

Delayed hypersensitivity to piperacillin

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• **PIPERACILLIN (PP)** is a wide-spectrum bactericidal ureidopenicillin. There have been a number of reports of cutaneous adverse reactions to PP, particularly in patients affected by cystic fibrosis. A cell-mediated immunopathogenic mechanism has been demonstrated (on the basis of patch-test or delayed intradermal-test positivity) in only two cases of maculopapular reactions to PP (1,2).

Late onset skin reactions

This report describes two cases of cutaneous reactions to PP that appear to have been caused by delayed hypersensitivity.

Patient 1: A 38-year-old male immediately after a hemorrhoidectomy had been started on PP (Avocin 4 g/day intramuscularly), and after 6 days of treatment a generalized erythematous rash developed. The antibiotic was discontinued and after 7 days of corticosteroid therapy the skin lesions resolved.

Patient 2: This 42-year-old male had undergone surgery for cranial trauma. Avocin (4 g/day intramuscularly) was administered during the postoperative period and a generalized maculopapular rash developed on the fourth day. The drug was then discontinued, and corticosteroid therapy was started. The rash resolved within 10 days, leaving generalized scaling.

Neither patient had a personal or family history of allergic diseases.

Two and seven months later, respectively, the patients underwent skin tests with penicilloypolylysine (Allergopen, Reinbeck, Germany), minor determinant mixture (Allergopen), benzylpenicillin (BP), ampicillin (AM), amoxicillin (AX) and PP, as well as cefaclor and ceftriaxone, as previously described (3). AM, AX and PP were used at concentrations of 1 and 20 mg/ml in 0.9% NaCl, cephalosporins at 2 mg/ml.

Both patients presented skin-test negativity after 20 min, and delayed intradermal reactions (after 24 h in case 1 and 48 h in case 2) only to AM, AX and PP: erythematous, indurated wheals larger than 10 mm, which began to fade after 72 h. Intradermal tests with PP were negative in 10 healthy control subjects, 4 of whom had previously tolerated PP.

Patch tests were done with BP, AM, and AX (5% in petrolatum), as well as with PP, cefaclor and ceftriaxone (200 mg/ml in 0.9% NaCl) as previously described (3). Only those with AM, AX and PP were positive at the 48- and 72- h readings (patient 1:+++for all haptens; patient 2:++for all haptens).

Single-blind challenges with BP (1000 000 IU), ceftriaxone (1 g) and cefaclor (500 mg) were also performed, the first two intramuscularly and the last orally. Increasing doses (0.01, 0.1 and 1.0 of the respective therapeutic doses indicated in parentheses) were administered at 1 week intervals, and were well tolerated.

The characteristics of these two cases (i.e., cutaneous reactions appearing more than 48 h after the initiation of therapy, as well as patch-test and delayed intradermal-test positivity) are indicative of delayed hypersensitivity to PP.

Patch tests and delayed-reading intradermal tests are a simple and effective means of diagnosing this type of reaction.

Both of the previously described subjects displayed allergologic-test

negativity to penicillin determinants as well as to AM and AX (1,2). Thus, their reactions were probably caused by a selective sensitization to PP; however, they were not challenged with other β -lactams to assess such selectivity.

Our patients presented positive reactions to AM and AX, as well as to PP, but there were no reactions to penicillin determinants or to cephalosporins. The cross-reactivity between PP and the aminopenicillins may reflect the presence of antigenic structures shared by the side-chains of all three semisynthetic penicillins. However, considering that subjects tolerated cefaclor (an aminocephalosporin which shares the aminobenzyl side chain with AM and AX) recognition of the penicillin thiazolidin ring also appears to be important.

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