

Unexpected Cefazolin Anaphylaxis in a 5-Month-Old Girl

To the Editors:

β -Lactam antibiotics are the most common drugs that cause hypersensitivity, with an incidence of 0.7% to 8%.¹ Cephalosporins are widely used β -lactam antibiotics mainly for their efficacy in gram-positive and gram-negative infections and their few side effects.² Hypersensitivity reactions are the most important side effects of these drugs because of their potential seriousness, although life-threatening reactions have been reported only rarely.^{2,3} Here, we report a child with unexpected cefazolin anaphylaxis, which is reported only rarely after operation especially in children.

A 5-month-old girl was referred to our pediatrics department for an evaluation of experienced acute pyelonephritis and diagnosed ureteropelvic junction obstruction. She was referred for a consultation in our urology department and was decided to undergo an operation because of ureteropelvic junction obstruction.

The infant's drug profile was unremarkable, and her parents claimed to have no known drug allergies. Her mother reported that 1 month previously, because of a noncomplicated acute pyelonephritis, she administered 200 mg of amoxicillin by mouth 2 times daily for 10 days, and the infant had no allergic reaction for this drug. Her parents were sure that she had never received cefazolin previously until this time. Her medical records showed no cefazolin usage.

After successful surgery, intravenous administration of 250 mg of cefazolin was done in 45 minutes as prophylaxis against surgical infection. In a few seconds, she developed cyanosis, apnea, hypotension, bradycardia, and cardiovascular collapse. She was considered anaphylactic to cefazolin and was treated immediately with intramuscular epinephrine (0.01 mg/kg, 1:1000),

intravenous diphenhydramine (1 mg/kg), intravenous methylprednisolone (1 mg/kg), intravenous ranitidine (1 mg/kg), fluid expansion (30 mL/kg), and oxygen therapy (4 L/min). Thirty minutes after intervention, her vital signs and respiratory capacity began to normalize (respiratory rate, 36 breaths/min; heart rate, 110 beats/min; and blood pressure, 90/50 mm Hg). Over the next 3 hours, nasal oxygen supply was weaned slowly. She was followed up for 3 days, with oral diphenhydramine and methylprednisolone for late reaction, and was discharged with oral diphenhydramine. Before discharge, we used penicillin- and amoxicillin-specific immunoglobulins that were positive. We performed skin prick test with cefazolin at different concentrations: 2 mg/mL in normal saline was performed 1 month after the reaction, which was positive with a concentration of 2 mg/mL and a wheal of 10 mm. We also carried out prick and intradermal tests with penicillin that was positive. The results were considered positive if a wheal of 3 mm or greater than that of the saline control was obtained and was also associated with a flare. Thus, we confirmed cefazolin hypersensitivity.

The incidence of anaphylaxis after penicillin administration has been estimated to be around 0.01%, with mortality rate of up to 9%.⁴ Many studies have report the allergic mechanism of penicillin; a few have described the nature of cephalosporin allergies and identified the true allergic determinants of these reactions.^{2,3} Of the various cephalosporins used, the least cross-allergenicity was reported to apply to cefazolin.⁴ In a report provided by Fujisawa Pharmaceuticals in 1990, anaphylactic shock was suggested to have occurred in 5 of 84,799 cases of cefazolin administration.⁵ However, there were no reports about the incidence of cefazolin anaphylaxis in children.

Warrington and McPhillips⁶ reported 4 patients who experienced immediate anaphylaxis to cefazolin given before surgery, in patients lacking a history of penicillin allergy or documented cefazolin exposure. Cefazolin anaphylaxis can be experienced by children without a history of penicillin allergy or cefazolin

exposure like our patient. Therefore, patients who have an allergic reaction to a specific drug may be allergic to other agents and to penicillins and cephalosporins.³ Because the patient possesses numerous IgE antibodies that may be reactive to different determinants in structurally dissimilar compounds, our patient had an amoxicillin (a β -lactam antibiotic) exposure before she experienced anaphylactic reaction with cefazolin administration. We used performed penicillin- and amoxicillin-specific immunoglobulins that were positive and carried out skin prick test with cefazolin and penicillin that were also positive. Skin prick test with cefazolin at a therapeutic concentration seems a reliable and effective method for identifying patients allergic to this drug.² Hence, we confirmed cefazolin allergy and determined cefazolin anaphylaxis. Consequently, we considered cefazolin allergy as due to amoxicillin cross-reactivity.

As far as we know, our patient may be the first and the youngest case to experience cefazolin anaphylaxis in this age group. In conclusion, although it is very rare, children can experience cefazolin anaphylaxis without a documented cefazolin or penicillin allergy due to cross-reactivity among all β -lactam antibiotics. Pediatricians must be careful when administering cefazolin to patients through the parenteral route and be familiar with the management of anaphylaxis.

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