American Journal of Ophthalmology Case Reports 29 (2023) 101811

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Alpha-gal syndrome (AGS) in a glaucoma suspect with narrow iridocorneal angles

Aminatta Z. Tejan-Kamara [a,b], Joan M. Murhammer [c], John H. Fingert [a,d,*]

[a] Institute for Vision Research, University of Iowa, Iowa City, IA, 52242, USA
[b] Des Moines University, Des Moines, IA, 50312, USA
[c] Department of Pharmaceutical Care, University of Iowa Health Care, Iowa City, IA, 52242, USA
[d] Department of Ophthalmology and Visual Sciences, Carver College of Medicine, University of Iowa, Iowa City, IA, 52242, USA

ARTICLE INFO

Keywords:
Alpha-gal syndrome
AGS
Allergy
Glaucoma
Case report

ABSTRACT

Purpose: Alpha-gal syndrome (AGS) is an allergy to non-primate mammalian carbohydrate (galactose-alpha-1,3-galactose) which may cause anaphylaxis. Allergic patients must avoid ophthalmic drugs containing animal-derived ingredients.

Observations: We report a 59-year-old non-Hispanic white woman who was referred for a glaucoma evaluation. She had been diagnosed with AGS after a tick bite in 2017. Ophthalmic exam revealed potentially occludable, narrow iridocorneal angles and laser iridotomy was recommended. Prior to performing the iridotomy, we investigated the ophthalmic medications required for the procedure to identify options that are free of animal-derived products and safe to use. Laser iridotomy was performed without complications or allergy to medications.

Conclusions: Ophthalmologists need to be aware of both the presence of AGS as well as the identity of ophthalmic medications that are safe to use in patients with this condition to avoid potentially lethal allergic responses.

1. Background

Alpha-gal syndrome (AGS), also referred to as alpha-gal allergy, is a type I hypersensitivity allergy to galactose-α-1,3-galactose (alpha-gal), an oligosaccharide that is unique to non-primate mammals. AGS is thought to be caused by Lone Star tick bites which cause an immune response of IgE antibodies to haptens in tick saliva that cross-react with alpha-gal.[1] Once sensitized by a tick bite, patients may experience a hypersensitivity response to alpha-gal after eating non-primate, mammalian meat, i.e., beef, pork, lamb, rabbit, or venison (red meat) or products derived from them. AGS has been strongly linked with cetuximab (anti-epidermal growth factor) monoclonal antibody infusions[2] Hypersensitive patients were found to have IgE antibodies to galactose-α-1,3-galactose and not cetuximab. Cetuximab, which is produced from murine cell lines, contains an alpha-gal molecule glycosylated on the Fab fragment.[2] While most food allergies have an onset within 5–30 minutes of exposure,[3] the time course of AGS is delayed and occurs 3–6 hours following ingestion.[4,5] However, an immediate-onset of symptoms may occur following intravenous administration of alpha-gal containing products.[2] Affected individuals experience varying allergic responses ranging from mild urticaria to severe angioedema and potentially lethal anaphylaxis.[1,2]

Hypersensitivity to alpha-gal is a serious concern for ophthalmologists, considering numerous ocular medications that may contain alpha-gal from animal-derived ingredients (e.g., glycerin, polysorbate, magnesium stearate, gelatin).[5]

We present a patient with AGS that was evaluated as a glaucoma suspect to highlight the potential allergy risks to these patients from routinely used ophthalmic medications and an approach to identify medications that are safe for these patients. To our knowledge, this is the first case report describing ophthalmic care of a patient with AGS.

2. Case presentation

A 59-year-old non-Hispanic white woman was referred for a glaucoma evaluation after an intraocular pressure of 27 mm Hg was measured in her left eye. She had no prior ocular surgeries. During review of her past medical history, it was discovered that she had been diagnosed with AGS after a tick bite in 2017 while vacationing in Wisconsin. She reports severe gastrointestinal distress (vomiting and

* Corresponding author. 3111B, Medical Education and Research Facility Carver College of Medicine, University of Iowa Iowa City, IA, 52242, USA.
E-mail address: john-fingert@uiowa.edu (J.H. Fingert).

https://doi.org/10.1016/j.ajoc.2023.101811
Received 18 November 2022; Received in revised form 22 January 2023; Accepted 27 January 2023
Available online 28 January 2023

diarrhea), difficulty breathing, and dizziness that occurs 2-4 hours after eating red meat.

She had best corrected visual acuity of 20/20 OD and 20/25 OS with glasses (−2.50 spherical OD and plano + 1.00 × 180 OS). Goldmann tonometry indicated that her intraocular pressures were 12 mmHg in the right eye and 17 mmHg in the left eye on no glaucoma medications. Slit lamp examination revealed bilateral trace amounts of pigment on the corneal endothelium. However, no additional stigmata to suggest a diagnosis of pigment dispersion syndrome were detected. Neither heavy trabecular meshwork pigmentation, nor iris transillumination (with white light or infrared light sources) were detected. Gonioscopy revealed a non-occludable iridocorneal angle OD, (C-D30f1+, scleral spur visible for 360°) and a narrow potentially occludable angle OS (A-B25b1+, greater than 180° closed). No signs of prior acute angle closure (i.e., glaukomflecken or iris stromal changes) were detected. Finally, small cup-to-disc ratios (0.2 OU) were seen on ophthalmoscopy.

Prophylactic treatment of the narrow iridocorneal angles OS with a laser peripheral iridotomy was recommended. Given the diagnosis of AGS, treatment was delayed for 1 week while the formulation of several topical medicines used with laser peripheral iridotomy were investigated. Several topical drugs that are used before and after laser iridotomy (pilocarpine, brimonidine tartrate, and prednisolone acetate) were investigated by reviewing the ingredients listed in package inserts and contacting the respective manufacturers to determine if they contained any mammalian animal-derived ingredients that might be problematic for patients with AGS. Although laser iridotomy can be performed without cholinergic drugs, pilocarpine hydrochloride 1% ophthalmic solution (Akorn, NDC: 17478-223-12) was determined to be free of animal-derived ingredients and was judged safe to use as was brimonidine tartrate 0.2% ophthalmic solution (Akorn, NDC: 17478-715-10). Prednisolone acetate 1% ophthalmic suspension (Pacific Pharma/Allergan, NDC: 60758-119-05) contains polysorbate 80, which is derived from animals, and was judged unsafe to use. However, prednisolone sodium phosphate 1% ophthalmic solution (Bausch & Lomb, NDC: 24208-715-10) is animal-free and safe to use in place of prednisolone acetate. The safety of using additional pressure-lowering medications in a patient with AGS was investigated should they be needed to control a post-laser pressure rise. Dorzolamide 2%/timolol 0.5% ophthalmic solution (Akorn, NDC: 50383-233-10) and methazolamide 50 mg oral tablets (Oceanside/Bausch Health, NDC 68682-0023-10) are animal-free and would be safe to use if needed, while acetazolamide 125 and 250 mg oral tablets (Taro, NDC: 51672-4022-1, 51672-4023-1) contain animal-derived ingredients (i.e., gelatin, lactose, magnesium stearate) and would not be safe to use in this patient. Additional drugs frequently used in ophthalmology care, proparacaine hydrochloride 0.5% ophthalmic solution (Bausch&Lomb, NDC: 24208-0730-06) and fluorescein sodium ophthalmic strips (HUB, NDC: 17238-900-30) do not contain any animal-derived ingredients and would be safe to use in a patient with AGS.

The patient was pretreated with pilocarpine hydrochloride 1% and brimonidine tartrate 0.2% and a laser iridotomy was performed with a neodymium-doped yttrium alumninum garnet (Nd:YAG) laser. Brimonidine tartrate 0.2% was applied after the laser and followed with a 1-week course of prednisolone sodium phosphate 1%. The patient had no complications or allergic reactions.

3. Discussion and conclusions

AGS is rare and likely underdiagnosed.[6] As a result the precise prevalence of AGS is unknown. However, a total of 34,256 cases of AGS were reported in the United States in 2018.[6,7] Although the geographic distribution of AGS is largely unknown, a high frequency of individuals with elevated IgE antibodies against alpha-gal has been reported in the southeastern region.[2] These regions match the range of several ticks (e.g., Lone Star ticks) that have been linked with AGS,[4,6] which provides more evidence for the role of ticks in the pathophysiology of this condition. Moreover, such population-based measurements of IgE antibodies to alpha-gal suggest that frequency of AGS might be on the rise.[6] As a result, patients with AGS are increasingly likely to present for ophthalmic care. We identified some ophthalmic medications in this report that are formulated with no animal products and are safe for patients with AGS. However, drug formulations may change. Thus, consultation with pharmacists to identify drugs that are formulated with no animal products is necessary to avoid potentially fatal allergic reactions in patients with AGS.

The Zhongshan Angle-Closure Prevention (ZAP) trial investigated the effectiveness of laser peripheral iridotomy in preventing acute angle-closure attacks in Chinese patients judged to be primary angle closure suspects.[8] The ZAP trial determined the risk for acute angle closure in primary angle closure suspects is extremely low and consequently did not recommend widespread prophylactic laser iridotomy.[9,10] The patient in our case report meets the criteria for being a primary angle closure suspect. However, the results of the ZAP trial are only directly applicable to Chinese populations. It is unclear how they might apply to our patient who is of European ancestry.

Our case report highlights considerations for treating patients with AGS in a glaucoma clinic. Ophthalmologists need to be aware of the special needs of patients with AGS. This information might also be of interest to patients who wish to avoid drugs with animal products due to their beliefs (i.e., those with strict vegan diets).

Patient consent

Written consent to publish this case has been obtained.

Funding

Research to Prevent Blindness, The Hadley-Carver Chair in Glaucoma, and the Don Heineking Research Fund.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

All authors declare that they have no competing interests.

Acknowledgments

None.

References

1. Commins SP, James HR, Kelly LA, et al. The relevance of tick bites to the production of IgE antibodies to the mammalian oligosaccharide galactose-alpha-1,3-galactose. *J Allergy Clin Immunol*. May 2011;127(5):1286–12893 e6. https://doi.org/10.1016/j.jaci.2011.02.019.
2. Chung CH, Mirakhur B, Chan E, et al. Cetuximab-induced anaphylaxis and IgE specific for galactose-alpha-1,3-galactose. *N Engl J Med*. Mar 13 2008;358(11):1109–1117. https://doi.org/10.1056/NEJMoa074943.
3. Cianferoni A, Muraro A. Food-induced anaphylaxis. *Immunol Allergy Clin*. Feb 2012;32(1):165–195. https://doi.org/10.1016/j.iac.2011.10.002.
4. Hilger C, Fischer J, Swiontek K, et al. Two galactose-alpha-1,3-galactose carrying peptidases from pork kidney mediate anaphylactogenic responses in delayed meat allergy. *Allergy*. May 2016;71(5):711–719. https://doi.org/10.1111/all.12835.
5. Seddon I, Venincasa M, Farber N, Sridhar J. Alpha-gal syndrome in ophthalmology and medicine. *Int Ophthalmol Clin. Fall*. 2020;60(4):61–75. https://doi.org/10.1097/IIO.0000000000000330.
6. Binder AM, Commins SP, Altrich ML, et al. Diagnostic testing for galactose-alpha-1,3-galactose, United States, 2010 to 2018. *Ann Allergy Asthma Immunol*. Apr 2021;126(4):411–416 e1. https://doi.org/10.1016/j.anai.2020.12.019.
7. Steinke JW, Platts-Mills TA, Commins SP. The alpha-gal story: lessons learned from connecting the dots. *J Allergy Clin Immunol*. Mar 2015;135(3):589–596. https://doi.org/10.1016/j.jaci.2014.12.1947. quiz 597.

8. Jiang Y, Friedman DS, He M, Huang S, Kong X, Foster PJ. Design and methodology of a randomized controlled trial of laser iridotomy for the prevention of angle closure in southern China: the Zhongshan angle Closure Prevention trial. *Ophthalmic Epidemiol*. Oct 2010;17(5):321–332. https://doi.org/10.3109/09286586.2010.508353.
9. He M, Jiang Y, Huang S, et al. Laser peripheral iridotomy for the prevention of angle closure: a single-centre, randomised controlled trial. *Lancet*. Apr 20 2019;393(10181):1609–1618. https://doi.org/10.1016/S0140-6736(18)32607-2.
10. Friedman DS, Chang DS, Jiang Y, et al. Acute angle-closure attacks are uncommon in primary angle-closure suspects after pharmacologic mydriasis: the zhongshan angle-closure prevention trial. *Ophthalmol Glaucoma*. Nov-Dec 2022;5(6):581–586. https://doi.org/10.1016/j.ogla.2022.04.003.