

Allergy to cloxacillin with normal tolerance to amoxicillin and cefuroxime

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ABSTRACT

Background: Cloxacillin is a semisynthetic penicillin widely used in nonmethicillin resistant *Staphylococcus aureus* infections. Several hypersensitivity reactions to cloxacillin have been reported, although IgE-mediated allergic reactions to the drug are rare and there is little information about possible tolerance to other semisynthetic penicillins or cephalosporins in patients with cloxacillin allergy. We present 2 patients with demonstrated IgE-mediated allergy to cloxacillin and tolerance to amoxicillin and cefuroxime.

Case reports: Case 1. A 47-year-old woman began treatment with cloxacillin due to acute cellulitis. After ingesting 500 mg of the drug, she experience generalized maculopapular eruption and facial angioedema. Case 2. A 55-year-old woman presented an episode of acute urticaria and labial angioedema 60 minutes after ingesting 500 mg of cloxacillin for a skin abscess.

Methods and results: Skin prick tests were positive to cloxacillin in case 1 and negative in case 2. However, an intradermal test was positive to cloxacillin (2 mg/ml) in case 2. Simple-blind oral challenge tests with amoxicillin (1 g) and cefuroxime (500 mg) were well-tolerated by both patients.

Conclusions: We present 2 patients allergic to cloxacillin with normal tolerance to other betalactam antibiotics, confirming that cross-reactivity among these antibiotics seems to be uncommon. Complete allergy study, including an oral challenge test, should be considered in these patients.

Key words: Amoxicillin. Cloxacillin. Hypersensitivity. Tolerance. Allergy.

INTRODUCTION

Cloxacillin is a semisynthetic penicillinase-resistant penicillin widely used in non-methicillin resistant *Staphylococcus aureus* infections. Most frequent side effects of cloxacillin are gastro-intestinal manifestations like vomiting or diarrhea, although there have been reported different hypersensitivity reactions^{1,2}. However, IgE-mediated allergic reactions to the drug are rare and there is little previously reported information about the management of allergic patients to cloxacillin in order to demonstrate tolerance to other semi-synthetic penicillins or cephalosporins³. We present two different patients with demonstrated IgE-mediated allergy to cloxacillin with normal tolerance to amoxicillin and cefuroxime.

CASE REPORT

Case 1. A 47-year-old woman diagnosed of chronic lymphedema after a radical mastectomy, began treatment with cloxacillin due to an acute cellulitis. Short-

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ly after the intake of *Orbenin*® 500 mg (Glaxo-SmithKline-Beecham, Toledo, Spain) she experienced generalized pruritic maculo-papular eruption, hives and angioedema of the face.

Case 2. A 55-year-old woman, with a personal background of smoking, who had taken cloxacillin 500 mg for an abscess involving the bulbous end of a finger. 60 minutes after the intake of the first pill, she presented an episode of acute urticaria and labial angioedema. Both patients were completely recovered after the administration of parenteral treatment (40 mg of 6-methyl-prednisolone and intravenous diphenhydramine). They both had previously taken cloxacillin without any reaction and they had not eaten any food or had not been doing exercise in the previous 4 hours.

ALLERGIC STUDY

In the Allergy Unit at our Hospital, Skin prick tests (SPT) with benzylpenicillin (10.000 U/ml), major and minor determinants mixture of benzylpenicillin (BPO and MDM, Diater, Madrid, Spain), cloxacillin (20 mg/ml), amoxicillin (20 mg/ml) and cefuroxime (200 mg/ml) were performed 30 days later according to standardized procedures⁴. If they were negative, intradermal tests were carried out. Prick test was positive only to cloxacillin in case 1 with a mean diameter of the obtained wheal of 5mm. Prick test were all negative in case 2, but the intradermal test was positive to cloxacillin (2 mg/ml) presenting a 14 mm wheal of mean diameter, double that of the histamine wheal (1 mg/ml) at the 20 min. reading. All the other tests were negative and no positive results were obtained at the 24 h reading. Simple-blind oral challenge tests with increasing doses until an accumulative dose of amoxicillin (1 g) and cefuroxime (500mg) were performed, being well-tolerated in both patients.

DISCUSSION

Adverse reactions to betalactam antibiotics constitute a major hazard in medical practice. Although the use of cloxacillin is widely extended, data of immediate allergic reactions after using this drug are very

scarce. It could be explained due to it is not frequently involved in allergic reactions⁵ but there could exist an insufficient communication that leads to remain cloxacillin allergic reactions to be underdiagnosed. This fact could explain the lack of reported experience in clinical management of those patients. There is a general tendency to avoid using other betalactam antibiotics due to that there are similarities in chemical structure between them to justify a cross-reactivity mechanism between cloxacillin and amoxicillin or cephalosporins. However, if we remember that many of the allergic patients to penicillin or amoxicillin tolerate any cephalosporin, the allergologist might be asked to find out which of the other betalactam antibiotic could be used as secure alternatives in cloxacillin allergic patients. We should not forget that previous observations indicate that, in some instances, subjects allergic to cloxacillin may experience an allergic reaction after taking the drug orally but have good tolerance after being administered the same drug by parenteral route⁶.

In conclusion, we present two different patients allergic to cloxacillin with normal tolerance to other betalactam antibiotics, confirming that cross-reactivity seems to be uncommon among those tested antibiotics. A complete allergologic study, including an oral challenge test, should be considered in these patients.

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