

Correspondence

Reply

To the Editor:

The case study entitled “Successful treatment of idiopathic anaphylaxis in an adolescent” presented by Pitt et al¹ documents the effect of omalizumab on the frequency of anaphylactic events in a patient with anaphylaxis. The results of the allergy evaluation are not presented, but presumably no agent was identified that precipitated the episodes of anaphylaxis.

The patient had documented hypotensive events with a significant increase in serum tryptase levels above baseline values. Although the patient had a documented baseline serum tryptase level of greater than 20 ng/mL and 10% mast cells in the marrow, it is not clear whether focal collections of mast cells were found (the major criterion to diagnose systemic mastocytosis). If such lesions were not found, then the diagnosis of mastocytosis requires reliance on the remaining World Health Organization minor criteria (detection of the *ckit D816V* mutation, >25 spindle-shaped mast cells on bone marrow biopsy, and CD25⁺ mast cells), which have not been either completed or included.² Systemic mastocytosis is an important diagnosis to confirm because there are studies documenting a potential increased risk in certain clinical settings, such as venomous insect anaphylaxis,³ reactions to radioiodinated contrast dye,⁴ and evolution of associated hematologic disorders.⁵

There are case reports of patients with idiopathic anaphylaxis demonstrating a response to omalizumab therapy with and without the diagnosis of systemic mastocytosis.^{6,7} Also important is the relatively benign adverse event of local swelling, which has also been seen in other studies. In a follow-up to our study of 2 patients with mastocytosis who continue to receive omalizumab therapy, patients 1 and 2 in that report have now received therapy without serious adverse events for 5.5 and 4 years, respectively. Patient 1 had a breakthrough event on monthly therapy after missing a dose for 8 weeks.

The mechanisms that underlie the ability of omalizumab to decrease the frequency of anaphylaxis are poorly understood but

might include fewer IgE receptors for antigen engagement on the surfaces of basophils and mast cells,⁸ as well as a possible dampening of signaling events initiated by antigen binding to the IgE receptor. An essential question that has not been addressed is the duration of therapy required with omalizumab for continued control. Because of the sporadic nature of idiopathic anaphylaxis and the fact that the cause remains elusive, a finite period of therapy cannot be recommended with any certainty.

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REFERENCES

1. Pitt TJ, Cisneros N, Kalicinsky C, Becker AB. Successful treatment of idiopathic anaphylaxis in an adolescent. *J Allergy Clin Immunol* 2010; ■■■:■■■.
2. Valent P, Li CY, Longley BJ, Metcalfe DD, Parwaresch RM, Bennett J. World Health Organization classification of tumours, pathology and genetics of tumours of the haematopoietic and lymphoid tissues. Lyon: IARC Press; 2001.
3. Bonadonna P, Perbellini O, Passalacqua G, Caruso B, Colarossi S, Dal Fior D, et al. Clonal mast cell disorders in patients with systemic reactions to Hymenoptera stings and increased serum tryptase levels. *J Allergy Clin Immunol* 2009;123:680-6.
4. Weingarten TN, Volcheck GW, Sprung J. Anaphylactoid reaction to intravenous contrast in patient with systemic mastocytosis. *Anaesth Intensive Care* 2009;37:646-9.
5. Travis WD, Li CY, Yam LT, Bergstralh EJ, Swee RG. Significance of systemic mast cell disease with associated hematologic disorders. *Cancer* 1988;62:965-72.
6. Carter MC, Robyn JA, Bressler PB, Walker JC, Shapiro GG, Metcalfe DD. Omalizumab for the treatment of unprovoked anaphylaxis in patients with systemic mastocytosis. *J Allergy Clin Immunol* 2007;119:1550-1.
7. Warrier P, Casale TB. Omalizumab in idiopathic anaphylaxis. *Ann Allergy Asthma Immunol* 2009;102:257-8.
8. Beck LA, Marcotte GV, MacGlashan D, Togias A, Saini S. Omalizumab-induced reductions in mast cell FcεpsilonR1 expression and function. *J Allergy Clin Immunol* 2004;114:527-30.

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