

atopy where it is not necessary to identify the specific allergen.

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IgE-mediated allergy to bromelain

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Key words: allergy; bromelain; drug; IgE.

● BROMELAIN is a plant-derived enzyme, of the family of the Bromeliaceae, included in the group of proteolytic enzymes, which, because of their catalytic activity, are generally used by the drug and food industries, and in diagnostics. Together with papain, bromelain is used in the industrial preparation of meat and in brewing (1); it is also used as an anti-inflammatory drug.

We describe a patient presenting an IgE-mediated reaction to bromelain used as a drug (Ananase). This 47-year-old

woman had a history of allergic rhinoconjunctivitis and a negative family history in terms of drug reactions. She came to our attention because of an adverse reaction that occurred 10 min after she took the seventh tablet of Ananase. The reaction was characterized by generalized urticaria and angioedema, palpebral-labial edema, nausea, abdominal pain, and diarrhea.

Because she had suffered three adverse reactions with urticaria and angioedema after the administration of ASA, oral ibuprofen, and nimesulide, the patient had begun taking Ananase as a NSAID, and she had subsequently been using it with no problem for two consecutive therapeutic cycles.

Furthermore, 4 months before the visit, she presented an adverse reaction with generalized urticaria, dyspnea, and glottis edema, after ingestion of raw celery. After this reaction, celery manipulation caused contact urticaria.

After giving informed consent, the patient underwent a full allergologic examination:

- 1) The skin prick test (SPT) was done with bromelain provided by Rottapharm (Monza, Italy), diluted in 0.9% NaCl at concentrations of 10, 100, and 1000 µg/ml. Histamine chloride (0.1%) and NaCl (0.9%) were used as positive and negative controls, respectively (1). SPT for bromelain was positive.
- 2) SPT was performed for celery, latex, pineapple, fig, kiwi, fennel, carrot, wheat flower, and rye, and for grass pollen, cypress pollen, *Parietaria officinalis*, Compositae mix, olive pollen, *Dermatophagoides farinae*, *D. pteronyssinus*, dog dander, and cat dander. SPT was positive for celery, Compositae mix, cypress pollen, and grass pollen.
- 3) Prick by prick tests were executed for celery, fennel, and carrot. They were positive for celery.
- 4) Total IgE in the patient's serum was measured by PRIST (CAP System FEIA), and the result was 473 kU/l.

5) RAST was done for bromelain and for all allergens tested with SPT except for Compositae, and also for papain. A positive reaction for RAST was defined as >0.35 kU/l. Positivity was found for bromelain (15.4 kU/l), papain (3.1 kU/l), celery (27.2 kU/l), fennel (0.9 kU/l), carrot (1.2 kU/l), cypress pollen (8.3 kU/l), and grass pollen (*Lolium perenne*) (3.7 kU/l).

6) A patch test with immediate and delayed reading was performed for bromelain and celery. The patch preparations (celery as is and bromelain 10% in petrolatum) were applied with Finn chambers on Scampor according to the IRDGC recommendations (2).

Immediate reading of the patch test was negative for bromelain and positive for celery while the delayed reading was negative. SPT for bromelain and the immediate and delayed patch tests for bromelain and celery were also done on a control group of 10 people with a negative history of adverse reactions to drugs and foods, and their results were negative.

7) Oral challenge test with erythrosine (E127) contained in Ananase was negative. In this case, the adverse reaction documented in the patient's history was confirmed by the positive SPT and RAST for bromelain, showing that oral administration of this drug containing bromelain induced an immune IgE-mediated reaction.

There are adverse reactions to bromelain reported in the literature, characterized mainly by allergic asthma after inhalation of the substance. Bromelain is a powerful sensitizing substance and sensitization usually follows its inhalation, and not its ingestion (3). The positive prick and/or RAST for celery, papain, carrot, fennel and cypress pollen, grass pollen, and Compositae may confirm cross-reactivity between bromelain and these foods or pollens (4–6), particularly between bromelain and papain (4); furthermore, it has been shown that celery-allergic and

cypress pollen-allergic patients present IgE directed against carbohydrate epitopes which seem to be shared by bromelain (5, 6). Therefore, the administration of drugs containing bromelain should be carefully evaluated in patients presenting allergic reactions to foods which may cross-react with such enzymes.

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Hypersensitivity to ASA

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Key words: acetylsalicylic acid; sodium benzoate; sodium salicylate.

● THE pathomechanism of immediate-type hypersensitivity reactions to acetylsalicylic acid (ASA) is not yet clear. Several findings suggest nonimmunologic (nonallergic hypersensitivity) mechanisms.

We treated a 39-year-old female kindergarten teacher who had suffered for 10 years from recurrent episodes of flush, rhinoconjunctivitis, facial edema, dyspnea, and loss of consciousness after intake of analgesics containing ASA. For the last 2 years, she had several times developed flush and rhinoconjunctivitis, and twice also loss of consciousness, after eating ready-

cooked meals. There was no history of atopic diseases, asthma, urticaria, or nasal polyps.

Skin prick tests with ASA, a panel of food preservatives, and coloring agents yielded immediate-type reactions to ASA (1 mol/l in ethanol), sodium benzoate (1 mol/l in aqueous solution), and sodium salicylate (1 mol/l in aqueous solution). Skin prick tests were done twice and gave identical results. Ten controls had no skin test reactions to these substances.

Specific IgE antibodies to ASA in the patient's serum were not demonstrable by a commercial kit (Hycor Biomedical, Kassel, Germany). Incubation of a preparation of the patient's peripheral blood leukocytes with three concentrations (1.0, 0.1, and 0.01 mmol/l) of ASA, sodium salicylate, or sodium benzoate did not induce release of histamine or leukotrienes (CAST-ELISA, DPC Biermann, Germany).

Single-blind oral-challenge tests were done with analgesics, preservatives, and coloring agents administered in gelatin capsules at least 90 min apart. There were clear-cut immediate-type reactions after ingestion of 50 mg acetylsalicylic acid (after 5 min, rhinoconjunctivitis, flush, and edema), 250 mg sodium benzoate (after 5 min, flush and nausea), and 500 mg

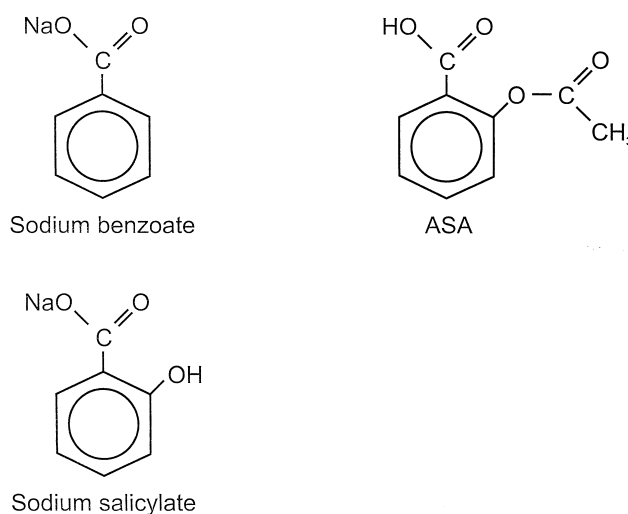


Figure 1. Chemical structure of ASA, sodium salicylate, and sodium benzoate.