

The first reported cases of meat allergy following tick bites in the UK

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Summary

Allergic reactions frequently involve the production of immunoglobulin E (IgE) antibodies to proteins. However, reactions directed against carbohydrate moieties are increasingly being recognised. Tick bites can contribute to the development of immunoglobulin E to the galactose-1,3-galactose (alpha-gal) moiety on tick salivary proteins. These IgE molecules can cross-react with alpha-gal found in red meats, causing Type I IgE-mediated hypersensitivity reactions to these foods. We present three cases of delayed reactions to beef, pork and lamb in patients with prior tick bites and in the presence of a positive-specific IgE to alpha-gal. Patients were advised to avoid red meat consumption and to carry emergency treatment in the form of anti-histamines with or without adrenaline autoinjector devices. This is the first published report of red meat allergy caused by tick bites suffered in the UK.

Keywords

Clinical, immunology (including allergy), other pathology, pathology

Background

Tick bites may induce delayed allergic reactivity to red meat by stimulating IgE antibodies to alpha gal carbohydrate moieties.

This has been reported in the USA and several European countries. Urticaria is evident in over 90%, with anaphylaxis and gastrointestinal symptoms seen in 60% each. Interestingly, the levels of specific IgE to alpha-gal were similar in those with and without anaphylaxis, atopy and between children and adults.¹ We detail the first report of UK patients with this unusual pattern of allergic reactivity.

Case presentations

Case 1

A 42-year-old male gardener suffered over 100 tick bites on his waist, back and knees over the course of two decades. His 20 or so reactions comprised of urticaria and angioedema accompanied with vomiting and diarrhoea, between 2 and 8 h after eating various red meat-containing dishes including steak and kidney pie, pork and roast beef. His worst reactions were with roast beef, where he experienced faintness. Treatment with antihistamines was helpful and he had never required adrenaline.

Case 2

A 30-year-old previously well man reported multiple tick bites in the 12 months prior to experiencing eight episodes of urticaria and angioedema with varying degrees of dyspnoea, occurring 4–5 h after eating red meat. There was no history of asthma. The reactions were mostly managed with antihistamines with additional adrenaline when there were severe respiratory symptoms. His risk factors for tick bites were unclear and he denied symptoms of other food or drug allergies.

Case 3

A 58-year-old male gardener living in an area of Surrey known to be populated with ticks, suffered over 20 incidents of tick bites over three years, affecting his arms and legs. His index reaction occurred 4–5 h after eating a sausage and comprised a widespread urticarial rash over his arms, legs and chest, followed

Table 1. Summary of cases.

Patient no.	Age of onset (years)	Gender	Number of reactions	Time between ingestion and first symptoms	Examples of foods ingested leading to reactions	Symptoms of reaction	Adrenaline given as treatment	Total IgE (kU/L)	Specific IgE alpha gal (kU/L)	Specific IgE beef (kU/L)	Specific IgE pork (kU/L)	Specific IgE lamb (kU/L)
1	42	Male	20	2–8 h	Steak and kidney pie Pork Roast Beef	Urticaria, angioedema, vomiting, and faintness (on one episode)	No	524	77.3	13.6	20.2	2.21
2	30	Male	8	4–5 h	Red meat	Urticaria, angioedema, difficulty in breathing	Yes	1215	>100	64.4	22.6	9.06
3	58	Male	20	4–5 h	Sausage	Urticaria, mild angioedema, diarrhoea and vomiting, mild difficulty in breathing	Yes	200	34.1	4.56	1.93	1.2

Reference ranges: Total IgE: 0–81 kU/L, Specific IgE: 0–0.34 kU/L

by vomiting, diarrhoea and then mild dyspnoea. He also reported some minor lip and eye swelling during this episode and felt shaky and faint. He was treated with intramuscular adrenaline followed by antihistamines and steroids. Table 1 summarizes the cases above and includes related blood test results.

Discussion

Gal α 1-3Gal β 1-(3)4GlcNAc-R (alpha-gal) is a mammalian blood group antigen not expressed by primates or humans. The discovery of alpha-gal allergy in patients with carcinoma of the bowel reacting to the mouse monoclonal antibody cetuximab which targets cell surface growth factor receptors on various cancers has been described in detail by Berg et al.² In 2009, 25 individuals with red meat allergy³ were reported from the Northern Beaches region of Sydney, an area known to be infested with several tick species. Subsequent cases of red meat allergy have been reported in the rural pre-Alps area of Northern Italy, Spain, Sweden, France and Denmark, where the black-legged tick (*Ixodes scapularis*) has been identified as the probable sensitising species. In Spain, the frequency of positive-specific IgE to alpha-gal in 160 patients with urticaria and anaphylaxis was 26.3%, with an observed correlation with prior tick bites, participation in outdoor activities and pet ownership [4]. Our cases confirm the ability of tick bites in the UK to cause delayed red meat allergy and with similar risk factors to these cases in the Spanish patient cohort.

It is presently unclear why only some individuals bitten by ticks become clinically sensitised to alpha-gal and why the reactions are delayed by several hours, in contrast to conventional IgE-mediated food reactions which usually occur within several minutes. This could in part be related to which species of tick has caused the bite; the lone star tick (*Amblyomma americanum*) and the black-legged tick (*Ixodes scapularis*) have both been found to have alpha-gal in their saliva and are able to activate basophils primed with the plasma of alpha-gal allergic subjects,⁴ whilst the Gulf-Coast tick (*Amblyomma maculatum*) and the American dog tick (*Dermacentor variabilis*) contained no detectable salivary alpha-gal. In Surrey, UK, the most common ticks are *Ixodes ricinus*, *Ixodes hexagonus* and *Ixodes canisuga*, which infect deer (and also sheep), hedgehogs and dogs, respectively.⁵

Other factors influencing sensitisation include the protective blood group B antigen which has structural similarity with alpha-gal, and the balance between pro-allergic IgE and protective IgM and IgG anti-gal

antibodies. Interestingly, it is possible that the basophil activation test may distinguish asymptomatic IgE alpha-gal sensitisation, from clinically important sensitisation.⁶

The reason for the delayed nature of red meat allergy may relate to exposure of the alpha-gal moieties post-ingestion and on chylomicron transfer via the thoracic duct, which is a process that takes several hours.⁷ However, alpha-gal requires lipids but not proteins for its transfer across intestinal monolayers and the delayed digestion of lipids could also explain the late onset of reactions.⁸ Additionally, the processing and degradation of alpha-gal can be delayed when present on the surface of proteins, with the latter perhaps reducing the rapid availability of suitably exposed IgE binding epitopes.⁹

More recently, as our understanding of alpha-gal allergy has improved, the link between this and other tick bite mediated pathology has been explored. Tjernberg et al. investigated the relationship between IgE antibodies to alpha-gal and the prevalence of Lyme borreliosis in 518 healthy blood donors in Sweden.¹⁰ There was no difference in the percentage of patients reporting a history of Lyme borreliosis when comparing the IgE alpha-gal positive and negative groups. This suggests that developing Lyme borreliosis and acquiring IgE alpha-gal sensitisation are two separate phenomena.

Conclusion

Red meat allergy arising from sensitivity to alpha-gal is a relatively rare, but likely under-reported cause of IgE-mediated food allergy with the potential to cause anaphylaxis. It should be considered in patients with delayed onset urticaria and even in those resident in countries where this has not been hitherto described.

Learning points

- Delayed allergic reactivity to red meat following tick bites can occur in the UK.
- This allergy involves specific IgE directed against carbohydrate groups which are present in mammalian red meat as well as certain protein-based drugs.
- The delayed nature of the reactions may relate to digestion-mediated exposure of the allergenic carbohydrate moieties.
- It is a rare but important cause of food allergy that could be missed due to delayed onset of symptoms.

Declarations

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