

Correspondence

Subgroups in cephalosporin allergy, making a patient-tailored approach redundant?

To the Editor:

We read with great interest the work of Romano et al,¹ elegantly demonstrating in a large cohort of patients that IgE-mediated cephalosporin hypersensitivity is not necessarily a class hypersensitivity. Cephalosporins form a heterogeneous group with important differences in their chemical structure and behavior. In terms of the antibiotic spectrum, currently 5 generations are available, with third- to fifth-generation broad-spectrum cephalosporins existing only in parenteral formulations, with some exceptions such as the third-generation cefpodoxime, ceftibuten, and cefdinir. From a drug allergy point of view, Romano et al now propose a classification of cephalosporins into 4 groups based on positivity of skin tests for 1 or more of the following: group A including second-generation cefuroxime, third-generation ceftriaxone, cefotaxime, cefodizime, and ceftazidime, and fourth-generation cefepime, and characterized by a highly similar side chain at position R1; group B encompassing aminocephalosporins (ie, first-generation cefalexin and cefadroxil and second-generation cefaclor); and group C containing cephalosporins other than those belonging to group A or B (ie, first-generation cefazolin, second-generation cefamandole, and third-generation cefoperazone and ceftibuten). Group D includes those with positive skin tests to cephalosporins belonging to 2 or more different groups. Their data suggest only limited cross-reactivity between these groups, corroborating data from previous studies and case series²⁻⁶ and providing a means for clinicians to determine a safe cephalosporin alternative after skin testing in patients with type I cephalosporin hypersensitivity.⁷ Although useful from a drug allergy point of view, it does not always provide a good alternative in terms of antibiotic spectrum, availability, and convenience of a regimen. For instance, if we were to seek a broad-spectrum cephalosporin alternative in a patient with confirmed immediate hypersensitivity to a cephalosporin of group A, a cephalosporin of group B or C would be proposed, leaving us only with narrow-spectrum first- or second-generation cephalosporins, or the third-generation cefoperazone, ceftibuten, and cefdinir, which are not widely available. In that respect, we report on a 74-year-old woman presenting with a grade II anaphylaxis (generalized urticaria, angioedema, vomiting, and diarrhea) 30 minutes after oral administration of cefuroxime, necessitating a treatment with intramuscular adrenaline. She reported recidivating urinary and respiratory tract infections and intolerance toward penicillin and quinolone antibiotics. Skin testing was positive for cefuroxime (skin prick test at 1 and 10 mg/mL) and cefotaxime (intradermal skin testing at 1 mg/mL) but negative for benzylpenicillin,

minor determinant mixture, penicilloyl-poly-lysine, amoxicillin/clavulanic acid, ceftriaxone, and ceftazidim. Basal tryptase was normal (2.3 µg/L; normal, <11.4 µg/L). The patient refused a provocation test with aminopenicillins because of anticipated gastrointestinal discomfort, even if a drug allergy would be disproven. A search for a safe alternative broad-spectrum betalactam antibiotic available for outpatient and in-hospital treatment led to ceftibuten, which is not regularly available in our country, or ceftriaxone, belonging like cefuroxime and cefotaxime to the aforementioned group A. A provocation test with ceftriaxone (cumulative dose of 1010.1 mg IV) was negative. We reasoned that our patient was sensitized to the R2 side chain, which is similar in cefuroxime and cefotaxime but different in ceftriaxone.

Our case confirms the observation that type I cephalosporin hypersensitivity is not always a class hypersensitivity. Patients preferably undergo an allergy workup to diagnose the culprit agent, identify potential cross-reactivities, and also provide an adequate alternative in terms of antibiotic spectrum, availability, and convenience, which, in some cases, can include the search for a valuable skin test negative alternative within group A cephalosporins, as in our patient.

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REFERENCES

1. Romano A, Gaeta F, Valluzzi RL, Maggioletti M, Zaffiro A, Caruso C, et al. IgE-mediated hypersensitivity to cephalosporins: cross-reactivity and tolerability of alternative cephalosporins. *J Allergy Clin Immunol* 2015;136:685-91.e3.
2. Antunez C, Blanca-Lopez N, Torres MJ, Mayorga C, Perez-Inestrosa E, Montañez MI, et al. Immediate allergic reactions to cephalosporins: evaluation of cross-reactivity with a panel of penicillins and cephalosporins. *J Allergy Clin Immunol* 2006;117:404-10.
3. Demoly P, Messaad D, Sahla H, Hillaire-Buys D, Bousquet J. Immediate hypersensitivity to ceftriaxone. *Allergy* 2000;55:418-9.
4. Guéant J, Guéant-Rodriguez R, Viola M, Valluzzi R, Romano A. IgE-mediated hypersensitivity to cephalosporins. *Curr Pharm Des* 2006;12:3335-45.
5. Pipet A, Veyrac G, Wessel F, Jolliet P, Magnan A, Demoly P, et al. A statement on cefazolin immediate hypersensitivity: data from a large database, and focus on the cross-reactivities. *Clin Exp Allergy* 2011;41:1602-8.
6. Poston SA, Jennings HR, Poe KL. Cefazolin tolerance does not predict ceftriaxone hypersensitivity: unique side chains precipitate anaphylaxis. *Pharmacotherapy* 2004;24:668-72.
7. Joint Task Force on Practice Parameters, American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology, Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. *Ann Allergy Asthma Immunol* 2010;105:259-73.

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