Could Cat Flea Bites Contribute to α-Gal Serum IgE Levels in Humans?

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About 25 million years ago, in an evolutionary event, ancestral humanoids lost their ability to synthesize the carbohydrate galactose-α,1,3-galactose (α-gal) [1]. The α-gal epitope has become highly immunogenic to humans, in contrast with other mammals [1]. Consumption of mammalian meat or administration of drugs of mammalian origin (cetuximab, snake antivenom, gelatin-containing vaccines or drugs) [1] can elicit anaphylaxis in individuals with specific IgE (sIgE) to α-gal. This novel allergy is termed α-gal syndrome. α-Gal-specific IgE is environmentally induced through bites by ticks and mites [1,2]. The following case report addresses other possible bloodsucking parasites that are potentially involved with α-gal sIgE formation.

A 30-year-old biology student was assessed at the allergy unit in October after 6 episodes of nocturnal angioedema and urticaria during the previous 3 months. These events occurred 3 to 4 hours after warm dinners with pork or beef. The patient had a medical history of allergic rhinitis but not of food allergy. He described reactions lasting for more than 1 week. A veterinarian had been consulted and treatment initiated, although this was not yet complete at the time of presentation. Upon questioning, the patient recalled tick bites 2 years previously, but not during the previous summer.

Prick-to-prick skin tests performed with fresh preparations of beef and pork meat and pork and beef kidney were positive. Intradermal testing with a 1:100 dilution of gelatine polysuccinate infusion solution (Gelafundin 4%) was also positive, while prick testing with commercially available and certified food and meat test solutions proved negative. Laboratory tests revealed elevated total IgE (IgE) of 137 kU/L and sIgE of 7.7 kU/L for pork, 12.3 kU/L for beef, and 57.2 kU/L for α-gal (bovine thyroglobulin) (ImmunoCAP, Thermo Fisher Scientific). Serum basal tryptase was 4.8 µg/L (reference range, <11.4 µg/L).

The patient was diagnosed with α-gal syndrome based on the clinical history and diagnostic findings.

The patient changed his diet to poultry and fish. At the follow-up appointment 6 weeks later, he reported no further episodes of generalized urticaria. Efforts to control the cat’s flea infestation were unsuccessful. In fact, the patient had experienced more flea bites in the meantime. Follow-up serological testing showed an increase in IgE levels, ie, the tIgE concentration was 312 kU/L, sIgE to pork 20.2 kU/L, sIgE to beef 33.1 kU/L, and sIgE to α-gal 115 kU/L. The patient reported not having received tick bites or developed a chigger rash since testing, and activities with a high risk of bites had not taken place. Given the seasonally low daily temperatures in autumn, activity may have reduced during the daytime temperature 8.4°C, activity for the most frequent local tick, Ixodes ricinus, was low, and the likelihood of unnoticed tick bites was assumed to be low.

We present the first case of a significant increase in α-gal sIgE titers in the context of cat flea bites. There is strong scientific evidence advocating that bites from hard ticks (Ixodidae, subclass Acari, class Arachnida) can induce α-gal sIgE and increase sIgE titers [1]. Based on clinical observations, it is also possible that bites from chiggers (Trombiculidae, subclass Acari, class Arachnida) can contribute to α-gal sensitization [2]. Ticks and mites are obligate parasites requiring a blood meal from mammals or other vertebrates for each stage in their lifecycle [3]. Hence, blood meal constituents are absorbed during hematophagy and stored in the hemolymph [3]. During the next bite, various constituents of the previous host, including α-gal–containing glycoproteins, are secreted into the wound with the tick’s saliva [4,5]. In order to undermine the host’s immune defense, a predominantly Th2 milieu is established in the wound, thus creating immunological conditions that stimulate the production of sIgE to α-gal [5]. Following a tick bite, clinical signs of α-gal sIgE-positive individuals include long lasting and severe local pruritic eruptions along with the boosting of α-gal sIgE titers [6].

Ticks/mites and fleas (Pulicidae, class Insecta) share certain physiological similarities. In the adult stage, fleas are also obligate hematophagous animals that ingest host blood meal constituents [7]. Fleas, however, are characterized by greater mobility and more frequent host changes and can take blood with bites several times within the same individual (“breakfast, lunch, and dinner sign” in humans) [7]. In Europe, approximately 15% of domestic cats are infested by Ctenocephalides felis, and measures for pest control can...
be laborious [7,8]. Although their main hosts are cats and dogs, cat fleas may also infest humans as accidental hosts. Considering the large numbers of cats kept as pets, human cat flea infestation is assumed to be underreported [8]. Cat fleas transmit various pathogens (eg, *Rickettsia* species) with their saliva [9]. Therefore, in a manner similar to ticks and mites (Figure), they likely transfer traces of α-gal–carrying glycoprotein from a previous blood meal on a cat during a further bite to an accidental human host. This can result in persistent itching and local inflammation around the bite area and increased sIgE to α-gal in susceptible individuals.

Figure. In contrast to adult female hard ticks feeding on a single host for several days, adult female cat fleas collect the blood required for laying eggs by multiple short-term bites on a single or multiple hosts (“breakfast, lunch, and dinner sign” in humans). According to this hypothesis, cat fleas can transfer traces of α-gal–carrying glycoprotein from a previous blood meal on a cat during a further bite to an accidental human host. This can result in persistent itching and local inflammation around the bite area and increased sIgE to α-gal in susceptible individuals.


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**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

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