

Selective type-1 hypersensitivity to cefuroxime

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Cefuroxime is a second-generation semisynthetic cephalosporin that is widely used for treatment of respiratory tract infections. Both the sodium salt for parenteral administration and the acetyloxy ethyl ester (cefuroxime axetil) for oral use are generally well tolerated. This report describes a case of anaphylactic shock provoked by cefuroxime axetil, in which specific IgE to the latter drug was demonstrated.

CASE REPORT

A 58-year-old woman was prescribed cefuroxime axetil tablets (500 mg three times a day) for pharyngitis. Fifteen minutes after taking the first tablet, she had generalized urticaria, facial

angioedema, shortness of breath, dizziness, tachycardia, and severe hypotension. Two hours after treatment in the emergency department with subcutaneous adrenaline, 6-methylprednisolone (80 mg intravenously), and chlorphenamine (10 mg intravenously), her symptoms had largely disappeared, and she was completely asymptomatic after 24 hours.

Eight months earlier, she had tolerated intramuscular cefuroxime, and before that she had tolerated ampicillin and amoxicillin. Her personal and family histories were negative for allergic disease.

One month after the reactive episode, an allergologic work-up was performed.

Skin tests

The patient underwent skin tests (skin prick and intradermal) with penicilloyl polylysine (Allergopen, Reinbeck, Germany), minor determinant mixture (Allergopen), sodium penicillin G diluted in 0.9% NaCl and administered at increasing concentrations (0.1 IU/ml to 10,000 IU/ml), ampicillin, amoxicillin, cefuroxime, cephalothin, ceftazidime, cefamandole, and ceftriaxone. Ampicillin, amoxicillin, cefuroxime, cephalothin, ceftazidime, cefamandole, and ceftriaxone were diluted in 0.9% NaCl and used at concentrations of 1 and 20 mg/ml.

All haptens were used for skin prick testing on skin of the

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volar forearm. Reactions were considered positive when wheals greater than 3 mm in diameter were present 15 to 20 minutes after testing. When results were negative, 0.02 ml of the drug solution was injected intradermally. Readings were made after 20 minutes and 48 hours, and wheals greater than 5 mm in diameter were considered as positive results.

Positive skin prick and intradermal controls with histamine (10 mg/ml and 1 mg/ml, respectively) and negative controls with normal saline were interpreted according to the same criteria used for β -lactam testing. Intradermal tests with the above cephalosporins were also administered to 30 healthy control subjects, 20 of whom had previously tolerated cefuroxime.

In vitro testing

Assays (CAP System RAST FEIA; Pharmacia, Uppsala, Sweden) were performed, according to the manufacturer's instructions, for specific IgE to penicilloyl G, penicilloyl V, ampicilloyl, amoxicilloyl, cephalixin, cefaclor, cefadroxil, cefuroxime, and ceftriaxone. Cephalosporin assays were performed with experimental immunoCAP prototypes. Total serum IgE was also determined (PRIST, Pharmacia).

Single-blind, placebo-controlled oral challenges

Single-blind, placebo-controlled oral challenges with penicillin V (therapeutic dose, 1,000,000 IU), ampicillin (1 gm), cephalixin (500 mg), and cefaclor (500 mg) were also performed (each on a different day). Increasing doses (0.01, 0.1, and 1.0 of the respective therapeutic doses) were administered at 1-hour intervals.

The patient had a positive reaction to skin prick testing with cefuroxime (1 mg/ml) (maximum wheal diameter, 8 mm; flare, 15 mm) after 15 minutes. Skin prick and intradermal histamine produced wheals 6 and 10 mm in diameter, respectively. No other reactions were observed. RASTs revealed class-2 levels (1.0 kU/L) of cefuroxime-specific IgE and negative results (< 0.35 kU/L) for all other drugs tested. Total serum IgE was 78 kU/L. There was no reaction to any of the oral challenges.

With regard to control subjects, histamine produced maximum skin prick test wheal diameters of 5 to 9 mm (mean, 6.6 mm) and intradermal wheal diameters of 9 to 20 mm (mean, 12.2 mm). There were no positive reactions to any of the haptens, although five subjects developed mild responses (maximum diameter, 3 mm) to intradermal cephalotin.

DISCUSSION

Immediate reactions to cefuroxime appear to be rare.¹⁻⁴ Only one reported case appears to involve a selective response to this drug, although both skin tests and RASTs were negative for all drug antigens tested (including cefuroxime).⁴ Our patient's selective reactivity was confirmed by skin test, RAST, and oral challenge results. It is noteworthy that the results of the experimental cephalosporin RASTs we used were fully concordant with those of skin testing and oral challenges.

The cefuroxime-specific IgE levels were too low for RAST inhibition studies to identify the chemical structure of the antigen recognized by these antibodies.

Monoclonal antibody studies indicate that cephalosporin molecules can generate several determinants, including those of the side-chain, the nuclear region (common to all cephalosporins), and the new antigenic determinant.⁵ Although the IgE in this case appears to have been directed toward the cefuroxime side-chain, involvement of other determinants cannot be excluded.

For patients who have negative results with the classic penicillin reagents, skin tests and RASTs should also be performed with the culprit β -lactams.

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