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Anaphylaxis triggered by alpha-gal allergy

SHORT CASE REPORT

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Background
Alpha-gal allergy or red meat allergy is a rare yet potentially severe allergy. Sensitisation usually occurs when alpha-gal present in the tick's saliva is transferred to humans during a tick bite, prompting the production of IgE antibodies to alpha-gal. Subsequent exposure to mammalian meat or other products containing alpha-gal can lead to allergic reactions.

Case presentation
A previously healthy man in his sixties was admitted with acute anaphylaxis. A history of multiple tick bites and recent consumption of mammalian meat raised suspicion of anaphylaxis caused by alpha-gal syndrome.

Interpretation
A diagnosis of alpha-gal syndrome was given based on elevated alpha-gal IgE antibodies, and further supported by medical history and clinical assessment. He was discharged with dietary instructions to eliminate food and products containing alpha-gal, and to manage allergy symptoms and anaphylaxis according to local guidelines.

This case report describes a case of anaphylaxis triggered by an alpha-gal allergy. Anamnestic information about the combination of previous tick bites and recent consumption of red meat was crucial for supplementary blood testing and correct diagnosis.

A previously healthy man in his sixties was admitted to hospital in late summer with acute anaphylaxis. Late in the evening he developed a generalised, pruritic rash, and about 30 minutes later, his lips became swollen. He contacted his local emergency medical communication centre, and an ambulance with a doctor was dispatched. Upon arrival, he had a pulse of 129 beats/min, blood pressure of 88/56 mmHg, temperature of 36.5°C, and mild respiratory distress, with a peripheral oxygen saturation of 90 % on room air. He had no known atopic diseases or previous allergic reactions. He stated that two months earlier he had received over 20 tick bites during a walk in the woods. They had itched, but there had been no rash around the bite sites. The clinical picture was assessed as anaphylaxis of unknown cause. He was given intravenous fluid,

oxygen supplementation, a total of 0.6 mg of intramuscular adrenaline, 10 mg of dexchlorpheniramine and 250 mg of intravenous hydrocortisone, with a stabilising effect. After arrival at the hospital, he remained stable and was admitted for observation until the next day.

Serum tryptase tests were performed, which showed a typical anaphylactic rise and fall pattern; s-tryptase was 14.2 µg/L (reference range < 12) on admission and 9.8 µg/L the following day. Total IgE level was elevated to 1801 kU/L (2–297). The patient's detailed medical history revealed that his diet was mainly plant-based, but approximately three hours before the acute event, he had eaten red meat in the form of beefburgers. This, together with the information about recent multiple tick bites, raised the suspicion of an alpha-gal allergy, and additional blood tests were performed. These showed specific galactose-alpha-1,3-galactose IgE antibody level > 100 kU/L (< 0.35) as well as antibodies to mammalian meat: IgE for lamb 1.13 kU/L (< 0.35), IgE for beef 14.1 kU/L (< 0.35) and IgE for pork 3.86 kU/L (< 0.35).

Based on clinical findings and biochemistry, the patient was diagnosed with anaphylaxis caused by alpha-gal allergy following the consumption of red meat. He was discharged with an adrenaline auto-injector and antihistamines, along with information on complete elimination of mammalian meat and gelatine-containing products from his diet until follow-up at the Regional Centre for Asthma, Allergy and Hypersensitivity. At an outpatient check-up two months later, he had persistent urticaria, and it emerged that he was still consuming alpha-gal in the form of fatty dairy products. Since eliminating these from his diet, the patient has been symptom-free. He will continue to require annual outpatient checks, including a medical history review and measurement of alpha-gal IgE levels. Reintroduction of mammalian meat will then be considered. It is not possible to predict whether he will be able to eat red meat again.

Discussion

Alpha-gal allergy, or alpha-gal syndrome, is a rare but potentially severe IgE-mediated allergy to the carbohydrate galactose-alpha-1,3-galactose (alpha-gal); an oligosaccharide present in mammalian lipids and proteins. Primary sensitisation occurs during a tick bite when the tick's saliva – which contains alpha-gal – is transferred to humans, triggering the production of IgE antibodies to alpha-gal. The production of alpha-gal IgE usually peaks after 4–6 weeks. Upon subsequent exposure to mammalian meat or other products containing alpha-gal, such as dairy products, gelatine and certain medicines, an allergic reaction can occur (Figure 1) (1). Treatment involves eliminating foods and products containing alpha-gal; poultry, fish and shellfish are generally tolerated. Patients should be trained in what to do and equipped with an adrenaline auto-injector, and other allergy symptoms should be treated as normal. Patients in Norway who have experienced anaphylaxis should be referred for evaluation at the Regional Centre for Asthma, Allergy and Hypersensitivity in their local health region.

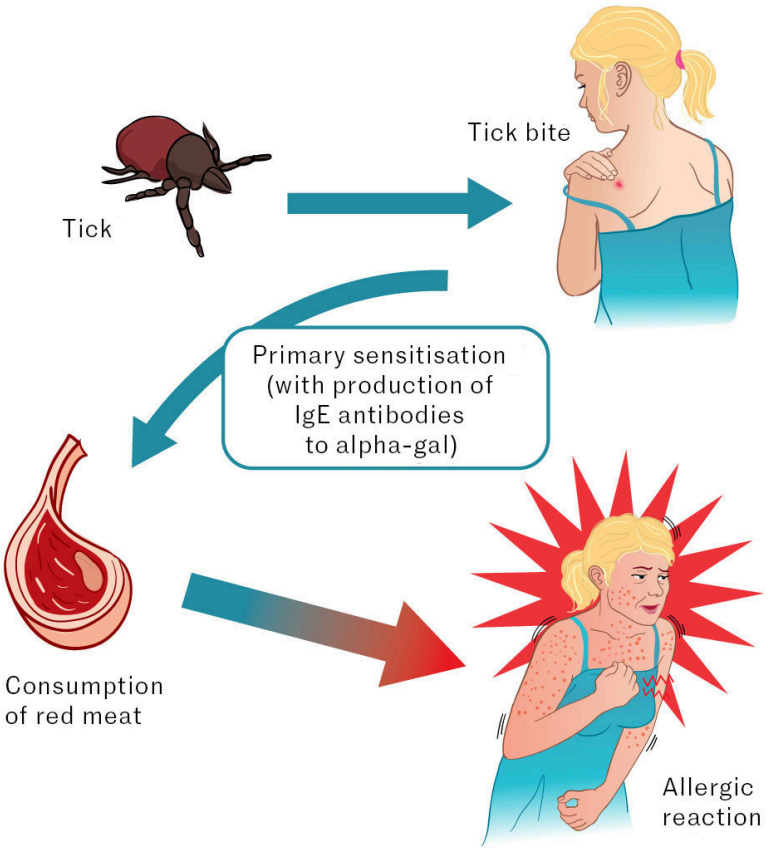

Figure 1 Primary sensitisation occurs during tick bites when the tick's saliva, which contains alpha-gal, is transferred to humans, triggering the production of IgE antibodies to alpha-gal. Upon subsequent exposure to mammalian meat or other products containing alpha-gal, an allergic reaction with typical IgE-mediated allergy symptoms, and potentially anaphylaxis, can occur. Illustration: Jeanette Engqvist / Illumedic

The relationship between the alpha-gal allergy and tick bites was first described in 2009 (2), but the condition is probably underdiagnosed as many clinicians are not yet familiar with the diagnosis. Several species of ticks are associated with alpha-gal allergy, including the castor bean tick (*Ixodes ricinus*) found in Norway (3). Despite tick bites being a common occurrence, only a small number of recipients will develop an alpha-gal allergy. It is unclear why only certain people develop the allergy. We know from clinical experience that sensitised individuals typically exhibit prolonged itching and redness around the tick bite. In contrast to most other IgE-mediated food allergies, an allergic reaction caused by alpha-gal can have a symptom onset in which typical IgE-mediated allergy symptoms (systemic itching, urticaria, angioedema and/or abdominal pain, and possibly anaphylaxis) first appear 2–8 hours after consuming mammalian meat (4, 5). Some people only experience gastrointestinal symptoms, which can be misinterpreted as conditions other than rapid-onset IgE-mediated allergy. Our patient's clinical anaphylaxis was confirmed in serum tryptase tests. A rise in tryptase is significant if the patient's baseline increases by 20 % + 2 µg/L, measured 1–4 hours after the

allergic reaction. This has a positive predictive value of 98 % and is the gold standard for biochemical differentiation of anaphylaxis from similar clinical conditions. The baseline can be measured after 12 hours, but after 24 hours is preferred (6). Factors such as alcohol intake, physical activity and various medications can lower the threshold and increase the severity of an allergic reaction in sensitised individuals (7). The diagnosis is based on the detection of serum-specific alpha-gal IgE antibodies along with a typical medical history and clinical findings. In some cases, skin prick tests and oral provocation tests with red meat are also performed, but these tests can be flawed. In cases of clinically probable alpha-gal allergy, such as in our patient, specific alpha-gal IgE > 1 % of total IgE has been shown to closely correlate with clinical allergy. No red meat provocation tests were performed on our patient as his clinical anaphylaxis, typical medical history and level of specific alpha-gal IgE were considered sufficient to diagnose alpha-gal allergy.

Asymptomatic sensitisation to alpha-gal is common, and only patients with allergic reactions to mammalian meat should cease consumption of this. The level of IgE against alpha-gal usually decreases if future tick bites are avoided, but it is unclear how much IgE levels need to fall before consumption of mammalian meat can be resumed (5). Some patients eventually experience declining and non-detectable levels of specific IgE to alpha-gal and can thus reintroduce red meat to their diet (8). This should be done in consultation with an allergist. In terms of exposure to alpha-gal-containing wound products, biological heart valves and medications, there is more uncertainty about when re-exposure is safe.

The patient has consented to publication of this article.

The article has been peer-reviewed.

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