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Red Meat Allergy Associated with NSTEMI

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Abstract Alpha-gal syndrome, also known as mammalian meat allergy, is characterized by a hypersensitivity reaction to galactose-alpha-1,3-galactose. Reactions typically manifest hours after consumption of red meat products such as beef, pork, and lamb. We describe the case of a 64-year-old male resident of rural Oklahoma who presented with anaphylaxis and myocardial infarction. The patient suffered complications that were attributed to porcine-derived heparin in the setting of undiagnosed alpha-gal syndrome. We describe the clinical course of this patient that lead to the diagnosis of alpha-gal syndrome to raise awareness of this disease.

Keywords: *Alpha gal, mammalian meat allergy, heparin*

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1. Introduction

Alpha-gal syndrome, also known as mammalian meat allergy (MMA), is defined as a hypersensitivity reaction to galactose-alpha-1,3-galactose (alpha-gal). [1] This carbohydrate moiety, found in red meat such as beef and pork, is transferred to humans worldwide via ticks. Since its introduction to the literature, cases have now been reported in Australia, Europe, Africa, and Central America. [2,3,4]. In the United States, the allergy occurs most often in the distribution of Lone Star tick (*Amblyomma americanum*) in the central and southern states. [5,6] Exposure to alpha-gal through tick saliva results in formation of IgE antibodies to alpha-gal. Successive exposure to alpha-gal through red meat or red meat-derived products (either food or medications) causes crosslinking of IgE:IgE complexes on mast cells to secrete mediators that lead to symptomatology consistent with anaphylaxis [7,8]. In the majority of cases, anaphylaxis, urticaria and angioedema develop 3 to 6 hours after ingestion of red meat, unlike other IgE mediated reactions that occur 5 to 30 minutes after ingestion of the offending agent. [9] Bovine and porcine derived medications, such as heparin and gelatin, may be triggers for patients with MMA resulting in delayed urticaria, angioedema and anaphylaxis. [10]

2. Case Report

A 64-year-old male, with past medical history of noninsulin dependent diabetes mellitus and hypertension, was transported to the nearest hospital emergency department after paramedics were called to his home around 2:00 a.m.

Our patient awoke from sleep with shortness of breath and a rash. The patient's wife injected him with two epinephrine auto-injectors while awaiting paramedics.

He reported that this was his fourth occurrence of an allergic reaction in past five years. He had epinephrine auto-injectors at home for these recurrences, despite no diagnosis of a specific allergy trigger. On arrival to the emergency department, initial vital signs were blood pressure 81/53, pulse 120, respiratory rate 28, and oxygen saturation 92% on room air, 96.5^0F oral. In the emergency department, our patient complained of an itchy rash and shortness of breath. Physical exam was positive for diffuse urticaria and respiratory distress. He was treated with intravenous steroids, diphenhydramine, and non-invasive ventilation over several hours. Fourteen hours after admission, troponin-I increased to 2.08ng/mL (0.00-0.06 ng/mL), and he was transferred to a tertiary care center for cardiac evaluation. Upon arrival to the tertiary care facility, laboratory testing revealed elevated serum troponin-I of 2.60 ng/mL without changes on electrocardiogram. Intervals (QTc, QRS, PR) were within normal limits. An intravenous heparin infusion was started for non-ST-segment elevation myocardial infarction (NSTEMI), and the patient was stabilized in the intensive care unit. He subsequently underwent left heart catheterization and 3-vessel coronary artery bypass grafting (CABG) five days after presentation. Postoperatively, the patient developed atrial fibrillation with rapid ventricular response, and intravenous heparin was re-initiated for anticoagulation. Following reinstatement of intravenous heparin, the patient developed abdominal pain, and a small bowel ileus was found on CT abdomen and pelvis. Decompression via nasogastric tube did not alleviate the ileus. Consequently, our patient underwent small bowel resection for small bowel obstruction and bowel wall edema.

With anaphylaxis being the patient's presenting symptom, further laboratory testing was performed to

determine the etiology of his urticaria and bowel dysfunction. Serum analysis revealed the patient was grossly positive for IgE to galactose-alpha-1,3-galactose. All heparin products were discontinued, and fondaparinux was used for anticoagulation for atrial fibrillation. The patient had return of bowel function as well as improved pain and nausea with cessation of all heparin products. Laboratory results from the tertiary care hospital are summarized in Table 1.

Table 1. Pertinent Laboratory Results

Laboratory Assay	Result	Reference (units)
IgE to galactose alpha-1,3-galactose	>100	<0.35 KU/L
Beef allergen Beef ASM Class	16.40 Class 3	<0.35 KU/L Class 0
Pork Allergen Pork ASM Class	7.44 Class 3	<0.35 KU/L Class 0
Tryptase (off heparin)	4.7	<10.9
Complement C4	27	15-59 mg/dL
C1 Esterase Inhibitor	27	31-67 mg/dL
C1 Esterase Inhibitor Functional Assay	83%	>40%

3. Discussion

Alpha-gal allergy has an atypical presentation when compared to other food allergy syndromes. It commonly affects adults rather than children, and can manifest as urticaria, angioedema, and anaphylaxis. In addition, patients often complain of gastrointestinal upset. [1,7] These reactions are typically delayed, with manifestation usually occurring up to 3 to 6 hours after consumption of red meat. [11] In this case, the patient developed an anaphylaxis reaction at 2:00 a.m., hours after consuming a meal of red meat. It is thought that the time of absorption from the gut and cholesterol metabolism is responsible for the delayed response as alpha gal is present on both glycoproteins and glycolipids found in beef, pork, venison, and lamb. [11] This delay makes the diagnosis of MMA difficult; as patients will report prior tolerance for meat, and may not make the connection with a meal they had hours before. Poultry and fish do not have alpha-gal, and therefore do not precipitate a reaction. Following his episode of anaphylaxis, our patient developed a NSTEMI. It is possible the patient could have suffered from Type II Kounis syndrome in the setting of MMA. Kounis syndrome is defined as acute coronary syndrome triggered by the release of inflammatory mediators in the setting of an allergic reaction. Type I occurs in patients without coronary artery disease, and Type II occurs in patients with pre-existing atherosclerotic disease. [12] Following development of the patient's acute coronary syndrome, he was placed on a continuous heparin infusion. Currently, the literature is lacking to support heparin cross-reactivity with alpha-gal. However, this patient's clinical status markedly improved proved after cessation of continuous heparin infusion. A serum tryptase level was drawn 3.5 hours after stopping the heparin infusion, and resulted at 4.7ng/mL.

4. Conclusion

A high index of suspicion must be held for diagnosis of MMA. The diagnosis should be considered in patients living in the south central United States that have a history of recurrent hypersensitivity reactions. Specifically, MMA must be high on the list of differential diagnoses when patients develop hives in the early morning hours. As in this case, if the diagnosis had been made during one of his prior episodes, avoidance of red meat would have prevented this hospitalization.

Additionally, avoidance of porcine-derived heparin could have prevented a small bowel resection. Patients diagnosed with MMA should be advised to avoid all red meat, bovine or porcine derived medications, and always carry an epinephrine auto-injector. In clinical practice, the diagnosis can be confirmed with serum IgE specific to alpha-gal. [13]

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