

CLINICAL REPORT

Prevalence and Clinical Characteristics of Chronic Urticaria and Positive Skin Prick Testing to Mites

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The aim of this study was to review chronic idiopathic urticaria patients with positive skin prick testing to mites and the clinical relevance of this positivity. Case records of patients with chronic idiopathic urticaria who underwent skin prick testing during the years 2000 to 2007 were reviewed. The studied allergens included house dust mite allergens; *Dermatophagoides pteronyssinus* and *farninae*. A total of 172 patients were enrolled in the study. The prevalence of positive skin prick testing to mites among patients with chronic idiopathic urticaria was high (34.9%), but had little clinical relevance (3.3%) to their urticarial symptoms. Patients with mite-sensitization were more commonly male and more often had a personal or family history of atopy compared with those without mite-sensitization. Key words: mite; skin prick testing; chronic urticaria.

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Urticaria is characterized by the rapid appearance of wheals and/or angioedema. Chronic urticaria (CU) is defined by spontaneous wheals occurring over a duration of longer than 6 weeks (1). In 80–90% of adults with CU, no external cause can be identified and the final diagnosis is chronic idiopathic urticaria (CIU) (2–6). Immediate hypersensitivity is believed by some to be involved in the pathogenesis of CU (7, 8). Therefore skin prick testing (SPT), which detects the presence of allergen-specific IgE on a patient's mast cells, has been used by some researchers and practitioners in the investigation of CU (9–12).

Mites are a common aeroallergen, colonizing beds, sofas, carpets, and any woven material (13). Mites sensitize and induce atopic disease, such as rhinitis and asthma, in predisposed individuals. House dust mites are an important deteriorating factor in patients with allergic rhinitis, asthma and atopic dermatitis (14). Avoidance of mites can effectively reduce symptoms in some of these patients (15–17).

Dixit (9) reported three patients with urticaria who showed presence of mites in their home environment and who also had a positive SPT to *Dermatophagoides* spp. Their urticaria symptoms became worse in the home environment and markedly improved when they removed themselves from the mite-atmosphere. It was concluded that *Dermatophagoides* spp. was the most likely causative factor in these patients (9). Two studies have implicated house dust mite sensitivity in CIU, both using intradermal skin testing and *in vitro* analysis of *Dermatophagoides* spp. (18–20). Numata et al. (18, 19) reported that 48.8–57.7% of CIU patients without atopic disease had a positive cutaneous reaction to the mite allergens. They found a direct correlation between skin test reactivity and *in vitro* mite-induced histamine release from leukocytes and concluded that patients with CU may be sensitized to mite allergens.

Caliskaner et al. (11) studied SPT to house dust mites and other aeroallergens in 259 patients with CIU and angioedema. In the CIU group, a reactivity to house dust mites was found in 24.7%, whereas SPT positivity to house dust mites in 300 healthy control individuals and 300 atopic patients without CU was 4.7% and 50.3%, respectively. The difference was statistically significant. They concluded that the significantly higher percentage of SPT positivity to mites obtained in their patients with CIU, compared with the healthy controls, is not coincidental. However, clinical relevance of mite to CIU was not reported. Mahesh et al. (12) reported that 78 out of 122 patients with CU (64%) had skin sensitivity to house dust mites. They suggested a relationship between house dust mite sensitivity and CU. Moreover, the presence of allergies in patients with CU seems to increase skin reactivity to dust mites.

Even though there are many studies that have reported a relationship between mite sensitization and CU, there are still no clear published data indicating clinical relevance of mite sensitivity to aetiology and treatment of CU. In addition, the prevalence of sensitivity to mites in healthy individuals and atopic patients varies from country to country. The purpose of our study, therefore, was to assess the prevalence, clinical relevance and characteristics of CU patients with positive SPT to mites in Thailand.

METHODS

Patients and study design

The study was approved by the ethics committee on research involving human subjects of Siriraj Hospital, Bangkok, Thailand. The case records of patients with CU (as defined in the Introduction) who underwent SPT at the Urticaria Clinic, Siriraj Hospital, during the years 2000 to 2007 were reviewed retrospectively. Only patients aged over 18 years were included.

The aetiology of CU was evaluated by conducting a complete history of possible causes, physical examination and laboratory tests. When obvious aetiological factors could be identified, i.e. physical urticaria, drug-induced urticaria, systemic lupus erythematosus, and urticarial vasculitis, patients were excluded from the study. Besides SPT, other laboratory investigations included complete blood count, urinalysis, erythrocyte sedimentation rate, stool examination, autologous serum skin testing and other investigations that were necessary in each individual case, i.e. renal function test, liver function test, hepatitis B surface antigen, anti-hepatitis C virus, antinuclear antibodies, cryoglobulins, serum complement level, chest X-ray, sinus X-ray, thyroid function and anti-thyroid auto-antibodies (i.e. anti-thyroglobulin and anti-microsomal antibodies).

All subjects were informed about the process of SPT and gave their written consent prior to the beginning of the SPT. The following data were collected: demographic data for age, sex, personal and family history of atopy, and history of aeroallergen-induced urticaria.

Patients were not tested if they had taken short-acting antihistamines within the preceding 3 days or long-acting antihistamine drugs within the preceding 7 days, or systemic corticosteroids equivalent to more than 10 mg of prednisolone per day at any point within the 28 days prior to skin testing. The application of high potency, topical corticosteroids to the tested area was avoided for 3 weeks prior to testing (11).

Skin prick testing

The SPT was performed by placing a drop of antigen extract on the skin then using a hypodermic needle to gently tent the skin and puncture it in order to introduce the allergen. In addition, 0.9% saline and histamine phosphate 10 mg/ml were used as negative and positive controls, respectively. In all patients, skin reactivity was tested on the volar surface of the forearm by the same trained and experienced person. The results were read at 15 minutes. A positive result yields a wheal of at least 3 mm larger diameter than the negative control. The studied allergens (Alk-Abello, Lincoln Diagnostics, Inc., Texas, USA), included house dust mite antigens, namely *Dermatophagoides*

pteronyssinus and *Dermatophagoides farninae* (10,000 Au/ml). Immediate cutaneous reactivity to at least one allergen was interpreted as a positive result.

Statistical analysis

The prevalence of positive SPT results to mites was recorded as a number and percentage. Descriptive statistics, e.g. mean, median, minimum, maximum and percentages, were used to describe demographic data, positivity of SPT and clinical correlation. Demographic and clinical data for CU patients with and without mite sensitivity were compared. Qualitative data were compared using Pearson's χ^2 test. Quantitative data with and without normal distribution were analysed using unpaired *t*-test or Mann-Whitney *U* test, respectively. Since some patients were lost to follow-up, a Kaplan-Meier survival curve was applied to determine the probability of symptom resolution at each time-point. All statistical data analyses were performed using SPSS for Windows version 10.0.

RESULTS

Table I shows the demographic and clinical data of CU patients with and without mite sensitization. A total of 172 patients were enrolled in the study, of whom 140 (81.4%) were female. The mean age (standard deviation (SD)) of the patients was 36.4 (12.2) years, with a range of 18–70 years. There were 49 patients (28.5%) with a positive personal history of atopy and 46 (26.7%) with a positive family history of atopy. The most common personal atopic histories were allergic rhinitis (20.4%) and asthma (4.7%). Similarly, the most common family atopic histories were allergic rhinitis (18%) and asthma (6.4%). Sixty (34.9%) of the 172 subjects had positive SPT result to mites. Multivariate analysis showed independent associations between mite sensitization and male gender and personal and family history of atopy (Table II).

There was no significant difference in laboratory findings, such as eosinophilia, urine analysis etc., between the two groups (data not shown). When we compared the severity scores of the urticarial symptoms of the mite-positive CU with mite-negative CU, neither wheal size, the extent of body involvement or itching score

Table I. Demographic and clinical data of patients with chronic urticaria (CU) with positive and negative skin prick testing to mites

| Characteristics | Number of patients with CU (%) | | <i>p</i> -value |
|--|---------------------------------------|---|-----------------|
| | With mite sensitivity (<i>n</i> =60) | Without mite sensitivity (<i>n</i> =112) | |
| Age, years (mean \pm SD) | 34.9 \pm 11.7 | 37.2 \pm 12.5 | 0.241 |
| Sex | | | |
| Male | 18 (30) | 14 (12.5) | 0.005 |
| Female | 42 (70) | 98 (87.5) | |
| Personal history of atopy | 23 (38.3) | 26 (23.2) | 0.036 |
| Family history of atopy | 22 (36.7) | 24 (21.4) | 0.031 |
| Systemic symptoms | 3 (5) | 4 (3.6) | 0.696 |
| History of urticaria induced by aeroallergen | 14 (23.3) | 13 (11.6) | 0.044 |
| Associated angioedema | 19 (31.7) | 36 (32.1) | 0.949 |
| Associated dermographism | 9 (15) | 8 (7.1) | 0.100 |

Significant *p*-values are shown in bold.

SD: standard deviation.

Table II. Multiple logistic regression analysis of demographic and clinical data of patients with chronic urticaria with positive and negative skin prick testing to mites

| | Adjusted OR (95% CI) | p-value |
|--|----------------------|--------------|
| Sex: male | 3.88 (1.68–8.96) | 0.001 |
| Personal history of atopy | 2.09 (0.99–4.39) | 0.050 |
| Family history of atopy | 2.26 (1.08–4.72) | 0.030 |
| History of urticaria induced by aeroallergen | 2.05 (0.83–5.06) | 0.118 |

Significant p-values are shown in bold.

OR: odds ratio; CI: confidence interval.

were significantly different. However, the mite-positive group had a higher mean number of days with wheals per week than the mite-negative group (5.9 ± 1.9 vs. 5.1 ± 2.4 days), although this difference was not statistically significant ($p=0.24$).

Table III shows the personal and family history of atopy in both the mite-positive and the mite-negative groups. The most common associated atopic conditions were allergic rhinitis and asthma. A positive personal and family history of atopy was significantly more common in the mite-positive group than in the mite-negative group.

Fig. 1 shows Kaplan-Meier curves demonstrating the duration of the disease in patients with CIU with positive and negative SPT, respectively. Median durations were 19 and 17 months, respectively, but this difference was not statistically significant (log rank $p=0.9893$).

In 2 out of 60 (3.3%) mite-sensitized CU patients the sensitivity was considered of clinical relevance to their urticaria. Both patients also had allergic rhinitis. Their urticarial symptoms together with allergic rhinitis were induced by exposure to a mite-rich environment.

DISCUSSION

Our study demonstrated a 34.9% prevalence of positive SPT to mites in CU patients. Mahesh et al. (12) and Caliskaner et al. (11) reported that 64% and 24.7%

Table III. Personal and family history of patients with chronic urticaria (CU) with positive and negative skin prick testing to mites

| Characteristics | Patients with CU (%) | |
|---------------------------|------------------------------|----------------------------------|
| | With mite sensitivity (n=60) | Without mite sensitivity (n=112) |
| Personal history of atopy | | |
| Allergic rhinitis | 13 (21.7) | 22 (19.6) |
| Asthma | 7 (11.7) | 1 (0.9) |
| Atopic dermatitis | 1 (1.7) | 1 (0.9) |
| Allergic conjunctivitis | 2 (3.4) | 2 (1.8) |
| Family history of atopy | | |
| Allergic rhinitis | 14 (23.3) | 17 (15.2) |
| Asthma | 7 (11.7) | 5 (4.5) |
| Atopic dermatitis | 1 (1.7) | 1 (0.9) |
| Allergic conjunctivitis | 0 | 1 (0.9) |

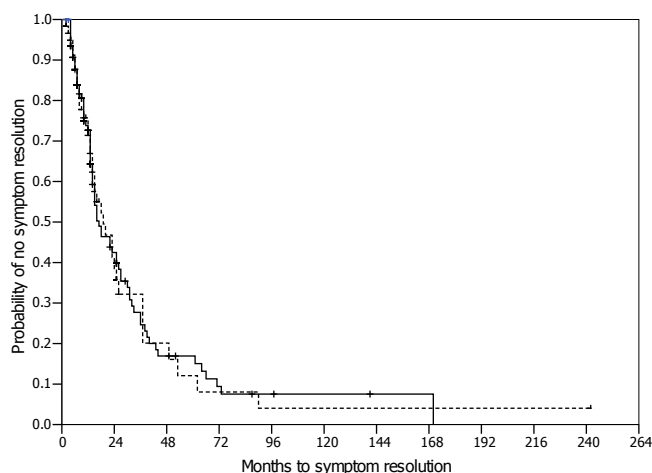


Fig. 1. The Kaplan-Meier curve demonstrates duration of the disease in patients with chronic idiopathic urticaria with positive and negative skin prick test (SPT) to mites: —: negative SPT to mite; - - - : positive SPT to mite; each plus sign (+) on the Kaplan-Meier curve shows duration of the disease in one unresolved patient. Median durations with positive and negative SPT to mites were 19 and 17 months, respectively, but this difference was not statistically significant (log rank $p=0.9893$).

of their CU patients had skin sensitivity to mites, respectively. The variation in prevalence may be due to different environments and study populations.

In Thailand, Daengsuwan et al. (21) reported 23 out of 71 (32.4%) of normal adults had sensitization to *Dermatophagoides* spp. In the present study, 34.9% of CU patients had positive SPT to mites. This implies that the prevalence of positive SPT to mites in our CU patients is not obviously higher than that in the normal population. Vichyanond et al. (22) reported that the prevalence of allergic rhinitis and asthma in Thai university students was 26.3% and 8.8%, respectively. The present study demonstrated that 28.5% of CU patients had atopic histories. The common histories were allergic rhinitis (20.4%) and asthma (4.7%). These data show that the prevalence of atopy was not increased in our population of patients with CU.

Mahesh et al. (12) reported that 53% of patients with CU alone and 79% of patients with both CU and atopic disease had mite sensitization. Our study showed that mite sensitivity in the group with CU alone and the group with both CU and atopic disease was 30.1% and 46.9%, respectively. Mite-positive CU patients had a significantly higher percentage of personal and family histories of atopy than did the mite negative group. These data suggested that patients with both CU and atopic diseases are more likely to be sensitive to mites than patients with CU alone.

In Thailand, Trakultivakorn & Nuglor (23) reported positive SPT to *D. pteronyssinus* in atopic adult was 23 out of 45 (51.1%). Daengsuwan et al. (21) reported 49 out of 71 (58.3%) asthmatic adult patients had positive SPT to *Dermatophagoides* spp. Pumhirun et al. (24) reported that adults with allergic rhinitis had positive

SPT to house dust mite, *D. pteronyssinus* and *D. farinae* at 72%, 76% and 79%, respectively. This implies that patients with atopic diseases (without CU) are more likely to be sensitive to mites than patients with CU.

Kulthanan et al. (25) reported that 356 out of 450 (79%) patients with CIU were female. Caliskaner et al. (11) reported that 33 out of 64 (51.6%) CU patients with mite sensitivity were male, which was a higher percentage of male than that among patients without mite sensitivity; however, the difference was not statistically significant. Our study showed that the group with mite sensitivity had a statistically significant higher percentage of males than the group without mite sensitivity.

Mites enter the body mainly by inhalation (26). Other entrance routes for mites are through ingestion or directly through the epidermis. Sanchez-Borges et al. (27, 28) reported "oral mite anaphylaxis" caused by the ingestion of foods prepared with contaminated wheat flour containing domestic or storage mites. The allergens responsible for this reaction seem to be heat-resistant (29). Caliskaner et al. (11) recommended to their mite-sensitive CU patients that they completely eliminate mite-contaminated food, such as bread and other flour-containing food. The patients found it induced relief to various degrees. Since the number of patients who underwent this elimination was so small, the researchers concluded that the results might not be statistically significant.

There is a diversity of mite species in our environment. The most common mite in Thailand is *D. pteronyssinus* (30). There are reports concerning cross-reactivity among house dust mite and/or storage mites (31, 32). Rice has historically been the staple diet for Thai people. They do not eat bread regularly. Franzolin et al. (33) studied mite contamination in polished rice grains in markets in Brazil. The predominant species was *Tyrophagus putrescentiae*, others were *Blomia tropicalis*, *Cheyletus* spp. and *Blattisocius tarsalis*. Further studies on mite contamination in Thai rice and the role of mites in causing urticaria are needed. We cannot conclude whether strict elimination of mite-contaminated food may be helpful to our mite-sensitized CU patients. However, only 2 out of 60 patients in our study showed a clinical correlation between the history of urticaria induced by mite inhalation and the positive SPT to mites. Therefore, the avoidance of exposure to mites by inhalation may not be very helpful for the majority of mite-sensitized CU patients.

To our knowledge, there is no conclusive study that indicates that mite elimination is useful in CU. CU is not included in the indication for allergen immunotherapy and the idea that patients will receive benefit from this form of treatment remains controversial. Further studies into the effect of mite elimination in CU patients are required.

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