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17th International Conference on ALLERGY AND CLINICAL IMMUNOLOGY

April 11, 2022 | Webinar

Allergy to galactose-alpha-1,3-galactose (Alpha-gal) update 2022

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Background: The story about Alpha-gal allergy in the United States starts with life-threatening allergic reactions to a cancer drug, which was later found to contain a mammal carbohydrate, Galactose-alpha-1,3-galactose (Alpha-gal). Significant overlap was observed between the location of known cases of allergy to Alpha-gal and cases of Rocky Mountain spotted fever and ehrlichiosis. These diseases can be transmitted by the tick species Amblyomma americanum (lone star tick). This led investigators to realize that in the United States, bites from the lone star tick triggered an allergic response to Alpha-gal, a carbohydrate present on mammals except humans and higher apes. The allergy can be caused by bites from adult and larval stage (seed) ticks. People who develop an allergy to Alpha-gal may have symptoms with exposure to red meat, mammal products, and certain medications (Platts-Mills, et al). Dr. van Nunen in Australia previously described an allergy to mammalian meat associated with tick bites and published a related article in 2009. Symptoms of allergic reactions to Alpha-gal range across most body systems, and vary from mild (e.g. rash, occasional headache, fatigue) to fatal (e.g. anaphylaxis, suicide from depression). In addition, many patients indicated that they are not getting better, despite months and even years of treatment. Others may after a period of latency, experience a return of symptoms, known in the medical literature as reactivation.

Methods: Literature review and review of abstracts from the 2022 AAAAI and WAO meeting in Phoenix, AZ.

Results: The saliva of certain species of ticks have been found to contain Alpha-gal. New research confirms the presence of Alpha-gal in the Lone Star Tick's saliva (Karim et al). Significantly, the study also reveals the presence of Alpha-gal in the saliva of the black-legged tick (Ixodes scapularis). The black-legged tick, which is heavily concentrated in the northeastern United States, is primarily known to transmit Lyme disease. The discovery that it may also transmit Alpha-gal has important implications for the diagnosis and treatment of patients for Lyme and other tick-borne diseases in the US. Both tick species are expanding their territory, and the reported cases of Alpha-gal allergy are expanding as well. Public comments often include the fear and frustration associated with this allergy, which is unique, it is more than just avoiding eating red meat, many people must worry about medications, products and cross-contamination which limits their daily lives. It is unclear how many people have Alpha-Gal Syndrome, but specimens in the United States from 105,674 persons were tested for Alpha-gal IgE during July 1, 2010, to December 31, 2018. Nearly one-third (34,256, 32.4%) had at least one positive result. (Armstrong et al) In a recent survey, the five most common reactants are beef, pork, dairy, gelatin (usually in medications), and personal care products. While 25% experienced reactions 4-6 hours after exposure, 7% also indicated reactions within 0-5 minutes. Exposure routes included ingestion, topical, and inhalation. Two-fifths of respondents have visited the ER due to reactions; 37% had 15+ reactions prior to diagnosis; and 25% still react once or more a month after diagnosis. The top autonomic (neurologic) symptoms include abnormal sweating and fainting. Over 60% reported anxiety. To learn how to prevent further reactions, 50% of patients get online support while 20% receive information from healthcare providers. (Platt and Merritt) Bianchi et al have developed a GalSafe pig that is FDA approved for human consumption in the United States.

Conclusions: The pathogenesis of reactions to Alpha-gal involves getting sensitized, or becoming allergic to Alpha-gal, and then the immune response after becoming allergic. In a recent paper from Dr. Iweala et al(6), the proposed immune mechanism for developing Alpha-gal allergy is described. During feeding, tick mouth parts induce physical trauma to the skin while introducing Alpha-gal, potentially disease-causing bacteria, and other particles that alter the immune response. This may trigger the production of cytokines that promote isotype switching from to IgE. The immune response to the tick saliva converts the antibody producing cells (B cells) in some people to switch to produce IgE, the allergy antibody.

Symptoms of food allergies differ significantly, depending on the immune mechanism involved and the affected target organ. (Davis et al) Severe symptoms include shortness of breath, wheezing and repetitive cough. Blood pressure may decrease, but in a subset of patients with Alpha-gal allergy, their blood pressure increases during a reaction (TBC United Survey). Some people with this allergy are extremely sensitive and report dizziness and even loss of consciousness with minimal exposure. Neurologic symptoms include feeling something bad is about to happen, anxiety, and confusion. Urticaria or hives are red, raised rash that itches, but some patients with Alpha-gal allergy report burning with the rash. Gut symptoms can be severe cramping pain, nausea, vomiting and severe diarrhea. Not everyone with this allergy has a life-threatening reaction. The symptoms of Alpha-gal allergy are usually delayed 3-6 hours after eating red meat or mammal ingredients such as gelatin (Commins). Another difficult factor is the level of allergy antibody against Alpha-gal does not always correspond with the level of reaction. A positive test result for IgE to Alpha-gal is greater than 0.10 kU/L.

Biography

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