

Severe systemic allergic reaction induced by accidental skin contact with cow milk in a 16-year-old boy. A case report

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Summary: The symptoms of food allergy are rarely induced by skin contact. A 16-year-old boy was referred to our Allergology Centre after an episode of systemic symptoms triggered by accidental skin contact with a drop of cow milk (CM) dripped from a sandwich containing fresh cheese. The patient had been allergic to CM from the age of 24 months and had experienced several episodes of urticaria-angioedema after the ingestion of tiny or "hidden" amounts of CM proteins. In vivo and in vitro diagnostic procedures showed intense sensitisation to all CM proteins (1/100 dilutions of allergenic extracts produced large wheals, and class 4 specific IgE antibodies. Total IgE antibodies were elevated (770.0 UI). A moderate degree of bronchial hyperresponsiveness was found (PC20 metacholine: 3.90 milligrams). This case report suggests that patients with a high degree of sensitisation to CM proteins should be alert to the danger of skin contact and should beware of "hidden" CM allergens.

Key words: Cow milk allergens, systemic reactions, food allergy, hidden allergens, skin contact, urticaria-angioedema.

Symptoms of food allergy are usually triggered by ingestion of the offending food. Food allergy subsequent to inhalation, skin contact and non-oral mucous membrane contact, which can induce severe and even life-threatening allergic reactions [1-5], is less frequently encountered. These less common modes of exposure are sometimes trivial or accidental and sometimes due to 'hidden' food allergens [6]. The ingestion of cow milk (CM) proteins is a common cause of food allergy, whereas allergic reactions triggered by trivial skin contact with CM proteins are very unusual. These reactions must be considered a contact urticaria syndrome as is the case of contact allergy to latex [5]. We will describe now the case of an adolescent with intense sensitisation to CM who experienced systemic symptoms after a drop of CM spilled on the intact skin of his shoulder.

Case report

A 16-year-old boy was referred to our Allergology Centre after a recent episode of systemic symptoms

(urticaria-angioedema, cough, bronchial obstruction etc.) triggered by accidental skin contact with CM. He was fed exclusively maternal milk for his first 6 months of life; there was no family history of allergy. At 24 months he had bronchial obstruction after eating ice cream containing CM. Respiratory symptoms disappeared after the use of inhaled B2 agonists and systemic corticosteroids. As the same symptoms reappeared only after the ingestion of CM, CM derivatives (cheese), ice cream and cakes containing milk, the patient underwent skin-prick tests and specific IgE determinations (RAST), which revealed intense sensitisation to CM proteins. Consequently, his parents were instructed to avoid foods containing CM.

At the age of 12 the patient experienced systemic anaphylaxis after eating a pizza (not containing cheese). Investigations showed that the *pizzaiolo* added a small amount of CM to the pizza dough. The boy was treated with epinephrine, corticosteroids and anti H1 receptor antagonists, and B2 agonists. At that time, diagnostic tests confirmed intense cutaneous and serological monosensitisation to CM proteins.

In August 2001 the patient experienced systemic

symptoms (urticaria-angioedema, cough, bronchial obstruction etc.) 2-3 min after a drop of milk from a sandwich containing *fior di latte* was accidentally dropped on the intact skin of his shoulder. *Fior di latte* is a typical fresh cheese containing cow milk. When a *fior di latte* is sliced, fresh milk gushes out. This systemic reaction occurred in the presence of one of the authors (FDF) who administered epinephrine, corticosteroids, anti H2 receptor antagonists and inhaled B2 agonists.

Methods

Five months after the last episode of systemic anaphylaxis the patient underwent further diagnostic procedures (skin prick tests, and total and specific IgE measurements). Written informed consent was obtained from the patient and his parents. Skin prick tests were carried out with a standardized method for the most common inhalant and food allergens [7]. The results were expressed as wheal area (mm²). Allergenic extracts were supplied by ALK Abellò (Milan, Italy). Skin prick tests for CM proteins were conducted on a different day. To avoid the risk of systemic reactions we diluted the CM allergenic extracts (containing whole milk, alpha lactoalbumin, beta globulin and casein) to 1/1000, 1/

100 and 1/10 with the same glycerinate solution usually used as a negative control. A blood sample was obtained for the evaluation of total and specific serological IgE determinations of inhalant and food allergens (Phadebas RAST, Pharmacia & Upjohn Diagnostics Uppsala, Sweden). Bronchial challenge with metacholine was performed according to a standard procedure on a different day [8,9].

After three reproducible FEV1 measurements, double concentrations of metacholine, starting from 0.1 mg/ml were inhaled at 5-min intervals. Solutions were delivered by a de Vilbiss 646 nebulizer attached to a dosimeter (Mefar MB3, Brescia, Italy). The challenge was discontinued when FEV1 fell by 20%. We did not perform a skin challenge (or a prick-by-prick test) with the offending food because of the high risk of inducing severe systemic reactions. Moreover, the last anaphylactic reaction occurred in the presence of one of the authors (FDF).

Results

In vivo and in vitro diagnostic procedures failed to demonstrate allergic sensitization to common inhalant and food allergens with the exception of CM proteins (Table 1).

Table 1. Diagnostic results

		DILUTIONS OF ALLERGENIC EXTRACTS		
		1/1000	1/100	
IN VIVO TESTS	SKIN-PRICK TESTS WHEALS AREAS (mm ²)	<u>ALLERGEN</u>		
		whole milk	15	98
		α Lactoalbumin	12	108
		β Lactoglobulin	14	106
		Casein	20	112
		POSITIVE CONTROL (HISTAMINE 10 mg/ml)	65	
NEGATIVE CONTROL (GLYCERINATE SOLUTION)	-			
IN VITRO TESTS	PHADEBAS RAST SPECIFIC SEROLOGICAL IgE ASSAY	ALLERGEN	PRU/ml	CLASSES
		whole milk	>17.50	4
		α Lactoalbumin	>17.50	4
		β Lactoglobulin	10.90	3
		Casein	> 17.50	4
TOTAL SEROLOGICAL IgE DETERMINATION: 770.0 UI/ml				
BRONCHIAL CHALLENGE WITH METHACHOLINE → PD20 methacholine value: 3.90 milligrams				

n.d. = not done

Table 2. Possible predictive risk factors to identify patients with hazard for severe food allergic reactions through non-ingestant routes of exposure

- High serum total IgE level
- Strong family history of atopy
- Early age of onset of symptoms despite having been breast-fed
- Strong reactivity to skin-prick-tests or RAST
- Clinical history

We performed skin-prick tests using only 1/1000 and 1/100 dilutions of allergenic extracts containing CM allergens. Since 1/100 dilutions of all allergenic extracts induced the onset of large cutaneous wheals we did not perform skin-prick tests using a 1/10 dilution or undiluted allergenic extracts to avoid the risk of systemic manifestations.

Discussion

Severe systemic and sometimes fatal reactions have been reported in children, adolescents and adults who ingested food to which they were highly allergic [10-13]. These reactions are often elicited by small amounts of foods containing the offending allergens that were "hidden" as ingredients in various manufactured products [6]. Symptoms usually occur following ingestion of minute quantities of food allergens but, in some cases, also by inhalation of food allergens carried in the air or in cooking fumes [3,14].

Although ingestion is the principal route of exposure to CM proteins, some highly sensitive patients develop severe symptoms (and can be fatal) after casual or professional inhalation of CM allergens [4,15-20].

To our knowledge, there are only few case reports about the development of severe systemic symptoms upon trivial skin contact with minute quantities of CM in infants or children [21-24]; no case has previously been reported in an adolescent.

Our case report raises two important considerations of general interest. First, the problem of "hidden" food allergens that may be ingested with many manufactured foodstuffs. Secondly, patients with a strong sensitization to food allergens and other peculiarities suggested by Tan et al. [22] (Table 2) are at high risk of developing severe allergic reactions through non-ingestant exposure to small amounts (such as those considered "hidden") of offending foods. In fact, with the exception of a strong family history of allergy, our patient shows all the peculiarities listed in Table 2.

In conclusion, our case report suggests that patients with a high degree of sensitization to CM proteins be alerted of the potential risk of developing severe symptoms upon skin contact with CM. Moreover these patients should also be aware that CM proteins can be "hidden" in many processed foods. Patients with a high

degree of sensitization to CM (and to other foods) should wear a Medic Alert bracelet and carry an epinephrine (adrenaline) self injector at all times [11]. Individuals with lower sensitization may need to carry antihistamines with them.

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