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## A case of protracted hypotension as unique symptom of a biphasic anaphylaxis to amoxicillin

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### KEY WORDS

*Anaphylaxis, biphasic reaction, drug hypersensitivity.*

### SUMMARY

*We are reporting a case of one patient who have experienced itching of palms and soles, thorax erythema, conjunctive injection immediately after oral administration of amoxicillin, and hypotension after 3 hours. In E.D. hypotension was monitored because he was a cardiopatic but it wasn't treated even if it was protracted. A positive result of immediate-reading intradermal test with amoxicillin at 2 mg/ml concentration was found confirming the diagnosis of allergic biphasic anaphylaxis to amoxicillin.*

Biphasic anaphylactic reactions have been reported to develop in as many as 20% of anaphylactic reactions (1-4). Late-phase severity varies from mild to severe (rarely fatal). No clinical features on initial presentation identified those likely to have a biphasic response.

We are reporting a case of one patient who have experienced a biphasic anaphylaxis after the administration of amoxicillin. U.Z. is a 68-year-old man who went to Emergency Department (E.D.) for loss of consciousness, thoracic oppression and feeling of tightness of the throat. The patient was affected by ischemic hearth disease, hypertension, diabetes mellitus in therapy with carvedilole, zofenopril, aspirin 160 mg, ticlopidine 250 mg b.i.d., oral hypoglycemic and hypolipidemic agents.

On arrival at the E.D. hypotension was found (BP: 85/55) with no other values out of normal range.

Electrocardiography and assay for cardiac enzymes excluded an acute cardiac event, chest x-ray was negative.

In the history he referred that 3 hours before he had taken one tablet of amoxicillin with onset after 15 minutes of itching of palms and soles, thorax erythema, conjunctive

injection. He spontaneously took H1-antihistaminic with resolution of symptoms. After 3 hours he complained weakness, thoracic oppression for which he took sublingual nitroglycerin, feeling of tightness of the throat and finally loss of consciousness, so he was admitted to E.D.

The patient remained in E.D. during 9 hours without a support therapy until blood pressure spontaneously returned to normal value (BP: 120/80). Note that after 6 hours values pressure were still very low (BP: 90/50).

The patient was discharged with diagnosis of thoracic pain and allergic reaction and a therapeutic course with H1-antistaminic and cortisone was prescribed.

The allergological evaluation was made 3 months later in November 2008. He was not affected by symptoms of rhinitis or asthma.

Assays for serum specific IgE to penicilloyl G, penicilloyl V, amoxicilloyl, ampicilloyl resulted negative with a value < 0.35 kU/L.

Patch tests at 5% in petrolatum were performed with benzylpenicillin, ampicillin, amoxicillin, cephalixin, cephalothin, cefazolin, cefradine, cefuroxime and resulted all negative.

The patient was prick and intradermal tested with PPL (final concentration  $1.07 \times 10^{-2}$  mM/l) and MDM (final concentration 1.5 mM/l) using Diater S.A. (Madrid, Spain) reagents, with aminopenicillins (ampicillin and amoxicillin) at a concentration of 2 and 20 mg/ml 0.9% NaCl, with cephalosporins (cefuroxime and ceftazidime) at 2 mg/ml 0.9% NaCl in order to evaluate cross-reactivity for a possible future use of them as alternative  $\beta$ -lactam antibiotics.

Positive control for prick test was performed with histamine at 10 mg/ml. As negative control for prick and intradermal test 0.9% NaCl was used. Tests were conducted and readings were taken according to the ENDA recommendations (5).

A positive result of immediate-reading intradermal test with amoxicillin at 2 mg/ml was found; so the amoxicillin concentration of 20 mg/ml wasn't tested.

The clinical history was suggestive for allergic biphasic anaphylaxis and the IgE nature of the reaction was confirmed by positive result of immediate-reading skin tests. No, tryptase levels weren't measured when the patient was admitted at the E.D. No basal tryptase levels weren't measured in our diagnostic approach because the patient never had allergy manifestations before this amoxicillin reaction for which was evaluated in our hospital.

The patient studied in our hospital had not potential risk factors reported in other studies (1-3) but actually there are no reliable predictors of biphasic anaphylaxis.

For this patient the diagnosis of biphasic allergic reaction was under recognized and undertreated, in spite of a protracted and profound hypotension he was not treated but

only maintained under observation. To note that these cases are normally poorly responsive to adrenaline (6). Biphasic responses occur with significant frequency and should be taken into consideration when one considers the observation period after the initial event which can be of various grade of severity. Biphasic allergic reactions were reported in 23% of drug/biological reactions (7). In front of a positive anamnesis for recent intake of drugs with referred adverse reactions, even in a patient with cardiovascular disease, we have to be suspicious of an allergic reaction with prompt treatment and sending for following allergological investigation.

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