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## Successful venom immunotherapy to paper wasp, in IgE-venom negative patient

To the Editor:

Venom immunotherapy (VIT) is indicated only in patients with anaphylaxis and detectable venom IgE.<sup>1,2</sup> However, some patients with severe anaphylaxis to insect stings, with negative skin test and RAST, need more than a set of adrenaline for protection.

A 44-year-old male roof maker was stung by a paper wasp during his work on a roof (common place of paper wasp nest) and after 30 minutes flushing of face, dizziness and difficulty in breathing occurred. A week later, another sting of an unknown insect caused no reaction at that time. It might have been a common wasp sting because it occurred in an open market place. A month later, another paper wasp sting occurred during his work and immediately he felt flushing, dizziness, difficulty in breathing and he lost consciousness within 10 min. Thanks to his profession he was able to recognise the culprit insect and in addition he brought us the polistes nest. Intradermal skin tests were negative in venom at concentration up to 1 µ/ml for all insects. RAST to all insect venoms were negative too. Serum tryptase was 9 µg/ml.

Three and six months later venom skin test and RAST remained negative. Diagnostic challenge with paper wasp sting was not carried out for ethical reasons. Although venom immunotherapy was not indicated according to recent guidelines, in this case we decided to perform it because of the severity of the reaction, the convincing history and his frequent exposure at his work place.<sup>2</sup> VIT was carried out with paper wasp venom (Pharmalgen ALK), and no reactions occurred. Paper wasp venom 100 µg as maintenance dose, every four weeks, had been administered.

A year later we challenged him with paper wasp sting in order to check the effectiveness of VIT but some concern was raised about the treatment's success because venom preparation was derived from American polistes which seems to differ from European polistes venom in the structure of antigen 5 and protease.<sup>3</sup> Despite that the patient tolerated the challenge test with two paper wasp stings in a 15 min interval. Challenge with two common wasp stings did not cause any reaction either.

According to EAACI-position paper, patients with anaphylaxis to hymenoptera sting but undetectable IgE to venom are not recommended to receive VIT.<sup>1,2</sup> Contrary to the common belief that skin test is positive in the majority of patients with a clear history of sting anaphylaxis, some studies showed negative skin test responses in up to 32% of patients with a convincing history.<sup>4</sup> This low sensitivity of the skin test and RAST might be the cause of undetectable venom specific IgE in our case. A supposed sensitization in an epitope existed only in European polistes venom but not in American commercial polistes venom did not occur in our case.<sup>3</sup> This group of IgE venom negative patients should not be ignored. In an interesting study the frequency of a future systemic reaction as it has been assessed by challenge test was the same in patients with convincing positive history, regardless of their skin test response to venom (21% in patients with positive skin test, and 22% in those with negative skin test).<sup>4</sup> The repetition of skin test and RAST three and six months later does not usually solve the problem. FAST (basophilic activation tests) may offer some help.<sup>5</sup> Western blot may be an alternative sensitive method but more studies are needed to verify this concept. Molecular components of polistes venom are not available.

Published practice guidelines and parameters state that patients with negative skin test responses are not candidates for immunotherapy, but no guidance is provided for managing these patients.<sup>1,2</sup> Skin test and RAST with venom seem to lack the necessary sensitivity to detect low level of venom specific IgE, thus we consider that venom immunotherapy may be a challenging option in patients with undetectable venom IgE, but only when the following criteria are fulfilled: (1) frequent severe anaphylactic reactions; (2) definite recognition of the offending insect; and (3) a job-related exposure. Venom immunotherapy was proven to be successful in this case because the patient tolerated two stings challenges tests with paper wasps after VIT.

## Conflict of interest

We declare that none of the aforementioned authors has conflict of interest.

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