

Anaphylaxis to beef in penicillin-allergic patient

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Key words: anaphylactic reaction; beef; penicillin hypersensitivity.

• In June 1999, 10 min after eating a minced steak, a 51-year-old man experienced anaphylactic shock (angioedema, dyspnea, and hypotension). He also suffered from hand urticaria 15 days before this anaphylactic shock, and this also happened 10 min after he ate a minced steak from the same manufacturer.

Probably due to penicillin residues in the meat.

In September 1999, skin prick tests with 25 common food allergens, including beef, and 29 pneumo-allergens were negative. Specific IgE to beef was undetectable.

In December 1999, the patient experienced another anaphylactic shock (generalized urticaria, lip angioedema, dyspnea, and hypotension) 10 min after finishing a bowl of vegetable soup. He had also just taken (about 10 min before) 500 mg of amoxicillin per os on day 1 of treatment, and nimesulide and tetrazepam on day 3 of treatment. He also took nefopam i.m. on day 3 of treatment, 1 h before the anaphylactic episode. He was admitted to hospital and treated by subcutaneous epinephrine, plasma expanders, intravenous methylprednisolone, and chlorphenamine.

The patient intentionally ate grilled steak after the second anaphylactic shock and there was no adverse event.

Two months after the second anaphylactic shock, we gave the patient skin prick tests with penicilloyl polylysine (Allergopen, Reinbek, Germany), a minor determinant mixture (Allergopen), benzylpenicillin at

25 000 UI/ml, ampicillin, amoxicillin at 25 mg/ml, and ceftriaxone and cefapirine at 25 mg/ml (all diluted in normal saline). All the reactions were extremely positive with pseudopods, and at the same time, the patient experienced anaphylactic shock, which was treated by the same protocol as above. Symptoms resolved completely and rapidly.

Three months later, we gave the patient an open patch test: one drop of amoxicillin at 25 mg/ml was placed on the skin of his forearm, without cutaneous breaking. Fifteen minutes later, he developed contact urticaria, which rapidly became generalized with conjunctivitis.

Two months later, oral provocation tests with the accompanying treatments (tetrazepam, nimesulide, and nefopam) and with alternative drugs (cefuroxime and cefpodoxime) were performed (each on a different day). No reactions were observed to the different challenges.

Our clinical findings and the positive skin tests with penicillins suggest that the patient developed IgE-mediated allergy to penicillins (β -lactam ring). He was not allergic to beef, as he ate steak from his butcher with no problems and specific IgE to beef was undetectable.

Another well-documented case of anaphylaxis due to penicillins present in beef and pork has been reported in the literature (1). Double-blind oral provocation tests with increasing doses of penicillin G diluted in milk compared with placebo (milk of the same bottle alone) induced bronchospasm with hypotension with a cumulative dose of 0.012 mg. Specific IgE to beef and pork was undetectable.

In 20 other cases discussed in that paper, hypersensitivity to benzylpenicillin residues in meat was highly suspected because of the negativity of food tests and the positivity of penicillin tests.

In our patient, traces of penicillin were certainly present in the frozen minced steak eaten twice by the patient and bought in the same supermarket, despite denial by the technical services. These traces were responsible for the two anaphylactic shocks immediately after eating the steak. The reactivity level of this patient was about 0.0005 mg per ml with the prick test. This was 100 times lower than the advisable maximal residues limit, which is 0.05 mg per mg for edible tissues in the European Community (2, 3). This limit is based on the determination of an acceptable daily intake. These recommendations are based on studies performed *in vitro* and *in vivo*. Finally, for each drug, a withdrawal period must be defined during which one cannot consume food from animals. For example, a farm animal treated by penicillin cannot be slaughtered within the following 30 days, but it is difficult to ensure that this legal delay is always respected.

We advised the patient strictly to avoid foods of animal origin from an unknown breeder and always to have with him autoinjectable epinephrine.

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Allergy to lipopolysaccharide?

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Key words: dermatology; endotoxin; inhalation.

● HUMAN volunteer inhalation challenges administering commercially available lipopolysaccharide (LPS) preparations are being used increasingly in experimental models to elucidate the biological effects of endotoxin exposure.

Previously reported symptoms after inhalation have included upper respiratory tract irritation, dry cough, dyspnoea, chest tightness, headache, tiredness, myalgia, arthralgia, and fever (1). We describe a 50-year-old, nonatopic, nonsmoking volunteer with no relevant medical history, who developed a macular rash after experimental inhalation of LPS.

On week 1, he inhaled a control solution of pyrogen-free saline solution, and on week 2, a 0.5 µg dose of LPS. Both were well tolerated, and not associated with any symptoms or rise in temperature. On week 3, he inhaled a dose of 5 µg LPS, which

initially was not related to any adverse effects. However, 24 h later, he complained of a mild, nonitchy, macular rash distributed on the volar aspect of both arms, extending up onto the top of the chest. This was not associated with any systemic upset, or fever. The rash was short-lived, and had completely settled by the following morning. As dermatologic problems with inhaled LPS had not previously been described, and the rash had been mild in nature, the volunteer agreed to proceed to the last dose of 20 µg. By 45 min after inhalation, this dose induced cough, chest tightness, and bronchospasm requiring salbutamol administration. These symptoms settled, but when he was reviewed the next day, he had again developed an identical rash of similar distribution. The rash progressed over the course of the same day and was associated with flu-like symptoms. By 72 h after inhalation, the volunteer had returned to normal.

Flow cytometry data (Fig. 1) demonstrated a marked peak in monocyte CD14 (the LPS receptor) 2 h after inhalation of 20 µg of LPS, an event which had not occurred after the control dose. This had returned to baseline by 6 h after inhalation. Fig. 1 also shows the rise in CD4 CD25-positive lymphocytes

(activated T-helper cell) that occurred after inhalation of 20 µg LPS; in this case, it took 2 days to settle back to baseline levels.

We believe this to be the first case of a dermatologic response to inhaled LPS, and that this may have an underlying allergic mechanism. We suggest that experimental inhalation of LPS may cause a dermatologic response in healthy volunteers, and those demonstrating such symptoms or signs should not be further exposed. Furthermore, it may be necessary to monitor volunteers for more than the 24 h that has previously been suggested (1).

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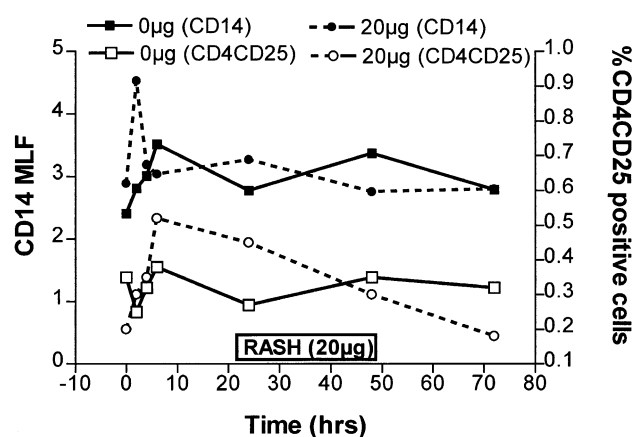


Figure 1. Whole-blood immunologic responses to inhaled control and 20 µg lipopolysaccharide, as measured by monocyte CD14 (mean linear fluorescence), and T-helper cell activation (percentage CD4 CD25-positive lymphocytes).