

Clinical Communications

α -Gal—a new clue for anaphylaxis in mastocytosis

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Clinical Implications

- Anaphylactic reactions based on food allergy in patients with systemic mastocytosis have been rarely described. Here, we present the first case of galactose- α -1,3-galactose-associated anaphylaxis in a patient with co-occurring indolent systemic mastocytosis.

TO THE EDITOR:

Mastocytosis is a disease defined by an accumulation of mast cells in the skin and/or internal organs.¹ Clinical symptoms in allergic patients with mastocytosis have been described as more severe than those in allergic patients without mastocytosis.² The coexistence of indolent systemic mastocytosis and anaphylactic allergic reactions due to hymenoptera venom is often described, whereas anaphylactic reactions based on food allergy in patients with systemic mastocytosis are rarely reported.^{2,3} Here, we present the first case of galactose- α -1,3-galactose (α -gal)-associated anaphylaxis in a patient with co-occurring indolent systemic mastocytosis.

A 47-year-old patient presented with more than 10 recurrent severe anaphylactic reactions during the last 4 years. The patient could not identify a common trigger. KIT D816V-positive indolent systemic mastocytosis was diagnosed in 2011 by bone marrow biopsy (with aberrant coexpression of CD25). Urticaria pigmentosa and signs of atopic diseases were absent. The patient did not take any medication. The baseline tryptase level was measured as 25.1 μ g/L (norm: <11.4 μ g/L). A typical reaction occurred several hours after a meal and manifested as palpitations, dyspnea, and shivering. The most recent reactions occurred after a steak dinner, respectively, muesli and greaves on a slice of dark bread.

Skin prick tests with commercial extracts (Allergopharma, Reinbek, Hamburg, Germany and ALK-Abelló A/S, Hørsholm, Denmark) of standard food, spices, and grains were performed as well as prick and/or scratch tests with native pork kidneys and Gelafundin (a gelatin-based volume expander) and an intradermal test with Gelafundin (dilution used for prick test 1:1, for intradermal test 1:10). The levels of specific IgE to meats, grains, and α -gal (ThermoFisher Scientific, Waltham, Mass) were measured. In addition, basophil activation tests (Flow CAST, Bühlmann Laboratories AG, Switzerland) with pork kidney and cetuximab and oral provocation tests (OPT) with gluten, gluten plus cofactor (physical training), and pork kidney were performed.

The skin prick tests with commercial extracts were negative. An intradermal test with Gelafundin yielded a positive reaction (4 mm $\times$ 6 mm). Specific IgE antibodies to beef and pork were measured with 0.51 kU/L and 0.43 kU/L, respectively. Moreover, the specific IgE to α -gal was 1.68 kU/L. No further elevation of specific IgE antibodies was detected. Basophil activation tests with pork kidney (89.1% at a concentration of 10 μ g/mL) and cetuximab (76.5% at a concentration of 5 μ g/mL) were positive. In the OPT, the patient showed no reaction to a cumulative dose of 60 g gluten and gluten plus cofactor (physical training). In contrast, 30 minutes after ingestion of 3 g of pork kidney (the lowest dose of the 3 planned doses), the patient developed a generalized flush and was sweating. Moreover, the patient's tryptase level was 47.2 μ g/L at 0.25 hours after the reaction compared with 25.1 μ g/L before OPT. Although the patient was treated immediately (dimetindene 8 mg i.v., prednisolone 200 mg i.v.), a second episode of an allergic type I reaction appeared 1 hour later (including flush, palpitation, dyspnea, hypotension, and a decline in peripheral oxygen saturation). At this time, the treatment included 0.6 mg epinephrine i.m. to stabilize the patient's condition.

In 2008, Platts-Mills et al⁴ disclosed the underlying cause of allergic reactions during the first application of cetuximab and simultaneously found that the responsible specific IgE to α -gal was associated with a new form of food allergy. α -Gal is a carbohydrate present in mammalian cells, except in humans and Old World monkeys. Thus, this carbohydrate may cause allergic reactions because of its immunogenicity in humans.⁵

Specifically, red meat and its derived products contain α -gal. Thus, the consumption of red meat and innards can result in IgE-mediated anaphylaxis.⁴ In 2011, Commins et al⁶ identified tick bites as the primary cause of IgE antibody responses to α -gal.

Our patient did not remember any tick bites in the past, but he did report frequent work in the forest. In his medical history, he described allergic reactions several hours after the ingestion of red meat, but showed anaphylaxis only 30 minutes after OPT with 3 g of pork kidney, which is approximately one-fiftieth of a traditional kidney meal. In 2014, Commins et al reported on 10 patients who had positive open food challenge tests with mammalian meat. Each reaction began at least 150 minutes after the consumption of mammalian meat (150 g of pork sausage consumed as a single dose).⁷ In contrast, Morisset et al⁸ described 1 patient who tolerated mammalian meat but experienced anaphylactic shock after ingesting only 2.1 g of pork kidney. Until recently, the largest group of patients with a history of at least 1 allergic reaction to pork kidney was examined in Germany (n = 25). Among these patients, 35 OPT were performed in 4 patients with exclusive pork-kidney allergy and in 4 patients with additional red meat allergy. The conclusions of the study were that (1) pork kidney elicits red meat allergy more consistently compared with muscle meat; (2) consequently, patients who also react to muscle meat may be at higher risk because much lower levels of accessible α -gal may trigger red meat allergy in these patients; and (3) subgroup analyses showed a shorter delay in the appearance of allergic reactions in these patients.⁹

Higher amounts of α -gal determinants in the kidney compared with meat may explain why some patients react only after kidney ingestion and why symptoms generally occur with a shorter delay than that of previously described anaphylactic reactions to mammalian meat.⁸ The occurrence of allergic symptoms in our patient shortly after the ingestion of kidney is consistent with the data obtained by Morisset et al,⁸ who reported anaphylaxis with a delay ranging from 10 minutes to 5 hours after kidney ingestion, and Fischer et al,⁹ who described that patients with hypersensitivity to both pork kidney and red meat (n = 11) reacted earlier than patients with hypersensitivity only to pork kidney. Thus, we concluded that the allergic reaction observed in our patient is related to α -gal sensitization.

The presence of a second episode of an allergic reaction despite previous medical treatment may be explained by the underlying systemic mastocytosis. In this case, symptoms are the result of a massive release of mast cell mediators and range from mild symptoms, such as pruritus and flush, to life-threatening symptoms, such as anaphylaxis.⁴

Our report underlines the importance of also considering rare triggers, such as food allergens, and even an underlying allergy to α -gal as a potential cause of anaphylaxis in patients with systemic mastocytosis. We recommend screening for α -gal allergy in patients with systemic mastocytosis and episodes of anaphylaxis.

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