

When alpha-gal hides: A case series of atypical presentations of alpha-gal syndrome in children

Tharindi Suriapperuma

svtp.nadeesha@kln.ac.lk

Department of Paediatrics, Faculty of Medicine

Nadisha Badanasinghe

Department of Medical Microbiology and Immunology, Faculty of Medicine

Sachith Mettananda

Department of Paediatrics, Faculty of Medicine

Case Report

Keywords: Alpha-gal syndrome, galactose-alpha-1,3-galactose, tick bites, Ig-E mediated delayed food allergy

Posted Date: July 15th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-9438539/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Journal of Medical Case Reports on August 25th, 2026. See the published version at <https://doi.org/10.1186/s13256-026-06549-z>.

Abstract

Background

Alpha-gal syndrome is an IgE-mediated allergy resulting from sensitisation to galactose-alpha-1,3-galactose (alpha-gal). Although classically associated with delayed urticaria or anaphylaxis following red meat ingestion, it can present with diverse and atypical manifestations. We report four paediatric patients with rare and atypical manifestations of alpha-gal syndrome.

Case presentations

Case 1: An 18-month-old boy with recurrent respiratory symptoms was on treatment for allergic rhinitis and poorly controlled asthma for six months. His symptoms showed an inconsistent association with dairy consumption; however, there were no cutaneous manifestations.

Case 2: An 11-year-old boy with recurrent abdominal pain and altered bowel habits for one year was managed as irritable bowel syndrome. His symptoms frequently followed ingestion of dairy products.

Case 3: An 8-year-old boy had been experiencing brief episodes of urticaria for four months. He was treated as having chronic spontaneous urticaria with poor response to standard treatment.

Case 4: An 18-year-old girl had 19 episodes of idiopathic anaphylaxis since the age of six years, with symptoms that were not consistently associated with an identifiable food trigger.

All patients recalled a history of tick bites. Detailed history revealed delayed symptom onset and inconsistent reactions to alpha-gal-containing foods. The diagnosis of alpha-gal syndrome was confirmed in all four patients by skin prick testing and elevated specific IgE for alpha-gal. Elimination of the implicated food allergens led to complete resolution in all cases.

Conclusions

This case series illustrates the diverse and atypical clinical presentations of alpha-gal syndrome in children which can lead to delayed recognition and misdiagnosis. Increased clinician awareness is the key to early diagnosis, thus preventing recurrent episodes of symptoms and anaphylaxis and improve overall outcomes.

Background

Alpha-gal syndrome (AGS) is an IgE-mediated delayed food allergy resulting from sensitisation to galactose-alpha-1,3-galactose (alpha-gal), a disaccharide, which is found in non-primate mammalian meat such as pork and beef. As alpha-gal is not found in humans, exposure following tick bites, where the allergen is introduced through saliva, leads to sensitization and production of specific IgE in humans (1).

AGS is an emerging and increasingly recognised food allergies in adult worldwide, but less reported in children. The clinical presentation of AGS can vary from skin manifestations to anaphylaxis (1). The wide range of delayed and variable clinical manifestations makes the diagnosis challenging. In this case series, we report four patients with AGS presenting with rare and atypical clinical manifestations.

Case presentations

Case 1: Alpha-gal syndrome presenting with exclusive respiratory symptoms

An 18-month-old boy had recurrent episodes of sneezing, rhinorrhoea and an itchy nose for a 6-month duration. He was initially managed as allergic rhinitis with cetirizine. Due to subsequent recurrent episodes of cough, he was commenced on regular inhaled beclomethasone and inhaled salbutamol as required for a presumed diagnosis of asthma. Despite treatment, his symptoms showed minimal improvement, and he was labelled as having poorly controlled asthma with perennial allergic rhinitis.

On further inquiry, his mother revealed a possible but inconsistent association between ingestion of dairy products and the onset of respiratory symptoms, however, no immediate reactions were observed. He never experienced cutaneous manifestations, such as urticaria or angioedema. His diet included dairy products, but he had no prior exposure to red meat. The mother recalled that the child had been exposed to tick bites a few months ago.

Based on the history, AGS was suspected. The skin prick test (SPT) demonstrated sensitisation to beef, pork, dairy, and gelatine. The specific IgE for alpha-gal was 5.7 kUA/L, confirming the diagnosis of AGS. Following strict avoidance of dairy and mammalian-derived products, the patient showed marked clinical improvement. Antihistamines and inhaled medications were discontinued. At the 6-month follow-up after cessation of medication, he remained asymptomatic without further respiratory exacerbations.

Case 2: Alpha-gal syndrome presenting with isolated abdominal symptoms

An 11-year-old boy presented with recurrent abdominal pain and altered bowel habits over one year. He reported that abdominal pain often occurred on days he consumed dairy products, symptoms developing several hours after ingestion, with no immediate reactions. On some days, he was asymptomatic despite dairy consumption. He reported a history of tick bites in the past.

He was initially diagnosed as having functional abdominal pain and irritable bowel syndrome. He was treated with omeprazole, famotidine and antacids (aluminium hydroxide/magnesium carbonate) on several occasions with minimal symptom improvement. A trial of mebeverine also failed to improve his symptoms.

SPT revealed sensitisation to red meat, dairy and gelatine. The specific IgE for alpha-gal was elevated at 3.56 kUA/L, confirming the diagnosis of AGS. Following the avoidance of dairy and mammalian-derived products, his symptoms improved significantly.

Case 3: Alpha-gal syndrome presenting as chronic spontaneous urticaria

An 8-year-old boy presented with recurrent urticaria for four months. The urticarial episodes occurred intermittently but frequent enough to meet the diagnostic criteria for chronic spontaneous urticaria (CSU). He was initially treated with fexofenadine and loratadine for six weeks, which provided reasonable symptom control, however, symptoms recurred upon discontinuation of antihistamines.

A detailed evaluation revealed that, even though he developed urticaria every week, individual episodes were very brief and resolved with a single dose of antihistamines. The patient recalled having been bitten by ticks previously. His diet was rich in dairy and gelatine-containing foods, and he occasionally ate red meat. AGS was suspected, and avoidance of dairy, gelatine and red meat was advised. Following this, his symptoms improved dramatically.

His SPT revealed sensitisation to red meat, dairy and gelatine, and specific IgE for alpha-gal was 2.47 kUA/L, confirming the diagnosis of AGS. He remained well on a diet free of alpha-gal-containing foods without the requirement for further antihistamines.

Case 4: Alpha-gal syndrome presenting as recurrent anaphylaxis of unknown trigger

An 18-year-old girl was referred following 19 episodes of anaphylaxis since the age of six years, with no identifiable trigger. She was unable to associate any specific foods with her episodes of anaphylaxis, as none were associated with immediate reactions. Consequently, she had not avoided any foods in her diet, which included dairy products. Some episodes were temporally associated with exercise, prompting evaluation for wheat-dependent exercise-induced anaphylaxis, however, specific IgE to omega-5-gladine was undetectable. She also reported intermittent and brief episodes of abdominal pain on some days, for which she had not sought medical treatment. Recently, she experienced an anaphylaxis episode after consuming a fruit juice. A review of the ingredient label revealed milk-derived substances used as flavouring agents, raising suspicion of AGS. She also recalled several tick bite episodes in the past.

The skin prick test revealed sensitisation to the alpha-gal panel (red meat, dairy and gelatine) and specific IgE for alpha-gal was markedly elevated at 23.7 kUA/L, categorised as very high. No further episodes of anaphylaxis were reported following strict avoidance of all food containing alpha-gal.

Discussion

AGS is a unique form of food allergy characterised by delayed hypersensitivity to the disaccharide, galactose- α -1,3-galactose, typically occurring three to eight hours after ingestion of mammalian meat or related products (1). Due to the delayed and inconsistent nature of reactions, in which individuals may not react to all exposures and may react unpredictably to foods containing alpha-gal, the diagnosis of AGS is particularly challenging. Due to these distinct features, patients often present with several episodes of allergy before the definitive diagnosis of AGS is established. These characteristics have been widely recognised as key contributors to under-recognition and or delayed diagnosis of AGS (2).

The classic presentation of AGS involves an allergic reaction to red meat several hours after consumption in an individual who previously tolerated red meat. Notably, while AGS has been described predominantly in adults, emerging evidence underscores a significant paediatric burden (1).

Alpha-gal, a carbohydrate epitope, is present in muscles, blood cells, parenchymal tissue, and secretions of all non-primate mammals. Exposure to a wide range of non-primate mammalian products (red meat, kidneys, milk, gelatine, and blood products) could trigger allergic reactions in sensitised individuals. Other rare sources of alpha-gal include, carrageenan, a food additive and polysaccharide derived from red algae (E407 on food labels), and flounder roe(4).

Amblyomma americanum (lone star tick), *Ixodes ricinus*, *Ixodes holocyclus*, and *Haemaphysalis longicornis* are among the tick species identified as capable of inducing alpha-gal sensitisation in humans (5). The tick species or vectors that induce alpha-gal sensitisation in Sri Lanka are yet to be identified. The source of alpha-gal in ticks is not clearly understood. The hypotheses include endogenous production of alpha-gal by ticks, persistence of residual amounts of alpha-gal in tick secretions following a prior blood meal from a non-primate mammal, or synthesis of alpha-gal in tick saliva by microbial symbionts (5).

Sri Lankan data on AGS were published in 2025, describing its clinical and demographic characteristics, and representing the first report from the Indian subcontinent (6). The study included 57 patients with AGS, of whom 31 were ≤ 12 years. No significant differences in clinical features or reaction timing were identified between children and adults. The most common food trigger was red meat while only 5.2% reacted to cow's milk, with 66.7% of patients presented with anaphylaxis and 38.6% reported gastrointestinal manifestations.

In this case series, we highlight several rare and variable clinical manifestations of AGS in children that extend beyond those commonly described in the limited existing literature on AGS.

Unlike many published cohorts where urticaria and systemic reactions were the most frequent manifestations, one patient in our series presented exclusively with respiratory symptoms that mimicked allergic rhinitis and poorly controlled asthma. This child had presented with several episodes of anaphylaxis with respiratory compromise, which were managed as acute exacerbation of asthma, before the diagnosis of AGS was made. Episodes mimicking allergic rhinitis, such as sneezing and rhinorrhoea,

and isolated wheezing in the absence of other classic allergic features, are rarely emphasised in prior AGS reviews. This case highlights that clinicians should consider AGS in children with recurrent respiratory symptoms following ingestion of alpha-gal-containing foods, even in the absence of typical cutaneous symptoms or prior tolerance to these foods.

Case two presented exclusively with abdominal symptoms, and the patient suffered recurrent episodes of abdominal pain before the diagnosis of AGS was made. Isolated gastrointestinal presentations have been documented in paediatric cohorts, particularly in gastroenterology clinics, where positive specific IgE for alpha-gal was associated with recurrent abdominal pain and symptomatic improvement with dietary elimination (7). Clinicians should therefore consider AGS as a differential diagnosis in children who present with recurrent abdominal pain with unidentified aetiology, even in those who have previously tolerated food containing alpha-gal.

Another important observation in our case series was the misclassification of AGS as chronic spontaneous urticaria (CSU) in case 3. A previous case report has also highlighted a similar misdiagnosis (8). Identification of food triggers is particularly challenging when the delayed onset of symptoms obscures the link to ingestion of mammalian products, further complicated by the inconsistent nature of reactions and the occurrence of allergic symptoms to foods that were previously well tolerated. Without their awareness, allergens such as dairy products may be routinely consumed as components of processed foods and additives, resulting in almost daily symptoms that mimic CSU. This patient had initially been mislabelled as CSU based on the recurrent urticaria; however, complete resolution of his symptoms was achieved following an exclusion diet.

Case 4

in our case series experienced an unacceptably high number of anaphylactic episodes before the correct diagnosis was established. Her clinical course illustrates the highly variable nature of clinical manifestations of AGS. Although she had occasionally reacted to foods containing alpha-gal since age 6, she was able to tolerate the same foods at other times without symptoms, making it nearly impossible to identify the triggers in her diet. Some episodes were likely influenced by co-factors such as exercise, infections and menstruation, which modulate immune thresholds and symptom expression, further complicating the identification of the trigger (9).

Collectively, these cases expand our understanding of AGS beyond the classical descriptions of cutaneous and systemic allergic responses. They reflect the heterogeneous and multifaceted nature of this disease in the paediatric population and underscore the need for heightened clinical vigilance.

Conclusions

In this case series, we reported four rare and diverse clinical manifestations of AGS in children, including isolated respiratory symptoms, recurrent abdominal pain, presentations mimicking CSU and idiopathic anaphylaxis. These atypical presentations lead to repeated misdiagnoses and prolonged diagnostic

delays. Our findings reinforce previous observations that AGS is a highly variable and often under-recognised condition, particularly in paediatric populations. Increased awareness of these unusual clinical patterns is essential for clinicians evaluating children with recurrent, unexplained allergic reactions. Early recognition of AGS and identification of dietary triggers can significantly reduce morbidity by preventing recurrent allergic reactions and potentially life-threatening anaphylaxis. Furthermore, this case series contributes valuable paediatric evidence to the limited global literature on AGS and underscores the need for prospective, population-based studies to better define the epidemiology, mechanisms of variability in clinical expression, and optimal diagnostic strategies for this unique food allergy.

Declarations

Ethics approval and consent to participate:

Written informed consent from the parents of all children and assent from children 10–18 years were obtained.

Consent for publication:

Written informed consent from the legal guardians of all children were obtained for publication of this case series. The copies of the written consent forms would be available on request for review by the Editor-in-Chief of this journal.

Competing interests:

The authors declare that they have no competing interests

Funding:

No funding

Author Contribution

Author's contributions: TS and NB participated in making the diagnosis and management of the children. TS, NB and SM wrote the manuscript. All authors reviewed and approved the final manuscript.

Acknowledgements:

Not applicable

Availability of data and material:

Not applicable

References

1. Kaushik P, Bhatti FS, Bangale T, Marak CP. Alpha-Gal Syndrome: A Concise Review. *Allergies*. 2025; 5(4):42. <https://doi.org/10.3390/allergies5040042>
2. Commins SP. Diagnosis & management of alpha-gal syndrome: lessons from 2,500 patients. *Expert Rev Clin Immunol*. 2020;16(7):667–677. doi: 10.1080/1744666X.2020.1782745. Epub 2020 Jul 8. PMID: 32571129; PMCID: PMC8344025.
3. Tobacman JK. The common food additive carrageenan and the alpha-gal epitope. *J Allergy Clin Immunol*. 2015;136(6):1708–1709. doi: 10.1016/j.jaci.2015.08.048. Epub 2015 Oct 27. PMID: 26518095.
4. Fujiwara M, Araki T. Immediate anaphylaxis due to beef intestine following tick bites. *Allergol Int*. 2019;68(1):127–129. doi: 10.1016/j.alit.2018.08.002. Epub 2018 Aug 23. PMID: 30146464.
5. Commins SP, James HR, Kelly LA, Pochan SL, Workman LJ, Perzanowski MS, Kocan KM, Fahy JV, Nganga LW, Ronmark E, Cooper PJ, Platts-Mills TAE. The relevance of tick bites to the production of IgE antibodies to the mammalian oligosaccharide galactose- α -1,3-galactose. *J. Allergy Clin Immunol*. 2011;127.
6. Dasanayake D, Karunatilake C, Karunaratne C. *et al*. Alpha-gal allergy in a South Asian country. *BMC Immunol*. 2025;26(37).
7. Busing JD, Stone CA Jr, Nicholson MR. Clinical Presentation of Alpha-Gal Syndrome in Pediatric Gastroenterology and Response to Mammalian Dietary Elimination. *Am J Gastroenterol*. 2023;118(7):1293–1296. doi: 10.14309/ajg.0000000000002268. Epub 2023 Mar 28. PMID: 36995329; PMCID: PMC10511000.
8. Bellutti Enders F, Elkuch M, Wörner A, Scherer Hofmeier K, Hartmann K. Alpha-gal syndrome initially misdiagnosed as chronic spontaneous urticaria in a pediatric patient: a case report and review of the literature. *J Med Case Rep*. 2023;17(1):6. doi: 10.1186/s13256-022-03718-8. PMID: 36611183; PMCID: PMC9826568
9. Fischer J, Hebsaker J, Caponetto P, Platts-Mills TAE, Biedermann T. Galactose-alpha-1,3-galactose sensitization is a prerequisite for pork-kidney allergy and cofactor-related mammalian meat anaphylaxis. *J. Allergy Clin Immunol*. 2014;134.