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Delayed-type allergy to systemic corticosteroids

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Key words: allergy; corticosteroids; cross-reactivity; dermatitis; dexamethasone; drug allergy.

• WITH reference to the recently published paper on anaphylactoid symptoms due to paramethasone (1), we would like to draw attention to another type of steroid-intolerance reaction, which has been very rarely reported.

A 59-year-old woman, with no past medical history of allergies or intolerances, and suffering from encephalomyelitis disseminata, was put on oral dexamethasone during an acute phase of her disease. On the third day after starting

Positive patch tests in a patient treated for encephalomyelitis.

this medication, she developed a macular rash with an exfoliate component involving the face, the upper chest, and intertriginous areas. Dexamethasone treatment was immediately stopped; subsequently, the skin disorders resolved over several days. The patient had never received corticosteroids before. An allergic reaction to the administered corticosteroid was suspected as the cause of the rash, and allergologic investigations were initiated.

Patch testing revealed a positive crescendo reaction to dexamethasone, betamethasone, and clobetasol-17-propionate. Other tested corticosteroids, including prednisolone, hydrocortisone-17-butyrate, methylprednisolone, and triamcinolone-acetonide, were negative. Prick tests using the same set of substances were completely negative. Finally, we tested oral exposure with methylprednisolone to confirm tolerance to this alternative treatment for future exacerbations of encephalomyelitis disseminata, and the patient tolerated this drug without complications.

Allergic reactions, particularly delayed reactions to applied systemic corticosteroids, are rarely reported in the literature (2). In this context, two main types of systemic allergic reactions have been described: an anaphylactoid type, with symptoms such as angioedema, bronchospasm, shock, or urticaria, occurring minutes or hours after systemic exposure; and a so-called delayed type of systemic reaction, which is described as generalized macular or maculopapular exanthematous dermatitis, characteristically appearing several days after the start of systemic corticosteroid medication (3, 4).

In our case, the clinical presentation already suggested a delayed systemic reaction, as skin changes occurred 2 days after oral dexamethasone treatment was started, and were not accompanied by anaphylactoid symptoms. Moreover, the

typical exanthematous rash with an exfoliate component, which our patient developed, fitted into this picture. Finally, we could confirm the diagnosis by a positive result in the patch test for dexamethasone.

Interestingly, the patch test was also positive for betamethasone and clobetasol-17-propionate, suggesting a cross-reaction. According to Coopman et al., cross-reactions occur primarily (6–7 times more often) within certain groups of corticosteroids (5). Four different groups of structurally related substances are distinguished:

- 1) group A comprising hydrocortisone-related steroids such as methylprednisolone
- 2) group B comprising triamcinolone acetonide and related compounds
- 3) group C comprising betamethasone-like substances including dexamethasone
- 4) group D comprising steroid esters such as clobetasol-17-propionate.

Our patient showed a cross-reaction between substances of group C and group D. This interesting phenomenon (especially as both groups are considered rarely to cause delayed-type reactions [6]) can be explained by the similar molecular structure of these steroids (7, 8). The fact that dexamethasone, betamethasone, and clobetasol-17-propionate all have a methyl-group at the C16 position in the D-ring seems to be associated with the reaction (9). This explains why, in our patient, methylprednisolone, a member of group A, which is not substituted on C16, was tolerated well upon oral exposure.

In general, corticosteroid allergy, especially to group-C corticosteroids, is difficult to establish, as skin reactions in allergologic testing may be suppressed by the anti-inflammatory and immunosuppressive properties of the tested substance (8). Therefore, it is important to keep the possibility, and the whole spectrum, of corticosteroid allergy in mind.

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Exercise-induced anaphylaxis to wheat flour

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Key words: exercise-induced anaphylaxis; food allergy; gliadin; wheat flour.

● Food-dependent, exercise-induced anaphylaxis is a severe form of allergy that occurs only when the patient exercises within 2-4 h of ingesting a food, but in the absence of exercise the patient can ingest the food without any apparent reaction (1). We report on a 44-year-old woman who suffered from exercise-induced food allergy to wheat flour.

About 20 min after consumption of wheatmeal products – rolls, noodles – and subsequent intensive walking or jogging, the patient suffered from itching, generalized urticaria, and finally short-term unconsciousness. Some episodes necessitated intravenous emergency therapy with an antihistamine, a corticosteroid, and fluid substitution. If the patient avoided subsequent physical stress after consumption of wheatmeal products, no reaction appeared.

Furthermore, the patient complained of face dermatitis and rhinitis in the morning.

An atopic woman with generalized urticaria.

In a previous prick test, positive reactions were found to house-dust mites.

To elucidate the exercise-induced anaphylactic events, we carried out prick tests with baking ingredients and various sorts of flour. Performance and assessment of the prick tests followed the recommendations of the EAACI (2). For detection of specific IgE antibodies in the serum, we used RAST (CAP-RAST FEIA, Pharmacia Freiburg, Germany) for the baking ingredients and flours. The test results are summarized in Table 1. Positive prick test reactions were obtained for different flours (wheat, malt, and spelt) and gluten and powdered milk. A control test with wheat and the other flours in 10 volunteers gave negative results. In addition, specific IgE antibodies were detected to wheat flour, rye flour, spelt flour, and gluten, each with RAST class 3.

Furthermore, we carried out an exercise test on the bicycle ergometer (20 min at 150 W) and an oral challenge test with different flour products (wheatmeal roll, spelt noodles, and rye bread). The challenge tests were carried out double-blind (neither the patient nor the physician knew the contents of the challenge). The fasting exercise test on the bicycle ergometer produced no reactions. Oral challenge alone with wheatmeal roll, spelt noodles, and rye bread did not elicit any reactions, nor did spelt noodles or rye bread with subsequent

Table 1. Test results

Test substance	Prick test	RAST classes
Flours and baking ingredients		
Wheat flour	++	3
Rye flour	Negative	3
Buckwheat flour	+	0
Gluten	++	3
Malt flour	++	1
Spelt flour	++++	3
Ground guar endosperm flour	Negative	0
Powdered milk	++	0
Baker's yeast	Negative	0
NaCl 0.9%	Negative	
Histamine 0.1%	++	