



Letter

Anaphylaxis to the amoxicillin skin prick test: utility of the basophil activation test in diagnosis

Anaphylaxis in response to a skin prick test (SPT) with the culprit drug rarely occurs in patients with a suspected drug allergy.¹ The diagnosis of β -lactam hypersensitivity is usually based on the patient's clinical history, positive skin test results, or specific IgE antibody measurements. The basophil activation test (BAT) should be performed in cases in which the diagnosis of a drug allergy is highly suspected but is not supported by the results of skin testing or in vitro IgE measurements are not available.^{2,3}

We report the case of a 77-year-old woman with a medical history of itchy erythema while taking oral amoxicillin who was referred to the Allergy Unit of San Giovanni di Dio Hospital. The patient was receiving ramipril and lansoprazole therapy for high blood pressure and gastroesophageal reflux respectively since 60 years of age.

A SPT with amoxicillin was performed at a concentration of 20 mg/mL. The allergy workup was conducted according to the European Network for Drug Allergy recommendations.⁴ Basophilic cells were selected from the lymphocyte population using anti-CCR3 according to the method of Ebo² (Flow-CAST High Sense; Buhlmann Laboratorie AG, Shonenbuch, Switzerland). At least 300 basophils were assessed in each assay. The up-regulation of the activation marker CD63 and CD203c was calculated as the percentage of the CD63- and CD203c-positive cells. A positive result required the percentage of activated basophils after incubation with the allergen to exceed 5%. In addition, the percentage of basophils activated after allergen stimulation should be at least double the percentage of spontaneously activated basophils (stimulation index, ≥ 2).

The result of the SPT with amoxicillin was highly positive with pseudopods. Shortly after the SPT, the patient developed profuse sweating and became unconscious. The patient was given epinephrine at 0.01 mg/kg intramuscularly, and the injection was repeated 5 minutes later because of persistent hypotension (blood pressure, 70/40 mm Hg). The patient's tryptase level was 17 $\mu\text{g/mL}$ (basal level, 5 $\mu\text{g/mL}$) 3 hours later. The patient was discharged 4 hours later. The patient had positive penicillin V, ampicillin, and amoxicillin serum specific IgE. Two months later the BAT was performed with amoxicillin, clavulanic acid, minor determinant mixture, penicilloyl-polylysine, and cefuroxime. The results were positive to amoxicillin, clavulanic acid, and minor determinant mixture. The results were negative to penicilloyl-polylysine and cefuroxime. A SPT and intradermal test with cefuroxime (20 mg/mL) were performed and produced negative results. On the basis of these results, we performed an oral drug provocation test (DPT) with cefuroxime, and the patient tolerated the drug. The BAT was repeated 1 month later with cefuroxime, and the result was positive.

Skin testing remains the most important method to confirm β -lactams allergy; the sensitivity of skin testing is up to 70%.

Currently, it is not possible to calculate the specificity because a DPT in those patients with positive skin test results cannot be used as a gold standard.⁵

β -Lactam skin tests are generally safe. However, systemic reactions ranging from generalized cutaneous reactions to anaphylactic shock can occur in 0.02% to 1.3% of tested patients.¹ According to the literature, the main risk factor to predict a systemic reaction during SPTs to penicillin is a previous immediate systemic reaction to penicillin.¹ Our case is atypical because the patient had a prior minor reaction (itchy erythema) with amoxicillin 3 years before she came to our hospital. Therefore, in vivo investigations to address severe allergic reactions should be performed in a specialist setting by health care professionals.⁵

BAT is a safe in vitro diagnostic tool for patients with a history of immediate reactions to β -lactams, especially cephalosporins, when immunoassays are not available.³ In a multicenter study,⁶ BAT sensitivity and specificity to β -lactams was 50% and 89% to 97%, respectively. The clinical utility of BAT remains limited by the requirement of fresh blood, specialized laboratory equipment, and technician time and therefore remains a research tool until its role can be fully defined.⁵

Patients retested approximately 1 month after negative results on allergy workup, including a DPT, develop resensitization, with a frequency ranging from 0.9% to 27.9%,⁷ even if the presence of skin resensitization is not associated with more positive results on DPTs. Unfortunately, the patient refused to undergo a provocation test with cefuroxime; therefore, we cannot clinically prove cefuroxime allergy.

This case shows the importance of performing a drug allergy evaluation in an appropriate hospital setting with emergency care facilities. The in vivo tests may provoke severe, life-threatening reactions.¹ BAT could be considered a valid and safe diagnostic tool. In this case, the BAT correctly identified the severe amoxicillin allergy, and the negative BAT test results to cefuroxime supported a cephalosporin challenge, which was tolerated. The clinical relevance of the subsequent positive BAT result to cefuroxime is unknown, but it suggests that patients may have sensitization on BAT after oral challenges, as previously reported for skin testing.

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