



Correspondence

Basophil activation test, skin prick test, and anaphylaxis after drug hypersensitivity



Barni et al reported a case of anaphylaxis to amoxicillin caused by a skin prick test (SPT). To improve diagnostic assays and prevent severe life-threatening reactions caused by SPTs, they suggested the use of the basophil activation test (BAT) in allergy units.¹ However, BAT refers to basophils rather than mast cells. Because mast cells are particularly abundant in the forearm, they are the main immune frontline for allergy response after SPTs, even before basophils, which are rapidly recruited into any skin lesion or inflammatory site within the next 15 to 20 minutes.² The existence of infiltrated basophils should be closely related to chronically inflamed skin.² Basophils are particularly able to elicit a T-cell response at the inflammatory site, and although apparently normal, the immune microenvironment may be particularly active in an allergic response.

The case reported by the authors involved a 77-year-old man with itchy erythema probably due to drug hypersensitivity.¹ The patient had undergone therapy with ramipril since 17 years of age. Interestingly, ramipril might worsen the anaphylactic reaction observed by the authors because this drug could prime skin mast cells.³ Primed mast cells formed synapsis with infiltrated CD4⁺ T cells, promoting the generation of T_H22 and interferon γ -producing T_H cells, which are a causative source of primed mast cells.⁴ Mast cells only drive memory CD4⁺ T cells to an interleukin 22 response in the skin⁵; therefore, early allergy reaction after SPTs may be driven by only skin mast cells, which then recruit basophils to interact with memory CD4⁺ T cells and increase T_H17-mediated response by augmenting the release of interleukin 22 and then exacerbating the immune reaction.⁶ Ramipril, by priming mast cells, might induce a proanaphylactic state, which can be unveiled by SPTs. Depending on the clinical state, it should be clear that the SPT has to be performed with the patient's therapeutic schedule in mind. The SPT-induced skin response does not seem to reveal differences between atopic and nonatopic individuals if the mechanism accounts for the immediate allergic response (≤ 15 minutes) or a delayed hypersensitivity test (24 hours) probably triggered by CCL2 and CCL3 chemokines. A major role is exerted also by cysteinyl leukotrienes, which should act as vasoactive agents, and their receptors. At least for eosinophils, cysteinyl leukotrienes are associated with the recruitment of these leukocytes at the site of allergic inflammation,⁷ although no data yet exist for basophils. Basophils express leukotriene C₄, finally transformed in leukotriene D₄ and leuko-

triene E₄, and actively participate in chronic allergy inflammation. Furthermore, they control, through cysteinyl leukotrienes, the induction of a T_H2-mediated response to allergens.⁸ Actually, past data from cysteinyl leukotriene receptor antagonists confirm the role of these mediators in allergic asthma.⁹

Circulating basophils, which interact with allergens in a complex way, may affect BAT reliability, although the BAT appears safer than the SPT.¹⁰ The latter may generate severe life-threatening reactions if skin was previously inflamed by allergic reactions. Therefore, despite the fundamental role of the SPT, the BAT needs to be highly considered when only a SPT is included in the allergy diagnosis.

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