

## Case report

# Immediate contact allergy from hydrolyzed wheat in a cosmetic cream

Immediate contact allergy to cosmetics seems to be rare, since only a few case reports on it have been published. We report on a case of IgE-mediated allergic contact urticaria caused by hydrolyzed wheat in a body cream.

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A 27-year-old healthy woman without personal or family history of atopy had used a moisturizing body cream for 1 week without any problem. When she continued to use the product, she noticed shortly after every application a pruritic, erythematous, urticarial rash that became more intense with time.

The open application test on intact skin on the volar site of the forearm with the product as such revealed an extensive wheal and flare reaction, which spread beyond the 3 × 3 cm test area within 15 min (Table 1). Skin prick tests (SPTs) with commercial preparations of common inhalant allergens, natural rubber latex, and cereal grains including wheat were negative. SPTs were also performed with negative results with a series of 21 protein allergens from plant and animal sources that are often used in cosmetics (e.g., hen's egg, cow's milk, milk casein, almond, silk protein, aloe gel, papaya fruit, and hydrolyzed collagen). The total IgE was slightly elevated at 160 kU/l (reference value <110 kU/l).

The product was composed of 42 ingredients (15 liposoluble and 27 hydrosoluble), which were provided to us by the manufacturer. The open application test with the ingredients at the concentration suggested by the manufacturer was negative, but the SPT revealed a positive 8-mm reaction with pseudopods to one component, hydrolyzed wheat protein (Fig. 1). Histamine dihydrochloride (10 mg/ml) used as a positive control gave a 5-mm wheal, but no wheal

was induced with saline diluent in 50% glycerol used as a negative control. A patch test with the product as such was also performed with negative result. The open application test and the SPT with the product were negative in 10 control subjects.

In order to clarify the reaction mechanism, the patient's serum was evaluated for specific IgE antibodies by the immunospot method (8). Only water-soluble cream ingredients ( $n=27$ ) were tested for IgE binding on a nitrocellulose paper. In addition, an SPT preparation of timothy pollen (Soluprick, 10 HEP, ALK, Denmark) and a wheat extract (1:5 w/v) were used.

A nonatopic serum was used as a negative control, and pooled serum from grass-pollen- and wheat-IgE-positive sera as an atopic control. Specific IgE binding from the patient's serum was demonstrated to only one ingredient (wheat hydrolysate). Both control sera remained negative to all ingredients. Strong IgE binding to timothy and wheat was demonstrated from the atopic control, but not from the patient's serum. The commercial wheat-flour RAST (CAP FEIA, Pharmacia & Upjohn, Uppsala, Sweden) was also negative with the patient's serum. There was not enough hydrolysate for in-house RAST or any other laboratory tests.

## Discussion

This is the first report on hydrolyzed wheat in cosmetics causing immediate IgE-mediated contact urticaria. In a

Table 1. Test results

|                                                         | SPT | Open test | Specific IgE    |
|---------------------------------------------------------|-----|-----------|-----------------|
| Skin cream as such                                      | ND  | +         | ND              |
| Hydrolyzed wheat (hydrosoluble)                         | +   | –         | +               |
| 15 liposoluble ingredients                              | –   | –         | ND              |
| 26 hydrosoluble ingredients                             | –   | –         | –               |
| Wheat                                                   | –   | ND        | –               |
| Common inhalant allergens                               | –   | ND        | Timothy grass – |
| 21 animal- and plant-derived allergens and hydrolysates | –   | ND        | ND              |

SPT: skin prick test, +: positive, –: negative, ND: not done.

previous study, 22 protein hydrolysates, including two wheat-protein hydrolysate preparations, were tested in 11 hairdressers with hand dermatitis, with negative results for both wheat hydrolysates (6). The mechanism of most cases of immediate contact reactions to cosmetics or their ingredients seems to be nonimmunologic, since in the previous case reports no specific IgE to the suspected ingredients has been found or even looked for (1–5).

In only two studies has specific IgE been determined against a collagen hydrolysate present in hair conditioner, pointing to an immunologic contact urticaria (6, 9). Today, a popular trend in cosmetic industry is the use of substances from animal and plant sources in a variety of cosmetic products. These natural proteins and their hydrolysates are capable of producing IgE-mediated allergic reactions. The frequency of these immediate contact reactions is not known, but, according to reported cases, they seem to be rare. However, most people certainly do not even seek medical help unless the reaction is severe. Some cases may also go undetected if the possibility of this kind of immediate allergic reactions is not recognized and therefore appropriate skin tests are not performed.

In addition to proteins, some low-molecular-weight substances, such as formaldehyde and chlorhexidine, are also capable of causing immediate allergic contact reactions (10, 11). Both of these substances are widely used as preservatives in topical products including cosmetics. The symptoms of contact urticaria vary from itching and redness to widespread urticarial reactions even with systemic symptoms (4) and may, although rarely, lead to anaphylaxis (11).

Atopic patients with immediate reactions from animal- and plant-derived proteins in foods should be advised to avoid cosmetics containing these substances (5, 12). Pecquet et al. reported two patients who had suffered for years first from generalized urticaria after eating and later urticarial rashes from



Figure 1. Skin test reaction with hydrolyzed wheat. Open application test on marked square above (19) with negative result. SPT reaction on right with positive 8-mm wheal reaction.

contact with cosmetic products. In both cases, the tests revealed immediate allergy to sesame seed and oil with primary sensitization to foods (5). One of these potential sensitizers was carmine, which already has been reported to cause IgE-mediated anaphylactic reactions to beverages and sweets (13, 14). Carmine is a natural red dye extracted from an insect (cochineal, E120) and is widely used in both the food and cosmetic industries; therefore, it is likely that cases of immediate contact reactions caused by cosmetics will be reported. Physicians should be aware of these causes of immediate hypersensitivity in order to perform the skin tests and to advise their patients adequately.

The peculiarity in our case was that the patient had no personal or family history of atopy, and she had negative test results (SPT and RAST) to wheat. Although the product as such gave a strongly positive open test reaction, this test remained negative with the wheat hydrolysate. This probably resulted from the relatively small open test areas used, since all the 42 ingredients were tested simultaneously on the upper extremities (Fig. 2).

It remained unknown what happened during wheat protein hydrolysis to make this protein derivative able to act as a potent allergen. New epitopes may appear during the hydrolysis, or the additives (e.g., enzymes) used (data not available to us) may act as allergens. The time of sensitization remained open, too. This may have occurred already before the use of the present preparation, since hydrolyzed wheat is widely used in cosmetics. However, it seems more probable that the sensitization occurred while the patient was using the product, since no immediate reactions were observed during the first applications.



Figure 2. Open application tests on marked squares with all 42 ingredients of product performed simultaneously on both arms.

When immediate-type allergy to cosmetics is suspected, we skin-prick-test the patient with a series of 28 allergenic ingredients commonly used in cosmetics.

Annually, more than 200 patients have been tested with this series at our clinic. More than 10% have shown a positive test result to wheat or wheat germ. Occasionally, skin tests are performed with the product used by the patient and, when necessary, they are continued with the individual ingredients of the causative product. The ingredients have been kindly provided by the manufacturers. IgE antibodies to cosmetics or their ingredients have also been screened *in vitro* by the immunospot method (8).

After the present study, an atopic male hairdresser with hand eczema and natural rubber latex allergy did not show significant improvement with strict avoidance of latex-containing materials. Further SPTs revealed positive reactions to wheat and wheat germ and to wheat-containing hair cosmetics which he used daily. In the immunospot, his serum revealed IgE antibodies to four out of seven hair cosmetic products. All of the positive ones contained hydrolyzed wheat proteins. Avoidance of these hair-care products resulted in substantial improvement of his eczema, although occasional exacerbations still occurred mainly due to irritation from wet work.

In conclusion, in addition to other reported protein hydrolysates, hydrolyzed wheat may also produce immediate allergic contact urticaria. Besides the more common allergic type IV contact dermatitis from cosmetics, the possibility of immediate contact reactions should be kept in mind, because of the modern frequent use of proteins and their hydrolysates in skin and hair care products. We recommend the open application test and the SPT first with the product as such when immediate contact reactions are suspected.

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