

Acknowledgments

We thank UW-ICTR.

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IRB approval status: Reviewed and approved by University of Wisconsin and Oregon Health and Science University, approval #00018823.

Conflict of interest: None.

Funding source: None.

doi: 10.1111/ijd.14892

References

- 1 Rubio-Tapia A, Van Dyke CT, Lahr BD, *et al.* Predictors of family risk for celiac disease: a population-based study. *Clin Gastroenterol Hepatol* 2008; **6**: 983–987.
- 2 Song MS, Farber D, Bitton A, *et al.* Dermatomyositis associated with celiac disease: response to a gluten-free diet. *Can J Gastroenterol* 2006; **20**: 433–435.
- 3 Dahan S, Shor DB, Comaneshter D, *et al.* All disease begins in the gut: celiac disease co-existence with SLE. *Autoimmun Rev* 2016; **15**: 848–853.
- 4 Caio G, Volta U, Sapone A, *et al.* Celiac disease: a comprehensive current review. *BMC Med* 2019; **17**: 142.
- 5 Guz-Mark A, Feldman BS, Ghilai A, *et al.* High rates of serology testing for coeliac disease, and low rates of endoscopy in serologically positive children and adults in Israel: lessons from a large real-world database. *Eur J Gastroenterol Hepatol* 2020; **32**: 329–334.
- 6 Demirezer Bolat A, Akin FE, Tahtacı M, *et al.* Risk factors for polyautoimmunity among patients with celiac disease: a cross-sectional survey. *Digestion* 2015; **92**: 185–191.
- 7 Freeman HJ. Adult celiac disease followed by onset of systemic lupus erythematosus. *J Clin Gastroenterol* 2008; **42**: 252–255.

Mammalian meat allergy – beyond urticaria?

Dear Editor,

Mammalian meat allergy (MMA) after tick bites¹ is an emerging IgE-mediated hypersensitivity reaction against the oligosaccharide galactose- α -1,3-galactose (α -gal) found in mammalian meat. Patients typically present with delayed anaphylaxis, angioedema, and urticaria following meat ingestion.^{1,2} Anaphylaxis has also been seen with cetuximab treatment, as α -gal residues have been found on the Fab segments of the

monoclonal antibody.³ Herein, we report the case of a patient with MMA presenting with exfoliative erythroderma, which, to our knowledge, has not been previously described.

An 88-year-old male presented with a 2-month history of a generalized, pruritic rash. The patient had an ill-defined history of an eruption on the back that had progressively worsened. Physical examination revealed widespread, exfoliative, erythematous plaques involving >90% of his body surface area (Fig. 1). Histologic examination of skin biopsies from the arms and scalp demonstrated a subacute spongiotic dermatitis with slight acanthosis and a superficial perivascular infiltrate of lymphocytes and eosinophils consistent with an exfoliative erythroderma secondary to a hypersensitivity reaction (Fig. 2). The patient was treated with topical corticosteroids in combination with soriatane, followed by methotrexate, with little improvement.

After acquiring outside records, we discovered that the patient had developed an anaphylactic reaction to his first dose of cetuximab for metastatic squamous cell carcinoma of the head and neck. Further history taking revealed that his rash progressively worsened and became erythrodermic shortly after his cetuximab infusion. The patient also related a history of numerous tick bites throughout his lifetime, the most recent of which occurred a few months prior to the onset of rash. After elucidation of the above history, serologic testing revealed elevated serum IgE against α -gal (33.20 kU/l), beef (21.50 kU/l), lamb (2.27 kU/l), and pork (14.10 kU/l). The patient was instructed to eliminate meat from his diet. His erythroderma gradually resolved over the subsequent 2–3 weeks and has remained clear for over 8 months.

MMA after tick bites is an emergent tick-mediated, type I hypersensitivity reaction to the oligosaccharide α -gal. MMA was first reported by van Nunen *et al.*¹ in Australia and has since been reported on all six continents where humans are bitten by hard ticks. While the involved ticks vary between countries, *Amblyomma americanum*, the Lone Star tick, has been implicated in the United States. MMA commonly presents with delayed urticaria, angioedema, and anaphylaxis following ingestion of meat. To our knowledge, this is the first report of MMA presenting with exfoliative erythroderma.

While the pathogenic mechanism underlying this presentation is unclear, it may represent a systemic contact dermatitis (SCD) to mammalian meat. SCDs are thought to be type IV hypersensitivity reactions, most commonly to medications, metals, and food.⁴ Contrary to other causes, food-induced SCD is refractory to traditional treatments and is often persistent, as many patients are unaware they are ingesting their allergen, as seen in our case. SCDs are known to present with erythroderma clinically and demonstrate spongiotic changes histologically.⁴

Additionally, recent evidence suggests that MMA may not be limited to a type I, IgE-mediated hypersensitivity reaction. Lauer *et al.*⁵ reported probable T cell-mediated hypersensitivity reactions to mammalian meat in the gastrointestinal tract of three patients, suggesting that there may be a role for type IV

Figure 1 Exfoliative erythroderma involving >90% body surface area, most prominent on arms, back, and legs

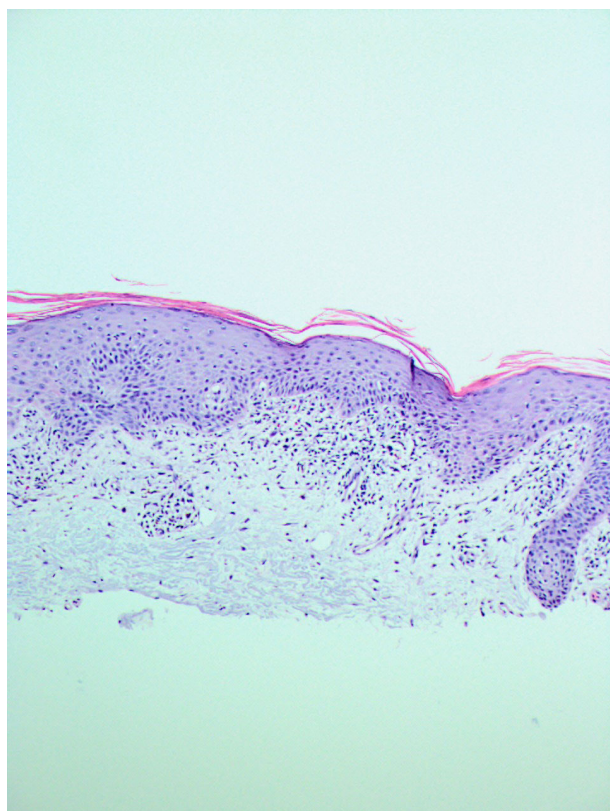


Figure 2 Subacute spongiotic dermatitis with slight acanthosis and a superficial perivascular infiltrate of lymphocytes and eosinophils (hematoxylin and eosin, $\times 100$)

hypersensitivity reactions in MMA. Our patient's localized rash became erythrodermic shortly after his anaphylactic reaction to cetuximab. This event suggests the possibility of an initial IgE-mediated, localized eruption, which subsequently transformed into a T cell-mediated SCD following cetuximab treatment. It also suggests a potential role for cetuximab in the reconstitution of the patient's immune system leading to this phenomenon. However, further studies are warranted to elucidate all potential pathogenic mechanisms in MMA.

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Conflict of interest: None.

Funding source: None.

doi: 10.1111/ijd.14897

References

- 1 van Nunen SA, O'Connor KS, Clarke LR, *et al.* The association between *Ixodes holocyclus* tick bite reactions and red meat allergy. *Intern Med J* 2007; **39**: A132.
- 2 Commins SP, Satinover SM, Hosen I, *et al.* Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose- α -1, 3-galactose. *J Allergy Clin Immunol* 2009; **123**: 426–433.
- 3 Chung CH, Mirakhur B, Chan E, *et al.* Cetuximab-induced anaphylaxis and IgE specific for galactose- α -1, 3-galactose. *N Engl J Med* 2008; **358**: 1109–1117.
- 4 Aquino M, Rosner G. Systemic contact dermatitis. *Clin Rev Allergy Immunol* 2019; **56**: 9–18.
- 5 Lauer S, Burk M, Broadfoot A, *et al.* Food carbohydrate induced enterocolitis syndrome. *Intern Med J.* 2019; **49**: 23.