

# Successful desensitization to penicillin after diagnostic reassessment

V. Soriano<sup>a</sup>, E. Niveiro, J. Fernández, J.-V. Castelló y P. González

Sección de Alergia. Hospital General Universitario de Alicante. Alicante. Spain.

## SUMMARY

Clinical situations for which penicillin is indicated as the sole effective treatment are not infrequent, in these circumstances penicillin allergy complicates their medical management. No proven alternatives to penicillin are available for treating neurosyphilis, congenital syphilis, or syphilis in pregnant women, it is not possible choosing an alternative non betalactam antibiotic. The management of the patient who has a history of penicillin allergy include skin testing to determine if penicillin-specific IgE antibodies exist, and desensitization if penicillin is the choice treatment. We report a case of successful desensitization to penicillin in a 30 year-old pregnant woman with latent syphilis and penicillin allergy, where the first penicillin study was not positive, but the repetition of diagnosis test (reassessment) with the same betalactam reagents than in the first study two weeks later the initial evaluation was positive, detecting allergic sensitization not detected at the previous examination.

**Key words:** Syphilis. Pregnancy. Penicillin allergy. Reassessment. Desensitization.

## RESUMEN

No son infrecuentes los cuadros clínicos en los que la penicilina está indicada como único tratamiento eficaz; en estas circunstancias, la alergia a la penicilina complica su tratamiento médico. No se dispone de alternativas más adecuadas que la penicilina con las que tratar la neurosífilis, la sífilis congénita o la sífilis en mujeres embarazadas, y no es posible elegir un antibiótico no betalactámico alternativo. El diagnóstico integral del paciente con antecedentes de alergia a la penicilina consiste en la realización de pruebas cutáneas para determinar si existen anticuerpos IgE específicos de la penicilina y desensibilización si este antibiótico es el tratamiento de elección. Describimos un caso en el que se logró una desensibilización satisfactoria a la penicilina en una mujer embarazada de 30 años con sífilis latente y alergia a la penicilina. El primer análisis de penicilina no fue positivo, pero la repetición de la prueba diagnóstica (reevaluación) con los mismos reactivos betalactámicos que en el primer estudio, 2 semanas después de la evaluación inicial, fue positiva, pues se detectó sensibilización alérgica no identificada en el examen anterior.

**Palabras clave:** Sífilis. Embarazo. Alergia a la penicilina. Nueva evaluación. Sensibilización.

### Correspondencia:

Dr. V. Soriano  
Sección de Alergia  
Hospital General Universitario de Alicante  
C/ Maestro Alonso, 109.  
0310 Alicante (Spain).  
E-mail: soriano\_vic@gva.es

## INTRODUCTION

The management of the patient who has a history of penicillin allergy include skin testing to determine if penicillin-specific IgE antibodies exist, and desensitization if penicillin is the choice treatment<sup>1</sup>. Especially when no proven alternatives to penicillin are available

for treating neurosyphilis, congenital syphilis, or syphilis in pregnant women and it is not possible choosing an alternative non betalactam antibiotic<sup>2</sup>.

We report a case of successful desensitization to penicillin in a pregnant woman with latent syphilis and penicillin allergy, where the first penicillin study was not positive, but the repetition of diagnosis test (reassessment) with the same betalactam reagents than in the first study two weeks later was positive, detecting allergic sensitization not detected previously.

## CASE REPORT

We studied for a second time, a 30 year-old pregnant woman with latent syphilis (RPR positive, IgM ELISA positive and FTA Abs positive) and penicillin allergy. One year before was evaluated in our outpatient clinic because a history of immediate angioedema to penicillin when she was only two years old, resulting in a positive intradermal skin test to the minor determinant mixture reagent (wheal of 7 × 5 mm with a flare). She had a past history of previous abortions, nephritic colics and adverse reactions to Sulfonamides and Streptomycin.

This time, the patient underwent skin tests with standard concentrations of Penicilloylpolylysine (Allergopen®, Reinbek, Germany), Minor Determinant Mixture (Allergopen®) and Ampicillin, Amoxicillin, Cefazoline, Cefotaxime diluted in 0.9 % sodium chloride and used at concentrations of 20 mg/ml in prick method and 0.2 mg/ml and 2 mg/ml in intradermal method, with positive and negative controls. Specific IgE to penicilloyl G, penicilloyl V, ampicilloyl and amoxicilloyl (UniCAP specific IgE; Pharmacia, Uppsala, Sweden) were negative too (< 0.35 kU/l). Upon negative skin tests and specific IgE results, we performed single-blind, placebo-controlled oral challenge test in the hospital with oral potassium fenoximetilpenicillin. Increasing amounts (5 mg, 50 mg, 500 mg) of the therapeutic doses (555 mg = 880.000 IU), indicated in parentheses, were administered at 1-h intervals, with excellent tolerance. But owing to private problems the patient could not be admitted to the hospital and came back two weeks later.

As we were not confidence with the result of the tolerance test we performed a second skin tests with the same reagents (reassessment) with positive results to Penicilloylpolylysine, Minor Determinant Mixture, Ampicillin, Amoxicillin, Cefazolin and Cefotaxime (table I), but negative specific IgE to reagents above mentioned.

**Table I**

**Skin test results with betalactams reagents**

Drugs	Concentrations (mg/ml)	Prick-test	Intradermal tests (1/100)	Intradermal tests (pure)
PPL	0.035	Negative		7 × 5 mm
MDM	1.1	4 × 4 mm		6 × 6 mm
Ampicillin	20 mg/ml	Negative	7 × 5 mm	
Amoxicillin	20 mg/ml	Negative	7 × 6 mm	
Cefazoline	20 mg/ml	Negative	7 × 6 mm	
Cefotaxime	20 mg/ml	Negative	6 × 4 mm	

All skin test results are given as size of largest diameter of wheal and its perpendicular diameter minus control wheal diameters.

So therefore and after obtaining written, informed consent the patient was proposed to desensitization. Doses of 500, 5000 and 40000 IU of fenoximetilpenicillin was prepared. The specific amount of drug was diluted in 30 mL of water and administered orally with 15 minutes interval between doses, and elapsed time 4 hours and cumulative dose, 1.288.000 units. The patient was treated with 2.400.000 UI of Penicillin G i.v. every 4 hours during 10 days. The patient was admitted in ICU and monitorized during all the procedure, including the first two i.v. doses of penicillin. No reactions were observed during the desensitization protocol and treatment.

A follow up study was done one year later with new skin tests with the same reagents and positive results to Penicilloylpolylysine, Minor Determinant Mixture, and Ampicillin, but negative to Amoxicillin, Cefazolin and Cefotaxime. Specific IgE was again negative. By the second year all the tests were negative, including skin and serologic tests, challenge test and a new reassessment.

After oral controlled administration of penicillin in patients with skin tests and RAST negative, repetition of diagnostic tests (reassessment) with betalactam reagents two to four weeks after initial evaluation can be of value to detect allergic sensitization not detected at the previous examination<sup>3-5</sup>.

## DISCUSSION

Detection of IgE antibodies in the skin or serum depend on the time interval between the reaction and the study, because skin test sensitivity decrease with time<sup>6</sup>. This loss of sensitivity varies individually, but no sufficient studies have been carried out to examine it. The reason for the variability in the skin test response may be genetic or environmental because uncontrolled or hidden contact with beta-

lactams antibiotics can occur, which could maintain sensitization<sup>7</sup>.

Allergic diseases are unpredictable more, less severe, or unchanged in pregnant women<sup>8</sup>. Little specific information is available concerning the relative susceptibility of pregnant women to anaphylaxis or acute desensitisation<sup>9</sup>. This case demonstrates that in a patient allergic to penicillin, in whom there is a vital indication to administer this compound, the drug can be given safely after tolerance induction or desensitization.

## REFERENCES

1. Sullivan TJ, Yecies LD, Shatz GS, Parker CW, Wedner HJ. Desensitization of patients allergic to penicillin using orally administered  $\beta$ -lactam antibiotics. *J Allergy Clin Immunol* 1982; 69:275-82.
2. Centers for Disease Control and Prevention. Primary and secondary syphilis—United States, 1997. *MMWR Morb Mortal Wkly Rep* 1998;47:493-7.
3. Mendelson LM, Ressler C, Rosen JP, Selcow JE. Routine elective penicillin allergy skin testing in children and adolescents: study of sensitization. *J Allergy Clin Immunol* 1984;73:76-81.
4. Lopez L, Mateo B, Beristain A, Armisen M, Perelló S, Alvarez-cuesta E. Importance of reprovocation in penicillin allergy study. *Allergy* 1993;48:147.
5. Lopez-Serrano MC, Caballero MT, Barranco P, Martinez-Alzamora F. Booster responses in the study of allergic reactions to beta-lactams antibiotics. *J Invest Allergol Clin Immunol* 1996;6:30-5.
6. Blanca M, Torres MJ, Garcia JJ et al. Natural evolution on skin test sensitivity in patients allergic to betalactams antibiotics. *J Allergy Clin Immunol* 1999;103:918-24.
7. Blanca M, Garcia J, Vega JM, Miranda A, Carmona MJ, Mayorga C et al. Anaphylaxis to penicillins after non therapeutic exposure: an immunological investigation. *Clin Exp Allergy* 1996;26:335-40.
8. Schatz M, Hoffman CP, Zeiger RS, Falkoff R, Macy E, Mellon M. The course and management of asthma and allergic diseases during pregnancy. In: Middleton E, Allergy, Principles and Practice, 1998.
9. Wendel GD, Stark BJ, Jamison RB, Molina RD, Sullivan TJ. Penicillin allergy and desensitization in serious infections during pregnancy. *N Engl J Med* 1985;312:1229-32.