Clinical Communications

Implications of a fatal anaphylactic reaction occurring 4 hours after eating beef in a young man with IgE antibodies to galactose-α-1,3-galactose

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Clinical Implications

- The circumstances of fatal anaphylaxis 4 hours after eating beef draw attention to the importance of understanding galactose-α-1,3-galactose syndrome, which includes the role of ticks, the severity of delayed attacks, and the wide variety of symptoms.

The recognition of galactose-α-1,3-galactose (alpha-gal) syndrome (AGS) arose from the availability of the assay for IgE to alpha-gal, which in turn arose from the investigation of severe reactions to the monoclonal antibody cetuximab.[1] The syndrome is now well recognized in many areas of the south but not in the areas where the tick is spreading.[2] We report here the first documented fatal case of AGS occurring after consuming mammalian meat. The authors shared the manuscript with the widow of the patient discussed here; she reviewed it with her family and gave consent for publication.

In the summer of 2024, a 47-year-old airline pilot with no significant past medical history went on a camping trip with his wife and children. After a day outside, they ate supper at 10:00 PM, including beef steak, which was unusual because the family typically ate chicken. The man awoke at 2:00 AM with abdominal discomfort, which became so severe that he was writhing in pain, having diarrhea and vomiting. After 2 hours, his condition improved, and he went back to sleep. In the morning, he felt well enough to walk 5 miles and then ate breakfast. Discussing the event with his wife, they considered consulting a doctor but concluded "what would we say happened?" On the other hand, he told one of his sons that during the episode "I thought I was going to die."

Two weeks later at home in New Jersey, he and his wife went to a barbecue where he ate a hamburger at approximately 3:00 PM. After going home, he mowed the lawn for an hour, but he still had no gastrointestinal symptoms when his wife left the house at 7:00 PM. At 7:20 PM, he went to the bathroom, and by 7:30 PM, their son was on the phone with his mother saying, "dad is getting sick again." Shortly thereafter he found his father unconscious on the floor of the bathroom with vomit around him; the son called 911 at 7:37 PM and initiated resuscitation. The paramedics continued resuscitation efforts for 2 hours, which included transferring the patient to hospital, but at 10:22 PM, he was declared dead.

The postmortem examination showed no significant abnormalities in the cardiac, respiratory, neurological, or abdominal systems, including on microscopic examination of the heart, right lung, and liver, as well as on cardiac pathology examination. Toxicology revealed blood ethanol of 0.049% and a diphenhydramine level of 440 ng/mL. The conclusion of the autopsy was "Sudden unexplained death." His wife wanted to know why her husband had died, and she asked her friend, Dr Erin McFeely, to review the autopsy report. They then contacted our group in Virginia to address the possible role of AGS and gave permission for the Medical Examiner's Office to send the postmortem blood to Virginia.

The blood was received on April 7, 2025, and was tested using ImmunoCAP for IgE to a range of allergens (Table I). The sample was positive for the seasonal allergens of rye grass and ragweed, which was in keeping with the presence of diphenhydramine in his blood. The total IgE was low, 16.7 IU/mL, and IgE to alpha-gal was 0.57 IU/mL; in addition, the IgE to beef was positive. This level of IgE to alpha-gal represents 3.4% of his total IgE, and values over 1% are generally regarded as relevant. The Mayo Clinic lab provides a specific test for postmortem tryptase (TRYPA), and the tryptase value was reported as >2000 ng/mL, a level that is in keeping with the highest values reported in sera from cases of fatal anaphylaxis (Figure 1).[5]

When asked whether he had tick bites, his wife replied, "yes, in the past, but none this year." On further questioning, she said that earlier in the summer he had 12 or 13 "chigger" bites around his ankles that left pruritic papules. In the eastern United States, what are often called "chiggers" are more often larvae of *Amblyomma americanum* (ie, Lone Star ticks), which are known to bite humans and are an important cause of sensitization to alpha-gal.[2] However, chiggers are not generally recognized as ticks.

The death in suburban New Jersey in 2024 is notable because it is the first documented anaphylactic death related to AGS where the symptoms started several hours after consuming mammalian meat. There are some possible factors that might have contributed to the severity of his anaphylaxis, including drinking a beer with the hamburger, exposure to ragweed pollen, and exercise that afternoon, which ended 1 hour before the start of symptoms. However, none of those are a possible cause of anaphylaxis occurring 4 hours after eating beef. We consider that there are several aspects of the case that are of public and general medical importance. It is recognized that the deer population of many southeastern states increased dramatically between 1950 and 2020.[6] Indeed the deer in New Jersey were recently described as "an unsustainable statewide emergency."[7] What is less well known is that these deer are the primary breeding host of the Lone Star tick and are thought to be an important reason why this species of tick is moving North.[8]

The fact that severe abdominal pain without any other allergic features can be an important and indeed dangerous form of anaphylaxis is not well recognized.[2,9,10] Even though the first episode scared the patient, neither he nor his wife considered it to be "anaphylaxis," and therefore, they did not connect the pain with the beef eaten 4 hours earlier. Thus, he had no reason to avoid eating a hamburger 2 weeks later. The event that occurred in September, 4 hours after eating beef, progressed rapidly, but

TABLE I. Total serum IgE and specific IgE antibody levels in postmortem blood

Food allergens	IgE level (IU/mL)*	Percentage of total IgE†	Inhalant allergens	IgE level (IU/mL)*	Percentage of total IgE†
Total IgE	16.7				
Alpha-gal	0.57	3.4	Rye grass	0.99	5.9
Beef	0.17	1	Ragweed	0.42	2.5
Pork	0.12		Birch pollen	0.14	
BSA	<0.1		Dust mite	0.13	
Chicken	<0.1		Oak pollen	<0.1	
Peanut	<0.1		Cat	<0.1	
Gelatin	<0.1		Alternaria	<0.1	
Egg white	<0.1		Horse dander	<0.1	
Wheat	<0.1				
ω-5-Gliadin	<0.1				
Milk	<0.1		Honey bee	<0.1	
			Yellow jacket	<0.1	

Alpha-gal, Galactose-α-1,3-galactose; *BSA*, bovine serum albumin.
*Both specific IgE and total IgE are in International Units/mL (IU/mL).
†The relevence of different levels of sIgE to alpha-gal as a percentage of total IgE has been addressed in the paper by Platts-Mills et al.[2]

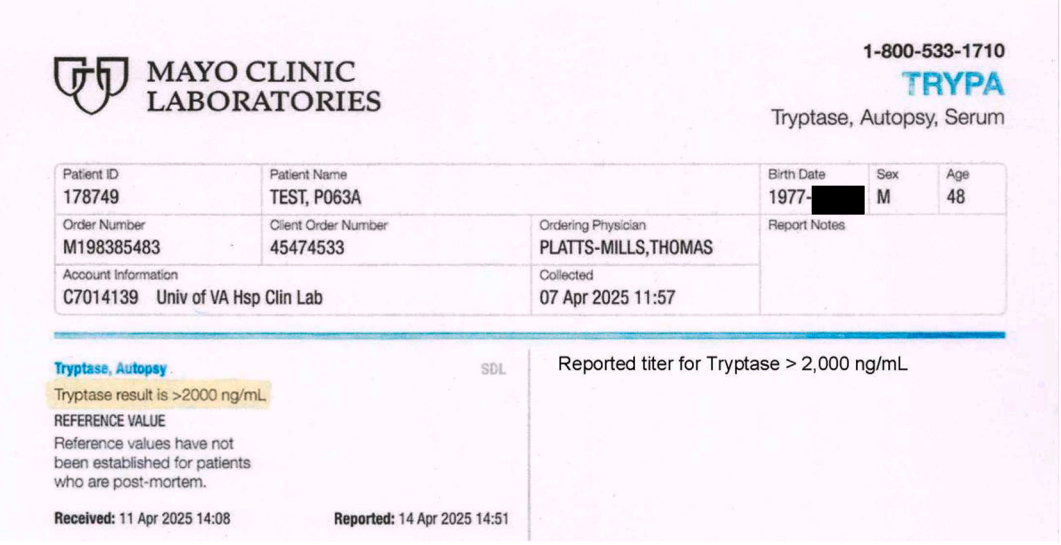

FIGURE 1. The assay for tryptase in serum was developed by Dr Schwartz.[3] The first report on values in postmortem samples came from Yunginger at the Mayo Clinic.[4] The normal upper limit of the assay is 200 ng/mL; to measure values up to 2000 ng/mL, the sera were diluted 10-fold. The prevalence of tryptase values >2000 ng/mL among samples tested at the Mayo Clinic lab during the period from May 1, 2024, to May 1, 2025, was as follows. TRYPT (living patients): 47,045 total samples; 5156 >11.5 ng/mL, 1 >2000 ng/mL; TRYPA (postmortem): 40 total samples; 19 >11.5 ng/mL, 2 >2000 ng/mL. Values from Mayo Clinic, courtesy of Dr Melissa Snyder, PhD.

the postmortem examination did not recognize anaphylaxis as a possible cause of death.

In conclusion, we report here the first well-documented death related to eating mammalian meat in a patient with specific IgE to alpha-gal. The symptoms, which started 4 hours after eating a hamburger, lead rapidly to collapse and unconsciousness, and his postmortem blood had >2000 ng/mL of tryptase. The significance of this case is that a large and increasing population of the United States is being exposed to the Lone Star tick, both because the tick is moving north and because there are now large populations of deer in many states.[2,7,8] The result is that there are many sensitized individuals who are unaware of the fact that (1) both larvae ("chiggers") and mature ticks can cause sensitization to alpha-gal; (2) the delay between eating meat and an allergic reaction in patients with AGS is, in most cases, 3-5 hours; and (3) abdominal symptoms, particularly pain, can be isolated symptoms in this form of allergic disease. Finally, it is clear that there is a need for better education of both the professionals and the public. The CDC has documented that a large number of physicians are not aware of the AGS; however, we

would argue that there is a major need for public education in areas where the tick is increasing.[11]

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T.A.E. Platts-Mills and J. M. Wilson report support from the National Institutes of Health/National Institute of Allergy and Infectious Diseases (grant R37 A120565-41) and for supplies of reagents for IgE assays from Phadia Thermo Fisher.
Conflicts of Interest: The authors declare that they have no relevant conflicts of interest.
Received for publication July 25, 2025; revised September 26, 2025; accepted for publication September 29, 2025.
Available online ■■

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2213-2198

https://doi.org/10.1016/j.jaip.2025.09.039

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