Title: Innovative Desensitization Protocol for Mammalian Meat Allergy in alpha-Gal Syndrome: A Case Report

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Presenters: **Vaishnavi Parchuri, MD, Kaitlyn Knurek, BS, PharmD**
Additional: Rebecca Cino, PharmD, Joseph Reilly, BS, PharmD, BCGP, Manish Trivedi, MD

Abstract:
Individuals bitten by the lone star tick (Amblyomma americanum) may develop alpha-Gal syndrome (AGS), characterized by an IgE-mediated allergic reaction upon exposure to galactose- α-1, 3-galactose (α-Gal) found in mammalian meat. This meat contains the carbohydrate α-Gal and can elicit severe and potentially life-threatening reactions in patients with AGS. A report from the Centers for Disease Control indicates there have been more than 34,000 suspected AGS cases in the US identified between 2010 to 2018. This number appears to be rising annually, with a notable increase in positive α-Gal-specific IgE antibody test results. Currently, there is no recommended treatment for AGS with mammalian meat allergy (MMA), except to avoid ingestion and exposure to mammalian-based products. This report describes the case of a man with AGS and severe MMA who was successfully desensitized to meat utilizing a novel oral immunotherapy (OIT) protocol. Our subject was a 38-year-old male with no significant past medical history or allergies. He was bit by a lone start tick in Missouri in August 2024. He is an avid hunter, in good physical condition, and works as a home builder. He started having reactions to meat weeks after the tick bite. His first reaction occurred 3 hours after ingesting steak. The symptoms included severe abdominal pain, full body hives, and tightening of the throat. The patient had 4 subsequent reactions to meat products with symptoms ranging from abdominal pain, rash, changes in vision, dizziness, and difficulty breathing. He completed laboratory testing for an α-Gal IgE Panel in October 2024. The results of the panel showed that his total serum IgE was 985 IU/mL, and he had positive IgE antibodies specific to beef, pork, lamb, and α-Gal. Based on the lab panel, he was diagnosed with AGS. Investigators created a meat desensitization protocol utilizing concepts from other allergen OIT protocols. The patient was instructed to report any allergic symptoms and keep doses of diphenhydramine, famotidine, and an epinephrine injector on hand always. For the first 7 days, the patient initiated twice daily micro-dosing of a liquid meat broth prepared to provide 0.00025 mg (0.25 mL) and escalated to 0.004 mg (4 mL). The dosing was 6-7 hours apart throughout the desensitization period. Broth preparation consisted of boiling 6 mg of meat in 600 mL of water for 15 minutes. Then 10 mL of broth (0.01 mg/mL) was further diluted in 90 mL of water, for a final concentration of 0.001 mg/mL. The broth and measured meat doses were prepared in 7-day supplies and provided to the patient. On days 9-14, the patient changed to twice daily cooked meat doses ranging from 0.25 mg to 40 mg per dose in an escalating fashion. Days 15-21, the patient continued ingesting twice daily cooked meat starting at 60 mg and increasing to 1 g of beef. By day 28, the patient was consuming 2.8 oz of steak and switched to once daily dosing. He then transitioned

into a maintenance dose phase where he consumed 3 oz of steak, at least 3 times per week to help maintain tolerance, but was instructed not to ingest larger quantities of meat. He increased meat portions over time and tolerated servings exceeding 10 oz of steak. Our subject reportedly did not develop any significant reactions during the desensitization period. The success of this experimental protocol may help this patient avoid hospitalization related to hypersensitivity reactions that occur via cross-contamination, ultimately improving his quality of life. This is the second successful adult MMA desensitization completed with our protocol. Our success can potentially provide hope for those living with AGS and MMA where ingestion of α-Gal can result in severe or life-threatening reactions. Further examination of this novel treatment for patients with AGS would be prudent.