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# Food-Dependent, Exercise-Induced Anaphylaxis : First Case Report in Thailand

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## Abstract

A forty-year-old military personnel presented with generalized urticaria, syncope, shortness of breath and headache associated with jogging after ingestion of a taro-filled bun and a red bean-filled bun. Skin prick test was positive for bread, taro and wheat but negative for red bean and preservative. Exercise challenge tests were performed. Exercise alone failed to induce any allergic reaction but exercise following ingestion of a taro-filled bun and a red bean-filled bun induced generalized urticaria. Since the patients stopped taking these types of food, the urticaria has not returned. This is the first case report of food-dependent, exercise-induced anaphylaxis in Thailand.

**Key word :** Exercise, Urticaria, Anaphylaxis, Food

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Exercise-induced anaphylaxis is a form of physical allergy characterized by pruritus, urticaria and erythema, progressing to upper respiratory obstruction or vascular collapse, occurring in association with physical exertion<sup>(1)</sup>. In 1979, Maulitz et al reported a case of urticaria, facial flushing and laryngeal edema after shellfish ingestion before long-dis-

tance running<sup>(2)</sup>. Neither exercise nor shellfish alone could reproduce the symptoms. Since then, many cases of food-dependent exercise-induced urticaria and anaphylaxis have been reported<sup>(1,3-5)</sup>. In this paper, a case of food-dependent exercise-induced anaphylaxis was described. To the best of our knowledge, this is the first case report in Thailand.

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## CASE REPORT

A 40-year-old Thai military personnel was referred to Phramongkutklo Hospital with a history of generalized urticaria, syncope and shortness of breath. He had a 20-year history of recurrent urticaria after long distance jogging, which was relieved with antihistamine. These exercise-induced urticarial episodes were repeated several times without any systemic symptoms.

One year prior to consultation, he developed generalized urticaria after ingestion of a sweetened taro-filled bun and a sweetened red bean-filled bun, one hour before jogging. The lesions occurred without any systemic symptoms. Since then, the urticaria occurred whenever he ate the buns before jogging.

Four months prior to consultation, he did a long distance jogging 15 minutes after taking a sweetened taro-filled bun and a sweetened red bean-filled bun. Thirty minutes later, he developed generalized urticaria, headache, shortness of breath and syncope. He was rushed to a hospital. His vital signs at the time of admission revealed blood pressure of 57/26 mmHg, with 100/min-pulse rate and normal body temperature. He was treated with intravenous fluid, chlorpheniramine and dexamethasone. His blood pressure rose to 130/90 in ninety minutes and the headache was resolved within 3 hours. He was discharged without any sequelae.

The patient had a history of lip edema and diarrhea after seafood ingestion. He had neither history of itching nor hives associated with the increase in core body temperature from fever or warm bath. No one in his family had urticaria or asthma.

Laboratory examination including complete blood count, urinalysis, serum electrolytes, liver function tests, blood urea, creatinine, chest X-ray and electrocardiogram were all normal. His complement level was within normal limits. His total serum IgE was 475 KU/L.

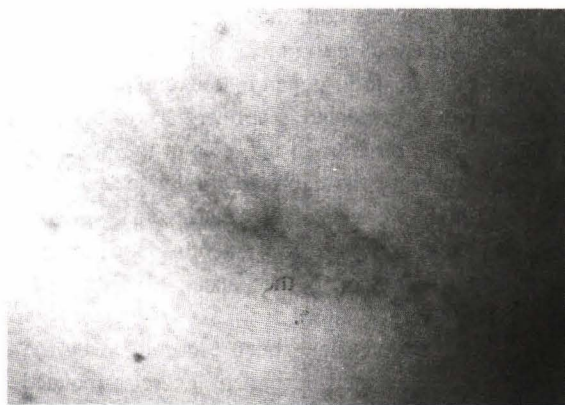
Skin prick tests with various commercial allergens revealed positive wheal and flare reactions to seafood, yeast and mosquito but negative reaction to whole wheat antigen (Greer Laboratories, Inc., Lenoir, NC 28645 US).

Allergen extracts from crude foods including bread, sweetened taro, sweetened red bean, wheat flour and calcium propionate powder (preservative used in the bun) were done by mixing 1 gram of each crude food with normal saline under agitation. The

supernatant of each solution was filtered with filter paper. The supernatants obtained were further diluted to 1 : 10, 1 : 20, 1 : 100 and 1 : 1000 with buffered albumin.

Skin prick tests with crude food extracts were then carried out. Normal saline and histamine were used as negative and positive control respectively. Food allergens eliciting wheals at least 3 mm in the longest diameter larger than those induced by the negative control were considered positive; all others were considered negative. The patient showed positive reactions to 1 : 10 concentrations of bread, sweetened taro and sweetened red bean. He showed positive reactions to 1 : 100 concentrations of bread and taro. He also had positive wheals and flares reaction to 1 : 10 and 1 : 20 concentrations of wheat flour extract. He had a negative reaction to calcium propionate.

To confirm the diagnosis of food-dependent exercise-induced anaphylaxis, an exercise challenge test was done. He was asked to run on a treadmill, using the Bruce protocol of exercise stress test. The test consisted of 2 parts. First, treadmill exercise alone was done. Dyspnea and sweating were noted at high workload (15 minutes after the exercise) without any skin lesion. In the second part, the test was repeated 30 minutes after the taro-filled bun ingestion. The patient experienced headache, erythema, pruritus, wheals and flares after 15 minutes into the exercise (Fig. 1). Considering the patient's



**Fig. 1.** Urticarial lesion found from exercise challenge test after taro-filled and red bean filled buns ingestion.

condition and the potential risk of developing anaphylaxis, the exercise challenge tests with bread, taro or red bean ingestion alone were abandoned.

The patient was advised to avoid taking bread and wheat-containing food. Exercise should be avoided until 3-4 hours after meal. Since then, he has never had any problem with his long distance jogging and remains free of urticaria.

## DISCUSSION

There are three major types of exercise-induced urticaria and anaphylaxis<sup>(6)</sup>; cholinergic urticaria, classical exercise-induced anaphylaxis and variant type of exercise-induced anaphylaxis. Cholinergic urticaria is characterized by generalized flushing and small punctate 2-4 mm wheals surrounded by red flare occurring in response to increased core body temperature<sup>(7)</sup>. Vascular collapse is not found in this type of urticaria<sup>(8)</sup>. Exercise-induced anaphylaxis starts with fatigue; generalized warmth, pruritus and erythema associated with exercise that progress to an urticarial eruption, angioedema and vascular collapse<sup>(6)</sup>. The urticarial lesion in this type of urticaria is larger (10-15 mm) than cholinergic urticaria. Variant type of exercise-induced anaphylaxis is characterized as punctate urticaria similar to cholinergic urticaria that is precipitated by exercise only and not by passive warming<sup>(9)</sup>.

Food-dependent exercise-induced anaphylaxis is a variant of exercise-induced urticaria and anaphylaxis. This type of urticaria was first reported in 1979 by Maulitz *et al*<sup>(2)</sup>. It is an immediate allergic reaction that requires both the ingestion of an allergenic food and exercise to induce anaphylaxis. In this paper, a case of food-dependent exercise-induced anaphylaxis was presented. Cholinergic urticaria was excluded by the absence of urticaria in the presence of sweating during the exercise challenge test. The urticarial lesions were also larger than typical punctate lesions of cholinergic urticaria. Exercise induced anaphylaxis was excluded by the absence of the skin lesion with exercise alone.

Many foods have been reported to be the causative agents in food-dependent, exercise-induced anaphylaxis including wheat, celery, shellfish, cabbage, peaches, grapes, chicken, hazelnuts, apples, shrimp and grains flowers<sup>(1,3-5)</sup>. Most reported that the episodes occurred within 2 to 3 hours after food ingestion. Even though specific causative food could

be identified in most cases, some cases developed urticaria when they exercised in a postprandial state independent of specific food<sup>(10)</sup>. These cases are called postprandial exercise-induced anaphylaxis. In addition to food, drug-dependent exercise-induced anaphylaxis has also been reported<sup>(11)</sup>.

The history of repeated urticarial episodes after a sweetened taro-filled bun and a sweetened red bean-filled bun intake before exercise strongly suggested that these foods were responsible for the patient's problem. The positive skin prick test for bread, sweetened taro and sweetened red bean together with the positive exercise challenge test after the buns ingestion confirmed this. The postprandial exercise-induced anaphylaxis was excluded by the history of urticarial episodes associated only with the sweetened taro-filled and the sweetened red bean-filled buns intake and the resolution of the problem on wheat-containing food avoidance.

Although the skin prick test using commercial wheat antigen was negative, the positive result to wheat flour extract and the disappearance of urticaria after avoiding wheat-containing food suggested wheat as the causative agent. Commercially prepared food extracts frequently lack the labile proteins responsible for IgE mediated sensitivity<sup>(12)</sup>. Negative skin prick test responses with commercially prepared extracts that contradict convincing histories of food-induced allergic reactions should be repeated with fresh food before concluding that food allergen-specific IgE is absent<sup>(13)</sup>. Although the skin prick tests using taro and red bean were also positive, these foods were unlikely to be the important causes because the patient's problem resolved after avoiding only the wheat-containing food.

Wheat is a frequent cause of food-dependent exercise-induced anaphylaxis<sup>(14)</sup>. Kushimoto and Aoki<sup>(15)</sup> found that peptides from pepsin-digested gluten caused a positive skin response in prick tests more effectively than non-digested gluten, while trypsin digestion of gluten abolished the ability of the allergen to induce a positive skin response. They also performed skin tests in patients with type I wheat hypersensitivity, using gel-filtrated fractions of pepsin-digested gliadin and glutenin and found wide molecular distribution of the allergens and variable individual reactivity. These findings support that wheat allergens in type I hypersensitivity are multiple. Palosuo *et al*<sup>(14)</sup> studied wheat allergen in 18 patients

with food-dependent exercise-induced anaphylaxis and found that the major allergen was a gamma-like gliadin.

The pathogenesis of food-dependent exercise-induced anaphylaxis remains unknown. The observations that skin response in these patients after exercise was increased only to compound 48/80 and not to histamine or the control suggest a direct effect on mast cell releasability and not to increased sensitivity to histamine(16). This implies that the interaction between the food antigen and IgE may lower the mast cell threshold to another stimulus such as exercise that enables the mast cell release to become clinically apparent. The reverse is also possible, that exercise in these patients lowers the threshold for mediator release as a result of specific IgE-allergens interaction on the cell surface.

The management of an acute attack of food-dependent exercise-induced anaphylaxis is similar to that for anaphylaxis of any cause. Airway maintenance, epinephrine, intravenous fluids, oxygen and antihistamine are essential. Endotracheal intubation and assisted ventilation may be needed(17). A detailed history must be obtained in order to find the precipitating factors.

Although terfenadine(18), disodium chromoglycate(19) and sodium bicarbonate(20) have been found to be effective in the prevention of the attack in a few cases, elimination of the causative foods or medications before exercise remains the most effective way of treatment(3,21). However, since the pathophysiology of postprandial exercise-induced anaphylaxis remains unknown, exercise should be avoided for 4-6 hours after food intake in all patients with exercise-induced anaphylaxis(3). Modification of an exercise program by reduction in intensity and duration of exertion may be required. The patients should be advised to stop exercise at the earliest symptoms of itching or cutaneous warmth. They should carry a self-injectable epinephrine kit and learn how to use it in case of emergency. Medical identification bracelets are also necessary.

Since more people participate in physical activity, food-dependent exercise-induced anaphylaxis has become increasingly common. Moreover, because this is a serious but preventable condition, dermatologists should be able to recognize and manage the disease appropriately.

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## Food-dependent, exercise-induced anaphylaxis : รายงานผู้ป่วยรายแรกของประเทศไทย

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ผู้ป่วยชายไทยอายุ 40 ปี อาชีพรับราชการทหาร มีลมพิษเกิดขึ้นทั่วตัวร่วมกับเป็นลมหน้ามืด หายใจไม่ออก หลังจากรับประทานขนมปังไส้เผือกและขนมปังไส้ถั่วแดงแล้ววิ่งออกกำลังกาย เมื่อทดสอบภูมิแพ้ด้วยการสะกิดผิวหนัง พบผลบวกต่อเนื้อขนมปังไส้เผือก แต่ให้ผลลบต่อไส้ถั่วแดงและสารกันบูด การทดสอบด้วยการวิ่งออกกำลังกายบนสายพานเพียงอย่างเดียวไม่เกิดปฏิกิริยา แต่มีลมพิษเกิดขึ้นเมื่อให้ทำการทดสอบซ้ำอีกครั้งหนึ่งหลังจากผู้ป่วยรับประทานขนมปังไส้เผือกและขนมปังไส้ถั่วแดง เมื่อแนะนำให้ผู้ป่วยหยุดรับประทานขนมปังไส้เผือกและถั่วแดงแล้วไม่มีลมพิษเกิดขึ้นอีก ผู้ป่วยรายนี้เป็น food-dependent, exercise-induced anaphylaxis รายแรกของประเทศไทย

**คำสำคัญ :** การออกกำลังกาย, ลมพิษ, อะนาฟัยแล็คซิส, อาหาร

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