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Urticaria-angioedema reaction caused by propafenone

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Key words: drug allergy; propafenone; urticaria-angioedema.

Hypersensitivity reactions to drugs mainly involve the cutaneous, respiratory, and cardiovascular systems, but the rate and kind of reactions may widely change according to the different drugs. Propafenone is an agent used in cardiac arrhythmias thus far reported as mainly responsible of respiratory reactions (1–4). Here we describe for the first time a skin reaction with urticaria-angioedema in a patient treated with propafenone.

The patient was a 51-year-old woman referred to our Allergy Unit for urticaria-angioedema with daily manifestations. Wheals were scattered in all the body but more abundant in the trunk and arms, and angioedema affected especially lips and eyelids. The patient was under treatment with enalapril 20 mg u.i.d., propafenone 150 mg b.i.d, and acetylsalicylic acid (ASA) 100 mg u.i.d. for hypertension and extrasystolic arrhythmia.

The clinical history was negative for atopy or previous hypersensitivity reactions to drugs.

Considering the major role for ASA in skin reactions and the current absence of arrhythmia we discontinued the treatment with ASA but no changes in symptoms were observed. Also ACE-inhibitors agents are frequently involved in angioedema and thus enalapril was substituted with the calcium antagonist amlodipin for treating hypertension, but also this measure did not have any effect on symptoms. Since 6 weeks had elapsed from their first presentation, standard investigations for chronic urticaria, and namely for allergic, physical, infectious and (by means of autologous serum skin test) autoimmune causes, were done, but all the results were negative.

Finally, to rule out a responsibility of propafenone, at first not considered because of the absence of reports of urticaria-angioedema reactions to such agent, and following consultation with the cardiologist, the drug was withdrawn. After 48 h urticaria and angioedema began to decrease in intensity, and a complete resolution occurred in 1 week. To achieve certainty, after 1 month the drug was readministered with rapid reappearance of wheals and angioedema of the lips and a new resolution following the definitive stopping of treatment.

It has been suggested that the asthmogenicity of propafenone is because of its structural similarity to the beta-blocker propanolol (2), and thus the respiratory reactions seem caused more by the drug's mechanism of action than by hypersensitivity. Regarding skin reactions, only recently a case of exanthematous pustulosis was reported (4), and the present description adds a classical picture of hypersensitivity with urticaria and angioedema, which suggests to reconsider propafenone as a possible cause of allergic reactions.

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Ranitidine-induced anaphylaxis: detection of serum specific IgE antibody

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Key words: anaphylaxis; IgE; ranitidine; skin tests.

Although an IgE-dependent mechanism was suggested for anaphylactic reactions to ranitidine, the presence of serum specific IgE antibodies to ranitidine has not been demonstrated (1, 2). We report a case of severe anaphylaxis to ranitidine, in which specific IgE antibody was demonstrated.

A 55-year-old asthmatic man was presented with skin rash with pruritus, dyspnea, irritability, and syncope which developed 30 min after taking one tablet of ranitidine (150 mg, Zantac®; Glaxo-SmithKline-Korea, Seoul, Korea). His blood pressure (BP) was 60/40 mmHg, and forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), and FEV₁/FVC were 1.35 l (44% of predicted), 3.16 l (81% of predicted), and 43%, respectively. After treatments with epinephrine, antihistamine, steroid, bron-

Our case suggests that ranitidine could induce an IgE-mediated anaphylaxis.

chodilator, and dopamine, the anaphylactic symptoms were resolved, BP returned to normal, and FEV₁ was 2.47 l (80% of predicted). One month later, he had experienced same anaphylactic symptoms 30 min after taking medications including one tablet (150 mg) of ranitidine (Ponaltin®; Daehwa Pharm., Seoul, Korea). These two episodes of anaphylaxis were presumed to be caused by ranitidine ingestion.

A total serum IgE was 2330 IU/ml. Skin prick test with common aeroallergens showed negative response. Skin prick tests with ranitidine (Urantac®; Whanin Pharm., Seoul, Korea) were positive (mean wheal diameter of 2, 6, and 8 mm for 0.25, 2.5, and 25 mg/ml, respectively; 5 mm for histamine positive control). Three unexposed healthy control subjects exhibited no reactions. Skin prick tests with other H₂-receptor antagonists, including cimetidine (Tagma®; Samsung Pharm., Seoul, Korea) and famotidine (Gaster®; Dong-A Pharm., Seoul, Korea), were negative. After written informed consent was obtained, a single-blind, placebo-controlled oral challenge test with ranitidine, cimetidine, and famotidine was performed in the patient until a therapeutic dose was reached or an adverse reaction appeared. The oral challenge test resulted in the reappearance of symptoms 7 min after the administration of 100 mg of ranitidine (Zantac®). Cimetidine (Himetin®; Ildong Pharm., Seoul, Korea) and famotidine (Gaster®) were well tolerated.

To determine ranitidine-specific serum IgE, ELISA was performed. Ranitidine-HSA conjugate was prepared in our laboratory according to a method described previously (3), and were used to detect specific IgE in serum using ELISA. Eleven nonatopic healthy subjects with no history of exposure, who had negative skin prick tests to ranitidine, were enrolled as controls. The final absorbance value of the patient was determined from the subtraction of the HSA-coated value from that of the ranitidine-HSA-coated value. The positive cut-off value for specific IgE (0.06) was determined using the mean + 2 SD of the absorbance values of controls. The patient had high specific IgE level

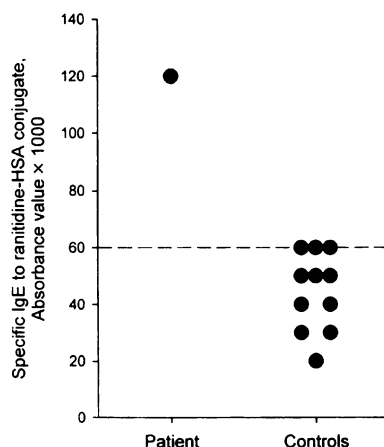


Figure 1. Serum specific IgE levels to ranitidine-HSA conjugate determined by using ELISA in our patient and 11 unexposed nonatopic controls. Dotted line indicates the cut-off value for positive specific IgE bindings, which was determined as mean + 2 SD of absorbance values of controls.

to ranitidine-HSA conjugate (0.12, Fig. 1).

This is the first report to succeed in detecting serum specific IgE reacting to ranitidine, as previous evidences of the presence of specific IgE antibodies were indirect and derived from positive skin tests (1, 2, 4) and leukocyte histamine release test (4) with ranitidine. This case suggests that ranitidine could induce the IgE-mediated anaphylaxis based on positive skin prick test, high serum specific IgE antibody, and immediate response to oral challenge test. It was unlikely that there was cross-reactivity between ranitidine and cimetidine or famotidine based on negative oral challenge tests in our case, which is consistent with the findings by Lazaro et al. (1) and Morisset et al. (4). A diagnostic method based on skin tests and specific IgE determination could be proposed in case of ranitidine-induced anaphylaxis.

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Is ethanol-induced bronchospasm an inflammation-driven event?

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Key words: asthma; ethanol; inhalant steroids; TRPV1.

Ethanol is used as a co-solvent in the preparation of new pressurized metered dose inhalers to enhance the solubility of the principal agents (beclomethasone, flunisolide, formoterol) in hydrofluoroalkane propellents.

We recently reported that the ethanol content in inhalant corticosteroid (ICS) formulations can induce bronchospasm (1). This result is consistent with those yielded by animal models, which demonstrate that ethanol is able to induce bronchospasm via stimulation of sensory airway nerves by a transient receptor potential vanilloid-1 (TRPV1) activation

Topical anti-inflammatory therapy can reverse ethanol-induced bronchospasm.