



Anaphylaxis caused by mosquito allergy in systemic mastocytosis

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Culex pipiens

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In the summer of 1996, a 56-year-old man was bitten on his arm by a mosquito in his garden in Bavaria, Germany. About 15 min later he had diarrhoea, felt nauseous, and lost consciousness. He was bitten again by a mosquito in May, 2001, and August, 2001. Following the bite in August, 2001, the reaction developed rapidly, and he immediately lost consciousness and went into cardiac arrest before the ambulance arrived. Because of delayed resuscitation, he had hypoxic brain damage to the basal ganglia, resulting in spastic tetraplegia. Red-brown maculopapular skin lesions were seen on his upper legs and a skin biopsy showed increased mast cell numbers. In 2006, he was bitten a fourth time by a mosquito. Despite immediate administration of rescue medication consisting of epinephrine, H₁-antihistamine, and corticosteroid, he again had a severe reaction and cardiac arrest. In 2012, the patient was referred to the department of dermatology and allergy, Charité—Universitätsmedizin Berlin, Germany, for further investigation.

On the basis of the history of maculopapular skin lesions and increased mast cell numbers on skin biopsy, we suspected systemic mastocytosis. WHO diagnostic criteria for systemic mastocytosis were confirmed. Despite having only slightly raised serum tryptase of 11.5 µg/L (normal range <11.4 µg/L), bone marrow examination showed spindle shaped mast cells expressing CD25, and the typical Kit-mutation (D816V) was detected by PCR of peripheral blood leucocytes.¹

From the patient's description of the appearance of the mosquitoes that bit him, and knowledge of the geographic region where the incidents occurred, *Culex pipiens* was identified by an expert from the Bernhard Nocht Institute, Hamburg, Germany, as the most likely of the 100 known mosquito species in central Europe to be responsible for inducing such reactions. As an alternative possibility, the patient's skin prick test reaction and basophil release in response to *Aedes communis*, another common European species, was also tested. Total serum IgE of 48.4 kU/L was within normal range (<100 kU/L). ImmunoCAP (ThermoFisher, Uppsala, Sweden) failed to detect mosquito-specific IgE. Measurement of serum *Culex pipiens*-specific IgE by indirect ELISA showed no difference between the patient and four healthy controls (patient 0.067 optical density; controls 0.049, 0.05, 0.106 and 0.082; blank 0.062).

To test for functional reactivity to mosquito allergens, skin prick testing was done on the patient and in healthy controls. Additionally, the patient showed a very strong basophil activation response to *Culex pipiens* and a weaker response to *Aedes communis* (appendix).

Previous studies have shown that desensitisation treatment of individuals with strong local immediate or delayed reactions to mosquito bites are effective and safe.² However we did not consider immunotherapy as a therapeutic option in this patient because of his unpredictable and severe reactions to mosquito bites. Instead he is taking desloratadine 5 mg daily prophylactically and is meticulously avoiding mosquitoes. He is also equipped with emergency medication including epinephrine, H₁-antihistamine, and corticosteroid. The patient was instructed to carry two epinephrine autoinjectors at all times.^{3,4} We have also offered him prophylactic treatment with omalizumab during the mosquito season (usually April–October). Omalizumab had a protective effect against severe anaphylactic reactions in a mastocytosis patient who had had several near-fatal anaphylactic reactions to bee stings.⁵

Anaphylaxis to mosquito bite has been previously reported but at present remains unexplained.^{6–8} The unique nature of this case of a grade IV allergic reaction to mosquito bites is that a clonal mast cell disorder was identified as concomitant disease without remarkable increase in serum tryptase. Unidentified mosquito allergy could be an underestimated cause of anaphylaxis, especially in combination with occult systemic mastocytosis.

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NR and FS looked after the patient. NR, MR, and SA did skin prick test, ELISA, and basophil release tests. TK and SB-O did Kit mutation analyses. SB assisted in identifying the mosquito species. FS and MKC wrote the paper. MMA and MME gave critical input to the manuscript. Written consent by the patient to publish was obtained.

References

- Kristensen T, Vestergaard H, Møller MB. Improved detection of the KIT D816V mutation in patients with systemic mastocytosis using a quantitative and highly sensitive real-time qPCR assay. *J Mol Diagn* 2011; **13**: 180–88.
- Peng Z, Simons FE. Advances in mosquito allergy. *Curr Opin Allergy Clin Immunol* 2007; **7**: 350–54.
- Bonadonna P, Perbellini O, Passalacqua G, 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**: 680–86.
- Lieberman P, Nicklas RA, Oppenheimer J, et al. The diagnosis and management of anaphylaxis practice parameter: 2010 update. *J Allergy Clin Immunol* 2010; **126**: 477–80.
- Kontou-Fili K, Filis CI, Voulgari C, et al. Omalizumab monotherapy for bee sting and unprovoked "anaphylaxis" in a patient with systemic mastocytosis and undetectable specific IgE. *Ann Allergy Asthma Immunol* 2010; **104**: 537–39.
- McCormack DR, Salata KF, Hershey JN, et al. Mosquito bite anaphylaxis: immunotherapy with whole body extracts. *Ann Allergy Asthma Immunol* 1995; **74**: 39–44.
- Hassoun S, Drouet M, Sabbah A. Anaphylaxis caused by a mosquito: 2 case reports. *Allerg Immunol (Paris)* 1999; **31**: 285–87.
- Galindo PA, Gómez E, Borja J, et al. Mosquito bite hypersensitivity. *Allergol Immunopathol (Madr)* 1998; **26**: 251–54.

See Online for appendix