



Protracted severe food anaphylaxis: Should we incriminate expired epinephrine pen or clonal mast cell disorder?

We read with great interest the report by Doll et al¹ on severe anaphylaxis in a 70-year-old woman after ingestion of pumpkin seed, beginning with nausea and a sense of impending doom, followed by several syncopal episodes, despite the use of an expired epinephrine pen. Three hours later, the patient was still found to be in shock and started recovering only after a second dose of epinephrine. Diagnostic workup found normal baseline serum tryptase levels at 6 ng/mL and positive skin prick test reactions to pumpkin seed. Specific immunoglobulin E levels to pumpkin seed were not assessed, although they were lower than 0.10 kU/L to pumpkin flesh, which has been described in previous case reports on pumpkin seed anaphylaxis.²

Symptom severity might have been due to the lack of efficacy of an expired epinephrine pen or inadequate epinephrine dose administration in relation to the woman's weight. However, it is noteworthy that the patient presented with severe cardiovascular symptoms in the absence of urticaria at the time of anaphylaxis. In patients with anaphylaxis in this type of clinical setting, an underlying clonal mast cell disorder (c-MCD) should be suspected and, if present, would equally explain symptom severity.^{3,4}

Prevalence of anaphylaxis in adult patients with mastocytosis is estimated to be 22%, 43%, and 49% in different study populations, whereas it is evaluated at 0.3% in the general population (approximately 100 times higher).^{4,5} Hymenoptera stings are the most common elicitors of anaphylaxis in adults with c-MCD (50%),^{3,4} and food is responsible in 6% to 10% of these patients.³

Gülen et al⁶ found that 72% of their patients with mastocytosis presented with syncope attacks. Danish investigators identified mastocytosis in 7.7% of adults presenting with suspected anaphylaxis by *KIT* D816V mutation screening of peripheral blood. Mastocytosis was significantly associated with severe anaphylaxis in the absence of skin lesions. Interestingly, none of the patients diagnosed with c-MCD had increased baseline serum tryptase (sBT) levels.⁷ Recent publications have emphasized the fact that normal sBT levels do not rule out an underlying c-MCD^{3,4,8,9} (10% of patients with mastocytosis and without skin lesions in a Spanish series).³

Spanish investigators developed and validated the Red Española de Mastocytosis (REMA) score as a diagnostic tool for predicting c-MCD in patients with systemic mast cell activation symptoms including anaphylaxis. This model scores sex (male, +1; female, -1), absence (+1) or presence (-2) of itching, urticaria, or angioedema,

presence of pre-syncope and/or syncope (+3), and sBT levels lower than 15 ng/mL (-1) or higher than 25 ng/mL (+2). A score of at least 2 has a predictive value of approximately 90% in identifying patients with anaphylaxis and an underlying c-MCD.⁸ The REMA score has proved to be more efficient than sBT levels alone for the identification of patients with an underlying c-MCD; accordingly, it has been incorporated in the updated consensus algorithm for the diagnosis of mastocytosis developed by the European Competence Network on Mastocytosis.⁹ When applying this tool in the patient described by Doll et al, a REMA score of +2 is calculated and therefore would suggest that an underlying c-MCD should be sought.

Catharina Chatain, MD*

Isabelle Boccon-Gibod, MD†

Laurence Bouillet, MD, PhD†

Marie-Thérèse Leccia, MD, PhD*

*Department of Dermatology, Allergology and Photobiology
Centre Hospitalier Universitaire de Grenoble
Grenoble, France

†Department of Internal Medicine
Centre Hospitalier Universitaire de Grenoble
Grenoble, France
cchatain@chu-grenoble.fr

References

- [1] Doll R, Johnson J, Peppers BP, et al. IgE-mediated anaphylactic shock caused by pumpkin seed in an adult. *Ann Allergy Asthma Immunol*. 2017;118:377–378.
- [2] Patel A, Bahna SL. Hypersensitivities to sesame and other common edible seeds. *Allergy*. 2016;71:1405–1413.
- [3] González-de-Olano D, Álvarez-Twose I. Insights in anaphylaxis and clonal mast cell disorders. *Front Immunol*. 2017;8:792.
- [4] Schuch A, Brockow K. Mastocytosis and anaphylaxis. *Immunol Allergy Clin North Am*. 2017;37:153–164.
- [5] Muraro A, Roberts G, Worm M, et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy*. 2014;69:1026–1045.
- [6] Gülen T, Hägglund H, Dahlén B, et al. High prevalence of anaphylaxis in patients with systemic mastocytosis—a single-centre experience. *Clin Exp Allergy*. 2014;44:121–129.
- [7] Ruiz Oropeza A, Bindslev-Jensen C, Broesby-Olsen S, et al. Patterns of anaphylaxis after diagnostic work-up: a follow-up study of 226 patients with suspected anaphylaxis [published online ahead of print May 19, 2017]. *Allergy*. <https://doi.org/10.1111/all.13207>.
- [8] Alvarez-Twose I, Gonzalez-de-Olano D, Sanchez-Munoz L, et al. Validation of the REMA score for predicting mast cell clonality and systemic mastocytosis in patients with systemic mast cell activation symptoms. *Int Arch Allergy Immunol*. 2012;157:275–280.
- [9] Valent P, Escribano L, Broesby-Olsen S, et al. Proposed diagnostic algorithm for patients with suspected mastocytosis: a proposal of the European Competence Network on Mastocytosis. *Allergy*. 2014;69:1267–1274.

Disclosure: Authors have nothing to disclose.

Authors' response

Thank you for the further inquiries and interest in our publication "IgE-Mediated Anaphylactic Shock Caused by Pumpkin Seed in an Adult" by Doll et al.¹ We hope that the following discussion will clarify some of the issues surrounding our case that were discussed in the article "Protracted Severe Food Anaphylaxis: Should

We Incriminate Expired Epinephrine Pen or a Clonal Mast Cell Disorder?" by Chatain et al.²

Anaphylactic episodes can occur in 3 distinct patterns: uni-phasic, biphasic, or protracted.³ Most episodes of food-induced anaphylaxis are uni-phasic, with a smaller number of reported cases being biphasic or protracted.⁴ Protracted anaphylaxis is defined as an anaphylactic reaction that lasts for hours, days, or even weeks and might require vasopressor or ventilatory support.⁵ There have been only a limited number of case reports and small series available

Disclosures: Authors have nothing to disclose.

