

Gelatin-containing sweets can elicit anaphylaxis in a patient with sensitization to galactose- α -1,3-galactose

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Clinical Implication

- Gelatin-containing sweets can elicit anaphylaxis in mammalian meat allergic patients. A warning regarding gelatin-containing foods and medical products should be included in recommendations for patients with IgE recognizing Galactose- α -1,3-Galactose.

TO THE EDITOR:

Galactose- α -1,3-galactose (α -Gal) is known to be the responsible allergen for delayed onset anaphylaxis 3 to 6 h after ingestion of mammalian food products.¹ Recently Mullins et al² detected α -Gal in meat-derived gelatin. With correlation of gelatin skin testing and anti- α -Gal IgE measurements a strong relation to red meat anaphylaxis was shown. It was hypothesized that α -Gal is one of the targets of reactivity to gelatin.²

Recently, we were able to examine the clinical relevance of meat-derived gelatin in food in 1 of our 21 patients with diagnosed red meat anaphylaxis. This 58-year-old hunter had presented with a 10-year history of episodes of anaphylaxis (flush, urticaria, hypotension, diarrhea) during night time after consuming meat and entrails from beef, pork, and game. The most severe reactions started <3 hours after eating entrails. Anaphylaxis after consumption of meat was regularly associated with symptoms that started 3 to 8 hours after eating and brought on by exercise. Remarkably, the patient reported multiple tick bites with persisting local reaction.³ Prick-to-prick skin testing of pork meat, pork kidney, and beef kidney was reactive (Table I). Laboratory measures showed an elevated total IgE of 595 kU_A/L and a specific IgE to pork of 4 kU_A/L, to beef of 4.3 kU_A/L, and to α -Gal of 29.2 kU_A/L (ImmunoCAP; Phadia GmbH, Freiburg, Germany). Baseline levels of tryptase were elevated on 3 occasions (12.6–16.1 μ g/L; normal range, <11.4 μ g/L), but no cutaneous mastocytosis was detected, and bone marrow biopsy showed no histologic signs for systemic mastocytosis.⁴ During 1 episode of anaphylaxis tryptase was further elevated to 82.7 μ g/L. To assess the patient's individual risk, oral challenge tests were performed: The consumption of cooked pork kidney (12 g and 36 g separated by 2 hours) elicited a severe and therapeutically difficult to manage allergic reaction that included diarrhea and urticaria lasting for 8 hours within 1.5 hours after the last portion of pork kidney. Twenty hours after this reaction occurred, elevation of serum tryptase to 28.9 μ g/L was detected. After consumption of grilled beef (350 g), mild self-limiting, generalized urticaria occurred 7.5 hours later. In contrast, after ingestion of grilled pork (350 g), no allergic symptoms were detectable. However, provocation tests with grilled pork (350 g) in combination with physical exercise on a bicycle ergometer (70 W for 20 minutes; 60 minutes after eating) elicited urticaria

TABLE I. Skin testing of meat, kidney, gelatin-containing gums (Haribo) and bovine gelatine-derived colloid (GelaFundin 4%) in a patient with sensitization to galactose- α -1,3-galactose

	Test result	Wheal (diameter)	Erythema (diameter)
Prick-to-prick meat & gelatin			
Histamin	++	4 mm	10 mm
NaCl 0.9%	-	1 mm	0 mm
Pork	++	4 mm	6 mm
Pork kidney	+++	10 mm	13 mm
Beef	-	1 mm	0 mm
Beef kidney	++	5 mm	10 mm
Gums (Haribo)	-	1 mm	0 mm
GelaFundin 4%	-	1 mm	0 mm
Intracutaneous test gelatin			
Histamin	++	15 mm	31 mm
NaCl	-	3 mm	0 mm
GelaFundin 4% (1:100 dilution, NaCl)	+	12 mm	27 mm

5 hours later, showing the role of exercise in the induction of delayed type I allergic reactions.^{5,6}

In addition to his severe reactions to red meat, our patient also complained of recurring dizziness, abdominal pain, and diarrhea with delayed onset after ingestion of his favored sweets (gums with pork-derived gelatin; Haribo GmbH & Co KG, Bonn, Germany). Prick-to-prick skin testing of gelatin-containing gums (Haribo) and bovine gelatin-derived colloid GelaFundin 4% (B. Braun, Melsungen, Germany) was not reactive, but additional intracutaneous testing with a 1:100 dilution of GelaFundin 4% was (Table I). Specific IgE to gelatin (0.04 kU_A/L) was not detectable. Next, an oral challenge test was performed. Within 60 minutes, the patient consumed 250 g of gelatin-containing Haribo gums (most likely corresponding to about 30 g of gelatin), followed by physical exercise 60 minutes later (70 W for 20 minutes) on a bicycle ergometer. About 10 hours after eating, flatulence and abdominal cramps began, which were followed by flushing, tachycardia, and diarrhea after 11.5 hours. Important to note, physical exercise on its own was always tolerated by the patient and in 4 healthy controls, consumption of the same 250 g of gelatin-containing sweet gums (Haribo) failed to elicit any intestinal discomfort or allergic reactions. As a consequence, the patient was advised to ban gelatin in his diet, leading to complete remission of periodic abdominal pain and diarrhea. In addition, a strict warning about the application of gelatin colloids was included into the patient's anaphylaxis emergency card. After the patient had removed all mammalian products from his diet baseline tryptase levels declined to 9.9 μ g/L (<11.4 μ g/L), indicating that previous to this diet tryptase levels were likely elevated because of IgE-dependent mast cell stimulation.

Our observations show that gelatin-containing sweets can elicit type I allergic symptoms in patients sensitized to α -Gal. In our opinion it is important to include a general warning about gelatin-containing foods and medical gelatin products into diet recommendations for patients with anaphylaxis to red meat and

disease-specific anaphylaxis emergency cards. Especially, an intravenous application of gelatin colloid as volume substitute could endanger patient's lives.² In case of a nongastrointestinal application, anaphylaxis will not be delayed, but rather occur within minutes. On the basis of the course of the oral challenge tests, especially the time points of elicitation, we assume that minimal amounts of gelatin in food or in medical products, for example, in capsules or pills, are unlikely to cause severe allergic reactions, but further analysis is warranted. Our investigations confirm and extend the studies by Morisset et al⁷ which show that the concept of food-dependent exercise-induced anaphylaxis is relevant for the understanding of red meat anaphylaxis. In our opinion individual risk assessment with oral challenge tests can offer valuable information for the allergologic guidance of these patients.

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