Anaphylactic Reaction to Oral Cefaclor in a Child

ABSTRACT. Adverse drug reactions are a common clinical problem. It has been estimated that 6% to 15% of hospitalized patients experience some sort of adverse drug reaction. Clinical manifestations of adverse drug reactions include skin rash; a serum sickness-like reaction; drug fever; pulmonary, hepatic, and renal involvement; and systemic anaphylaxis. Many of these adverse events are not immunologically mediated. Actual allergic or immunologic drug reactions probably account for <25% of adverse drug reactions overall.1

Antibiotics are one of the major contributors to drug hypersensitivity. Cefaclor, an oral second-generation cephalosporin with a β-lactam ring, is used against various infectious diseases of the respiratory tract, especially in children. Several cases of cefaclor hypersensitivity have been reported.2,3 The most common presentations are either erythematous or papular eruptions, although serum sickness-like reactions have also been described. Anaphylactic reactions, although rare, have been observed in adults. Here we report a case of anaphylactic reaction to cefaclor in a 2½-year-old patient.

METHODS

Cefaclor, in a 1-mg/mL solution, was used for epicutaneous prick testing. We also used cefuroxime, cefazolin, and cefadizime in a 2.5-mg/mL solution for testing. A solution of phosphate-buffered physiologic saline at pH 7.4 with 0.4% phenol was used for negative control. For positive control, we used histamine 1/200 in water (Bencard Allergy Laboratories, Mississauga, Ontario, Canada).

We performed a battery of penicillin prick, intradermal, and oral challenge tests. As major determinants, we used penicillin G at 1000 U/mL and 100 U/mL, and benzylpenicilloyl polylysine 6 × 10⁻⁵ M (Pre-Pen; Richmond Pharmaceuticals, Richmond Hill, Ontario, Canada). For minor determinants, we used penicilloate and penicillate sodium 10 mM. For oral challenge, 250 mg of penicillin G was given. The patient’s parent gave consent for us to carry out the tests, which were done according to the guidelines of our hospital ethics board.

CASE REPORT

A 27-month-old, nonatopic, white boy, previously healthy, was referred to our allergy/adverse drug reaction service for assessment of his anaphylactic reaction to cefaclor.

At the age of 2 years, he developed generalized hives 1 day after ingesting cefaclor suspension for otitis media. The eruption was pruritic. The rash resolved the same day, after one dose of diphenhydramine. He did not have any associated respiratory symptoms, hypotension, or gastrointestinal symptoms. He had been treated with cefaclor on two previous additional occasions, without adverse reaction.

Two months later, the patient redeveloped otitis media, and unfortunately, ignorant to the previous reaction, cefaclor was prescribed. Thirty seconds after ingesting the first dose of the drug, he developed a severe systemic reaction comprised of vomiting, generalized hives, shortness of breath, and wheezing with grunting. He lost consciousness on the way to the local hospital. The patient was not on any other medication at this time. He was treated on arrival with subcutaneous epinephrine, intravenous diphenhydramine, intravenous fluids, and inhaled salbutamol with oxygen. He was noted to have tachypnea (60 breaths/minute); however, his blood pressure was unreported. He was observed for 24 hours and discharged from the hospital in stable condition. Acute serum tryptase and urinary leukotriene E4 levels were not measured.

Subsequently we tested the patient for penicillin and cefaclor. All penicillin tests were negative, including the epicutaneous, intradermal, and oral challenges. However, epicutaneous prick testing with histamine revealed a wheal-and-flare reaction of a 5 × 5 mm induration; and there was an 8 × 10 mm induration at the site of the cefaclor epicutaneous test. Epicutaneous and intradermal testing with cefuroxime, cefazolin, and cefadizime were also negative. A simultaneous cefaclor skin test on a control, whom was noted to be an atopic individual, was negative.

DISCUSSION

Hypersensitivity to cefaclor has been recognized since its early clinical introduction. In 1981, Kammer reviewed more than 3000 adult and pediatric patients treated with cefaclor and found an incidence of hypersensitivity of 1.1%. Rash and diffuse pruritus were the most common findings. In 1980, McLinn reviewed the efficacy of cefaclor in the treatment of otitis media and noted no serious adverse reactions, except for one case of vascular purpura. This occurred during the sixth day of treatment of a 5-year-old boy with otitis media, who was taking cefaclor, 250 mg, three times a day. Other reports suggested a serum sickness-like syndrome, with symptoms including malaise, fever, cutaneous eruption, and arthralgias.6-8

Penicillin remains the most common cause of drug-induced anaphylaxis. It has been estimated that nearly 75% of fatal anaphylactic reactions result from the administration of penicillin. Anaphylaxis because of cefaclor is rare. Nishio and colleagues described 3 adult patients who developed urticarial rashes with asphyxiation immediately after an administration of cefaclor. In 1988, Hama and Mori reported 4 adults with anaphylactic reactions. But never before were similar reactions reported in the pediatric age group.

We report a case of anaphylaxis to cefaclor in a child who developed urticarial rash, vomiting, respiratory distress, and loss of consciousness immediately after cefaclor ingestion, requiring immediate treatment. This reaction to cefaclor is most likely to be IgE-mediated, which was confirmed by a strongly
positive epicutaneous prick test. Because the breakdown products of cefaclor are unknown, in vitro testing for this drug was not done. However, the positive epicutaneous test is indicative of IgE involvement. Furthermore these IgE antibodies are more likely to be side chain specific to cefaclor because our patient did not show any reaction to other cephalosporins including cefuroxime, cefazolin, and ceftazidime.

Our patient gradually developed hypersensitivity to cefaclor; his first three exposures to cefaclor were without significant reactions. This presentation is unusual compared with anaphylaxis from penicillin, which usually appears after the first or second exposure. There is a risk of cross-reactivity between penicillin and cephalosporins, occurring in 4% to 15% of cases10–12; therefore, most clinicians avoid cephalosporins for patients with a history of immediate reactions to a penicillin.12 In our patient penicillin testing (including oral administration of penicillin was negative).

CONCLUSION

In summary, we report a case of an anaphylactic reaction to cefaclor in the pediatric population. Because cefaclor is widely used in children for common infections such as otitis media, we will likely see more cases of anaphylactic reaction to this antibiotic. Physicians should anticipate the possibility of anaphylactic reaction in children treated with this agent, particularly in cases of multiple exposure.

REFERENCES
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