

Allergy to two drugs in a patient

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Key words: ampicillin; cephaloridine; delayed and immediate hypersensitivity; patch tests.

● EVEN though both anaphylactic and serum sickness-like reactions to a single dose of penicillin have been reported (1), to our knowledge, reactions by the same subject to both a penicillin and a cephalosporin, which are based on different immunopathogenic mechanisms, have never been described.

We examined a 49-year-old woman who had experienced two adverse reactions to different β -lactams. The first occurred a few minutes after intramuscular administration of 1 g cephaloridine, when she developed diffuse giant urticaria, facial angioedema, and dyspnea. Unspecified treatment was administered by a physician, and all symptoms rapidly regressed.

The second reaction took place 2 years later: on the second day of therapy with ampicillin three times a day orally, she developed a diffuse maculopapular rash accompanied by edema of the face, hands, and feet. The symptoms disappeared after 1 week of 6-methylprednisolone (20 mg/day intravenously).

Her personal history was negative for allergic diseases.

Five years after the first reaction, the patient underwent skin tests with penicilloylpolylysine (Allergopen, Reinbek, Germany), minor determinant mixture (Allergopen), benzylpenicillin, ampicillin, and amoxicillin, as well as cephaloridine, cephalothin, cefuroxime, and ceftriaxone, as previously described (2). Cephalosporins

were used at a concentration of 2 mg/ml in 0.9% NaCl.

At the 20-min reading, the intradermal test with cephaloridine produced a 14-mm diameter wheal, while all other intradermal tests were negative. However, positive reactions to intradermal injections of ampicillin and amoxicillin appeared after 10 h; by 24 h, indurated, erythematous lesions were present at the reactive sites (maximum diameters: 13 and 20 mm for ampicillin, and 12 and 18 mm for amoxicillin, at concentrations of 1 and 20 mg/ml, respectively), and remained for 3 days.

Prick and intradermal histamine tests produced wheals with maximum diameters of 7 and 11 mm, respectively. Intradermal tests with the aforementioned cephalosporins were negative in 40 healthy control subjects, six of whom had previously tolerated cephaloridine.

Patch tests were done with benzylpenicillin (5000 IU/g petrolatum), ampicillin, and amoxicillin (5% in petrolatum), as previously described (3). Only those with ampicillin and amoxicillin were positive (++) at the 48- and 72-h readings.

Assays (UniCAP specific IgE; Pharmacia & Upjohn, Uppsala, Sweden) for specific IgE to penicilloyl G, penicilloyl V, ampicilloyl, amoxicilloyl, cefaclor, and cephaloridine were negative (<0.35 kU/l). The cephaloridine assay was an experimental prototype.

We performed single-blind challenges with penicillin V (1 000 000 IU), cephalothin (1 mg), cefuroxime axetil (500 mg), and ceftriaxone (1 g) on different days. Increasing amounts (0.01, 0.1, and 1.0) of the therapeutic doses, indicated in parentheses, were administered at 1-h intervals, with negative results.

Clinical findings and the positive intradermal test with cephaloridine suggest that the immediate reaction to this drug involved an IgE-mediated pathogenic mechanism. The fact that an experimental prototype was used and that our assays were

performed five years after the reaction could explain the RAST negativity. The IgE titer may have meanwhile fallen under the cutoff value, as observed with penicilloyl IgE antibodies (4). Our patient showed skin-test and challenge negativity with other cephalosporins. Thus, her type-I sensitization seems to regard the entire cephaloridine molecule, as previously shown with cefaclor (5).

The maculopapular rash experienced during ampicillin therapy involved a delayed hypersensitivity mechanism, indicated by positive patch-test and delayed intradermal-test responses (3).

The clinical findings and results of allergologic tests suggest that type-I hypersensitivity to cephaloridine and type-IV allergy to ampicillin coexisted in our subject.

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Accepted for publication 22 March 2001
Allergy 2001; 56:786–787
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ISSN 0105-4538

References

1. FELLNER MJ, BALL EH, BAER RL. Double reaction to penicillin. Anaphylactic and serum sickness-like reactions to a single dose. *Arch Dermatol* 1967;**96**:687–688.
2. ROMANO A, MAYORGA C, TORRES MJ, et al. Immediate allergic reactions to cephalosporins: cross-reactivity and selective responses. *J Allergy Clin Immunol* 2000; **106**:1177–1183.
3. ROMANO A, QUARATINO D, DI FONSO M, et al. A diagnostic protocol for evaluating nonimmediate reactions to aminopenicillins. *J Allergy Clin Immunol* 1999; **103**:1186–1190.
4. ADKINSON NF Jr. Risk factors for drug allergy. *J Allergy Clin Immunol* 1984;**74**: 567–572.

5. BALDO BA. Penicillins and cephalosporins as allergens – structural aspects of recognition and cross-reactions. Clin Exp Allergy 1999;29:744–749.

Allergen-specific immunotherapy to mosquitoes

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Key words: delayed hypersensitivity; immunotherapy; mosquitoes.

● SKIN reactions to mosquito bites are usually harmless; however, delayed reactions have been reported (1). We report a case of delayed hypersensitivity to mosquito bites. Since childhood, a 19-year-old man had presented with persistent pruriginous lesions several hours after being bitten by a mosquito. On several occasions, a trace of lymphangitis was observed at the root of the limb.

ASIT is effective in delayed reactions.

Allergy evaluation revealed positive prick tests to *Dermatophagoides pteronyssinus* and birch. Prick tests to commercial extract of whole-body extracts (*Culex pipiens*, Stallergènes) were negative. The intradermal test was positive at 1:10 000: the initial diameter of papula (3 mm) reached 14 mm. Specific mosquito (*Aedes communis*) IgEs were at a level of 1.06 kIU/l (CAP-RAST Phadebas, Pharmacia).

Histologic examination of a pruriginous lesion revealed a lymphoplasmocytic dermal infiltrate with some polynuclear neutrophils and polynuclear eosinophils. The lymphoid elements were CD45Ra⁺, mainly T cells (60% CD8⁺, 40% CD4⁺).

Specific immunotherapy with a whole-body extract (*C. pipiens*, Stallergènes) was carried out initially with weekly injections beginning at a concentration of 0.01–1 IC. At the concentration of 10 IC, the injections were given twice a month, increasing the dose progressively to 0.6 ml. Nine months later, the desensitization was carried out with 0.05 ml at 100 IC. Local and general tolerance was good. Furthermore, the patient reported the disappearance of inflammatory manifestations with lymphangitis after being bitten by a mosquito.

There are 2000 to 3000 species of mosquito distributed throughout the world. The common species is *C. pipiens*. Male mosquitoes feed on nectar and water, but the females are hematophagous. Cutaneous manifestations after mosquito bites are most often banal, slight, and transitory with pruritis, rash, and papula of several millimeters. Nonetheless, some immediate and delayed allergic reactions have been described (2). Immediate reactions appear as inflammatory, extended, painful areas of edema larger than 50 mm. These manifestations last less than 24 h. Anaphylactic reactions have been reported. Delayed reactions occurred 2–6 h after the bite in the form of a hard, pruriginous lump that can persist for up to a week.

Phlyctenous and bullous reactions have been described. Lastly, an exceptional manifestation called Skeeter syndrome, which is defined as mosquito-bite-induced large local inflammatory reactions accompanied by fever, has been reported (3). Peg & Simons identified allergens (from three to 16) in the saliva with a molecular weight of 16–95 kDa among different species of mosquitoes (4). The recombinant allergens of *Aedes aegypti* (Aed a 1 [68 kDa] and Aed a 2 [37 kDa]) were found in other mosquito species. The most frequently found allergen had a band of 36 kDa, and was common to *A. communis* and *A. aegypti*.

Preventive treatment for mosquito bites is based on the use of repellents (citronella, vitamin B₁, diethyltoluamide). Curative treatment, apart from emergency treatment in cases of anaphylaxis, is based on the use of antihistamines; in this case, ceterizine and dermocorticoids. Specific immunotherapy with whole-body extracts was proposed with success in cases of anaphylactic reaction or major and extended local reactions (5). This observation underlined the possibility of successful specific immunotherapy with a whole-body extract (*C. pipiens*) in this type of severe delayed reactions with attacks of lymphangitis.

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Accepted for publication 12 March 2001
Allergy 2001; 56:787
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ISSN 0105-4538

References

1. FEINGOLD B, BENJAMINI E, MICHAELI D. The allergic response to insect bites. Annu Rev Entomol 1968;13:137–158.
2. LAVAUD F, BOUCHET F, MERTES P, KOCHMAN S. Allergies aux piqûres d'insectes hématophages: manifestations clinique. Allerg Immunol (Paris) 1999;31:311–315.
3. SIMONS FER, PEG Z. Skeeter syndrome. J Allergy Clin Immunol 1999;104:705–707.
4. PEG Z, SIMONS FER. Immunoblot analysis of salivary allergens in 10 mosquito species with worldwide distribution and the human IgE responses to these allergens. J Allergy Clin Immunol 1998;101:498–505.
5. MCCORMACK D, SALATA K, HERSHEY J, CARPENTER G, ENGLER R. Mosquito bite anaphylaxis: immunotherapy with whole body extracts. Ann Allergy 1995;74:39–44.