



Correspondence Clinical Letters

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Urticaria and angioedema after consumption of red meat

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Dear Editors,

In recent years increasing numbers of cases of delayed anaphylactic reactions after consumption of beef, pork and lamb have been reported, especially from the Southeastern USA. Typically the patients had tolerated these meat types for years without problems. These patients not only have elevated specific IgE antibodies against red meat, they also have IgE antibodies towards galactose- α -1,3-galactose (α -Gal), an oligosaccharide that is typically expressed in glycoproteins and -lipids of mammals with the exception of primates [1].

A 47-year-old man first presented in November 2010 with a history of several episodes of generalized urticaria with difficulty in breathing 4–6 hours after consumption of raw and grilled pork as well as pork kidneys. He developed similar symptoms after consumption of beef and lamb. Poultry was tolerated without problems.

The immunoassay revealed type I sensitizations to pork (CAP 4), beef (CAP 4) and lamb (CAP 3). As a striking connection of the symptoms with the consumption of red meat existed, specific IgE antibodies against galactose- α -1,3-galactose were determined and found to be highly positive with > 100 kU/l (CAP 6) (Table 1). The skin prick test with fried, homogenized pork and lamb as well as pork kidneys was positive (Table 2). In addition, the intradermal test with the colloidal volume replacement solution Gelafusal 4 % (gelatin polysuccinate in Ringer acetate), a derivative of bovine collagen, that also contains α -Gal was positive (Table 3). Foodstuffs containing gelatin have to date always been tolerated by the patient. He received a medical alert card and an emergency kit. He was informed that due to the danger of anaphylaxis he must refrain from the consumption of red meat, not receive volume replacement solutions containing gelatin during surgery or emergency situations and that he has a potential risk of anaphylaxis after consumption of foodstuffs containing gelatin. As gelatin has diverse uses in the food industry, he was instructed to always carry an emergency kit. At a later visit the patient reported that he was not willing to limit his meat consumption. In order to prevent symptoms after pork consumption he had taken shortly before eating Fexofenadin in a self-experiment. After several hours hives appeared, but he had no difficulty breathing. The lack of adherence to therapy by the patient demonstrates the general dilemma between physician's recommendations

Table 1 The patient's allergen-specific IgE against different kinds of meat, gelatin and galactose- α -1,3-galactose (α -Gal).

Total IgE	949.0 kU/l	
Specific IgE galactose- α -1,3-galactose (α -Gal)	> 100 kU/l	CAP 6
Specific IgE pork	25.7 kU/l	CAP 4
Specific IgE beef	29.3 kU/l	CAP 4
Specific IgE lamb	5.3 kU/l	CAP 3
Specific IgE chicken	< 0.1 kU/l	CAP 0
Specific IgE duck	< 0.35 kU/l	CAP 0
Specific IgE gelatin	< 0.1 kU/l	CAP 0

Table 2 Skin prick test with homogenized, fried meat.

	20 minutes Wheal/erythema
Histamine	5 mm / 7 mm
NaCl 0.9 %	0 mm / 0 mm
Pork	3 mm / 4 mm
Pork kidney	4 mm / 20 mm
Beef	1 mm / 2 mm
Lamb	3 mm / 6 mm
Chicken	0 mm / 0 mm

Table 3 Skin prick test and intradermal test with Gelafusal 4 % infusion solution (contains gelatin of bovine origin).

Prick test	20 minutes wheal/erythema
Histamine	5 mm / 7 mm
NaCl 0.9 %	0 mm / 0 mm
Gelafusal 4 % (pure)	0 mm / 0 mm
Intradermal test	20 minutes wheal/erythema
Histamine	20 mm / 30 mm
NaCl 0.9 %	0 mm / 0 mm
Gelafusal 4 % (pure)	15 mm / 40 mm
Gelafusal 4 %/NaCl 0.9 % (1 : 10)	10 mm / 30 mm
Gelafusal 4 %/NaCl 0.9 % (1 : 100)	5 mm / 10 mm

and patient reality. The patient was again informed that consumption of red meat and particularly of entrails, especially pork kidneys, could have fatal consequences even in small amounts, as was recently reported by Morisset et al. [2].

Foods are frequent triggers of anaphylactic reactions, that are usually mediated by IgE and usually occur within 5–30 minutes, sometimes even up to 2 hours later (immediate-type reaction). The delayed anaphylactic reactions due to red meat can be explained by the time required for digestion. Degradation products containing α -Gal are presumably liposoluble. Via VLDL and chylomicrons they reach the lymphatics and subsequently the general circulation. In contrast, water-soluble allergens enter the circulation directly [3].

In many patients in the Southeastern USA anaphylactic reactions to red meat developed only after tick bites. The bite of the tick *Amblyomma americanum* has been shown to induce the production of specific IgE against α -Gal [4].

Specific IgE against α -Gal also plays a role in anaphylactic reactions towards cetuximab, a recombinant chimeric IgG1 monoclonal antibody towards the EGF receptor that is employed in the treatment of colon and squamous cell carcinomas of the head and neck. Even during the first administration, severe anaphylactic reactions can occur that are attributed to preformed antibodies against galactose- α -1,3-galactose. α -Gal is found in the Fab portion of the heavy chain of cetuximab [5].

Mullins et al. were able to show that colloidal volume replacement solutions containing gelatin derived from bovine collagen contain α -Gal. They demonstrated that most patients with allergy to red meat also are sensitized to gelatin and that a subgroup of these patients reacts allergically to both [6]. In medicine they play a role especially in surgical and emergency situations. Patients with α -Gal-dependent allergy towards red meat should not receive volume replacement solutions containing gelatin due to the danger of anaphylaxis. This must also be included in the medical alert card.

α -Gal is the first oligosaccharide for which clinically relevant IgE-mediated anaphylactic reactions have been reported. It has long been assumed that immediate-type reactions are mainly directed against proteins. Many specific IgE antibodies against carbohydrate side chains of proteins are known, but no clinically relevant anaphylactic reactions have been attributed to these CCDs. Thus the delayed anaphylactic reactions towards the oligosaccharide α -Gal result in an altered understanding of our immunologic clash with car-

bohydrates. In the future this may possibly lead to the identification of “new” allergens [7].

Conflict of interest

None.

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