

Myocardial ischemia due to severe amoxicillin allergy

R. López-Abad, F. Rodríguez, J. L. García-Abujeta, D. Martín-Gil, J. Jerez

Allergy Section, Hospital Universitario Marqués de Valdecilla, Santander (Spain)

Summary: A patient suffered a myocardial injury as a manifestation of anaphylactic reaction to amoxicillin-clavulanic acid administration. A cardiologic study (ergometry and catheterization) showed no obstructive coronary disease and prick test to amoxicillin was positive. Anaphylaxis may cause myocardial injury and the mechanism is likely to be vasospasm induced by mast cells and basophil mediators.

Key words: myocardial ischemia, anaphylaxis, adverse drug reaction, amoxicillin.

Introduction

Acute anaphylactic reactions are sudden, frightening and potentially lethal responses to various allergens. They are often elicited by drugs, and the most frequent ones are penicillin derivatives [1,2].

It is well known that heart may be a target organ in human anaphylaxis [3-7]. Acute cardiac injury has been previously described in severe allergic reactions but only in a few cases the patient had normal coronary arteries. In medical literature we have found several studies which explain the pathophysiologic mechanisms that cause coronary vasospasm and myocardial injury due to anaphylaxis. It has been postulated before by several authors that histamine may cause coronary vasoconstriction and consequent angina and myocardial injury [5,7], although another anaphylaxis mediators such as leukotrienes are also potent vasoconstrictors and could be involved in the response [8]. We also found some published cases that suggest a drug-associated anaphylactic reaction with concomitant myocardial ischemia [7, 9-11].

Case report

A 43-year-old man was referred to our Allergy Section for evaluating betalactamic antibiotics allergy. Two months before, during a treatment with amoxicillin-clavulanic acid for a dental infection, he showed an

immediate episode of itching and erythema, which began on palms, soles and genital area and then became generalized. He also complained of a constricting chest pain with no irradiation and loss of consciousness. The patient was admitted in the Emergency Room. He was hypotensive with a systolic blood pressure of 70 mmHg and his pulse was barely palpable. He was treated with specific drugs for angor, intravenous fluid, steroids, antihistamines and oxygen. He did not receive epinephrine. The patient improved and then was transferred to the Coronary Unit with a diagnosis of angor of recent onset with an important hemodynamic repercussion. The electrocardiogram initially showed ST segment elevations and negative T-wave in leads II, III and aVF, indicating acute inferior injury (Figure 1). A few hours later, repeated electrocardiograms showed only minor non-specific ST-T changes (Figure 2). Daily electrocardiograms remained normal. Laboratory tests only revealed a moderate leukocytosis with normal series. Serial creatine phosphokinase levels over three days were absolutely normal, with no evidence of necrosis. Chest radiography revealed a normal heart size without pulmonary alterations. A subsequent cardiologic study (ergometry and catheterization) was normal and showed no obstructive coronary artery disease.

A skin prick test was done with clavulanic acid at a concentration of 10 mg/ml (Beecham Pharmaceuticals, Spain) and a high-diluted concentration of amoxicillin (0.1 mg/ml), obtained from Beecham Pharmaceuticals, due to the history of severe reaction. We also determined

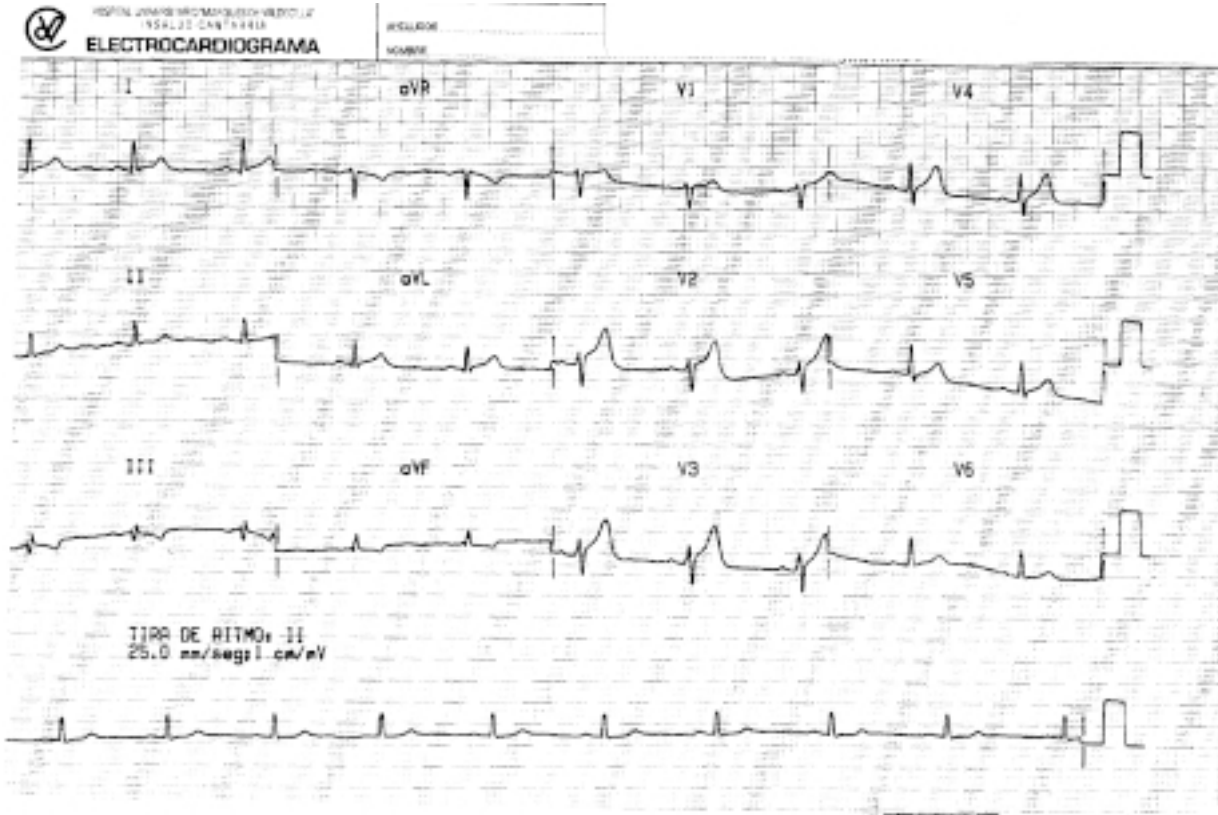


Figure 1.

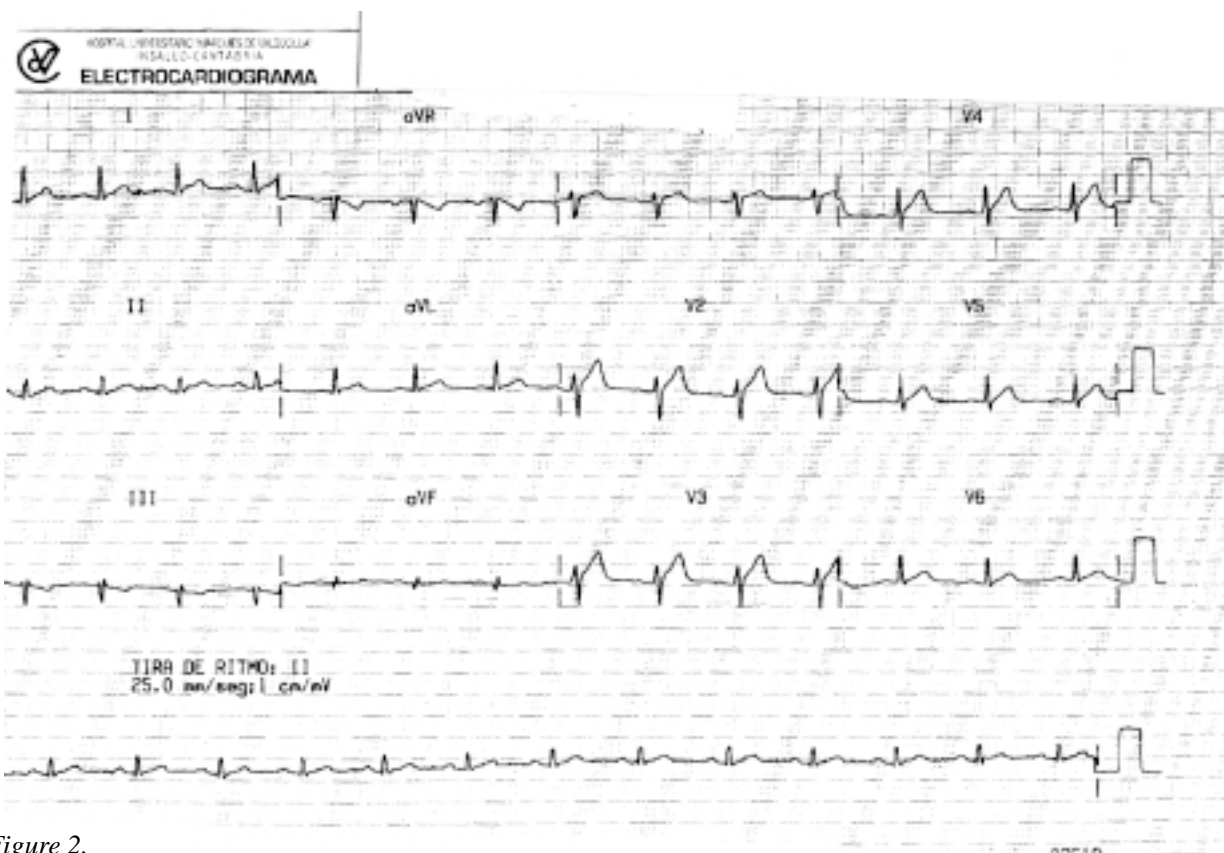


Figure 2.

serum specific IgE antibodies to amoxicillin, ampicillin, penicillin and cefaclor by the CAP system (Pharmacia).

For safety and ethical reasons, we did not perform intradermal and challenge tests with amoxicillin and other betalactamic antibiotics. The patient had a negative reaction to clavulanic acid but he showed an immediate positive response to a highly diluted concentration of amoxicillin. A pruriginous wheal with a mean diameter of 8 mm and associated surrounding erythema was found at the side of the prick test. He also complained about an immediate episode of generalized pruritus, which rapidly subsided with antihistamine therapy.

In clinical practice we do not test clavulanic acid due to its great instability. In this case and with research purposes, we included this drug in our study, making the solution immediately before performing the cutaneous test.

Determinations of serum specific IgE antibodies to amoxicillin, ampicillin, penicillin and cefaclor were all negative.

Discussion

A number of mechanisms have been proposed to explain the phenomenon of anaphylaxis-induced myocardial injury: hypoperfusion which occurs in anaphylactic shock; pharmacologic agents which may cause vasospasm such as epinephrine (used to treat anaphylaxis) and, last but not least, the mediators of anaphylaxis [6, 7].

We present a patient with normal coronary arteries who suffered a myocardial injury as a manifestation of anaphylactic reaction due to amoxicillin-clavulanic acid administration. On the basis of the symptoms and allergy study a diagnosis was made of severe allergic reaction caused by amoxicillin.

To our knowledge, this is the first published report in which sensitization to the suspected antibiotic is shown by the positive skin prick test to amoxicillin. The negative result of the serum IgE determination could be explained if we knew that the CAP system determined only the presence of serum IgE antibodies against the amoxycilloil (major determinant). IgE-mediated reactions to betalactamics may be caused by major determinants and in some cases by minor determinants, particularly in anaphylactic reactions. It has been claimed that immediate reactions to penicillins are more often a response to minor rather than to major determinants [12]. That is the reason why we think that our patient had a hypersensitivity type I reaction to minor determinants.

Other reports only suggest it but we can confirm that the allergic reaction was responsible for the coronary involvement producing the angina and this can be confirmed through the positive result of a skin prick test with the drug involved. As previously mentioned before we did not perform intradermal and challenge tests with amoxicillin and other betalactamics antibiotics for safety reasons.

This case provided further evidence about how anaphylaxis may cause myocardial injury and the mechanism is likely to be vasospasm induced by mast cells and basophil mediators, histamine being the most frequent one.

References

1. Vega JM, Blanca M, García JJ, Carmona MJ, Miranda A, Pérez-Estrada M, Fernández S, Acebes JM, Terrados S. Immediate allergic reactions to amoxicillin. *Allergy* 1994; 49 (5): 317-322.
2. Audicana M, Bernaola G, Urrutia I, Echechpía S, Gastamiza G, Muñoz D, Fernández E, Fernández de Corres L. Allergic reactions to betalactams: studies in a group of patients allergic to penicillin and evaluation of cross-reactivity with cephalosporin. *Allergy* 1994; 49 (2): 408-113.
3. Stein Isidore and Wecksell Irving. Cardiac disease accompanying allergic drug reactions. *J Allergy* 1970; 45: 48-53.
4. Criepp LH and Woehler TR. The heart in human anaphylaxis. *Annals of Allergy* 1971; 29: 399-409.
5. Capurro N and Levi R. The heart as a target organ in systemic allergic reactions. Comparison of cardiac anaphylaxis in vivo and in vitro. *Circulation Research* 1975; 36: 520-528.
6. Sullivan TJ. Cardiac disorders in penicillin-induced anaphylaxis. Association with intravenous epinephrine therapy. *JAMA* 1982; 248: 2161-2162.
7. Rich MW. Myocardial injury caused by an anaphylactic reaction to ampicillin/sulbactam in a patient with a normal coronary arteries. Texas Heart Institute. *Journal* 1998; 25: 194-197.
8. Michelassi F, Landa L, Hill RD, Lowenstein E, Watkins WD, Petkau AJ, Zapol WM. Leucotriene D4: a potent coronary vasoconstrictor associated with impaired ventricular contraction. *Science* 1982; 217: 841-3.
9. Cistero A, Urias S, Guindo J, Leonart R, García-Moll M, Geli A, Bayes de Luna A. Coronary artery spasm and acute myocardial infarction in naproxen-associated anaphylactic reaction. *Allergy* 1992; 47 (5): 576-8.
10. Ahmad S. Allopurinol and enalapril. Drug induced anaphylactic coronary spasm and acute myocardial infarction (letter). *Chest* 1995; 108: 586.
11. Stephen M Austin, Banajit Barooah, Chung S Kim. Reversible Acute Cardiac Injury during Cefoxitin-Induced anaphylaxis in a Patient with Normal Coronary Arteries. *Am J Med* 1984; 77: 729-732.
12. Baldo BA. Penicillins and cephalosporins as allergens structural aspects of recognition and cross-reaction. *Clin Exp Allergy* 1999; 29: 744-749.

Dra. Raquel López Abad

Allergy Section
Hospital Universitario Marqués de Valdecilla
39008 Santander (Spain)
Tel.: +34-942202543, +34-942202583
Fax: +34-942202543
E-mail: mabadl@terra.es