Letter to the Editor

Author's reply

Réplica a la carta al Editor

Dear Editor,

The diagnostic algorithm for drug-allergy combines both *in vivo* (prick test) and *in vitro* (specific IgE) tests. The basophil activation test (BAT) is a functional *in vitro* assay that could help in case of allergen-sensitization suspicion. The indication of BAT could be addressed when specific-IgE test is not commercially available, the allergic patient is at high risk of anaphylactic reaction after new exposition to allergen or due the low sensitivity of specific-IgE test in drug-sensitization cases. In all cases the BAT could support the allergy diagnosis.

An increase of total serum IgE levels could suggest an immediate IgE reaction but also another clinical overlap of food and inhalant allergy or parasite infection should be ruled out. Furthermore, total IgE is not especially increased in cases of drug hypersensitivity. To our knowledge, there is no omeprazole specific-IgE test in the reference system (CAP, Thermo Fisher), so the BAT could be used as *in vitro* diagnostic tool to confirm sensitization.

The letter to editor comments about several points in order to improve the immunophenotypic assessment of basophils as $CD45^{dim}CD123^{bright}HLA\text{-}DR^{neg}$ instead of FSC/SSC dot plot. The authors regret that the format of case report does not allow describe the methods in detail. However, the FSC/SSC dot plot showed in Figure 1 (Belmar et al.)[1] represents the backgating, there is neither gate in the plot nor mention in the figure legend about the gating strategy of basophils based on FSC/SSC, due to space constraints. Moreover, as suggested by the authors, the use of CD203c could help in the identification of basophils. After the performance of the omeprazol-BAT we include the CD203c marker in our routine flow cytometry panel and >97% $CD123^{+}HLA\text{-}DR^{neg}$ were $CD203c^{+}$, confirming the high concordance of basophils identification with both panels.

The authors are aware about the interpretation of the BAT is controversial,[2] most of the studies use a single cut-off value, stimulation index (SI) or %CD63. The study with 43 patients with omeprazole-allergy cited by the authors uses a single cut off above 2 SI,[3] moreover the same research group in the context of quinolone-allergy used SI >2 or CD63 >5%.[4] In the case report both conditions SI and %CD63 were fulfilled.[1]

The formil-Metionin Leucin Prolin (fMLP) activate basophils in a IgE-independent way, the authors assume that it is not the best positive control for basophil IgE-dependent degranulation and anti-IgE should be used instead. Nonetheless, the fMLP allows validate the BAT, confirming the ability of basophils to degranulate.

We could not exclude a possible immune-mediated reaction through the binding of the drug to H2 and H4 in basophils, as indicated by the authors in their reply. It could modulate the Th2 immune response by producing IgG that would induce the nephritis. Despite the suggested inhibition by omeprazol on basophils that we could not discard, we demonstrated an *in vitro* basophils degranulation after exposure to the drug.

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