust mite (HDM) in atopic dermatitis (AD) is still controversial.**

Objective **The aim of the study is to assess the prevalence, clinical relevance and characteristics of adult-onset AD patients with positive skin prick tests (SPT) to mites.**

Methods **The case record forms of adult-onset AD patients who underwent SPT at the Skin Allergy Clinic, Siriraj Hospital were reviewed.**

Results **Forty-one of 62 patients (66.1%) had positive SPT to mites. The frequency of intrinsic AD among adult-onset AD was 4.8% (3/62). SPT to HDM tended to be positive in patients who had personal or family history of atopy, positive SPT to several specific antigens or who presented with elevated serum IgE, chelitis, recurrent conjunctivitis and perifollicular accentuation, respectively.**

Conclusion **The prevalence of adult-onset AD patients with mite sensitivity was high. There were some notable features that tended to be present in mite sensitive adult-onset AD patients.** ***(Asian Pac J Allergy Immunol 2011;29:318-26)***

Key words: *adult, atopic dermatitis, mite, skin prick testing*

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Submitted date: 22/7/2011
Accepted date: 8/11/2011

Introduction

Atopic dermatitis (AD) is a multifactorial disease for which the pathophysiology is not clearly understood.[1,2] Genetic susceptibility, environmental factor, epithelial barrier dysfunction and immunologic response dysregulation have been implicated in the pathogenesis. A previous review[3] proposed that the most common airborne proteins which have the significant potential to contribute to AD include house dust mite (HDM), cockroach, pet dander and multiple pollens. By innate proteolytic activity, airborne proteins produced from HDM can directly impair skin barrier function and delay barrier recovery in patients with AD.[3]

AD with an onset between the age of 18 and 20 or older, known as adult-onset AD, is a subset of AD.[4-6] Apart from the typical flexural dermatitis in adult, this subgroup of AD patients often have a nonflexural rash distribution and atypical morphologic variants, such as nummular or prurigo-like lesions.[6]

Among general adult AD patients, more than 85% have aeroallergen specific IgE, mostly against dust mite[7]. Kulthanan, et al.[4] reported that among Thai adult-onset AD patients with positive skin prick testing (SPT), the most frequent allergen is Dermatophagoides mites.

Several meta-analyses on sublingual immuno-therapy (SLIT) have been carried out; they showed clinical efficacy of SLIT in allergic asthma and rhinitis caused by sensitization to pollens and HDM. SLIT has also been considered for new applications, such as AD.[8,9] Although the association between HDM and AD has remained inconclusive,[10] SLIT with HDM extracts in AD patients with mite sensitivity has been reported to effectively reduce the severity of the disease.[11,12]

A number of studies[12-16] on AD have previously been conducted. Most of them, however, focused on childhood AD and the early onset AD which extends to adult life. To date, no studies have been conducted on adult-onset AD and HDM sensitization. Therefore, the aim of this study was to assess the prevalence, clinical relevance and

characteristics of adult-onset AD Thai patients with positive SPT to mites.

Methods

Patients and study design

This study was approved by the Siriraj Institute Review Board, Siriraj Hospital, Mahidol University and was performed at Siriraj Hospital, a medical school and tertiary referral centre, Thailand. The case record forms of patients with adult-onset AD who underwent SPT at the Skin Allergy Clinic, Siriraj Hospital, from June 2008 to September 2010 were reviewed.

The diagnosis of AD was established according to the criteria of Hanifin and Rajka[17] when at least three major and three minor criteria were met. The severity of AD was assessed using the Rajka and Langeland score,[18] range of score 0–9 (mild, 3-4; moderate, 4.5-7.5; severe, 8-9), and eczema area and severity index (EASI),[19] range of score 0 -72 (mild, <6; moderate, ≥6; severe, ≥18). The age of 18 years old or above was used as a cut-off mark to determine adult-onset AD. Subjects who had concomitant skin diseases that might interfere with the clinical features of AD were excluded.

The following data were collected: demographic data for age, sex, age of onset, personal and family history of atopy, clinical symptoms and severity and previous investigation including SPT and total serum IgE.

Skin prick testing

All subjects were informed about the process of SPT and gave their written informed consent prior to the procedure. Patients were not tested if short-acting or long-acting antihistamines had been taken within the preceding 3 or 7 days respectively, or systemic corticosteroids equivalent to more than 10 mg per day of prednisolone had been taken within 28 days prior to the test. High potency topical corticosteroids applied to the tested area were omitted for 3 weeks prior to testing.[20] SPT was performed by placing a drop of antigen extract on the volar surface of the forearm. Then, the skin was gently punctured and tented to introduce the allergen by hypodermic needle. In addition, normal saline and histamine phosphate 10 mg/ml were used as negative and positive controls, respectively. The result was read at 15 minutes. A wheal of at least 3 mm larger diameter than the negative control was interpreted as a positive result. The procedures were performed by the same well-trained and experienced technician. Besides *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* allergens, 12 aeroallergens (aspergillus, penicillium, cladosporium, para grass, bermuda grass, careless weed, sedge, sugar cane, American cockroach, house dust, cat hair and dog epithelium) and 15 food allergens (egg white, egg yolk, cow's milk, wheat, banana prawn, giant tiger prawn, giant freshwater prawn, green mussel, undulated surf calm, blue swimming crab, sea crab, snapper, cuttlefish, butterfish and eaglefish), from Alk-Abello, Lincoln Diagnostics, Inc., Texas, USA were also tested.

The total serum IgE of the patients was also studied using the Nephelometry method (Dade Behring; Marburg, Germany). The level of 100 kU/l and lower was interpreted as normal.

All subjects were further subclassified into intrinsic and extrinsic AD subtypes. Patients who had a total serum IgE level lower than 200 kU/l with no other atopic diseases, absence of specific serum IgE antibodies to common aeroallergens and food allergens and negative SPT for common allergens were classified as intrinsic AD. The others were classified as the extrinsic form.[21]

Statistics

The prevalence of positive SPT results to mites was recorded as a number and percentage. Descriptive statistics, e.g. mean, median, maximum, minimum and percentages were used to describe demographic data, positivity of SPT and clinical correlations. To compare qualitative clinical data between patients with and without mite sensitivity, Pearson's Chi-square test or Fisher's exact test was used. The unpaired *t*-test or the Mann-Whitney *U* test were applied for quantitative data with and without normal distribution respectively. A *p*-value < 0.05 was considered as a significant result.

All statistical data analyses were performed using SPSS for Windows version 17.0.

Results

A total of 62 subjects were enrolled into the study, of whom, 9 (14.5%) were men, 53 (85.5%) were women. The age range of the patients was 18 to 59 years (mean: 33.5) with the age of onset ranging from 18 to 59 years (mean: 29.5). The majority of the patients (56.5%) developed AD during their 3rd decade of life (18-29 years). The median duration of the disease, from the onset to enrollment, was 1.0 year. Forty-six patients (74.2%) had a positive personal history of atopy, of which, allergic rhinitis (91.3%) was the most common

Table 1. Characteristics of patients with adult-onset atopic dermatitis (AD) with positive and negative skin prick testing (SPT) to mites (n =62).

Characteristics	Number patients with adult-onset AD (%)		*p*-value
	With mite sensitivity (*n*=41)	Without mite sensitivity (*n*=21)	
Age, years (mean ± SD)	33.0±11.0	34.5±10.1	0.586[1]
Sex			1.000[2]
Male	6 (14.6)	3 (14.3)	
Female	35 (85.4)	18 (85.7)	
Age of onset, years: median (min-max)	26.0 (18.0-59.0)	30.0 (20-50)	0.576[3]
Duration of disease, years: median (min-max)	1.0 (0-25.0)	2.0 (0-24)	0.298[3]
Personal history of atopy (with or without family history of atopy)	34 (82.9)	12 (57.1)	**0.028**[4]
Allergic rhinitis	30 (73.2)	12 (57.1)	0.201[4]
Allergic conjunctivitis	23 (56.1)	7 (33.3)	0.090[4]
Asthma	11 (26.8)	2 (9.5)	0.187[2]
History of food allergy	12 (29.3)	7 (33.3)	0.742
Family history of atopy (with or without personal history of atopy)	32 (78.0)	9 (42.9)	**0.006**[4]
Atopic dermatitis severity score: median (min-max)			
Rajka and Langeland Scoring System	6.0 (2.0-8.0)	5.0 (3-8)	0.970[3]
EASI	1.9 (0-22.7)	1.8 (0.3-13.3)	0.734[3]
Serum IgE level, kU/L: median (min-max)	216.0 (11.7 – 36,400)	61.4 (14.4-730.0)	0.103[3]
Subtype of atopic dermatitis, No.(%)			**0.035**[2]
Extrinsic	41 (100.0)	18* (81.0)	
Intrinsic	0	3 (19.0)	

SD: standard deviation; EASI: Eczema Area and Severity Index
*Diagnosis of extrinsic AD by total serum IgE level ≥ 200 kU/l or having other atopic diseases, presence of specific serum IgE antibodies to common aeroallergens and food allergens or positive SPT for common allergens
[1]Unpaired *t*-test
[2]Fisher's exact test
[3]Mann-Whitney *U* test

manifestation, followed by allergic conjunctivitis (65.2%). There were 41 subjects (66.1%) who had at least one first degree family member with atopy. Of these, 34 were mite sensitive and 9 did not have mite sensitivity. The most common family atopic histories were allergic rhinitis (61.0%) and asthma (36.6%).

Forty-one of 62 adult-onset AD subjects (66.1%) had positive SPT results to mites. All mite-sensitized adult-onset AD patients (41 subjects) were classified as extrinsic AD subtype, while among the 21 patients without mite-sensitization, 18 subjects (85.7%) and 3 subjects (14.3%) fit the extrinsic and intrinsic subtypes, respectively. Therefore the frequency of intrinsic AD in all adult-onset AD patients in this study was 4.8% (3/62). The extrinsic AD subtype was significantly associated with mite-sensitization, while within the intrinsic AD group there was a significant association with the absence of mite sensitivity. Table 1 shows the demographic data and clinical data of adult-onset AD patients with and without mite sensitization. The positive SPT to mites was significantly associated with a personal history of atopy and a family history of atopic diseases. On the other hand, there was no significant difference in age, sex, duration of disease, previous history of contact dermatitis, AD severity score and serum IgE level in those with positive and negative SPT results to mites.

Even when there was no significant difference in serum IgE level between those with and without mite sensitivity, our study revealed that serum IgE at the titer of >100 kU/L was found mostly in mite sensitive cases rather than non-mite sensitive one.

Table 2. Diagnostic features in relation to the results of SPT to mites.

Diagnostic features	Number of patients with adult-onset AD (%)		OR	95% CI	*p*-value
	With mite sensitivity (*n*=41)	Without mite sensitivity (*n*=21)			
Pruritus	41 (100)	21 (100)	-	-	-
Typical morphology and distribution	27 (65.9)	13 (61.9)	1.19	0.40 – 3.54	0.758
Chronically-relapsing dermatitis	41 (100)	21 (100)	0.66	0.55 - 0.79	1.000
Personal or family history of atopy	37 (90.2)	15 (71.4)	3.70	0.91 – 15.0	0.064
Xerosis	24 (58.5)	14 (66.7)	0.71	0.24 – 2.12	0.534
Icthyosis	1 (2.4)	2 (9.5)	0.24	0.02 – 2.79	0.263
Immediate Type I reaction to test antigens (excluding mite)	37 (78.7)	4 (26.7)	10.2	2.7-38.9	**<0.001**
Elevated Serum IgE	16 (69.6)	3 (33.3)	4.56	0.88 – 23.71	0.109
Early age of onset	0	0	-	-	-
Cutaneous infection	2 (4.9)	1 (4.8)	1.03	0.09 – 12.01	1.000
Non-specific hand or foot dermatitis	12 (29.3)	6 (26.8)	1.03	0.32 – 3.31	0.954
Nipple eczema	7 (17.1)	2 (9.5)	1.96	0.37 – 10.38	0.705
Chelitis	6 (14.6)	1 (4.8)	3.43	0.39 – 30.55	0.406
Recurrent conjunctivitis	8 (19.5)	2 (9.5)	2.30	0.44 – 11.98	0.472
Dannie-Morgan infraorbital fold	13 (31.7)	4 (19.0)	1.97	0.55 – 7.04	0.290
Keratoconus	-	-	-	-	-
Anterior subcapsular cataracts	-	-	-	-	-
Orbital darkening	23 (56.1)	11 (52.4)	1.16	0.40 – 3.34	0.781
Facial pallor	3 (7.3)	1 (4.8)	1.58	0.15 – 16.18	1.000
Pityriasis alba	4 (9.8)	2 (9.5)	1.03	0.17 – 6.12	1.000
Anterior neck folds	12 (29.3)	7 (33.3)	0.83	0.27 – 2.56	0.742
Itch when sweating	30 (73.2)	15 (71.4)	1.09	0.34 –3.521	0.884
Food intolerance	9 (22.0)	5 (23.8)	0.90	0.26 – 3.13	1.000
Course influenced by environment or emotion	13 (31.7)	11 (52.4)	0.42	0.14 – 1.24	0.114
Intolerance to wool, lipid solvent or fabric	9 (22.0)	7 (33.3)	0.56	0.17 – 1.81	0.332
Nonabsorptive occlusive garments, and working conditions	4 (9.8)	2 (9.5)	1.03	0.17 – 6.12	1.000
Perifollicular accentuation	4 (9.8)	1 (4.8)	2.16	0.23 – 20.68	0.654
White dermographism, delay blanch	1 (2.4)	0	1.53	1.27 – 1.83	1.000

OR: odds ratio; CI: confidence interval

Significant *p*-value ($p < 0.05$) are shown in bold.

Considering Hanifin's and Rajka's criteria, there were non-significant ($p > 0.05$) positive associations between mite sensitivity and a personal or family history of atopy, elevated serum IgE, chelitis, recurrent conjunctivitis and perifollicular accentuation. However, there was a significant positive association between the result of SPT to mites and immediate type I reaction to test antigens as shown in Table 2.

The data showed no statistical difference in the clinical presentations, including morphology and location of the lesions, between adult-onset AD patients with and without mite sensitivity.

As shown in Table 3, adult-onset AD patients with mite sensitivity had significantly higher positive SPT results to pollens, insects and other danders such as house dust, cat hair and dog epithelium. In contrast, there was no statistical

Table 3. SPT and serum IgE in relation to the results of SPT to mites.

	Number of patients with adult-onset AD(%)				
	With mite sensitivity (*n*=41)	Without mite sensitivity (*n*=21)			
Allergens		Without mite sensitivity (n=21)	Without mite sensitivity (extrinsic) (n=18)	Without mite sensitivity (intrinsic) (n=3)	*p*-value*
Food	20 (48.8)	7 (33.3)	7 (38.9)	0	0.246
Egg white	0	0	0	0	-
Egg yolk	1 (2.4)	0	0	0	1.000
Cow's milk	0	0	0	0	-
Wheat	0	1 (4.8)	1 (5.6)	0	0.339
Banana prawn	3 (7.3)	0	0	0	0.545
Giant tiger prawn	12 (29.3)	1 (4.8)	1 (5.6)	0	**0.045**
Giant freshwater prawn	10 (24.4)	3 (14.3)	3 (16.7)	0	0.514
Green mussel	6 (14.6)	1 (4.8)	1 (5.6)	0	0.406
Undulated surf calm	5 (12.2)	2 (9.5)	2 (11.1)	0	1.000
Blue swimming crab	13 (31.7)	0	0	0	**0.003**
Sea crab	8 (19.5)	0	0	0	**0.043**
Snapper	2 (4.9)	0	0	0	0.545
Cuttlefish	2 (4.9)	2 (9.5)	2 (11.1)	0	0.599
Butterfish	1 (2.4)	0	0	0	1.000
Eaglefish	2 (4.9)	0	0	0	0.545
Molds	2 (4.9)	1 (4.8)	1 (5.6)	0	1.000
Aspergillus	1 (2.4)	1 (4.8)	1 (5.6)	0	1.000
Penicillium	1 (2.4)	0	0	0	1.000
Cladosporium	1 (2.4)	0	0	0	1.000
Pollens	19 (46.3)	3 (14.3)	3 (16.7)	0	**0.013**
Para grass	7 (17.1)	0	0	0	0.08
Bermuda grass	11 (26.8)	0	0	0	**0.011**
Careless weed	4 (9.8)	3 (14.3)	3 (16.7)	0	0.680
Sedge	6 (14.6)	0	0	0	0.088
Sugar cane	5 (12.2)	0	0	0	0.157
Insects	26 (63.4)	4 (19.0)	4 (22.2)	0	**0.001**
Mosquito	18 (43.9)	4 (19.0)	4 (22.2)	0	0.053
Mixed ants	13 (31.7)	3 (14.3)	3 (16.7)	0	0.220
House fly	7 (17.1)	2 (9.5)	2 (11.1)	0	0.705
Dander	41 (100)	3 (14.3)	3 (16.7)	0	**<0.001**
American cockroach	5 (12.2)	1 (4.8)	1 (5.6)	0	0.654
House dust	25 (61.0)	3 (14.3)	3 (16.7)	0	**<0.001**
Cat hair	17 (41.5)	0	0	0	**<0.001**
Dog epithelium	21 (51.2)	0	0	0	**<0.001**
Serum IgE, n=32					
Serum IgE (>100kU/L)†	17 (73.9)	3 (33.3)	3 (37.5)	0	**0.049**
Serum IgE (≥200kU/L)	11 (47.6)	2 (22.2)	2 (25.0)	0	0.249

**p*- value for the difference between adult-onset AD with and without mite sensitivity

Significant *p*-value ($p < 0.05$) are shown in bold.

† Cut-off point which is defined as high titer by Siriraj Hospital laboratory

in the results of SPT to overall foods and molds between those with adult-onset AD with and without mite sensitivity. However, when analyzed separately, adult-onset AD patients with mite sensitivity had a significantly higher number of positive SPT results to giant tiger prawn, blue swimming crab and sea crab, respectively.

Discussion

The reported prevalence of positive SPT to mites varies between different conditions ranging from 64-84% in allergic rhinitis with or without asthma and 51-52% in AD patients[20,22-29] Daengsuwan et al.[30] reported that SPT to mites yielded a positive result in 23 out of 71 (32.4%) normal Thai adults. In our study, 41 of 62 (66.1%) subjects had positive SPT results to mites. This implies that the prevalence of positive SPT to mites in our adult-onset AD patients, though similar to other atopic conditions, was higher than that in the normal population.

A study of the epidemiology of 1,019 AD patients, aged between 4 weeks to 57 years, in south-east Nigeria,[31] showed a statistically significant association between AD patients and family history of atopic diseases. Seo[32] studied 1,545 Korean children with AD and reported the association between HDM-sensitive cases and sensitization to food allergens, family history and clinical severity. Our study also showed significant association between mite-sensitive adult-onset AD patients and a family history of atopy. However, there was no association between our mite sensitivity AD patients and sensitization to overall food allergens or clinical severity. This may be because of the differences in the age groups of patients and the severity score used. Six Area, Six sign Atopic Dermatitis score (SASSAD) was used in Seo's study while the Rajka and Langeland scoring system and EASI were used in our study.

In our study, the median of Rajka and Langeland score was 6.0 which rated as moderate severity. The disease severity, on the other hand, seems to be less severe when using EASI with the median EASI score of 1.85, from the total of 72. The difference may be because EASI measures disease severity as a cross-sectional objective evaluation while the Rajka and Langeland scoring system includes retrospective self-assessment of the severity (intensity of pruritus and remission history). Previous treatments, therefore, may improve the condition and be responsible for low EASI score on the examination day. In addition, a previous study[33] reported that EASI did not show a correlation with the subjective severity.

A previous review[34] stated that the level of IgE is associated with severity of AD. Our study showed that serum IgE at the titer of >100 kU/L was found mostly in mite sensitive cases. However, there was no statistical difference in the clinical severity between mite sensitive and non-sensitive groups. A recent randomized, placebo-controlled study on omalizumab, an IgE blocker, by Heil et al.[35] also showed no correlation between IgE levels and clinical severity of AD by demonstrating that there was no improvement in clinical scores in AD despite reducing IgE level to normal.

Even our present study showed no significant association between adult-onset AD with mite sensitivity and most of the features of Hanifin's and Rajka's criteria; SPT to HDM tends to be positive in patients presenting with a personal or family history of atopy, elevated serum IgE, chelitis, recurrent conjunctivitis and perifollicular accentuation. When analyzed separately, an isolated personal history of atopy with or without family history of atopy was significantly associated with mite sensitivity. An isolated family history of atopy with or without personal history of atopy was also significantly correlated with positive SPT results to mite as shown in Table 1.

Some studies[36-38] have demonstrated the possibility of cross-reactivity between mites and shrimp, snail or insects. To our knowledge, there is no supportive data on the cross-reactivity between pollen or crab and HDM. Therefore, a larger study with more subjects is needed.

Cross-reactivity between dust mites and cockroach, by tropomyosin as a cross-reacting allergen, has been reported in patients with asthma and/or rhinitis.[39] Our study of adult-onset AD patients, however, did not reveal any association between mite sensitivity and sensitivity to cockroach allergen.

Van der Veen et al.[40] found that the association between positive SPT responses to dog dander and mite sensitivity was because of the contamination of dog dander SPT preparations with the HDM. Our study, however, not only showed the association between mite sensitivity and dog dander but also revealed a significant association with other dander such as cat hair and house dust.

Mites enter the body mainly by inhalation, ingestion or directly through the epidermis.[23] The

two main groups of mites are HDM and the storage mites. Both can be found in house dust and the later can also be found in food, grain, flour and on cheese.[41] Rice, a staple food for Thais, can also be contaminated with mites.[42] A cross-reactivity between HDM and storage mites can be found[37]. Reactions produced by ingestion of mite-infested food, whether heated or unheated, range from mild skin reactions to severe life-threatening anaphylaxis reaction.[43-45] However, we cannot conclude whether strict elimination of mite-contaminated food may be beneficial to our mite-sensitized adult-onset AD patients. Nevertheless, ingestion of mite-contaminated food may explain the discrepancies of the results among several mite avoidance trials.[46-48]

As shown by several trials,[49-51] the clinical role of HDM in AD is still a matter of debate. Our specific group of adult-onset AD patients often had positive SPT to HDM, but there was no clinical difference between patients with and without mite sensitivity.

In summary, our study demonstrates that there was no difference in the clinical characteristics between adult-onset AD, with and without mite sensitivity. However, in adult-onset AD patients with positive results for SPT to HDM were significantly more likely to have a personal and family history of atopy an immediate type 1 reaction to test antigen and positive SPT to several specific antigens. This may imply that adult-onset AD patients with mite sensitivity probably have a high dependence on atopic diathesis.

Conclusion

The prevalence of adult-onset AD patients with positive SPT to mites was 66.1%. There was no difference in clinical presentations between adult-onset AD with and without mite sensitivity.

Conflicts of interest

All authors have neither conflicts of interest nor financial support from the drug companies

Acknowledgment

We are grateful to Dr. Chulaluk Komoltri for her kind support.

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