

Diagnosis of Life-Threatening Alpha-Gal Food Allergy Appears to Be Patient Driven

Journal of Primary Care & Community Health
1-4

© The Author(s) 2017

Reprints and permissions:

sagepub.com/journalsPermissions.nav

DOI: 10.1177/2150131917705714

journals.sagepub.com/home/jpc



Mary Grace Flaherty, PhD, MS¹, Samantha Jan Kaplan, MLIS¹,
and Maya R. Jerath, MD, PhD¹

Abstract

Objective: Patients exhibiting life-threatening symptoms associated with the alpha-gal food allergy (delayed urticaria or anaphylaxis due to mammalian meat) are frequently undiagnosed, causing unnecessary emergency department (ED) and health care visits, and extensive pain and suffering. This study aimed to determine the path to diagnosis experienced by alpha-gal patients. **Methods:** Semistructured interviews were conducted from March to June 2016 with a chronological systematic sample of approximately 10% of patients diagnosed with alpha-gal and treated by the University of North Carolina Allergy and Immunology Clinic (n = 28). Main outcome measures included average length of time between first symptoms' appearance and diagnosis, number and type of health care encounters en route to diagnosis, and typical symptom severity. **Results:** Six interviewees (21%) were diagnosed within a year of experiencing symptoms, of the remaining 22, mean time to diagnosis was 7.1 years. In over 100 medical encounters (including 28 ED visits and 2 urgent care) the correct diagnosis or effective diagnosing referral occurred less than 10% of the time. Seventy-one percent (20/28) described their first symptoms as severe. More patients found the allergist specializing in this condition on their own (n = 12; 43%) than those who were formally diagnosed or received referrals (n = 10; 36%) through the health care system. **Conclusions:** The medical community is challenged to stay abreast of emerging and newly uncovered illnesses through traditional medical literature communication channels. Presently, patients more often discover a diagnosis of alpha-gal allergy by using information resources on their own than by presenting to the ED with anaphylaxis.

Keywords

emergency visits, health outcomes, access to care, disease management, patient-centeredness

Background

A well-documented food allergy, "alpha-gal," due to sensitization to the carbohydrate galactose- α -1,3-galactose, can explain some cases of idiopathic anaphylaxis.¹ The condition has been seen in over 2000 patients in Virginia and North Carolina, and in Europe, Australia, and Japan.

This "novel and severe food allergy," causes delayed anaphylaxis, angioedema, or urticaria and is due to mammalian meat consumption; its novelty largely lies in delayed presentation of symptoms and the putative causative agent (a tick bite).² Though it was first reported in the medical literature 8 years ago,² patients still report extreme frustration and hardship (including anaphylaxis resulting in repeated emergency department [ED] visits) caused by health care providers' (HCPs) lack of awareness of the alpha-gal allergy, resulting in the necessity to seek out their own diagnoses.

Reports of alpha-gal made their way into popular media before information on the allergy gained traction in the medical literature. It was discussed on national radio programs in 2011-2012,^{3,4} in *Reader's Digest* in 2013⁵; in 2014, added to Wikipedia⁶ and WebMD (after a CBS news segment).⁷ Coverage increased dramatically in 2016, most recently with an article in *The Guardian*.⁸ Because patients are engaging in self-diagnosis through media reports and informal information networks, they are learning about new conditions before HCPs discover them.

¹University of North Carolina, Chapel Hill, NC, USA

Corresponding Author:

Mary Grace Flaherty, School of Information and Library Science,
University of North Carolina, 216 Lenoir Drive, Chapel Hill, NC 27599-
3360, USA.

Email: mgflaher@email.unc.edu



Health care providers need to be alerted to the unique delayed reaction of the alpha-gal allergy, otherwise delay in diagnosis results in considerable expense. This study aimed to determine the diagnostic path experienced by alpha-gal patients. Primary outcome measures were average length of time between first symptoms' appearance and diagnosis, and the number and type of health care encounters en route.

Methods

Participants included patients diagnosed with the alpha-gal allergy at the University of North Carolina (UNC) Allergy and Immunology Clinic. In late 2015, this patient pool included approximately 250 individuals. A sample size of 36 was calculated to detect factors with a 50% prevalence and precision of $\pm 15\%$. The sample was systematically selected based on date of patients' first clinic visit. Every seventh individual was chosen and invited to participate, via mail. The first mailing yielded 20 participants; a second mailing was sent to 16 individuals, and yielded 8 more. Twenty-eight individuals were successfully interviewed.

Semistructured interviews were conducted by the primary researcher and her research assistant. These took place from March to June 2016, and averaged 50 minutes in length. The same interview guide was used in each case; questions focused on path to diagnosis, interactions with the health care system, and impact of the allergy on lifestyle. Informed consent was obtained; all agreed to being audio-recorded. Participants were compensated with a \$100 gift card. The protocol was approved by the University of North Carolina Institutional Review Board (15-2747; January 6, 2016).

Results

Twenty-eight individuals (14 females; 14 males) completed interviews, 11% of the UNC Allergy and Immunology Clinic's alpha-gal patient population at the time, and 77% of the 36 total patients initially sought. Average age was 56 years (range 32-81 years); none were African-American or Hispanic. Four participants (14%) had not completed college; 8 (28%) had an undergraduate degree, and 16 (57%) had completed some graduate school or possessed a graduate degree.

Time to diagnosis was determined as difference between date of first symptoms and date of diagnosis as provided by participants. Six interviewees (21%) were diagnosed within a year of experiencing symptoms, of the remaining 22 (79%), the mean time to diagnosis was 7.1 years. Nine patients (32%) went without diagnosis for 5 years or more. Twenty of 28 cases occurred after the first report of alpha-gal appeared in the medical literature (2009). Sixteen of those 20 were not diagnosed in a health care encounter; 3 were diagnosed after more than 1 health encounter; and in 1

case, the participant's primary care provider recognized alpha-gal. Seventy-one percent (20 of 28) of participants described their initial symptoms as severe.

Every patient who was diagnosed in 2 or fewer years of first experiencing symptoms ($n = 19$; 68%) met one or more of the following criteria: they were HCPs or had close relationships with HCPs (eg, spouse or parent of HCP); had prior experience with severe allergies (and relationship with allergist and/or primary care provider); or knew someone who had been diagnosed with alpha-gal.

In over 100 medical encounters (average = 3.8/person), correct diagnosis occurred 9% of the time (Table 1). Of 17 patients (61%) who experienced anaphylaxis and went to an ED (totaling 28 visits), including 2 who visited urgent care clinics, none were diagnosed with alpha-gal or were asked any questions that would have led to diagnosis (eg, have you eaten meat within the past 3-6 hours?). Two individuals were admitted to the hospital repeatedly. One participant reported the paramedic identified his condition as possibly being alpha-gal, and did inform ED personnel. All others were treated for idiopathic anaphylaxis and discharged. Nine patients (32%) were diagnosed or received referrals to an allergist; 7 by their primary care provider, 1 by their dermatologist, and 1 by the nurse while visiting their allergist for a different condition.

Twelve of 28 (43%) reported finding an allergist on their own. Of those, 2 (7%) found information online and went directly to the UNC clinic; 2 received information from People's Pharmacy (radio/online program; original broadcast October 1, 2011); 2 received information directly from individuals with alpha-gal; 6 (21%) received information from health care insiders.

The remaining 6 patients (21%) advocated with HCPs for further allergy testing. Of those, 1 discovered alpha-gal in a hunting magazine (after 3 ED visits); 2 had other allergies, one's son had alpha-gal, one's mother was a nurse, and 1 had been advised by her dermatologist to keep a food diary.

Discussion

Despite >40 Medline citations from 2009 to 2015,⁹ and an entry in the physician's electronic reference (UpToDate),¹⁰ it appears the alpha-gal allergy is still relatively unknown. This results in unnecessary financial and emotional expense, significant delay in diagnosis and hence, in patients' finding relief from symptoms. Because diagnosis rarely occurs, it is likely related deaths are not detected; therefore, population prevalence and mortality rate are unknown.

Some diagnostic missteps can be attributed to the unique presentation of delayed reaction. As one participant, also a medical doctor, noted, "it violates all the rules." Most food allergies arise immediately; alpha-gal typically appears 3 to 6 hours after consumption. Even so, 12 participants (43%)

Table 1. Health Care Encounters and Diagnosis.

Type of Encounter	No. of Encounters Not diagnosed	Encounters With Diagnosis or Referral	Total Encounters
Emergency department	28	1 ^a	29
Urgent care clinic	2		2
Primary care provider	20	7	27
Outpatient clinic physician	19		19
Allergist	7		7
Dermatologist	5	1	6
Cardiologist	3		3
Gastroenterologist	3		3
Gynecologist	2		2
Otolaryngologist	2		2
Electrophysiologist	1		1
Hospitalist	1		1
Naturopath	1		1
Neuroradiologist	1		1
Pulmonologist	1		1
Unspecified specialist	1		1
Nurse		1	1
Total	97	10	107

^a Paramedic, not emergency department staff.

immediately suspected their symptoms were due to a food reaction. Unless they encountered a HCP who knew about alpha-gal, their suspicions were dismissed. The individual who received the paramedic's supposition that alpha-gal caused their anaphylaxis immediately visited the allergist, resulting in a timely diagnosis.

Less than 15% (4) of participants had not completed college; all other participants had an undergraduate degree, and 57% (16) had completed some graduate school or acquired a graduate degree. The high education level of our sample raises questions about patients who successfully obtained diagnosis. Combined with the characteristics of those who were diagnosed relatively early, it suggests that more educated and determined patients are more likely to be diagnosed. Therefore, prevalence could be far more common.

Despite the relative privilege of most of our participants, many had to request to be tested for alpha-gal and often were met with resistance. Alpha-gal is diagnosed via a blood test that costs less than US\$50, yet many individuals report visiting several specialists and undergoing many expensive tests, either because their HCP was unaware of alpha-gal or reluctant to test for it.

Limitations of the study include self-reported data, which may be subject to recall bias, and possible survivor and/or selection bias in those who agreed to be interviewed. In addition, routine laboratory testing for alpha-gal sensitization has only been available for 5 years, so confirmed clinical diagnosis is relatively new.

The current system of communication of medical information among providers is challenged to stay abreast of

newly uncovered illnesses. This can create extreme difficulties for patients and tax the health system. Presently patients are more likely to discover alpha-gal online, on the radio, or through personal information networks than by visiting the ED with anaphylaxis. Health care providers need to be alerted to the unique delayed reaction characteristic of the alpha-gal allergy. If not, it is likely patients with this condition will continue to experience long paths to diagnosis and concomitant consequences.

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.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Wolver SE, Sun DR, Commins SP, Schwartz LB. A peculiar cause of anaphylaxis: no more steak? *J Gen Intern Med*. 2013;28:322-325.
2. Commins SP, Satinover SM, Hosen J, et al. Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose- α -1,3-galactose. *J Allergy Clin Immunol*. 2009;123:426-433.
3. Kroen GC. Rare meat allergy caused by tick bites may be on the rise. National Public Radio. *The Salt, Eating and Health*. November 27, 2012. <http://www.npr.org/sections/>

- thesalt/2012/11/21/165633003/rare-meat-allergy-caused-by-tick-bites-may-be-on-the-rise. Accessed December 9, 2016.
4. People's Pharmacy. Alpha-gal allergy. <https://www.peoplespharmacy.com/2013/08/03/830-alpha-gal-allergy/comment-page-1/#comments>. Accessed December 9, 2016.
 5. Blumberg PO, Weinhouse B. Did you know . . . a bug bite can make you a vegetarian. *Reader's Digest*. 2013;May:34.
 6. Wikipedia. Alpha-gal allergy. https://en.wikipedia.org/wiki/Alpha-gal_allergy. Updated September 29, 2014. Accessed December 9, 2016.
 7. WebMD. Tick bites linked to red meat allergy. August 13, 2014. <http://www.webmd.com/allergies/news/20140813/tick-bites-red-meat-allergy>. Accessed December 9, 2016.
 8. Hunt E. Tick bites that trigger severe meat allergy on rise around the world. *The Guardian*. October 6, 2016. https://www.theguardian.com/society/2016/oct/07/tick-bites-that-trigger-severe-meat-allergy-on-rise-around-the-world?cmp=oth_b-aplnews_d-1. Accessed December 9, 2016.
 9. US National Institutes of Health. National Library of Medicine. PubMed. [https://www.ncbi.nlm.nih.gov/pubmed/?term=\(alpha-gal%20allergy\)%20AND%20\(%222009%2F01%2F01%22%5BDate%20-%20Publication%5D%20%3A%20%222015%2F12%2F31%22%5BDate%20-%20Publication%5D\)](https://www.ncbi.nlm.nih.gov/pubmed/?term=(alpha-gal%20allergy)%20AND%20(%222009%2F01%2F01%22%5BDate%20-%20Publication%5D%20%3A%20%222015%2F12%2F31%22%5BDate%20-%20Publication%5D)). Accessed December 9, 2016.
 10. UpToDate. Alpha gal=Galactose-alpha-1,3-galactose. <http://www.uptodate.com/contents/search?search=alpha-gal&x=0&y=0>. Accessed December 10, 2016.

Author Biographies

Mary Grace Flaherty is an assistant professor at the School of Information and Library Science at the University of North Carolina at Chapel Hill.

Samantha Jan Kaplan is a doctoral student at the School of Information and Library Science at the University of North Carolina at Chapel Hill.

Maya R. Jerath is an associate professor of Medicine and Pediatrics, serves as associate chief of Clinical Allergy and Immunology, and is director of the University of North Carolina Allergy & Immunology Clinic.