

Anaphylactic reaction due to cefuroxime axetil: A rare cause of anaphylaxis

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Abstract

One of the most used cephalosporins in clinical practice is cefuroxime axetil. Anaphylaxis due to the administration of cefuroxime is considered a rare event. We report a case of anaphylactic reaction after the administration of cefuroxime in a child who had tolerated the drug in past exposures. Diagnostic workup is recommended for all patients with at least a moderate anaphylactic reaction (hypotension, tachycardia, bronchial hyperreactivity). This should include a detailed history of the event, previous allergies, and underlying conditions. Unfortunately, all currently available diagnostic approaches (IgE, skin-prick-test, tryptase) leave a significant percentage of non-diagnostic results and false positive or negative outcomes.

Keywords

anaphylactic reaction, anaphylaxis, antibiotic, cephalosporins

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Introduction

Cephalosporins are among the most commonly used antibiotics in the treatment of routine infections (bronchitis, otitis media, pneumonia, and cellulitis).¹ Studies suggest that anaphylactic reactions to cephalosporin are rare,¹ although these incidents are increasing.^{2,3}

Common reactions to cephalosporins include a maculopapular or morbilliform skin eruption, drug fever, and a positive antiglobulin or Coombs test. Less common reactions may include urticaria, eosinophilia, serum-sickness-like reactions, and anaphylaxis. Acute interstitial nephritis and drug-induced cytopenias are rarely observed.¹

Case report

A 12-year-old girl, who had no personal or family history of allergic disease, was referred to us. Also, the patient's medical history included attention-deficit hyperactivity disorder, which was being treated with methylphenidatehydrochloride. Previously, cefuroxime axetil had been

administered twice with no adverse reaction (in 2010 and 2013). In this case cefurixime axetil was administered under suspicion of acute otitis and respiratory infection (first dose).

After a few seconds our patient developed the following symptoms: itchy throat; swelling tongue and hands; generalized urticarial and dyspnea (without increased breathing effort, or stridor). On arrival at the health center, she had a significant fall in blood pressure and loss of consciousness for approximately 10 s. In this circumstance, systemic corticosteroids were administered by intramuscular injection along with subcutaneous adrenaline and intravenous perfusion of adrenaline later.

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Table 1. Monitoring the change of serum tryptase values during time.

Time	Concentration of serum tryptase (mcg/L)
30 min	41
2 h	31
24 h	3

Normal concentration of serum tryptase <13 mcg/L.

The patient was posteriorly referred to the emergency department with evidence of an anaphylactic reaction. However, after a period of 24 h, the patient was completely asymptomatic.

The concentration of serum tryptase sampled in the emergency department at arrival was 41 mcg/L (normal <13 mcg/L). This concentration decreased to 31 mcg/L after 2 h and it was 3 mcg/L after 24 h (Table 1).

Specific IgE levels of cefuroxime were not detected. Only skin prick test was performed with cefuroxime (20 mg/mL) and it was positive (wheal of 10 mm in diameter; histamine, 3 mm). Reactions were considered positive when wheals greater than 3 mm in diameter were present 15–20 minutes after testing. Additional cutaneous test for assessment of cross-reactivity were performed to complete the diagnosis. Skin tests with PPL, MDM, amoxicillin, and amoxicillin clavulanic were negative.

The patient's family provided written informed consent for a challenge with increasing doses of amoxicillin under intensive medical monitoring. This investigation revealed that amoxicillin was well tolerated up to therapeutic dose.

Discussion

Cefuroxime is a second-generation semi-synthetic cephalosporin that, despite its use for a wide variety of pediatric infections, has been reported to cause anaphylaxis only in a few cases. Furthermore, it is exceedingly rare for children to develop anaphylaxis from cephalosporins.⁴

Regarding near-fatal cephalosporin anaphylaxis, although the possibility of developing anaphylaxis is very low, deaths following cephalosporin have been reported.¹

Cephalosporins can cause a range of hypersensitivity reactions, from mild, delayed-onset cutaneous reactions to life-threatening anaphylaxis in patients with immunoglobulin E (IgE)-mediated allergy.^{5,6}

The most important risk factor for allergy to cephalosporins is a history of allergy reactions to penicillin or cephalosporins which increases the risk by eight times.¹

Unlike penicillin tests, attempts to develop a skin test for allergy to cephalosporins have been unsuccessful, and skin testing with the native drug alone has little predictive value.⁷

Skin testing for cephalosporin allergy is sometimes performed, but is not standardized because the antigenic determinants of a serious allergic reaction have not been established.¹

Skin testing for penicillin allergy can be useful in patients with an allergy history of cephalosporin who require penicillin. If penicillin skin tests are negative, penicillin can be administered safely; if positive, patients should either receive an alternative medication or undergo desensitization to penicillin.¹ Also, the detection of IgE antibody to penicillin or cephalosporins or of cross-reactive IgE antibody does not predict a definite clinical reaction.⁹

A negative skin test to cephalosporin does not rule out the presence of drug-specific IgE antibodies.⁸ Furthermore, the presence of IgE antibodies to penicillin and cephalosporin is predictive of possible subsequent immediate, IgE-mediated allergic hypersensitivity reactions, but many patients with detectable IgE antibodies may not display a clinical allergic reaction.⁸

Hence, the role of both testing for IgE antibody to cephalosporin or penicillin and skin testing prior to administration are still uncertain. Test dosing with titrated doses could be considered as an alternative approach; but, it is still far from a flawless method.¹

Due to uncertainties in predicting anaphylaxis to cephalosporin, medical histories regarding previous antibiotic allergies should then include a comprehensive description of the symptoms such as: urticaria; pruritus; angioedema or respiratory difficulties; severity and timing of reaction after drug therapy.⁹ This could facilitate a quick response in case of a moderate anaphylactic reaction (hypotension, tachycardia, bronchial hyperreactivity).

In summary, we present a case report of cefuroxime-induced anaphylaxis in which IgE-mediated responses appear to be involved in the pathogenic mechanism and, thus, avoidance of the cephalosporin or induction of drug tolerance would be recommended if no alternative drugs were available.

Physicians should be aware of this potentially life-threatening complication which can occur even after first dose and should be vigilant of recognizing anaphylaxis and provide prompt treatment accordingly.

Declaration of conflicting interests

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