

Anaphylaxis during skin prick testing for amoxicillin allergy

Ekaterini Syrigou, MD, PhD^a, and

Konstantinos Syrigos, MD, PhD^b

Clinical Implication

- This is a report of a case of anaphylaxis during skin prick testing with β -lactams of a patient with a history of anaphylactic reaction to amoxicillin. Clinicians performing skin prick testing should be alert to the possibility of skin prick test–induced anaphylaxis.

TO THE EDITOR:

Skin prick testing (SPT) is generally considered as the preferred first-line diagnostic method in the workup of IgE-mediated allergies because of its rapidity, cost-effectiveness, minimal invasiveness, and excellent safety profile. According to previous studies, the occurrence of systemic reactions during performance of SPT is extremely low (range, 0.02%–0.4%), whereas SPT-induced anaphylaxis in particular is an exceptionally rare event.^{1,2} We herein report a case of anaphylaxis during SPT with β -lactam antibiotics in a patient with a history of anaphylactic reaction to amoxicillin. To the best of our knowledge, fewer than 5 similar cases have been reported in the English literature.

A 43-year-old man was referred to the allergy department at “Sotiria” General Hospital, Athens, Greece, for further evaluation of suspected amoxicillin-induced anaphylaxis. Six months before, the patient had had an episode of anaphylactic reaction immediately after oral administration of amoxicillin at home for treatment of periodontal abscess; less than 5 minutes after the first dose of amoxicillin, he developed generalized urticaria and angioedema, gastric pain, tachycardia, dyspnea, difficulty in swallowing, dizziness, and loss of consciousness. He was transferred to the emergency department where he recovered after receiving standard treatment with epinephrine, antihistamines, corticosteroids, and volume resuscitation. The patient reported that he had tolerated amoxicillin in the past with no adverse reactions and had no known personal or family history of an atopic disorder. His medical history was significant only for idiopathic hypertension, which was well controlled on combination therapy with olmesartan-amlodipine (20 mg/5 mg, once daily) for the past 2 years.

Initial diagnostic workup at the patient's presentation to our department included *in vitro* assays for specific IgE determination; allergen-specific IgE antibodies to penicilloyl G (C1), penicilloyl V (C2), ampicilloyl (C5), amoxicilloyl (C6), cefaclor (C7), and latex (K82) were evaluated by using CAP System FEIA (Pharmacia Diagnostics, Uppsala, Sweden), with negative results.³ Total IgE and tryptase also were found to be within normal limits (IgE, 30.2 kU/L [reference value, <100 kU/L]; and tryptase, 4.8 μ g/L [reference value, <11.4 μ g/L]). SPT was performed with penicilloyl-polylysine (PPL, 1:1), minor determinant mixture

(MDM, 1:1), amoxicillin (20 mg/mL), ampicillin (20 mg/mL), and cefuroxime (2 mg/mL). Histamine and saline solution also were used as positive and negative controls, respectively. Approximately 5 minutes after application of allergens on the volar surface of the forearm, the patient started experiencing oropharyngeal pruritus and abdominal pain, quickly followed by conjunctival redness and tearing, dyspnea, generalized urticaria, and angioedema. He was immediately treated with adrenaline (intramuscular), corticosteroids and antihistamines (intravenous) with prompt and uneventful recovery. An electrocardiogram was conducted with normal findings. The patient also was evaluated by an ENT specialist who confirmed the absence of any residual laryngeal edema. SPT results showed a strong positive reaction to amoxicillin and ampicillin (25 $\times$ 19-mm and 15 $\times$ 12-mm wheal, respectively) and a negative reaction to PPL, MDM, and cefuroxime. Histamine control was positive (7 $\times$ 5.5-mm wheal). The serum tryptase level at 1 hour after the onset of symptoms was 17.7 μ g/L. Baseline serum tryptase level obtained at 2 weeks follow-up was found to be within normal limits (5.2 μ g/L).

β -Lactams are the most frequently reported cause of hypersensitivity reactions to antibiotics.⁴ However, approximately 90% of patients with a reported allergy to penicillin or other β -lactam antibiotics are not truly allergic because they lack drug-specific IgE antibodies and may be unnecessarily denied the most appropriate antibiotic treatment.⁵ Therefore, for patients with a history of systemic reactions to β -lactams, diagnostic skin testing, with oral challenge if the SPT is negative, may be used to confirm the diagnosis of IgE-mediated allergy and to properly identify which patients can safely receive these antibiotics.^{1,5,6}

SPT with β -lactams is generally a very safe procedure, with a very low rate of systemic reactions. For the most part, these reactions are mild, whereas severe reactions are extremely rare and mainly associated with use of higher than recommended allergen concentrations and/or intradermal testing not preceded by SPT.⁷ Notably, anaphylactic reactions during SPT with β -lactams, most commonly with penicillin and amoxicillin, may rarely occur in patients who are highly sensitive, especially patients with a history of anaphylaxis.⁸ Furthermore, use of high-dose amoxicillin (20–25 mg/mL) for SPT compared with the use of approximately 2 mg/mL (or 0.01 M), may potentially increase the risk of systemic reactions, as previously emphasized¹; this also may explain the higher rates of systemic testing reactions reported by some research groups.⁹

In line with previous data,⁸ the present case further supports that even a minimally invasive technique, such as SPT, is capable of inducing anaphylactic reactions in predisposed individuals. Acute elevation of serum tryptase levels, which typically peak within an hour after the onset of symptoms, may confirm the clinical diagnosis of an anaphylactic reaction and exclude the possibility of a variety of other conditions that mimic anaphylaxis.⁸ The latter include, but not limited to, vasovagal syncope, severe asthma attacks, foreign body aspiration and pulmonary embolism, generalized hives, acute anxiety, hypoglycemia, and cardiovascular events.¹⁰ Baseline tryptase levels also may be helpful in excluding the presence of an underlying systemic mastocytosis.⁸

In conclusion, anaphylaxis during SPT for β -lactams antibiotics, albeit extremely rare, may occur, especially among patients with a

history of severe systemic reactions to these drugs. Using penicillin skin test reagents at 2 to 3 mg/mL, or roughly 0.01 M, should help reduce reactions and still provide an accurate assessment. Clinicians who perform allergy SPTs should always be alert to the possibility of this potentially fatal complication, and SPT should be conducted only in settings equipped to assess and manage anaphylaxis.

^aAllergy Department, "Sotiria" General Hospital, Athens, Greece

^bThird Department of Medicine, Athens School of Medicine, "Sotiria" General Hospital, Athens, Greece

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication February 18, 2014; revised March 29, 2014; accepted for publication April 3, 2014.

Corresponding author: Ekaterini Syrigou, MD, PhD, Allergy Department, "Sotiria" General Hospital, Mesogion 152, 115 27 Athens, Greece. E-mail: esyrigou@hotmail.com.

2213-2198/\$36.00

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<http://dx.doi.org/10.1016/j.jaip.2014.04.001>

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