

Involvement of Hidden Allergens in Food Allergic Reactions

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■ Abstract

Background: Hidden allergens in foods can induce allergic reactions. Currently it is not possible to estimate the exact prevalence of these reactions but they are clearly a growing problem.

Objective: The purpose of this study was to provide an overview of the role of hidden allergens (their importance, the types of food involved, and the severity of reactions) in allergic reactions in our geographical area.

Methods: A retrospective study was carried out in an adult population. Over a five year period, a total of 530 food reactions were reviewed.

Results: One hundred nineteen reactions (22.4%) were considered to be due to hidden allergens. Thirty-two percent of these were anaphylactic reactions. The most common hidden allergen was the *Anisakis simplex* larvae present in fish and shellfish. Fish allergens hidden in other foods caused reactions in 35% of fish-allergic patients. Twenty-two per cent of allergic reactions caused by eggs were due to egg allergens hidden in foods. All but one of the reactions caused by hidden legume allergens occurred in soy-allergic patients. Reactions caused by hidden fruits and hidden nuts were very uncommon.

Conclusion: Hidden allergens were the cause of a quarter of all food allergic reactions, mainly as a result of contamination and carelessness on the part of the patient. *A simplex* was the hidden allergen most frequently involved. Fruits and nuts were not frequent hidden allergens in our area. Reactions due to other uncommon foods such as soy, mustard, flavourings, and honey were multiple and usually went unnoticed. Only if the sources of hidden allergens are determined will it be possible to avoid such substances and thus guarantee the safety of the allergic patient.

Key words: Food allergy. Hidden allergens. Anaphylaxis. Foods. *Anisakis simplex*. Fruits. Nuts. Fish. Shellfish. Soy.

■ Resumen

Antecedentes: Alérgenos ocultos en alimentos pueden causar reacciones alérgicas. Actualmente es imposible conocer la prevalencia exacta de estas reacciones, pero es un problema creciente.

Objetivos: El propósito de esta revisión es analizar el papel de los alérgenos ocultos (importancia, tipo de alimentos implicados, gravedad de las reacciones, etc.) como causa de reacciones alérgicas en nuestro área.

Métodos: Se realizó un estudio retrospectivo en población adulta. Se revisaron 536 reacciones alimentarias recogidas en un periodo de 5 años.

Resultados: Se consideraron debidas a alérgenos ocultos 119 reacciones (22.4%), 32 % de ellas fueron reacciones anafilácticas. El alérgeno oculto más frecuentemente implicado fue la larva de *Anisakis simplex* presente en pescados y mariscos. Alérgenos de pescado ocultos en otros alimentos indujeron frecuentes reacciones en alérgicos a pescado. Un 25% de las reacciones alérgicas causadas por huevo fueron debidas a alérgenos de huevo ocultos en alimentos. Todas, excepto una de las reacciones debidas a alérgenos ocultos de legumbres ocurrieron en pacientes alérgicos a soja. Fueron muy poco frecuentes las reacciones por alérgenos ocultos de frutas y frutos secos.

Conclusiones: Los alérgenos ocultos producen la cuarta parte de las reacciones alérgicas a alimentos, sobre todo debido a contaminación o descuidos del paciente. El *Anisakis simplex* es el alérgeno oculto más frecuente. En nuestro área, las frutas y frutos secos no son alérgenos ocultos frecuentes. A menudo, las reacciones debidas a otros alimentos poco frecuentes como soja, mostaza, condimentos, miel, son múltiples e inesperadas.

Palabras Clave: Alergia a alimentos. Alérgenos ocultos. Anafilaxia. Alimentos. *Anisakis simple*. Frutas. Frutos secos. Pescado. Marisco. Soja.

Introduction

Hidden allergens in foods represent a major health problem for sensitized persons. A substance is a hidden allergen when it is unrecognised or not declared on the product label. This omission is not always intentional; and there are many ways for allergens to be hidden in food, for example through misleading labels, allergenic foods that can contaminate other safe foods, carelessness, food that is listed by an uncommon term, and ingredient switching, among others.

Hidden allergens can induce a wide variety of hypersensitivity reactions. Currently it is not possible to determine the exact prevalence of these reactions but they are clearly a rising problem.

The purpose of this study was to provide an overview of the role of hidden allergens as a cause of allergic reactions in our area. Food allergic reactions probably due to hidden allergens were investigated with the aim of estimating their importance, the foods most frequently involved, and the severity of the reactions.

Patients and Methods

A retrospective study was performed in an Allergy Unit which covers the adult population (individuals over 14 years of age) from a Public Health Area with 400 000 inhabitants. Over a five year period, 11 000 patients were examined and 436 patients (3.9%) were diagnosed with food allergy. In these patients, a total of 530 food reactions were reviewed.

Diagnosis of food allergy was made following the recommendations of the European Academy of Allergology and Clinical Immunology Nomenclature Task Force [1]. Thus, reactions were characterized by sudden allergic symptoms (urticaria and/or angioedema, oral allergy syndrome or anaphylaxis) on ingestion and were confirmed by positive skin tests and/or the presence of serum specific immunoglobulin (Ig) E to the food involved.

Skin tests were carried out using the prick test with common aeroallergens and the suspected foods based on individual clinical histories. Some foods were also tested by the prick test with fresh foods (for example fruits, spices, and processed foods). A skin test was considered positive when the size of the papule was 3mm larger than the negative control.

Serum specific IgE was determined using the CAP system (Pharmacia, Uppsala, Sweden) following the manufacturer's instructions.

If there was no anaphylaxis, an open oral challenge test was carried out when any discordance between clinical history and diagnostic tests was found.

A food reaction was considered as being caused by a hidden allergen when we highly suspected or demonstrated the involvement of foods, flavourings or additives that were not specified on the ingredients label by mistake or omission, or when ingestion went unnoticed due to personal carelessness, misunderstanding, misinformation, or contamination. All patients in whom the cause of the reactions remained unknown were excluded from the study.

Results

Of the 530 food allergic reactions analyzed, 119 (22.4%) were considered to be due to hidden allergens (Table 1). Both sexes were affected to the same degree. The mean age of the patients was 33.4 ± 15.4 years. Thirty percent of these patients were asthmatics and 53% also had sensitivity to inhalants, notably to pollens (40%). In 52% of cases, patients were known to have food allergy prior to the reaction to the hidden allergen and 18% of the patients had previously suffered an anaphylactic reaction due to food.

The reactions due to hidden allergens were frequently multiple. The mean number of food reactions was 1.98 per patient (range 1-10). Severity of the reactions was variable. Thirty-eight anaphylactic reactions (32%) were recorded (Table 2). No fatal reactions were reported.

The distribution by groups of the foods involved is shown in Table 1 and Table 2. Of all the hidden food allergic reactions reviewed, 45.3% were induced by fish and shellfish due to the presence of *Anisakis simplex* larvae.

Table 1. Total Allergic Food Reactions and Food Reactions Due to Hidden Allergens. Distribution by Groups of Foods Involved.

Food	No. of Allergic Reactions	No. of Hidden Foods Reactions (%)	Causes of Hidden Food Reactions (%)
Fruits	176	5 (2.8)	4.2
Nuts	131	11 (8.4)	9.2
<i>Anisakis Simplex</i>	54	54 (100)	45.3
Shellfish	50	8 (16)	6.7
Fish	31	11 (35.5)	9.2
Legumes	31	13 (42)	10.9
Egg	22	5 (22.7)	4.2
Others	35	12 (34.2)	10
Total	530	119 (22.4)	

Table 2. Anaphylactic Reactions Due to Hidden Food Allergens.

Hidden Food	No. of Cases of Anaphylaxis (%)
<i>Anisakis Simplex</i>	22 (58%)
Nuts	5 (13%)
Fish	3 (7.9%)
Fruits	2 (5.2%)
Shellfish	2 (5.2%)
Legumes (Soy)	2 (5.2%)
Egg	0
Others	2 (5.2%)
Total	38

These patients frequently suffered numerous and serious reactions (anaphylaxis in 41% of cases). The mean age at onset of symptoms was 46 ± 13.8 years. These reactions were associated with high levels of total serum IgE and serum specific IgE to *A simplex* (52.2 ± 35 kU/L). The fish most frequently involved were contaminated anchovy (60%), whiting (31%) and shellfish (22%).

Allergic reactions caused by fish allergens hidden in other foods were quite frequent in fish allergic patients (35.5%). Patients had usually suffered these reactions with a high or anaphylactic fish sensitivity since childhood. These reactions were severe and usually took place during meals or stays away from home. For example, a fish allergic patient suffered an anaphylactic reaction after the ingestion of a canapé containing salmon cream in a party; two patients had symptoms caused by inhalation of fish cooking vapors in a restaurant, another two through contact with a napkin and a fork contaminated with fish, another after the ingestion of a pâté with hidden fish and, another two through the consumption of other safe foods which had been fried in cooking oil previously used to fry fish.

Eight (16%) of all the allergic reactions to shellfish were due to hidden allergens. Seven occurred at restaurants caused by the use of grills and oil previously employed for cooking shellfish. Only one of the hidden shellfish reactions was caused by contact with a contaminated napkin.

Egg allergy is uncommon among adults. It represented only 4.1% of our food allergic reactions. Twenty-three per cent of allergic reactions caused by eggs were due to egg allergens hidden in foods. The sources were hidden egg proteins in ice creams and pastries ingested by mistake.

Legumes caused 5.8% of food allergic reactions in our patients. All the reactions caused by hidden allergens of legumes occurred in soy-allergic patients but one lentil-allergic patient suffered urticaria after contact with a contaminated napkin. Thirty-nine percent of the soy-allergic patients had some reaction caused by soy as a hidden allergen. The most frequent sources of hidden soy allergens were boiled ham, sausages, cheese puffs, precooked dishes, desserts and gravy.

Although fruit was the most frequent cause of food allergy in our study (33%), reactions by hidden fruits were very uncommon (2.8%). Two of these reactions were due to kiwi, one was caused by melon, another by peach and the last by apple, hidden in ice-creams or by indirect contact through kisses or utensils. All the patients affected had previous anaphylactic sensitivity to these fruits. Nuts were the second cause (25%) of allergic reactions, acting as hidden allergens in 11 cases (8.4%). The most frequent sources of hidden nuts were chocolates, cookies, pastries and cakes. Peanut was the nut most frequently involved (8 cases).

The other 12 reactions recorded were due to foods consumed in very small amounts (flavourings, honey, cinnamon, lupin, grasspea) that usually act as hidden allergens, thus making diagnosis difficult. The flavourings involved were mustard, present in gravy at restaurants, mayonnaise (3 cases) and paprika present in sausages (5 cases). We must also highlight the case of a patient diagnosed with anaphylaxis due to honey that suffered two episodes

of urticaria after the ingestion of white coffee probably due to contamination by incomplete cleaning of the containers previously used for serving infusions containing honey.

Of all the food allergic reactions, 65 (12%) were anaphylaxis; and 38 (58.5%) were due to hidden allergens. That is to say, 32 % of the food reactions caused by hidden allergens were anaphylaxis. Among the causes of anaphylaxis induced by hidden food allergens (Table 2), the most frequent were *A simplex* (58%), nuts (13%) and fish (7.9%). Nearly 41% of the reactions caused by *A simplex* were anaphylactic reactions, accounting for 34% of all the anaphylactic reactions due to foods. Uncooked anchovy was the food most frequently responsible for these reactions.

Discussion

Changes in eating habits, coupled with progress in the food industry, new technologies and globalization, have contributed to making the variety of food available increasingly large. Allergic patients are a growing minority who are becoming more and more exposed to allergenic resources that are not always adequately pointed out.

There are many ways for allergens to be hidden in foods. Probably the most common cause is unintentional contamination in the manufacture, handling or cooking process, when common equipment or the same cooking oil are used for different foods. Other causes are trace foods that do not exceed 25% (5% in the current legislation) of product final weight and which do not legally need to appear on the label. Meals at restaurants and public places where food ingredients are not specified; labels which are incomprehensible due to the use of technical or uncommon terms, code numbers, or foreign languages, labels which are misleading (because they are absent, ambiguous, inaccurate, in bad condition, poorly placed and designed), unnoticed changes in the food composition; chemical or genetic manipulation of food and carelessness of the patient are all the cause of further problems.

One of the first references to hidden allergens in food allergy was reported by Balyeat [2] who described asthma symptoms in two peanut-allergic children after they had drunk milk from a cow fed on peanut plants. A large variety of food reactions caused by hidden allergens has subsequently been reported in the literature. Most are anecdotal and trivial but others can result in patient death. Risk factors for serious or fatal food reactions include young age, multi-sensitivity, presence of uncontrolled asthma, previous serious food reactions, epinephrine not immediately available, eating out of the home and the presence of hidden allergens in the food [3-6]. Bock et al [5] reported 32 serious food reactions, all caused by hidden food allergens, of which peanuts were the most frequent cause. In the Food Allergy and Anaphylaxis Network study on food-induced reactions, Sicherer et al [7] reported 27% to be serious reactions, half of which were caused by hidden allergens, especially by contamination, with peanuts again being the most frequent cause (67%).

Usually the foods which are consumed most are those most frequently involved in allergic food reactions and contain the hidden allergens most commonly reported in all the published

series. Hidden egg proteins have been reported in candies [8,9], wines [10], pastry [11] or drugs [12]; hidden milk proteins may be in jam, boiled ham, sausage, cereals, biscuits, candies, canned tuna fish, ices, "pareve" foods, chocolate, hydrolysed cow milk proteins, coffee, wines, vegetarian soy cheese, glove powder and drugs [13-15]. Hidden soy proteins have been reported in boiled ham, sausage, and other similar products [16,17]. Hidden peanut proteins have been found in many processed foods (corn crisps, wafers, cereal bars, halva, curry sauces for pizzas, ice-creams, pastry, and sauces in oriental restaurants [18-23]. Other nuts such as hazelnuts are less frequent [29,30]. Because of its intense taste, the presence of fish protein in foods rarely goes unnoticed. However, there have been reports of fish-allergic patients, who suffered reactions after the ingestion of eggs and meat from poultry fed on fish flour [24].

Over the last decade there has been a great increase in allergic reactions induced by parasites hidden in foods. *A simplex* is the main agent involved in these reactions. This is an helminth capable of infecting shellfish, molluscs and fish. It has been one of the most frequent causes of anaphylaxis in our country in recent years [25], and is probably the leading cause of anaphylaxis in the adult population. Other surprising cases include food reactions induced by parasites due to allergic reactions after the ingestion of jam, pastries, batter and flour contaminated with different mites which acted as hidden allergens [26].

Few cases are caused by foods recently introduced into the diet; such as sesame that may be involved in reactions after the ingestion of cereals, burgers, oriental sauces and pasta, ice creams, biscuits, appetizers, margarine, vegetarian or exotic foods. Although sesame is traditional in oriental food, it is hardly used in European foods and frequently goes unnoticed. As a consequence, most patients allergic to this food suffered several reactions before the exact diagnosis was established or were misdiagnosed as "idiopathic anaphylaxis" [27].

Other hidden allergens reported are flavourings (ginger, paprika, oregano and especially garlic and mustard) which sometimes can result in serious reactions. Mustard has been found in sauces and pizza [28].

There are potentially a large number of other unnoticed allergens in food. For example, latex proteins have been detected in foods that had been handled with latex gloves or in drug pushers who ingested latex packages containing drugs [31,32]. Poppy seed can be used as decoration in ice creams or pastries [33]. Generally we can accept that any food allergen may be a potential hidden allergen.

The present study shows that reactions caused by hidden food allergens are frequent. In our series, hidden allergens accounted for almost a quarter (21%) of all food allergic reactions, affecting both sexes equally. Reactions were more frequently the result of contamination or carelessness on the part of the patient than incorrect labeling. Although fruits and nuts are the most frequent cause of food allergy, they do not represent a major problem as hidden allergen sources in this adult population. Only patients with high sensitivity to fruits suffered reactions from unnoticed sources, usually from utensil contamination.

Peanut consumption in Spain is lower than in other countries. Peanuts are usually consumed as nuts whereas

the use of by-products like oil, butter or flour is rare. This difference in cooking traditions could probably explain the lower probability of finding peanut as a hidden allergen and the lower frequency of peanut allergy when compared with other reported series in countries where peanuts represent the first cause of reactions from hidden allergens.

In our series, the most frequent cause of allergic reactions from a hidden allergen is *A simplex* that infects fish or shellfish. This might be due to the habit of eating fresh raw anchovy marinated in vinegar. This is an increasing problem that frequently causes serious reactions. Because of this, we believe that it is necessary to carry out educational campaigns informing people of the dangers and promoting the consumption of previously frozen fish and shellfish.

Another relatively frequent hidden allergen is soy. Due to its almost unlimited use, soy is a particularly insidious hidden allergen. The use of soy has spread in such a way that today it is almost impossible to make up a diet without soy. As a result, soy-allergic patients frequently have multiple allergic reactions.

Reactions due to other uncommon foods like mustard, flavourings, and honey, are also multiple and usually go unnoticed because they are difficult to identify and diagnose.

Only patients with a high sensitivity to fish and shellfish suffer reactions after unnoticed contact with these foods. The intense and special taste of these foods means that they rarely go unnoticed. Reactions occur by ingestion of small quantities of allergens due to container or grill contamination, contaminated oil use or by the unexpected inhalation of cooking vapors.

Due to the difficulty in diagnosing these reactions (where the final decision is based more often than not on clinical suspicion), undiagnosed cases are a real possibility, so the incidence could be still higher than we found.

Food allergy, which can sometimes be fatal, clearly limits the quality of life of patients and their families. Allergists, patients, public administrations and food manufacturers must work towards protecting allergic consumers. Allergists must insist on the importance and necessity of a strict elimination diet, giving the allergic patient the list of high-risk foods with all the information (possible pseudonyms, specific codes, and so on) to make identification easier and we must be alert to newly recognised hidden food allergens. Patients must read in detail the ingredients, not change utensils, clean tables, containers and surfaces thoroughly, carry to extremes hygiene in the handling of food, and avoid the inhalation of vapors of high-risk foods. Patients must be familiar with and also carry emergency treatment. Staff at restaurants and eating-places must be instructed about the measures to avoid cross contamination in the handling, cooking and serving of foods. The public authorities have to guarantee the safety of foods for consumers. Fraud must be pursued and allergen controls must be included in food hygiene controls. As for imports and exports of both food ingredients and packaged foods, steps toward uniform regulations will aid consumers and the food industry alike. Only if we know the hidden allergen sources can we avoid them and guarantee the safety of the allergic patient.

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