

Successful beef desensitization in 2 adult patients with a delayed-type reaction to red meat



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Clinical Implications

- In this report the first successful desensitization protocol to red meat in 2 adult patients with a delayed-onset red meat allergy and alpha-gal sensitization is presented.

TO THE EDITOR:

Allergic reactions to red meat are relatively uncommon and responsible for approximately 3% of all food allergies.¹ Recently, a new syndrome has been described in which delayed onset of anaphylaxis occurs 3 to 6 hours after mammalian meat consumption. This reaction is associated with IgE antibodies directed against oligosaccharides galactose-alpha-1,3-galactose (alpha-gal).² Following this finding it was concluded that some patients previously diagnosed with “spontaneous” or “idiopathic” anaphylaxis may have had delayed anaphylaxis to red meat that was not immediately recognized because of the significant delay between the exposure to meat and the appearance of symptoms.³ Although avoidance is the main treatment option for food allergies, it can cause difficulties especially in children who are allergic to common foods.^{4,5} For that reason, food immunotherapy trials have been undertaken with children to selected foods, such as milk and peanuts.⁶ Since the avoidance of beef or lamb is not difficult for adults, desensitization has not been commonly considered as an option for “red meat” cases.⁷ Here, we present 2 cases of delayed-onset red meat allergy that were successfully desensitized to beef.

CASE 1

A 21-year-old female patient was referred to our Allergy Outpatient Clinic because of a history of delayed anaphylaxis episodes from the consumption of beef with no concomitant food additives or spices. The patient had had angioedema and urticaria attacks since the age of 7 years, but her family was not aware of her red meat allergy until she was 15 years old when she experienced her first anaphylactic episode 4 hours after beef consumption. Although she has avoided red meat including lamb since that time, she has still experienced occasional anaphylaxis episodes because of accidental exposures to beef, even in trace amounts. She could not definitively state the last time she was accidentally exposed, but tentatively identified it as 4 years earlier. She and her parents were not aware of any tick bites during her childhood, but noted that she played in hayfields and could have been exposed to a tick bite. Also, she added that she might have had tick bites in the hazel nut grove in which she worked every summer. She tolerated all administered vaccines during her childhood. A skin prick test with cooked beef resulted

in a 7-mm wheal, whereas prick test results with cooked lamb, milk, cat, dog dander, turkey, chicken, and fish were negative. Because of religious rules, pork consumption is not common in our country; therefore, she was not skin tested for pork. Alpha-gal specific IgE level in the serum was 1.5 kU/L. Serum specific IgE levels for beef and lamb meat were both negative. Finally, an intradermal test with cetuximab of 1/1000 dilution was positive with a wheal and flare diameter of 6 mm.

We planned to determine if 4 years of red meat avoidance had decreased the patient’s sensitization⁸; a single blind provocation test was undertaken with an initial dose of 2 g followed by a doubled dose (4 g) 6 hours later. Five hours after the second dose, dyspnea, palpitations, and hypotension began and were treated with anaphylaxis measures including 0.25 mg of intramuscular adrenaline.

The patient was then informed of treatment options and she consented to be desensitized to beef. A 27-step beef desensitization protocol (Table 1) was prepared. The protocol began with 10 drops (0.00005 mg meat) of beef extract twice daily for 2 days. On the first day, the patient’s arm began to itch 4 hours after the first consumption, but she recovered without treatment within an hour of the onset of the reaction. The second dose of beef extract was tolerated without any complaints. On the second day, the same procedure was repeated without any symptoms. On the third day, the administered dose was doubled. By the fifth day, the patient transitioned to consuming increasing amounts of cooked beef. Beef consumption doubled every day, with 2 doses a day given 4 hours apart, every day. On weekends, she ate meat at home in the amount administered the day she was last at the hospital. No further reactions occurred for the remainder of the procedure. She tolerated the final 60-g dose without difficulty. The patient subsequently became tolerant to a serving size of 100 g of beef and has continued eating it every day for at least 6 months (at the time of this report) without any adverse reaction. Skin prick tests with fresh and cooked beef repeated 6 months after the treatment revealed negative results (wheal diameter, 2 mm). Serum alpha-gal sIgE displayed a 7-fold increase (10 kU/L) in 2 months, which is an expected finding in oral immunotherapy.⁹

CASE 2

A 55-year-old male patient was referred to our Allergy Outpatient Clinic because of a history of delayed urticaria episodes due to the consumption of beef and lamb. The patient had experienced urticaria attacks occurring several hours after meals containing beef since the age of 30 years. He had his first tick bite when he was 30 years old and experienced tick bites several times since then. His last tick bite was 4 years ago. Skin prick test results with cooked beef, lamb, milk, turkey, chicken, fish, cat, and dog dander were negative. Alpha-gal specific IgE level in the serum was 84 kU/L. Specific IgE levels for beef and lamb meat were both negative. A single blind oral provocation test with 6 g of beef resulted in generalized itchy urticaria after 6 hours and was treated immediately. As the patient strongly desired to be able to eat red meat, the desensitization option was explained to him. After obtaining his consent, the desensitization protocol was followed (Table 1) and there were no adverse reactions until the

TABLE 1. Red meat desensitization protocol

Day's dose	First dose	Second dose	Daily cumulative dose
Starting solution: % 0.1 Cooked meat extract*			
Day 1	10 drops [†]	10 drops	20 drops
Day 2	10 drops	10 drops	20 drops
Day 3	20 drops	20 drops	40 drops
Day 4	40 drops	40 drops	80 drops
Cooked pure meat			
Day 5	0.5 mg	0.5 mg	1 mg
Days 6-8	1 mg	1 mg	2 mg
Day 9	2 mg	2 mg	4 mg
Day 10	4 mg	4 mg	8 mg
Day 11	8 mg	8 mg	16 mg
Day 12	16 mg	16 mg	32 mg
Days 13-15	32 mg	32 mg	64 mg
Day 16	64 mg	64 mg	128 mg
Day 17	128 mg	128 mg	256 mg
Day 18	256 mg	256 mg	512 mg
Day 19	500 mg	500 mg	1 g
Days 20-22	1 g	1 g	2 g
Day 23	2 g	2 g	4 g
Day 24	4 g	4 g	8 g
Day 25	8 g	8 g	16 g
Day 26	16 g	16 g	32 g
Day 27	32 g	32 g	64 g

*Solution 1: 6 mg meat cooked in 600 mL water (1%). Solution 2: 10 mL solution 1 + 90 mL water (0.1%).

[†]1 mL: 20 drops (0.0001 mg meat).

26th day when the patient had itchy urticaria plaques, particularly on his arms and legs 6 hours after the first meat consumption of the day. Accordingly, the next day's dose of beef was reduced by half. No further reactions occurred for the remainder of the procedure. The patient subsequently became tolerant to a serving size of 100 g of beef and has continued eating beef every day for at least 2 months (at the time of this report) without any adverse reactions.

Since it was first described in 2009, there has been an increasing awareness of IgE-mediated food allergies to mammalian meat that are related to tick bites, known as an alpha-gal food allergy.¹⁰ Although the majority of patient reports have come from the United States, other patients were also reported from Australia, Western Europe, Japan, and Korea and were linked to tick bites. The delayed nature of hypersensitivity reactions to beef in our patients suggested an alpha-gal-related food allergy; elevated serum alpha-gal specific IgE levels and cetuximab skin test positivity in the first patient confirmed this

assumption. Although tick bite history was uncertain in the first patient, the possibility that such an incident occurred in her childhood is possible. In this context, these are the first reported alpha-gal-related meat-allergic patients from Turkey.

In addition, to our knowledge, these 2 cases are the first examples of red meat desensitization in patients with delayed-onset hypersensitivity to beef. Red meat-allergic patients are generally advised to avoid meat in their diets. However, serious incidents can occur despite careful avoidance measures, as seen in our first patient. Apart from that, avoidance of a common food item affects the patient's quality of life. For such circumstances, red meat desensitization can provide a better option for safer management.

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