Severe Anaphylaxis With Cardiac Arrest Caused by Prick Test With Cefuroxime

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Skin tests, including the skin prick test (SPT) and intradermal test (IDT), are useful for the in vivo diagnosis of IgE-mediated hypersensitivity reactions to drugs. SPT is considered a safe diagnostic approach, with only anecdotal fatal or near-fatal reactions, most of which are caused by prick testing with foods. No reactions caused by drugs have been reported [1,2]. According to previous studies, the occurrence of systemic reactions during performance of SPT is extremely low (range, 0.02%-0.4%), and SPT-induced anaphylaxis in particular is an exceptionally rare event [3]. We report a case of anaphylactic shock with cardiorespiratory arrest during SPT with cephalosporins in a patient with a history of perioperative anaphylaxis. To the best of our knowledge, this is the first report of anaphylaxis during SPT to cephalosporins reported in the literature.

A 62-year-old woman was referred to our allergy department for evaluation of perioperative anaphylactic shock. One month previously, she had experienced an anaphylactic reaction during cataract surgery. A few minutes after the intravenous (IV) administration of 750 mg of cefuroxime and 125 mg of methylprednisolone, she developed dizziness, vomiting, labial cyanosis, tachycardia, hypotension, and focal seizures. She was immediately intubated and treated with intramuscular (IM) epinephrine, clemastine 1 mg IV, methylprednisolone 125 mg IV, and volume resuscitation. The patient had no personal or family history of atopic diseases. Her medical history was significant for alcoholism, idiopathic hypertension, dyslipidemia, chronic obstructive pulmonary disease, and osteoporosis. She had been receiving long-term therapy with enalapril/lercanidipine (10 mg/10 mg, qd), rosuvastatin (10 mg qd), mirtazapine (30 mg qd), oxazepam (15 mg qd), acetylsalicylic acid (100 mg, qd), inhaled budesonide (400 µg, bid), tiotropium bromide (2.5 µg, qd) and indacaterol (150 µg, qd).

The initial diagnostic work-up was based on in vitro assays for determination of specific IgE to penicilloyl G, penicilloyl V,

amoxicillin, ampicillin, and cefaclor (CAP System FEIA, ThermoFisher Scientific). All results were negative. The patient's total IgE was 152 IU/mL and basal serum tryptase was 9.3 µg/L (reference value, <11.4 µg/L). In order to rule out allergy to corticosteroids, SPT and IDT were performed with betamethasone (7 mg/mL, 1:10), dexamethasone (4 mg/mL, 1:10), hydrocortisone (100 mg/mL, 1:10), methylprednisolone (40 mg/mL, 1:1000, 1:100, 1:10), and prednisolone (25 mg/mL, 1:10). Both immediate and late results were negative for all drugs tested. A few weeks later, SPT was performed with cefuroxime (10 mg/mL), cefazolin (33 mg/mL), and ceftazidime (10 mg/mL) on the volar surface of the forearm, at concentrations known to be nonirritant [4]. Histamine and saline solution were used as positive and negative controls, respectively. Approximately 2 minutes after the SPT with cephalosporins, the patient began to experience severe dyspnea and oropharyngeal tightness, which rapidly progressed to severe bronchospasm, cyanosis, and loss of consciousness. She was assisted immediately with epinephrine 1 mg IM, although she went into respiratory and cardiac arrest within seconds, with loss of sphincter control.

Advanced life support maneuvers were initiated, and the patient received an additional dose of epinephrine (1 mg IV), as well as methylprednisolone 125 mg IV, clemastine 1 mg IV, and oxygen through a nasal cannula. She was intubated and put on respiratory life support. About 2 minutes after the cardiac arrest, she recovered spontaneous circulation. Given the gradually increased consciousness and resistance to intubation, the patient was sedated with midazolam and propofol before being transferred to the intensive care unit. She was discharged from the unit 1 week after the reaction. A neurological evaluation 1 month later revealed no abnormalities.

During anaphylaxis, and even for some minutes after administration of epinephrine and recovery of heart function, the SPT result was strongly positive for cefuroxime (~15 mm) and negative for cefazolin and ceftazidime (histamine 6 mm). The serum tryptase level at 1 hour and 2 hours after the onset of symptoms was sharply elevated: 43.0 µg/L and 44.4 µg/L, respectively. The ECG result and high-sensitivity troponin I value (marker of myocardial necrosis) collected during the episode were normal.

Cephalosporins are one of the most widely prescribed classes of antibiotics owing to their broad spectrum of activity and low toxicity profile [5]. Most allergic reactions to cephalosporins consist of cutaneous rashes with a reported incidence of 1%-2.8% of treatments. Anaphylactic reactions to cephalosporins are rare, with a relative risk ranging from 1:1000 to 1:1 000 000 administrations [4]. However, cases of fatal anaphylaxis have been reported [6,7]. Skin tests are considered a useful tool for detecting patients with immediate hypersensitivity to cephalosporins [5].

Given their lower risk of systemic reactions than IDT, SPT is usually the first in vivo test to be performed in the diagnostic work-up of suspected IgE-mediated hypersensitivity reactions. They are easy to perform, cheap, and provide a positive/negative response within a few minutes [8]. In a 2015 British study on the incidence and features of systemic reactions to SPT [9], only 1 reaction was attributed to a drug (piperacillin). To the best of the authors' knowledge, this is the only case report in the English-language literature of a severe systemic reaction induced by SPT with cephalosporin.

Few studies have validated SPTs for the diagnosis of immediate hypersensitivity reaction to cephalosporins [4,5], and none have evaluated their safety with these drugs. Most studies on the safety of these procedures are with β-lactam antibiotics [10].

In the case we report, the acute elevation of serum tryptase levels, which typically peak within an hour after the onset of symptoms [3], confirms the clinical diagnosis of an anaphylactic reaction and rules out a variety of other conditions that could have led to cardiorespiratory arrest (eg, severe asthma exacerbations, pulmonary embolism, and cardiovascular events). In this particular case, the patient's comorbidities could have contributed to the severity of anaphylaxis.

Normal basal serum tryptase helps to rule out the presence of underlying systemic mastocytosis.

As reported elsewhere [3], the present case shows that a minimally invasive technique such as SPT is capable of inducing severe anaphylactic reactions in predisposed individuals. When performing skin tests, clinicians should be aware of this risk and must be capable of diagnosing and treating subsequent reactions. The case further stresses that these procedures should only be performed by trained staff and in settings equipped to assess and manage anaphylaxis.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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