Food-Dependent Exercise-Induced Anaphylaxis

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A 58-year-old farmer was admitted to our hospital because of repeated episodes of anaphylaxis. He had experienced 12 episodes of anaphylactic shock over the previous 17 years. These attacks included three episodes of bee sting. In general, the episodes occurred during farm work (exercise) and within two hours of eating cake in the afternoon. Because an immediate skin reaction to wheat flour was highly positive, a diagnosis of wheat allergy was considered. These findings suggested that his illness was consistent with food-dependent exercise-induced anaphylaxis. (Internal Medicine 31: 1052–1055, 1992)

Key words: physical allergy, food allergy

Introduction

Food-dependent exercise-induced anaphylaxis (FDEIA) is a distinct clinical entity, in which postprandial exercise induces an anaphylactic shock. Since Maulitz et al reported the first case in 1979, thirty-two cases have been reported (1–11). Here, we report a case with this disease and review the literature.

Case Report

A 58-year-old farmer was admitted to our hospital because of repeated episodes of anaphylaxis. He had been healthy until August 1973, when he had the first syncope attack. He had 12 episodes of anaphylactic shock over the last 17 years. The details of each episode are described below according to the information obtained from the patient, his wife and his family doctor.

1. He had cakes and milk at 3 p.m. in August 1973. He started to do farm work 30 minutes later. He had chest discomfort and stopped working, but lost consciousness very soon. His syncope lasted for 30–40 minutes and he recovered without treatment.
2. In September 1975, he had a bee sting (wasp) during farm work and lost consciousness. His family doctor visited him and gave him an injection of adrenalin. He soon recovered.
3. He had another (wasp) bee sting in 1977 and collapsed. The doctor again treated him and he recovered.
4. In September 1978, he had palpitation and similar chest

discomfort during farm work. At this time he did not lose consciousness and he recovered.

5. In April 1979, he climbed a hill by himself. He had chest discomfort, fell down to a valley and collapsed. After an unknown length of time he recovered and was able to go home without help.
6. He had cake and fruit juice at 3 p.m. in April 1980 and started working 40 minutes later. He had chest discomfort, vomited and lost consciousness. The doctor examined him and told his wife that his blood pressure was below 50. He was given an injection of adrenalin and recovered in 15 minutes.
7. In February 1983, he had a similar syncope attack during farm work 40 minutes after having cake and fruit juice. He was transferred to a hospital. A cardiologist performed electrocardiographic examination, exercise challenge test and cardiac catheterization. However, no definite diagnosis was made.
8. He fell into shock during farm work in July 1983. Related foods were not evident.
9. He had a syncope attack in the afternoon of March 1985, when he was doing farm work. Causative foods were not evident.
10. He had a third bee (yellow jacket) sting and collapsed in August 1986.
11. In October 1987, he had cake at 3 p.m. and started working 20 minutes later. He soon collapsed and was examined by the family doctor. He was given a subcutaneous injection of adrenalin and recovered.
12. When he was working one hour after lunch on

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December 21, 1990, he lost consciousness. He was treated by the doctor and transferred to our hospital at 5 o'clock in the afternoon.

He already recovered fully from the attack when he arrived. Physical examination on admission revealed no abnormal findings. He was a 58-year-old farmer with height and weight of 172 cm and 65.5 kg, respectively. He looked a little nervous but alert. The blood pressure was 122/78 mmHg, pulse was 72 and temperature was 36.5°C.

Routine blood tests were performed and the results (Table 1) were normal except for the presence of mild anemia. Urinalysis, electrocardiograph, X-ray film of the chest and pulmonary function tests were all normal. There was no family history of allergic disease.

Because a diagnosis of allergic disease was highly suspected, serum IgE, specific IgE and immediate skin reactions were tested (Table 2). Total IgE was 66 IU/ml. Although specific IgE to wheat flour was not detected by radioallergosorbent test (RAST), the patient showed a

positive immediate skin reaction to wheat flour. No positive results were obtained against other allergens. As a diagnosis of wheat allergy was considered, an informed consent was obtained and food challenge tests were carried out. However, no anaphylactic symptoms were induced (Table 2). The plasma level of histamine after food intake was not significantly higher than that before challenge (data not shown). Exercise challenge tests after food intake were not performed.

There were several common characteristics in his episodes. He had three bee stings and always had an anaphylactic attack, suggesting that he had bee venom allergy. His typical episodes occurred 4 times during farm work in the afternoon after eating cake. Although causative foods were not evident in other five attacks, a positive immediate skin test to wheat flour suggested the presence of wheat allergy. However, challenge tests with wheat-containing foods induced no anaphylactic symptoms. Furthermore, the patient did not necessarily have attacks when he had the wheat-containing foods. These facts suggested that his illness was not a simple wheat allergy but that other additional factors might be necessary to induce anaphylaxis. His episodes occurred mainly in the daytime when he was working. He never had attacks in the evening and at night. His attacks were closely related to postprandial farm work (exercise). These characteristics suggested that his illness was consistent with food-dependent exercise-induced anaphylaxis. His illness was distinguished from other physical allergies such as cholinergic urticaria in which symptoms are induced by a warm bath or shower and systemic manifestations were rare (12).

Discussion

Physical allergy is a group of disease in which physical stimuli such as low temperature, heat, exercise, sun light and mechanical pressure can cause allergic symptoms in patients (13). Exercise-induced asthma (EIA), exercise-induced anaphylaxis (EIAN) and cholinergic urticaria are categorized as exercise-induced allergy. Cases with EIAN whose symptoms are related to food intake are called food-dependent exercise-induced anaphylaxis (FDEIAN). Since the first case was reported by Maulitz et al in 1979, thirty-two cases have been reported (1–17). The characteristics of these patients are summarized in Table 3. Reported foods capable of inducing anaphylaxis were shellfish, shrimp, crab, squid, celery and wheat products. Attacks often occurred during exercise within two hours after food intake. Attacks consisted of allergic symptoms such as urticaria, air way obstruction and hypotension. Related exercise was running, tennis, baseball, volleyball, soccer and walking. It should be noted that not only strenuous exercise but light one caused anaphylaxis.

Patients with FDEIAN are divided into two groups. One is the group of patients whose symptoms are induced by specific foods. Specific IgE to food is detected by either

Table 1. Laboratory Data on Admission

White blood cells	6700/mm ³	ESR	18 mm/h
neutrophils	62%	CRP	0.4 mg/dl
lymphocytes	28%	Bilirubin	0.44 mg/dl
monocytes	7%	GOT	35 U/l
eosinophils	3%	GPT	11 U/l
Red blood cells	383 × 10 ⁴ /mm ³	ALP	89 U/l
Hemoglobin	10.9 g/dl	LDH	124 U/l
Hematocrit	32.1%	Total protein	6.8 g/dl
Platelets	30.2 × 10 ⁴ /mm ³	T3	0.89 ng/dl
BUN	16.3 mg/dl	T4	6.0 g/dl
Creatinine	0.8 mg/dl	TSH	0.81 IU/ml
Uric acid	5.6 mg/dl	ACTH	<4.0 pg/ml
Na	148 mmol/l	Cortisol	7.7 µg/dl
K	4.2 mmol/l		
Cl	110 mmol/l		
Glucose	83 mg/dl		

ESR: erythrocyte sedimentation rate.

Table 2. Allergic Examinations

Total IgE	66 IU/ml	Immediate skin tests	
RAST		Wheat	(+)
Wheat	<0.35 PRU/ml	Rice	(-)
Barley	<0.35 PRU/ml	Corn	(-)
Rye	<0.35 PRU/ml	Shrimp	(-)
Soybean	<0.35 PRU/ml	Crab	(-)
Corn	<0.35 PRU/ml	Meat	(-)
Shrimp	<0.35 PRU/ml	Milk	(-)
House dust	<0.35 PRU/ml	House dust	(-)
Candida	<0.35 PRU/ml	Candida	(-)
Bee venom		Cedar pollen	(-)
Yellow jacket	<0.35 PRU/ml	Pine pollen	(-)
Wasp	<0.35 PRU/ml	Food challenge tests	
Honey bee	<0.35 PRU/ml	Cake	(-)
		Shrimp	(-)
		Noodle	(-)

Table 3. Reported Cases of Food-Dependent Exercise-Induced Anaphylaxis

Reporter	Number of cases	Causative food	Time between eating and exercise	Exercise	Immediate skin reaction	RAST	Reference number
Maulitz 1979	1	Shellfish	5–24 hr	Running	+	–	1
Kidd 1983	1	Any	Within 2 hr	Running	–	–	2
	3	Celery	Within 2 hr	Tennis, basketball	+	–	
Novey 1983	1	—	1 hr	Running	NT	NT	3
Kushimoto 1985	3	Wheat	Within 0.5 hr	Running	+	+	4
Silverstein 1986	1	Celery	20–30 min	Aerobics	+	NT	5
McNeil 1988	1	Shrimp	3.5 hr	Tennis, volleyball	NT	NT	6
Miyake 1988	3	Shrimp, crab	Within 3 hr	Running	+	+	7
Miyake 1988	1	Squid	3 hr	Soccer, basketball	+	+	8
Akutsu 1989	3	Wheat	1–2 hr	Running, baseball	+	–	9
Dohi 1990	3	Shrimp, wheat	1–2 hr	Walking, baseball	+	–	10
Dohi 1991	7	Grape, crab, shrimp, squid, wheat		Running, pingpong, dancing, tennis, golf, walking	+	+	11
	4	—		Running, tennis, basketball	–	–	

NT: not tested.

immediate skin reaction or RAST in these patients (1, 2, 4–11). It is thought that these patients have food allergy to certain foods and symptoms are induced by exercise. Another is the group of patients who have no specific foods. Specific IgE is not detected in these patients (2, 3, 11). The present patient is thought to belong to the first group because specific IgE to wheat flour was detected by an immediate skin reaction.

Coexistence of bee venom allergy and FDEIAN is a characteristic of this patient. Although specific IgE against bee venom was not detected by RAST, he had an anaphylactic attack each time that he had a bee sting. It was reported that in 69 *Hymenoptera* hypersensitivity patients, 36 patients showed a negative RAST against yellow jacket and 45 patients showed a negative RAST to wasp (14). In spite of the fact that bee venom allergy patients do not necessarily have positive RAST, bee venom allergy is considered as a IgE mediated reaction. In this patient IgE mediated reactions might occur on both bee stings and food intake.

In EIAN, allergic symptoms are thought to be induced by chemical mediators such as histamine which is released from mast cells, because elevated levels of histamine in the plasma (15) and degranulating mast cells in the skin (16) are observed in patients during an attack. Challenge tests induce elevated levels of histamine in patients with FDEIAN (9–11), suggesting the presence of histamine mediated reactions as in EIAN.

As stated above, FDEIAN is a rare disease in which postprandial exercise cause anaphylaxis. However, several other factors such as fatigue, insufficient sleep, common cold, humid weather, low environment temperature and intake of aspirin are reported to aggravate anaphylaxis (10).

To prevent anaphylaxis, avoidance of both causative foods and exercise after meal is essential. Prophylactic use of anti-histamine, corticosteroid, β -stimulant and theophylline have been reported (10, 12), however, the definite effects of these drugs are not yet known.

References

- 1) Maulitz RM, Pratt DM, Schocket AL. Exercise-induced anaphylactic reaction to shellfish. *J Allergy Clin Immunol* **63**: 433, 1979.
- 2) Kidd JM, Cohen SH, Sosman AJ, Fink JN. Food-dependent exercise-induced anaphylaxis. *J Allergy Clin Immunol* **71**: 407, 1983.
- 3) Novey HS, Fairsher RD, Salness K, Simon RA, Curd GC. Postprandial exercise-induced anaphylaxis. *J Allergy Clin Immunol* **71**: 498, 1983.
- 4) Kushimoto H, Aoki T. Masked type I wheat allergy. Relation to exercise-induced anaphylaxis. *Arch Dermatol* **121**: 355, 1985.
- 5) Silverstein SR, Frommer DA, Dobozin B, Rosen P. Celery-dependent exercise-induced anaphylaxis. *J Emerg Med* **4**: 195, 1986.
- 6) McNeil D, Strauss RH. Exercise-induced anaphylaxis to food intake. *Ann Allergy* **61**: 440, 1988.
- 7) Miyake K, Kawamori J, Yoshida T. Food-dependent exercise-induced anaphylaxis in childhood. *Jpn J Pediatr* **92**: 1328, 1988 (in Japanese).
- 8) Miyake K, Kawamori J, Yoshida T. A pediatric case of food-dependent exercise-induced anaphylaxis. *Jpn J Allergol* **37**: 53, 1988 (in Japanese).
- 9) Akutsu I, Motojima S, Ikeda Y, Fukuda T, Ikemori R, Makino S. Three cases of food-dependent exercise-induced anaphylaxis. *Jpn J Allergol* **38**: 277, 1989 (in Japanese).
- 10) Dohi M, Suko M, Sugiyama H, et al. Three cases of food-dependent exercise-induced anaphylaxis in which aspirin intake exacerbated anaphylactic symptoms. *Jpn J Allergol* **39**: 1598, 1990 (in Japanese).
- 11) Dohi M, Suko M, Sugiyama M, et al. Food-dependent, exercise-induced anaphylaxis: A study on 11 Japanese cases. *J Allergy Clin Immunol* **87**: 34, 1991.
- 12) Sheffer AL, Austen KF. Exercise-induced anaphylaxis. *J Allergy*

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- Clin Immunol **73**: 699, 1984.
- 13) Miyamoto T. Physical Allergy. Medical Tribune, Tokyo, 1985, p.3 (in Japanese).
- 14) Shimizu T, Hori T. Evaluation of venom specific IgE and total serum IgE among forest administration workers. Jpn J Allergol **39**: 654, 1990 (in Japanese).
- 15) Sheffer AL, Sotor NA, McFadden ER, Austen KF. Exercise-induced anaphylaxis. A distinct form of physical allergy. J Allergy Clin Immunol **71**: 311, 1983.
- 16) Casale TB, Keahey TM, Kalinr M. Exercise-induced anaphylactic syndrome. JAMA **255**: 2049, 1986.
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