Case Report

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Alpha-Gal syndrome as a novel food allergy: a case report study

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Introduction and importance: Alpha-Gal syndrome (AGS), a distinct form of mammalian meat allergy, presents unique characteristics that set it apart from typical IgE-mediated food hypersensitivities. AGS induces an allergic response typically 3–6 h post-ingestion of mammalian meat, such as beef, pork, or lamb. This prolonged reaction time differentiates AGS from other food allergies, which usually provoke a more immediate response.

Case presentation: The authors present a case of a 35-year-old male patient who, unbeknownst to him, had been experiencing symptoms consistent with Alpha-Gal allergy for several years. His symptoms only subsided upon the complete elimination of mammalian meat from his diet. It was only then that the possibility of AGS was considered. Complete abstinence from mammalian meat, meat by-products, and other α-Gal containing foods is the most effective preventative strategy for AGS. No definitive cure for AGS has been established as of now. Treatment protocols for hypersensitivity reactions are contingent upon the severity of the reaction, with therapies ranging from antihistamine medications to the administration of epinephrine.

Conclusion: There is considerable variability among AGS patients concerning the consumption of dairy products. Some individuals with AGS can safely consume dairy products without any adverse reactions, while others are advised to abstain due to potential allergenic responses. This variability in dairy tolerance among AGS patients warrants further investigation.

Keywords: Alpha-Gal syndrome, case report, food allergy

Introduction

Alpha-Gal syndrome (AGS) denotes an allergy to a carbohydrate moiety, Alpha-Gal, common in most mammals, including livestock, but absent in humans and some primates. The human deficiency of the Alpha-Gal epitope results from ancestral inactivation of the α1-3GT gene[1].

Cetuximab, a chimeric monoclonal antibody primarily used in treating colorectal cancer and squamous cell carcinoma, alongside tick bite saliva, is a significant source of α-Gal, an antigen capable of inducing IgE production against itself. This IgE-mediated hypersensitivity towards α-Gal subsequently cross-reacts with certain red meats, specifically beef, pork, and lamb, precipitating an allergic reaction. Notably, the onset of these allergic symptoms commonly ensues within 3 to 6 hours post-ingestion, demonstrating a markedly delayed temporal profile relative to typical food allergies. This unique time course distinguishes AGS from conventional IgE-mediated food hypersensitivities. Furthermore, immediate anaphylactic reactions to tick bites and cetuximab, attributable to α-Gal sensitization, have been documented. Once again, this observation underscores the distinctive clinical characteristics of AGS compared to other food allergies, reinforcing its status as an exceptional variant within the spectrum of IgE-mediated food hypersensitivities[2].

Prior studies have elucidated that individuals with blood group B produce fewer anti-α-Gal IgE antibodies. Furthermore, a substantial association has been observed between the incidence of red meat allergy after tick bites and individuals with blood types other than B[3]. We present a case of a 35-year-old male exhibiting symptoms indicative of an α-Gal allergy that remained unidentified for several years. Symptom alleviation was achieved solely by eliminating mammalian meat from his diet. The work has been reported in line with the CARE criteria[4].

HIGHLIGHTS

According to the results of the study:

- α-Gal syndrome is a relatively rare condition and poses diagnostic challenges.
- Thus, a thorough patient history encompassing all clinical aspects is vital before initiating any laboratory investigations.

Case presentation

A 35-year-old male patient reported to the pediatric department in Gorgan City, Golestan province, with a 7-year history of late-

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onset anaphylaxis following red meat consumption. Symptoms, including urticaria, hives, itching, runny nose, and eczema, typically manifest with a significant delay after meat ingestion. Multiple clinic visits previously did not resolve the issue, and symptom relief was only observed upon the avoidance of red meat. Symptomatic relief was further managed with antihistamines such as Chlorpheniramine. Also, the patient does not have a history of allergies in herself or her family.

Despite these measures, the patient was admitted to the emergency department multiple times due to anaphylactic attacks. These episodes were mitigated with intravenous fluid therapy, Chlorpheniramine, and hydrocortisone, notably without administering Epinephrine. Subsequently, he was referred to the Allergy and Immunology Department of the Pediatric Hospital in Gorgan City.

Upon admission, the patient denied any history of tick bites, cetuximab use, or snake antivenom exposure. However, given the comprehensive history and physical examination, α-Gal allergy was suspected. Laboratory tests revealed eosinophilia and confirmation of the diagnosis was achieved via a skin prick test and the measurement of α-Gal-specific IgE antibodies. First of all, there is doubt about the occurrence of type 1 hypersensitivity reactions following the consumption of red meat. Chronic spontaneous urticarial Alpha-gal syndrome was initially misdiagnosed as chronic spontaneous urticarial.

On the morning of a subsequent visit, the patient had ingested several grilled meals to demonstrate his allergic response. By 11 AM, he exhibited extensive hives, respiratory distress, nasal flaring, wheezing, loss of consciousness, crampy abdominal pain, and diarrhea, accompanied by hypotension (90/60 mmHg) and tachycardia (pulse rate of 130). In response, we intramuscularly administered 0.5 ml of a 1:1000 epinephrine solution into his vastus lateralis muscle. The patient's critical condition persisted for approximately 30 minutes before stabilization. Alpha-gal IgE test results 0.25 kU/l were considered positive. Given the clear correlation between symptom onset and red meat consumption, the requirement for an oral food challenge to confirm the diagnosis was rendered superfluous. Subsequent laboratory investigations, including a complete blood count and serum tryptase level, were within normal limits.

Discussion

Alpha-Gal is a novel Immunologic adverse reaction to food that can be classified into three subgroups[5].

(1) IgE-mediated: oral allergy syndrome, asthma, rhinitis, and systemic anaphylaxis
(2) Mixed IgE/non-IgE-mediated: atopic dermatitis, eosinophilic gastrointestinal disease
(3) Non-IgE-mediated: celiac disease

Major symptoms observed in patients with AGS include urticaria, gastrointestinal disturbances, angioedema, and potentially life-threatening systemic anaphylaxis, typically following the ingestion of red meat or other α-Gal sources. Although numerous studies have identified IgE to α-Gal as a robust biomarker for diagnosing patients with red meat allergies, there appears to be no correlation between the level of α-Gal-specific IgE and the severity of the disease[5]. Hypersensitivity reactions in AGS can also be provoked by drugs containing cross-reactive epitopes such as cetuximab, measles-mumps-rubella-zoster virus vaccine, and Fenticonazole, collectively referred to as gelatin-containing products. As previously noted, allergic symptoms typically manifest 3–6 h after the consumption of red meat. The onset of reactions to red meat or other α-Gal sources may be expedited by factors such as exercise, alcohol consumption, and the use of nonsteroidal anti-inflammatory drugs[6].

While AGS is typically diagnosed in adults, children may also present with this potentially life-threatening allergy. Exposure to gelatin-containing pastry could be a precipitating factor for hypersensitivity reactions in the pediatric population[7].

The confirmation of AGS diagnosis involves skin prick tests (SPT), determination of serum-specific IgE antibodies, and food challenges. An oral food challenge, considered the gold standard method for diagnosing food allergies, entails the administration of an allergen in established doses followed by observation of the clinical response. However, its utilization for AGS diagnosis is not recommended due to the delayed nature of the reaction and the potential risk of triggering a severe, potentially fatal anaphylactic reaction[8].

The primary preventive strategy proposed for AGS and associated allergic reactions is the complete avoidance of mammalian meat, meat by-products, and other α-Gal containing foods. There is currently no definitive cure for AGS. The management of hypersensitivity reactions hinges on the severity of symptoms, administering treatments such as antihistamines and/or epinephrine as necessary. Regarding dairy product consumption, patient tolerances vary. While some individuals may safely consume dairy products, others are advised to avoid them[8].

Currently, the understanding of α-Gal is being harnessed for various novel strategies in scientific advancements. These include xenotransplantation from α1-3 galactosyltransferase (α1-3 GT) knockout pigs, and anti-cancer mechanisms involving the induction of a systemic protective anti-tumor immune response[9].

Conclusion

AGS is a relatively rare condition and poses diagnostic challenges. Thus, a thorough patient history encompassing all clinical aspects is vital before initiating any laboratory investigations. Further research is imperative to enhance our understanding of risk factors for AGS development, evaluation of diagnostic immunoassays, and establishing the epidemiology and distribution of AGS across diverse populations. Unlike other cases of anaphylaxis (life-threatening symptoms), the reaction in these patients is not fatal despite the severity. The patient is not afraid of eating grilled meat, and his interest has not decreased, but he knows that he will suffer from relatively severe side effects that have responded to the initial treatments and have become more frequent and have not been resistant to the initial treatments (he is cured with only hydrocortisone, serum therapy, and antihistamines without a history of epinephrine injection). This happens again and again for the patient, and the patient does not feel the need to go to the doctor except for a few special cases.

Ethical approval

None.

Consent to participate

An written informed consent was obtained from the parents of patient for possible publication of this information as the case report. The whole research was done under the permission of the Ethics committee of Golestan University of Medical Sciences and also Genetic Testing for parents was done because of their.

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Author contribution

M.G.G. revised the manuscript and finalized the draft; E.G. and S.D. writing draft manuscript; S.A.H. diagnosed and managed this patient and interpretation.

Conflicts of interest disclosure

The authors have no conflicts of interest to declare.

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