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INVESTIGATIVE REPORT

Atopy Patch Test Reactions to House Dust Mites in Patients with Scabies

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It is well known that the house dust and the scabies mites are related phylogenetically. We therefore performed atopy patch tests with house dust mite antigens (*Dermatophagoides pteronyssinus* (Dp) and/or *Dermatophagoides farinae* (Df)) in scabies patients without atopy and healthy controls. We studied 25 men with active scabies and 25 healthy controls. Skin prick tests with standardized house dust mite extract were performed for all patients and controls. An intradermal test procedure was carried out in skin prick test-negative patients, and for controls showing positive atopy patch test to Dp and/or Df. While atopy patch tests were performed directly in all healthy controls, patients with scabies were first treated and on the next day, atopy patch tests were performed. Twenty-two of 25 patients with scabies (88%) had skin prick test and/or intradermal test positivity against house dust mites, whereas 17/25 patients (68%) had atopy patch test positivity against house dust mites (Dp and/or Df). There was no statistically significant difference between skin prick test and/or intradermal test positivity and atopy patch test positivity in a regression analysis ($p=0.222$). The only statistically significant correlation was between atopy patch test positivity and the extent of scabies involvement ($p<0.05$). Only few of the healthy controls had positive tests. In this study, we have shown that a positive atopy patch test to house dust mite antigens is not specific for patients with atopic dermatitis, but also occurs in scabies patients without a history of atopic dermatitis.
Key words: atopy patch test; skin prick test; scabies; house dust mites.

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The atopy patch test (APT) is an epicutaneous patch test with aeroallergens commonly found in patients with atopic dermatitis (AD) (1, 2). Although there is no clear consensus on the importance of aeroallergens in the pathogenesis of AD, allergen exposure via inhalation or penetration through the scratched, abraded skin can provoke exacerbations of skin lesions (3, 4). It was suggested that large amounts of house dust mite (HDM) allergens induce immune and inflammatory reactions similar to those occurring in positive APT sites (5).

APT in patients with AD was first reported by Mitchell et al. (6) about 20 years ago. The APT reaction to aeroallergens was found to be specific for sensitized patients with AD, and negative results were obtained in healthy people or in patients with respiratory atopy (allergic rhinoconjunctivitis and/or bronchial asthma). There were significant correlations between APT results with history, skin prick tests (SPT), and specific IgE for HDMs, cat dander and grass pollens (7).

However, it should be kept in mind that high levels of allergen-specific IgE or SPT reactivity are not mandatory for APT positivity (2). Morover, APT was found to be positive not only in extrinsic AD, but also in intrinsic (non-allergic) AD (8, 9). Mites are ubiquitous organisms and an important source of allergens (10). HDMs are the most important allergens in respiratory atopy and AD. The most frequently detected mites are *Dermatophagoides pteronyssinus* (Dp), *Dermatophagoides farinae* (Df), *Blomia tropicalis* and *Euroglyphus maynei*. The faecal particles of HDMs contain most of the allergenic activity. There is a good cross-reactivity between Dp and Df (10, 11).

Sarcoptes scabiei (SS), which is also an 'astigmatid' mite like Dp and Df, is a true human parasite, classified in the family of sarcoptoidea (10). Cutaneous contact with scabies mite proteins (allergens) induces a systemic, inflammatory reaction. HDMs and SS are related phylogenetically. They show striking physical and antigenic similarities. The fact that 32–75% of patients with scabies without AD showed SPT and/or specific IgE positivity to Dp and Df antigens (12–15), clearly reveals the cross-reactivity between SS and HDM antigens. Similarly, we suggest that specific T cells developed against SS antigens (during the incubation period and/or clinical course of scabies) might be cross-reactive with HDM antigens. We documented – for the first time – APT positivity to HDMs in patients with scabies in an uncontrolled, preliminary study (16).

In the present study, we aimed to detect APT reactivity to HDMs in a larger study of scabies patients and healthy controls.

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MATERIALS AND METHODS

We studied 25 men with active scabies aged between 20 and 31 years (mean 21.2 ± 2.3), who had no past history of scabies. The diagnosis of scabies was verified microscopically. Twenty-five healthy controls aged from 19 to 32 years (mean: 21 ± 2.6) and who had also no past history of scabies were evaluated as a control group. Written informed consent forms were obtained. A history of AD was regarded as an exclusion criterion in both patients and controls. The individuals entered into the study had no signs, symptoms or history of AD. There was no patient using oral corticosteroids or antihistamines in either patient or control groups. Six of 25 scabies patients and 3/25 controls had allergic rhinoconjunctivitis, but none had bronchial asthma. The following criteria based on the extent of skin involvement were used for grading the severity of scabies in patients (14): mild, skin lesions in a few areas ($<20\%$ of body surface); moderate, skin lesions in many areas (20–50% of body surface); severe, generalized eruption ($>50\%$ of body surface).

Duration of disease was noted for each patient. Severity of itching was assessed on a visual analogue scale (0=absent to 10=very severe). SPT was performed in all patients and controls with a standardized HDM 'mixed' extract (5000 AU/ml Dp+5000 AU/ml Df; Center Laboratories, USA). SPT results were evaluated as positive if the HDM extract-induced wheal was at least 3 mm larger than that of the negative control (diluent containing 0.9% physiological saline).

For SPT-negative patients, the intradermal test (IDT) procedure was carried out by injecting 0.02 ml of HDM 'mixed' extract containing 500 AU/ml Dp and 500 AU/ml Df. A sterile diluent containing 0.9% physiological saline was used as a negative control. Wheals at least 4 mm larger in diameter than those of the negative control with or without pseudopods were regarded as positive. IDT was not performed for control patients except those showing APT positivity to Dp and/or Df.

While APT was performed directly after SPT for all healthy controls, patients with scabies were first treated with permethrin 5% cream after SPT/IDT evaluation, and on the next day, APT was performed. In this procedure, Dp and Df allergens in petrolatum at test concentration of 200 IR (index of reactivity – biological standardization of Stallergenes extracts combining *in vitro* and *in vivo* tests; Stallergenes, Antony, France) was applied to uninvolved skin on the backs of all patients and controls by using large Finn chambers (12 mm diameter) after 10 tape-strippings to facilitate allergen penetration (1). Pure petrolatum was used as negative control. Results were evaluated after 48 h according to the following criteria (2): negative, −, only erythema; questionable, ?, erythema; infiltration, 1+; erythema, few papules (≤ 3), 2+; erythema, ≥ 4 papules, 3+; erythema, many papules or spreading papules, 4+; erythema, vesicles, 5+.

Regression analysis and Mann-Whitney U test were used for statistical evaluation of the results.

RESULTS

Seventeen of 25 patients (68%) had APT positivity against HDMs (Dp and/or Df). Nine of 25 patients (36%) showed SPT reactivity to HDM-mixed extract, and IDT was found to be positive in 13/16 patients (81.25%) characterized by SPT negativity. These results revealed that 22/25 patients with scabies (88%) had 'immediate-type' reactivity (SPT and/or IDT positivity) against HDM. In the patient group, there was no statistically significant difference between SPT and/or IDT positivity and APT (Dp and/or Df) positivity in regression analysis ($p=0.222$). The only statistically significant correlation was between APT positivity and the extent of skin involvement (severity of scabies) ($p<0.05$). There was no statistically significant difference between APT and other parameters studied (duration of scabies, grade of itching and associated respiratory atopy; $p>0.05$).

In the control group, three patients who had allergic rhinoconjunctivitis showed SPT reactivity to HDM. Two controls who were non-atopic had APT positivity (Dp and Df, 1+), but were IDT-negative against HDM. A statistically significant difference was detected between patient and control groups for both SPT or IDT, and Dp and/or Df positivity using the Mann-Whitney U test ($p<0.005$).

APT with pure petrolatum (negative control) was found to be negative in all patients and controls.

DISCUSSION

The results of this controlled study cast doubt on the commonly held opinion that a positive APT with aeroallergens only occurs in AD. To the best of our knowledge, this is the second study demonstrating positive APT results with HDM antigens in scabies patients without AD. The first one, which presents the preliminary results of the present study was also performed by us, on 13 scabies patients. We demonstrated APT positivity against house dust mites in 9/13 patients (69%). The negative control patch tests with pure petrolatum excluded the possibility that APT reactivity against HDM in scabies patients might have resulted from heightened cutaneous reactivity typically seen in scabies (16). However, we cannot exclude the possibility that the treatment given the day before application of APT may have heightened the specific immune response.

van Voorst Vader et al. (17) asserted that all APT-positive patients with AD had concomitant respiratory atopy, and emphasized the necessity of the existence of active airway disease for the distribution of mediators and cytokines from activated inflammatory cells in the airway to the skin. However, it is clear that APT against HDMs is positive not only in AD cases with or without allergic airway disease (8, 9), but also in scabies patients. Morover, APT positivity may reflect the extent of skin involvement (or severity) in scabies. Therefore, our findings support the view that respiratory atopy is not a prerequisite for positive APT reactions.

Fertilized female scabies mites burrow into the stratum corneum and lay several eggs daily (18). In scabies patients, antigenic proteins induce the development of immediate and late immunologic reactions, which may be enhanced by scratching. As SS and HDM are closely related phylogenetically, SPT/IDT and APT

reactions to HDM antigens can be found in scabies patients without a history of AD or bronchial asthma, as shown in our study. Sensitization by only the cutaneous route appears to be sufficient for a high prevalance of APT positivity in scabies patients.

In scabies patients, changes in immunological parameters including SPT, specific IgE and/or IDT, and APT reactivity to HDM, and an increase in total IgE and blood eosinophil count suggest that scabies might cause transient atopy, or an 'AD-like' state. Some patients who previously had scabies were found to be SPT and/or IDT positive against HDM for 6 weeks to several months (14, 15, 19). Most of the scabies patients who were successfully treated eventually lost immediate-type reactivity against HDMs. There is no information regarding the duration of APT positivity in scabies patients. In the post-treatment period, we were able to follow 10 APT-reactive patients, and the APT was still positive in all of them at the end of the third month despite the absence of signs and symptoms of scabies.

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