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Alpha-gal anaphylaxis: the first case report in Italy

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KEY WORDS

Galactose-alpha-1,3-galactose (alpha-gal); red meat; Food allergy; delayed anaphylaxis

Summary

We report the case of a 55-year-old man who went into anaphylactic shock six hours after eating a meal containing meat. He reported having had several tick bites in months before the reaction. The serum specific IgE showed strong positivity to alpha-gal. This is clearly alpha-gal anaphylaxis with delayed onset after meat ingestion caused by tick bite, confirmed by alpha-gal IgE positivity.

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A new form of delayed anaphylaxis has been observed in the United States since 2009 (1), due to IgE antibody directed at a mammalian oligosaccharide epitope, galactose-alpha-1,3-galactose (alpha-gal).

Alpha-gal has been associated with two distinct forms of anaphylaxis: immediate-onset anaphylaxis during first exposure to intravenous cetuximab (2) and delayed-onset anaphylaxis 3-6 hours after meat ingestion.

Further studies strongly suggested that tick bites were a cause, if not the only significant cause, of IgE Ab responses to alpha-gal in the United States (3).

In Australia (4) and in Europe (5) cases of delayed anaphylaxis related to IgE-mediated alpha-gal sensitisation were subsequently observed, although the tick responsible seems to be *Ixodes*, whereas *Amblyoma americanum* seems to be the vector in the USA.

We report the case of a 55-year-old man who, in February and March 2013, experienced two generalised urticaria episodes,

the second one with associated angioedema and dyspnea. He was cared for in the Allergy Unit of Castelli Hospital, Verbania, Italy. The patient presented a personal history of hypertension treated with diuretic and sartanic, while no history of allergies or asthma had been reported in the past. Skin-prick tests, performed with commercial extracts for a standard panel of food allergens, resulted negative.

In August 2013 he reported itching, angioedema, dysphasia and dyspnea about six hours after having a meal containing meat. His wife administered betamethasone and marked bronchospasm was diagnosed in the Emergency Department. The patient was treated with methylprednisolone and epinephrin.

The patient reported not having taken any unusual medication or having eaten any food in the 6 hours prior to the anaphylactic episode. He also reported that he had not been stung or bitten by any insects. Skin-prick tests for food and inhalant allergens were again performed, with negative results. His basal serum

tryptase level was normal. The final diagnosis was “idiopathic anaphylaxis” and the epinephrine autoinjector was prescribed. In light of the time span since the meal, the reaction suggested alpha-gal anaphylaxis. In fact, the patient reported several tick bites during the summer as well as the previous summers. So prick-to-prick tests were performed with fresh meats (lamb, pork and beef) and sIgE for pork, beef, chicken and lamb and resulted negative.

In addition, prick-to-prick tests with beef liver and pork kidney (the alpha-gal richest organ) were performed and resulted positive. Finally the ImmunoCap technique (ThermoFisher, Sweden) was used to measure sIgE antibodies to alpha-gal *in sera*, which were collected in October 2013 and June 2014. The results were >100 kU/L and 41 kU/L, respectively.

Several species of tick are endemic in the alpine environment near Lake Maggiore. The patient was probably bitten by the *Ixodes ricinus* species, predominant in rural and woodland areas. The last episode described is clearly alpha-gal anaphylaxis with delayed onset after meat ingestion, caused by tick bite, confirmed by alpha-gal sIgE positivity.

In any case, we cannot rule out that the previous two cases of urticaria were due to an allergic pathogenesis. These episodes could have been milder as the most recent tick bite occurred the previous summer with a consequent decrease in sIgE level to alpha-gal. In fact, as reported in the literature, the temporal

proximity of tick bites - as well as the composition of meat - is the main trigger for allergic reactions (6). Consistent with the above observations, the patient reported having eaten roast beef at lunch the day the anaphylaxis occurred. Unfortunately we don't know what he had eaten in the two previous cases. In conclusion, to our knowledge this is the first reported case of alpha-gal anaphylaxis in Italy.

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