EMERGENCY CASEBOOK

Allergy evaluation after emergency treatment: anaphylaxis to the over-the-counter medication clobutinol

Cornelia S Seitz, Eva-B Bröcker, Axel Trautmann

Emerg Med J 2007;24:e19 (<http://www.emjonline.com/cgi/content/full/24/3/e19>). doi: 10.1136/emj.2006.042903

Anaphylaxis is traditionally diagnosed and treated as an acute emergency but should be always followed by a search for specific triggers, resulting in avoidance strategies. This case report highlights the relevance of a detailed evaluation after anaphylaxis for diagnosis of a rare but potentially life-threatening allergy. Considering the high frequency of clobutinol application, IgE-mediated allergic hypersensitivity seems extremely rare and has to be distinguished from infection-associated urticaria and angioedema as well as non-specific summation effects. Accidental re-exposure has to be strictly avoided and therefore after identification of clobutinol as the anaphylaxis trigger, the patient received detailed allergy documents including international non-proprietary and trade names of the culprit drug.

Anaphylaxis to clobutinol has not been described in the medical literature even though potential side effects such as itching, urticaria and angioedema are mentioned in the package insert of various clobutinol preparations. Anaphylaxis is a severe, systemic immediate-type hypersensitivity reaction that is rapid in onset and may cause death.¹ In most cases, itching of palms and soles and/or urticaria precede upper airway obstruction and hypotension. In the absence of cutaneous symptoms, clinical differentiation of anaphylaxis from other acute conditions such as vasovagal reactions or pulmonary embolism may be difficult. Common causes of anaphylaxis such as allergies to food, insect venoms and drugs as well as their pathophysiological mechanisms are summarised in table 1. Cofactors increasing the risk of anaphylactic reactions include ongoing infections, concomitant medications particularly β -blockers, mastocytosis prior food intake and physical exercise.¹

Clobutinol is a frequently used, European-wide, over-the-counter drug for upper respiratory tract infections, which was first introduced in Germany in 1952, and since then has been administered for decades to relieve cough symptoms.

Table 1 Immunopathological mechanisms and representative agents that cause anaphylaxis

Allergic anaphylaxis	IgE-mediated	Foods Venoms Natural rubber latex Drugs Allergen vaccines
	Non-IgE-mediated	Drugs Blood products General anaesthesia
Non-allergic anaphylaxis		Physical (exercise, cold) Drugs Idiopathic

Pharmacologically, clobutinol is a phenylalkylamine compound not related to opioids.² Interestingly, there is little evidence for the effectiveness of clobutinol and other over-the-counter antitussives compared with placebo controls.³ Nevertheless, these antitussives are popular self-medications for upper respiratory tract infection, accounting for a huge over-the-counter market.

CASE REPORT

A 38-year-old man suddenly developed a generalised urticaria followed by nausea, swelling of the tongue, difficulty swallowing, bronchospasm and sweating, while suffering from an upper respiratory tract infection. The patient received emergency treatment with intravenous fluids, steroids and antihistamines, was admitted to the hospital and monitored for 24 h.

Several months after the anaphylactic reaction, the patient was referred to our outpatient allergy clinic for further evaluation and testing. On thorough questioning he reported that the anaphylactic reaction started approximately 1 min after self-medication with Silomat syrup (Boehringer Ingelheim Pharma GmbH & Co KG, Germany). He did not take any other drug, specifically no β -blocker, denied prior intake of food and did not remember a previous exposure to Silomat syrup. His serum level of tryptase was within normal limits (3.03 μ g/L, UniCap, Pharmacia Diagnostics).

After obtaining informed consent, a skin prick test on the patient's volar forearm was performed and showed strong positive reactions after 20 min with Silomat pure syrup (clobutinol 4 mg/ml) (+++), with a dilution of 1:10 (++) and a dilution of 1:100 (++) respectively. To exclude reactions to additional ingredients of the syrup, such as sodium benzoate, saccharin and sorbitol, pure clobutinol was obtained and diluted to a stock concentration of 10 mg/ml. The patient also developed strong positive prick test reactions with the clobutinol stock solution (+++), as well as the 1:10 (++) and 1:100 dilution (++) whereas four control subjects had negative prick testing results with the same solutions, ruling out irritating reactions. The basophil activation test with clobutinol led to a dose-dependent activation of basophilic granulocytes and confirmed the diagnosis of IgE-mediated allergic hypersensitivity to clobutinol.⁴

The patient was educated about the identified allergy and received written allergy documents for clobutinol avoidance. Currently, there are no potentially cross-reacting drugs on the European market that have to be avoided.

Authors' affiliations

Cornelia S Seitz, Eva-B Bröcker, Axel Trautmann, Department of Dermatology, Venerology and Allergology, University of Würzburg, Würzburg, Germany

Competing interests: None.

Informed consent was given by the patient for publication of his details in this report.

Correspondence to: Mr A Trautmann, Department of Dermatology, Venerology and Allergology, University of Würzburg, Josef Schneider

Strasse 2, D-97080 Würzburg, Germany; trautmann_a@klinik.uni-wuerzburg.de

Accepted 11 October 2006

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