



Case Report

A tick-acquired red meat allergy



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ABSTRACT

Allergic reaction is a common clinical picture in the Emergency Department (ED). Most allergic reactions are from food or drugs. A detailed history is an integral aspect of determining the causative agent of an allergy. Galactose-alpha-1,3-galactose (alpha-gal) allergy is a tick-acquired red meat allergy that causes delayed-onset allergic reaction or anaphylaxis due to molecular mimicry. Alpha-gal allergy may not be widely known as a cause of allergic reactions. Lack of universal awareness of this phenomenon in the ED and Urgent Care setting could lead to misdiagnosis, or delayed diagnosis. Subsequently, lack of proper instruction to avoid red meat could put patients at risk for future attacks with morbidity or mortality. We report three cases of allergic reaction presumed from red meat consumption secondary to alpha-gal allergy.

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1. Introduction

An allergic reaction is a common bodily response to contact with an allergen. Allergens are usually harmless substances that trigger an immune response. Examples of common allergens include food, dust, pollen or medications. Allergic reactions can be mild upon first exposure to the offending agent, but serious and life-threatening reactions may occur. Anaphylaxis, an extreme clinical form of allergic reaction, is responsible for 500,000 Emergency Department (ED) visits annually [1]. Prompt recognition of the offending agent is integral to a successful management plan for patients suffering from this acute, systemic reaction. Failure to do so can put the patient at risk, as avoidance measures must be put in place to prevent recurrence of allergic reaction or anaphylaxis whenever applicable (e.g. discontinue medication, avoid food items and avoid using cloths and perfumes).

Galactose-alpha-1,3-galactose (alpha-gal) allergy, also known as Mammalian Meat Allergy (MMA), is a tick-acquired red meat allergy that causes delayed-onset allergy or anaphylaxis. This phenomenon was first described in the Journal of Allergy and Clinical Immunology in 2009 [2]. Flaherty et al. reviewed 28 patients with alpha-gal allergy, and found that many patients discovered their diagnosis on their own [3]. Out of 28 patients with alpha-gal allergy, 6 were diagnosed within

a year of their first symptoms, and the remaining 22 were diagnosed on average 7.1 years after [3].

We report three cases of presumed alpha-gal allergy in patients with history of red meat consumption and allergic reaction with an elevated alpha-gal titer.

2. Case presentation

2.1. Case 1

An 8-year-old Caucasian male without significant medical history presented to an urgent care center with a one week history of intermittent diffuse urticarial rash. The rash appeared on his face, chest and arms. The patient denied trying new foods, or using any new skin products, but he had eaten red meat multiple times during the week, including at a barbecue. His family mentioned that he recently became an avid camper over the past year, and reported a history of remote tick bite 10 months prior to presentation. The patient denied shortness of breath, cough, chest pain, wheezing, drooling or hoarseness. The remaining review of systems (ROS) was unremarkable. Vital signs were as follows at presentation: blood pressure (BP): 102/58 mm Hg, heart rate (HR): 58 beats per minute (bpm), respiratory rate (RR): 12 breaths per minute, Temperature (Temp.): 97.7° Fahrenheit (F). Physical examination was unremarkable except for the rash. The patient was given Zyrtec for his symptoms. A blood sample was sent out and revealed positive titers

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for immunoglobulin (Ig) E antibodies against alpha-gal (49.6 kU/L, normal range < 0.35 kU/L). The patient was advised to avoid red meat, and to follow up with his pediatrician.

2.2. Case 2

A 57-year-old Caucasian female with no history of atopy presented to an urgent care center with intermittent abdominal bloating and pain over the past three months. Her symptoms progressively worsened during this time period. She also complained of intermittent rash over the past three years. The patient denied trying new foods, or using any new skin products, but has eaten red meat several times during this period. The patient denied shortness of breath, cough, chest pain, wheezing, drooling or hoarseness. The remaining ROS was unremarkable. Vital signs were as follows: BP: 128/84 mm Hg, HR: 63 bpm, RR: 14 breaths per minute, Temp.: 98.2 °F. Physical examination including gynecological examination was unremarkable. At the time of the visit, no rash was present, but the patient revealed pictures of macular lesions on her hands and torso. She states that taking Benadryl is helpful when the rash appears. The patient was given Zyrtec. A blood sample was sent out and revealed positive IgE antibody titers against alpha-gal (14.0 kU/L). The patient was advised to avoid eating red meat. After two years of abstinence from red meat, repeat laboratory results showed a decreased IgE antibody level of 1.02 kU/L. The patient still occasionally feels itchy with beef consumption.

2.3. Case 3

A 64-year-old Caucasian female with no history of atopy presented to an urgent care center with new-onset urticaria. The patient denied trying new foods, or using any new skin products, but does eat red meat. Her history is significant for living in a region endemic to ticks, and getting bitten by an unknown bug recently on her right buttocks. The patient denied shortness of breath, cough, chest pain, wheezing, drooling or hoarseness. The remaining ROS was unremarkable. Vital signs were as follows: BP: 130/80 mm Hg, HR: 67 bpm, RR: 12 breaths per minute, Temp.: 98.2 °F. Physical examination including gynecological examination was unremarkable. The patient was given Zyrtec for her symptoms. A blood sample was sent out and revealed positive IgE antibody titers against alpha-gal (16.7 kU/L). The patient was advised to avoid eating red meat. Repeat laboratory testing after six months of abstinence from red meat showed a decreased IgE antibody level of 9.96 kU/L.

3. Discussion

Alpha-gal allergy is a fairly new phenomenon of importance. There are two distinct forms of this allergy: the first is an immediate-onset anaphylaxis observed following intravenous infusion of Cetuximab, a monoclonal antibody against epidermal growth factor receptor, and the second is a delayed-onset allergy or anaphylaxis 3–6 h following consumption of red meat in connection with a tick bite.

In a retrospective analysis of the 2004 clinical trials of Cetuximab, Maier et al. suggest that infusions of Cetuximab resulted in anaphylaxis in patients [4]. Additional studies have shown that patients with systemic infusion reactions (SIRs) in response to Cetuximab were also having allergic reactions to red meat, and that these patients were mainly distributed along the Southeast United States where many tick-borne illnesses are endemic [5–7]. Chung et al. found that these reactions were due to pre-existing IgE antibodies to alpha-gal, an oligosaccharide found both on the Fab portion of the Cetuximab molecule and in red meat [8]. The presumed pathophysiology is the production of antibodies against a protein in the Lone Star Tick's saliva that resembles alpha-gal. Due to molecular mimicry, consuming red meat or being infused by Cetuximab will cause allergic reaction [9].

Although the incidence of tick-acquired red meat allergy is not well described in the literature, the Centers for Disease Control and Prevention (CDC) suggests an increasing distribution of the lone-star tick following that of the white-tailed deer population. Consequently, this phenomenon should be more closely examined in the upcoming years. Due to minimal awareness of tick-acquired red meat allergy, a patient presenting with this condition is likely to be underdiagnosed, if not misdiagnosed. One diagnostic challenge is limited historical account of tick exposure or previous history of allergic symptoms [7]. In addition, patients presenting with these symptoms may visit different emergency departments or Urgent Care facilities. This lack of continuity of care may contribute to further delay of a proper diagnosis. Delayed diagnosis of the patient could lead to continued consumption of red meat, which risks repeated clinical symptoms, including life-threatening anaphylaxis.

All three patients presented above reported having an intermittent rash and consuming red meat prior to their onset of symptoms, which may suggest that the rash was from the red meat. The diagnosis of alpha-gal allergy is likely in these patients, given their high IgE titers. In addition, all three patients stated that their symptoms stopped after abstaining from red meat, which further strengthens the diagnosis.

Increased awareness of alpha-gal allergy can promote detailed history taking that may lead to prompt diagnosis and proper management strategies in the future (e.g. avoidance of red meat and proper tick prevention). Although not very sensitive, there is a skin test available to assist in the diagnosis of alpha-gal allergy. The confirmatory blood test that measures IgE antibodies to alpha-gal is more accurate and may be performed in suspected cases. Raising awareness in the ED and Urgent Care setting may help physicians make challenging diagnoses and ensure proper management of patients. Individuals who were bitten by a tick can exhibit a high alpha-gal titer; however, the presence of a high titer alone does not clinch the diagnosis of red meat allergy. The combination of the clinical symptoms of allergic reaction in association with red meat consumption and a high alpha-gal titer effectively reflect the overall picture.

4. Conclusion

Alpha-gal allergy is an emerging phenomenon that requires attention. Emergency Medicine physicians, especially those who practice in endemic regions, should be cognizant of this tick-borne reaction and include it in their differential diagnosis for allergic reaction and anaphylaxis. It is important to properly diagnose these patients, as misdiagnosis could lead to recurrent symptoms with the potential for complications. Although point-of-care testing (POCT) with a 20 minute skin test may not be a feasible practice for all patients that present with allergic symptoms, this may be a useful test that can be used in patients that present in endemic regions with risk factors for alpha-gal allergy. If alpha-gal is suspected, confirmatory blood work with IgE antibody titers should also be performed. Clear discharge instructions should be given so that the patient understands what to avoid in order to prevent continued allergic reactions or future anaphylaxis.

Meetings

This work has not yet been presented.

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Conflicts of interest

No conflicts of interest.

Author contributions

Joe Kevin Khoury and Neil Christian Khoury contributed equally as joint first authors. Getaw Worku Hassen oversaw the planning, organization, and execution of the paper. Deborah Schaefer saw and diagnosed the patients mentioned in the case series. Anup Chitnis contributed by advising and giving critique.

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