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Wheat Anaphylaxis in Children

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Food anaphylaxis is now the leading known cause of anaphylactic reactions treated in emergency departments, and wheat is one of the most common causes of anaphylaxis. Wheat is an important source of food worldwide. Wheat anaphylaxis is increasingly observed in our clinic. The purpose of this study was to describe the clinical features of wheat-induced anaphylaxis in 19 children for better elucidation of this disease. Children with severe reactions after ingestion of small amounts of wheat were referred to our clinic during a 4-year period. A detailed clinical history was recorded for each of the patients and a skin prick test was performed with wheat allergen extracts. The wheat-specific IgE and total IgE were measured. Grading of anaphylaxis episodes was performed according to a specific grading system. We identified 36 episodes of wheat anaphylaxis in 19 patients. All of the first attacks of wheat anaphylaxis occurred in the first-time ingestion. The most frequent manifestations of the reactions were skin and respiratory symptoms. In this study 78.9% of reactions were moderate and 21.1% of them were severe. All of our patients had positive skin prick tests to wheat. Mean total IgE level was 853.4 ± 455.27 IU/ml, and mean wheat-specific IgE was 70 ± 14.61 Ucs/ml. We conclude that wheat-induced anaphylaxis is a disease that is sufficiently severe, and, prevention of first wheat-induced anaphylaxis episodes is almost impossible. It would, however, probably be good practice to educate physicians to recognize the common clinical manifestations of this disease for early management.

Keywords Cereal, Wheat, Allergy, Anaphylaxis.

INTRODUCTION

Food allergy in childhood is common with a prevalence of between 6% to 8% (Wood, 2003) and six major foods—milk, egg, wheat, soy, peanut and fish—account for approximately 90% of food-allergic reactions in children (Ellman et al., 2002). Food allergy may manifest itself by local symptoms or systemic reactions as anaphylactic reactions. Anaphylaxis is the maximal variant of an

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acute allergic reaction involving several organ systems. In recent years, wheat has been increasingly recognized as a cause of food-dependent exercise-induced anaphylaxis (Romano et al., 2001).

Food induced anaphylaxis is a form of IgE-mediated hypersensitivity manifested by an abrupt onset of symptoms within minutes to hours of ingesting food. Food anaphylaxis is now the leading known cause of anaphylactic reactions treated in emergency department in the United States (Sampson, 2003). Anaphylaxis occurs in a remarkable number of patients who have wheat allergy (Pourpak et al., 2004). Wheat is the most widely cultivated cereal and an important source of food worldwide and wheat flour or wheat products are widely used in Iran.

Even if wheat-induced anaphylaxis is considered a life-threatening event, there is a lack of information on its prevalence and characteristics in our country, particularly in children. Because food anaphylaxis occurs commonly on the first known exposure and failure of prompt recognition and treatment of anaphylaxis can result in death it is important to elucidate this process in children better (Dibs and Baker, 1997).

It is imperative that all health care workers be familiar with the signs and symptoms of anaphylactic events and the need for rapid diagnosis and treatment. Any delay in recognizing the initial signs and symptoms of anaphylaxis can result in death (Pumphrey, 2004). So, the purpose of this study was to describe the clinical features and severity grading of 36 episodes of wheat-induced anaphylaxis in 19 children to help us for early diagnosis and treatment of this illness.

METHOD AND MATERIALS

Patients referred to the allergy and immunology clinic of the Children's Medical Center, in Tehran, Iran, between 2001 and 2004 with a previous diagnosis of wheat anaphylaxis were considered in this study. A detailed clinical history regarding the episodes experienced was recorded for each of the patients. A questionnaire was filled out to provide complete information, including demographic data, both personal and family history of allergy, the time of the introduction of solid foods, the allergic symptoms, treatment and allergologic evaluation of each child.

Definition of Anaphylaxis

To classify an event as anaphylaxis we required one symptom of a generalized mediator release such as erythema, maculopapular rash, flushing, urticaria, pruritus, angioedema, conjunctivitis, or chemosis in addition to at least one of the following additional organ systems involvement that are associated with hypoxia and/or hypotension (Yocum et al., 1999):

1. *Gastrointestinal symptoms:* Dysphagia, Nausea, Vomiting, Diarrhea, Abdominal pain.

2. *Respiratory symptoms:* Angioedema of the lips or tongue, Coryzal symptoms, Tachypnea, Cough, Stridor, Cyanosis, Hoarseness, Wheeze, Dyspnea, Laryngeal edema, Inability to swallow, Difficulty speaking or handling oral secretion, Accessory muscle use.
3. *Cardiovascular symptoms:* Tachycardia, Bradycardia, Hypotension, Shock, Chest pain, Asystole, Palpitation, Myocardial ischemia/infarction.
4. *Neurologic symptoms:* Headache, Anxiety, Seizure, Lethargy, Disorientation, Dizziness, Loss of consciousness, Syncope, Incontinence.

Skin features may be transient, subtle and therefore easily missed, in which case anaphylaxis may still be diagnosed if there is an otherwise typical presentation, especially where this follows exposure to a known precipitant (Brown, 2004).

Grading System for Generalized Hypersensitivity Reactions

1. *Mild:* Only skin and subcutaneous tissue involvement (erythema, angioedema, maculopapular rash, flushing, urticaria, pruritus, conjunctivitis or chemosis).
2. *Moderate:* Features suggesting respiratory, cardiovascular, gastrointestinal or nervous system involvement (dysphagia, angioedema of the lips or tongue, nausea, vomiting, diarrhea, abdominal pain, coryzal symptoms, tachypnea, accessory muscle use, cough, stridor, hoarseness, wheeze, dyspnea, laryngeal edema, inability to swallow, difficulty speaking or handling oral secretion, headache, anxiety, seizure, lethargy, disorientation, dizziness, tachycardia, bradycardia, hypotension, palpitation).
3. *Severe:* Cyanosis or $\text{PsO}_2 < 92\%$, hypotension (according to age of children), confusion, collapse, loss of consciousness, incontinence.

We regarded a simple scoring system that is immediately useful with regard to acute therapy without need for long reflection. The features listed in the moderate and severe grades support a definition of anaphylaxis as these are associated with hypoxia and/or hypotension. Reactions limited to skin defined are as "acute allergic reactions" but not anaphylaxis (Brown, 2004).

A programmed allergy study was set up for all of the patients. This study included eosinophil count, skin prick tests (SPT), serum total IgE and wheat-specific IgE measurement. An eosinophil count of more than 450 cells/ μl was considered as eosinophilia (Lim and Weller, 1998). In all subjects, stool samples were examined for ova and parasites to rule out the parasitic infection. Skin tests were performed with glycerinated wheat flour and wheat bran extracts on the volar side of the forearm with a lancet. A positive control

(histamine dihydrochloride 1 mg/ml) and a negative control (normal saline) were also included in this test.

The SPT responses were read for histamine at 10 min and for allergens at 20 min and were considered positive for histamine if the diameter of the wheal was at least 5 mm and for allergens at least 3 mm larger than the reaction to the negative control. The extracts were obtained from Dome Holister Stier (Miles, Canada).

The wheat-specific IgE and the total IgE were measured using the enzyme-linked immunosorbent assay (ELISA) method (Ownby, 1991). (Clone-systems, Hamburg, Germany). Total serum IgE levels were compared to the normal value for age (Sly, 2000). According to the Kit manual, the results of wheat-specific IgE were categorized in seven groups. (0–6+). The results equal to 1+ or more were considered positive.

RESULTS

We identified 36 episodes of nonfatal anaphylaxis in 19 patients. Twelve patients each had more than one reaction to wheat. Fourteen patients were male, and five were female. Patients' ages in the first attack ranged from 3 to 9 (Median 5.8 ± 1.5) months. All of patients had experienced the anaphylaxis within the first year of life. And, 7(36.8%) had past histories of atopic disease, and 13(68.4%) had positive familial history of atopic disease (include: rhinitis, asthma and eczema) (Table 1).

Table 1: Characteristics of patients with wheat anaphylaxis.

Characteristic	n (%)
Age at first attack (month)	
3–6	13(68.4)
6.1–9	6(31.6)
Sex	
M	14(73.6)
F	5(26.3)
Positive prior history of atopic disease	7(36.8)
Positive prior familial history of atopic disease	13(68.4)
Time between wheat ingestion and beginning of symptoms*	
0–15	10(52.6)
16–30	7(36.8)
31–45	2(10.5)
Number of reactions	
One episode	7(36.8)
Two episodes	8(42.1)
Three episodes	3(15.8)
Four episodes	1(5.3)
Wheat specific IgE	
+1,+2	1(5.3)
+3,+4	7(50)
+5,+6	6(31.6)

*We regarded the first attack in each patient in this item.

All of episodes occurred outside of the hospital on the first exposure to wheat-containing foods. Types of wheat-containing foods causing anaphylaxis were cakes, bread, biscuit and spaghetti. Amount of wheat-inducing symptoms ranged from a bite of cake to a little amount of spaghetti. Most symptoms occurred within 30 minutes after the ingestion and in 6 episodes the time between wheat ingestion and beginning of symptoms was less than 5 minutes. In this study 78.9% of reactions were moderate and 21.1% were severe.

The most frequent initial manifestations of the reactions were cutaneous manifestations (urticaria, erythema, periorbital edema), and during the entire course of their illness, all of patients had respiratory and dermatologic symptoms, and 8(42.1%) had gastrointestinal symptoms. Cardiovascular and neurologic manifestations were the least common presentations (Table 2; (Figure 1). We encountered no fatalities attributable to anaphylaxis. None of these patients had second-phase response.

Mean total IgE level was 853.4 ± 455.27 IU/ml. All of the patients had high total serum IgE for their age (Gower, 2005; Kardar et al., 2006; Sly, 2000). All of our patients had positive skin prick test with wheat flour and wheat bran and

Table 2: Symptoms and signs of patients after ingestion of wheat containing foods.

Symptom or sign	Patients n (%)
Mucocutaneous	19(100)
Erythema	12(63.7)
Maculopapular rash	3(15.8)
Flushing	4(21.1)
Urticaria	15(78.9)
Pruritus	16(84.2)
Angioedema	10(52.6)
Conjunctivitis	7(36.8)
Periorbital edema	8(42.1)
Respiratory	19(100)
Oral mucosa swelling	1(5.3)
Dyspnea	18(94.7)
Tachypnea	11(57.9)
Cough	7(36.8)
Cyanosis	3(15.8)
Wheeze	10(52.6)
Gastrointestinal	8(42.1)
Nausea	8(42.1)
Vomiting	8(42.1)
Abdominal pain	4(21)
Difficulty handling of oral secretion	1(5.3)
Neurovascular	7(36.8)
Irritability	6(31.6)
Lethargy	6(31.6)
Loss of consciousness	1(5.3)
Cardiovascular	2(10.5)
Hypotension	2(10.5)
Tachycardia	2(10.5)
Palpitation	1(5.3)

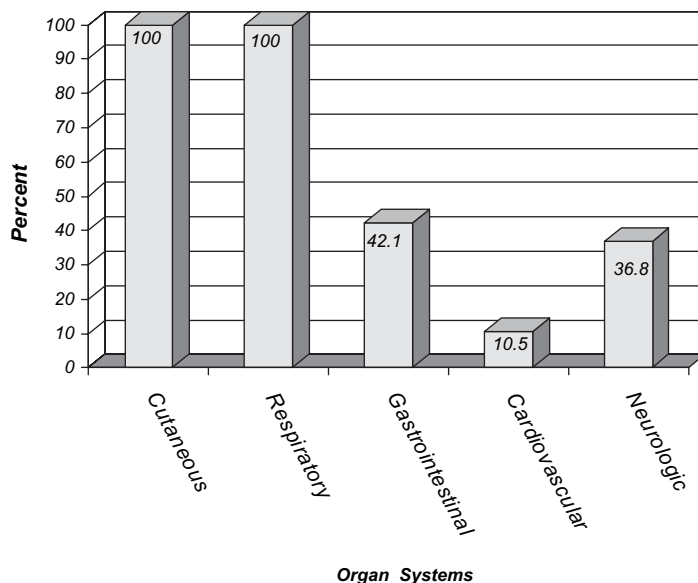


Figure 1: Percent of different organs involvement in patients with wheat anaphylaxis.

positive wheat-specific IgE and mean wheat-specific IgE was 70 ± 14.61 Ucs/ml. Eosinophilia (eosinophil $> 450/\mu\text{l}$) was detected in 6(33.3%) patients.

The medical treatment of patients in our series varied. All of our patients were admitted to the emergency room, and 12 children had more than one admission for wheat anaphylaxis. None of the patients with known past anaphylaxis had epinephrine self-administration devices available.

DISCUSSION

The types of foods triggering anaphylaxis varies between communities. And, six major foods that produce anaphylaxis in children are milk, egg, wheat, soy, peanuts and fish. Wheat is the most widely cultivated cereal that is widely used in Iran. There is limited knowledge about the exact incidence of wheat-induced anaphylaxis in the general population and in different age groups. But wheat anaphylaxis is increasingly observed in our clinic, probably for being a referral center in country.

According to some studies, sensitization to wheat may occur through maternal milk during exclusive breastfeeding (Palosuo, 2003). But in our study, in 13 patients, the first attack of anaphylaxis occurred at 4–6 months of age, which was simultaneous with introduction of wheat into the diet. In 6 patients the first attack of anaphylaxis occurred after the 6th month of age. Because wheat is introduced to the diet of these children around the age of 5 months, it seems that wheat allergens do not pass into the breast milk, and early introduction of solid foods may help to early

sensitization (Pourpak et al., 2004). There is also the possibility that the patients are sensitized in other ways, upon which further studies should be performed.

In our study, it was seen that all of the first episodes of wheat anaphylaxis occurred on the first exposure to wheat-containing foods, but patients with history of prior wheat anaphylaxis had no epinephrine self-administration devices available for use, although most reactions were sufficiently severe to warrant emergency room management. Also, 12 patients each had more than one reaction to wheat. It shows that patient education about wheat anaphylaxis has not been sufficient. Thus, patient education about avoidance and management of accidental ingestion of foods known to produce anaphylaxis is crucial. Perhaps these patients could use rice and corn as suitable substitutes for wheat (Pourpak et al., 2005).

Food-dependent, exercise-induced anaphylaxis is a severe form of allergy that occurs only when the patient exercises within 2–4 hours of ingesting a food, but in the absence of exercise, the patient can ingest the food without any apparent reaction (Kidd et al., 1983). Although various foods (tomato, peanuts, soybean, and seafood) have been associated with food-dependent, exercise-induced anaphylaxis, the most frequently reported cause of these reactions seems to be wheat (Gall et al., 2000). However, in our study there was not an obvious relationship between anaphylaxis and exercise. The possible reason of this event could be the age of our patients, which has been under 1 year old, experiencing the first attack of anaphylaxis.

We conclude that wheat-induced anaphylaxis is a disease that is sufficiently severe and the initial symptoms are generally dermatologic or respiratory. Most affected children have no stated histories of prior reaction to wheat; hence, prevention of the first wheat-induced anaphylaxis episode is almost impossible. In addition, because a high rate of mistreatment and misunderstanding regarding anaphylaxis has been noted in an emergency room setting (Clark et al., 2004). It would probably be good practice to educate the physicians to recognize the common presenting clinical manifestations of this disease for early management.

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