


No Bull: A Case of Alpha-Gal Syndrome Associated With Buffalo Meat Sensitivity

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Abstract

Introduction: Alpha (α)-gal syndrome (AGS) is an immunoglobulin E (IgE) antibody response against the glycoprotein carbohydrate galactose- α -1,3-galactose- β -1-(3)4-N-acetylglucosamine-R (Gal α -1,3Gal β 1-(3)4GlcNAc-R or α -gal) that is present in *Ixodida* (tick) saliva and noncatarrhine mammals as well as cetuximab, antivenom, and the zoster vaccine. The most frequently observed anaphylactic reactions in AGS are observed after beef, pork, lamb, and deer meat consumption. We present the first case of anaphylaxis to buffalo meat.

Case Report: A 55-year-old man presented with a history of recurrent urticaria that only developed approximately 7 hours after buffalo consumption. The patient denied history of *Ixodidae* bites but admitted to frequent hiking outdoors. Anti- α -1,3-gal IgE was positive (30.80 kU/L). The patient was advised to strictly avoid red meat.

Discussion: The prevalence of AGS has been increased in all continents in the past decade, and several *Ixodidae* species have been associated with this hypersensitivity. The list of IgE-mediated reactions to various types of meat has expanded to kangaroo, whale, seal, and crocodile, although these have not been associated with AGS. van Nunen only cautioned against consumption of exotic meats, such as buffalo, but no published case report describes AGS associated with anaphylaxis to this type of meat.

Conclusion: AGS is a mammalian meat allergy that has been increasingly prevalent worldwide, especially in *Ixodidae* endemic regions of Australia and the United States. Multiple AGS case reports published in the past decade demonstrate rapidly increasing understanding of underlying mechanisms provoking ongoing sensitization to help devise management strategies and dietary information. We offer the first case report of delayed anaphylaxis to buffalo meat.

Keywords

alpha-gal syndrome, buffalo meat, anaphylaxis

Introduction

Alpha (α)-gal syndrome (AGS) is an immunoglobulin E (IgE) antibody (Ab) response against the glycoprotein carbohydrate galactose- α -1,3-galactose- β -1-(3)4-N-acetylglucosamine-R (Gal α -1,3Gal β 1-(3)4GlcNAc-R or α -gal) that is present in *Ixodida* (tick) saliva and noncatarrhine mammals.^{1,2} Recurrent *Ixodidae* bites increase anti- α -gal IgE Abs that trigger immediate anaphylaxis to *Ixodidae* bites, xenotransplantation, and certain pharmaceuticals, such as cetuximab, and delayed hypersensitivity reactions to red meat consumption.^{1,2} The most frequently observed anaphylactic reactions in AGS are observed after beef, pork, lamb, and deer meat

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consumption.² We present the first published case of anaphylaxis to buffalo meat.

Case Report

A 55-year-old man presented with an 11-month history of recurrent urticaria that only developed approximately 7 hours after buffalo consumption. Similar hypersensitivity reactions occurred with lamb and beef. He reported that symptoms resolved within 24 hours and denied angioedema, respiratory distress, or other anaphylactic symptoms. The patient had eliminated buffalo and other red meat from his nutritional intake for 8 months and had not developed urticaria since. The patient denied history of *Ixodidae* bites but admitted to frequent hiking outdoors. Skin prick testing (SPT) to beef and lamb was negative. Buffalo meat SPT was not commercially available. Anti- α -1,3-Gal IgE was positive (30.80 kU/L). The patient was advised to strictly avoid red meat.

Discussion

AGS involves cross-reactivity against the glucose determinant Gal α -1,3Gal β 1-(3)4GlcNAc-R synthesized in nonprimate mammals and *Ixodidae*.^{1,3} Case reports from 17 countries across 6 continents have reported bites from the following *Ixodidae* family species: *Ixodes holocyclus* (Australia), *Amblyomma americanum* (United States), *Ixodes ricinus* (Europe), *Ixodes cajennense* (Panama), *Ixodes nipponensis* (Japan and Korea), *Amblyomma sculptum* (Brazil), *Amblyomma variegatum* (Ivory Coast), and *Haemaphysalis longicornis* (Japan).^{4,5} *Ixodidae* bites heighten anti- α -1,3-Gal IgE antibodies that induce delayed anaphylaxis to mammalian meats or other products containing α -gal as well as immediate anaphylaxis to further *Ixodidae* bites, xenotransplantation, and the chimeric monochromatic Ab cetuximab used to treat metastatic colorectal cancer and squamous cell carcinoma.³

AGS has been characterized by delayed anaphylaxis (2–10 h), urticaria, and angioedema after mammalian meat ingestion and is often preceded by an *Ixodida* bite.⁶ Symptoms may include intensive generalized pruritus, flushing, diffuse urticaria, a sense of impending doom, angioedema of the throat and mouth, dysphagia, dysarthria, tachycardia, wheezing, gastrointestinal pain, nausea, and vomiting, sudden weakness, hypotension, and syncope.⁷ AGS symptom manifestation may depend on lipid content and, thus, not present with anaphylaxis to every red meat ingestion.⁵ The delayed anaphylaxis may be attributed to the rate of lipid absorption that requires conversion and processing of lipids to chylomicrons and then to low-density lipoproteins.⁵ Increased risk of AGS may be associated with large

portion sizes of red meats, offal meats, unfamiliar meats when traveling abroad, and exotic meats, such as bear and squirrel in the United States or kangaroo and buffalo in Australia.^{1,6}

Serological testing for α -gal-specific IgE and mammalian meat-specific IgE is the standard for this diagnosis but may be substituted with cetuximab intradermal testing or SPT.⁶ The present case supported the lack of determinant findings achieved via SPT with mammalian meats. Dietary exclusion has been the mainstay of AGS management.⁶ Oral food challenge is only indicated for patients demonstrating α -gal antigen hypersensitivity but an unclear history of mammalian meat allergy.⁵

Case reports of mammalian meat allergy emerged in the literature about 2 decades ago, and the association of delayed anaphylaxis to the oligosaccharide α -gal in mammalian meat was first proposed about a decade ago.⁸ AGS has since increased prevalence in all continents, and several *Ixodidae* species have been associated with this hypersensitivity.⁸ Wilson et al. confirmed an AGS diagnosis (IgE to beef and pork) in 95% of 261 children and adults reporting mammalian meat allergy to the University of Virginia Allergy Clinic.⁹ Symptoms of urticaria (93%), anaphylaxis (defined as hypotension, lightheadedness, and/or dyspnea; 60%), and gastrointestinal symptoms (64%) averaged at 3 to 6 hours after mammalian meat consumption.⁹ Another American case in North Carolina involved a 67-year-old man with a history significant for anaphylaxis (pruritus, dyspnea, dysphagia, dysarthria, and angioedema of the tongue and hands) 3 hours after accidental consumption of sausage as well as multiple *Ixodidae* bites. AGS was verified by high α -gal IgE to beef, mutton, and pork.⁷

Mabelane and Ogunbanjo described a South African cohort that reported rapid hypersensitivity responses (within 45 min) and a prominence of gastrointestinal symptoms, following beef sausage ingestion.⁵ Abreu et al. detailed the second record of AGS in Portugal.¹⁰ This 76-year-old man experienced 2 immediate (within 1 h) anaphylactic episodes ((1) sickness, diarrhea, vomiting, and urticaria and (2) diarrhea, vomiting, cutaneous lesions, hypotension and syncope) to cooked beef and pork that were later confirmed by SPT to raw pork and cooked beef as well as an elevated α -gal IgE (35.3 kUA/L).¹⁰ The patient denied history of *Ixodidae* bites.¹⁰

The list of IgE-mediated reactions to various types of meat has expanded to kangaroo,^{4,6,11} whale, seal,¹² and crocodile,¹³ although these have not been associated with AGS. van Nunen cautions against consumption of exotic meats, such as buffalo.⁶ We now present the first published case of anaphylaxis to buffalo meat.

AGS is a mammalian meat allergy that has been increasingly prevalent worldwide, especially in *Ixodidae* endemic regions of Australia and the United States.⁶ The target allergen, oligosaccharide Gal α -1,3Gal β 1-(3)

4GlcNAc-R, is a constituent of many mammalian and offal meats, milk, and gelatin as well as cetuximab, antivenom, and the zoster vaccine.⁸ Multiple AGS case reports published in the past decade demonstrate rapidly increasing understanding of underlying mechanisms provoking ongoing sensitization to help devise management strategies and dietary information.⁸ We offer the first published case report of delayed anaphylaxis to buffalo meat.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

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Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

Statement of Informed Consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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