

Peculiarities of egg allergy in children with bird protein sensitization

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Background: Hen's egg is frequently implicated in food allergy in children. Sometimes this allergy is associated with bird protein sensitization.

Objective: A study was conducted to establish the possible role of bird protein sensitization in the clinical picture and evolution of egg allergy in patients with both egg and bird sensitization.

Methods: Epidemiologic and clinical characteristics and the results of allergic study of 27 patients with both egg and bird allergy were compared with those of a control group of 19 egg-allergic patients without bird protein sensitization. All patients were evaluated clinically each year during the 4 years subsequent to the beginning of the study or until clinical tolerance to egg was achieved.

Results: Patients with bird sensitization had more frequent digestive and respiratory symptoms related to egg ingestion compared with the control group. At the end of follow-up, 15% of the bird sensitized patients and 58% of the controls tolerated egg. Egg yolk sensitization was the major sensitization in bird-sensitized patients.

Conclusion: It is necessary to exclude sensitization to bird proteins in egg-allergic patients, mainly when they show respiratory or digestive symptoms after egg ingestion, the egg allergy persists over a long period of time or egg yolk sensitization is strong.

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INTRODUCTION

Hen egg white frequently causes food hypersensitivity in children.¹ Recently, several cases have been reported in whom egg allergy was the consequence of a previous sensitivity to avian allergens.²⁻⁵ This association is known as "bird-egg syndrome." Such patients, mainly adults, are sensitized to bird antigens (feathers, droppings, serum, and meat) as well as to egg, mainly soluble proteins or livetins from egg yolk. It can be assumed that alpha-livetin, which has been identified as serum albumin, is the cross-reacting protein responsible for the bird-egg syndrome.⁶ Some published series^{3,4} include cases in which the initial sensitivity is due to egg proteins,

followed by subsequent inhalatory sensitivity to bird antigens; "egg-bird syndrome" has been proposed to describe these cases.

Recently, we have been able to investigate the presence of bird protein sensitization in children with egg allergy, and, in the course of our investigations we have observed that children with both egg and bird sensitization have some peculiar characteristics, which we present in this article.

PATIENTS AND METHODS

Patients

We carried out a study of bird protein sensitization (bird feathers and chicken meat) in patients with egg allergy who visited our Hospital over a period of 1 year (1988). Diagnosis of egg allergy was made because of a clinical history of immediate symptoms (urticaria, angioedema, respiratory or digestive symptoms, or anaphylaxis) after egg

ingestion, with positive prick-tests and specific serum IgE to egg proteins.

Twenty-seven children (20 boys and 7 girls), mean age 5 years (SD = 3.8) were selected, all diagnosed with both chicken hen's egg and bird (feathers and meat) allergy. Patient characteristics were analyzed according to the following categories: epidemiologic (age, sex, personal and family history of atopy, presence of atopic dermatitis or other allergic disease, and bird exposure), clinical (symptoms after egg ingestion and bird exposure, age of first appearance, evolution-time and development of tolerance), and diagnostic (presence and degree of sensitivity to the different proteins from egg and bird).

These data were compared with those of a control group. The control group was 19 egg-allergic patients (14 boys and 5 girls) with an average age of 3.3 years (SD = 2.1). These patients were also evaluated in our hospital and selected during the same year as the study group (1988). The study of bird feathers and chicken meat sensitization was negative in all of them.

During the 4 years subsequent to the beginning of the study, all patients were reevaluated by one of the authors annually or until egg allergy was resolved and clinical tolerance to egg ingestion was confirmed.

Skin Tests

Skin tests were performed by the prick method. A wheal of 3 mm or more in diameter than the negative control wheal was considered positive. Histamine and glycerinated serum were used as positive and negative controls, respectively. The following antigens were tested: egg white, egg yolk and chicken meat (1/20 wt/vol, D.H.S. Madrid, Spain), ovalbumin and ovomu-

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coid (10 mg/mL), mixed feathers (duck and chicken, Bencard, Madrid, Spain), chicken feathers (5% wt/vol, Abello, Madrid, Spain), and canary feathers (1 mg/mL, Leti, Madrid, Spain).

Prick tests to common inhalants (mites, molds, pollen, and animal danders) were performed on those patients with suspected respiratory allergy. Prick tests to other foods (cow milk, fish, shellfish, nuts, and/or vegetables) were performed whenever other food allergies were suspected as well as on patients with atopic dermatitis.

In Vitro Study

Total serum IgE was determined by CAP-IgE FEIA (Pharmacia Diagnostics, Uppsala, Sweden). Specific serum IgE to chicken hen egg and bird proteins and other suspected allergens or those positive by prick testing were measured by CAP or RAST (Pharmacia Diagnostics, Uppsala, Sweden) according to the commercial availability of each antigen.

Oral Challenge Tests

Open oral challenge was performed with chicken hen egg and/or chicken meat only to confirm the diagnosis in those cases in which a discrepancy existed between the clinical history and the allergy study results, and also, when egg tolerance was suspected of having developed at follow-up. No challenge tests were performed when there was a highly suggestive clinical history with positive both prick tests and specific serum IgE, nor in instances of serious reaction (anaphylaxis).

Oral challenge tests were performed with the parent's consent during asymptomatic periods when the patient was receiving no medication. Progressively increasing doses of antigen were administered until the appearance of clinical symptoms, or until the total dose was reached (30 g of egg white and 50 g of chicken meat approximately). Clinical tolerance was assumed when oral challenge elicited no symptoms.

Statistical Analysis

Differences between groups were analyzed on a personal computer with a statistical software package (R-Sigma. Pkware, Inc. Glendale, WI, USA). Comparisons of the percentages were done by using the Mann-Whitney U test. Comparisons of means were done by using the t test. Data were expressed as mean $\pm$ SD. For all analyses, a *P* value of .05 was considered the limit of significance.

RESULTS

Table 1 shows the clinical characteristics of the subjects studied. We found no statistically significant differences between the study group and the control group with respect to the sex, family atopy or presence of atopic dermatitis. The presence of associated asthma (85%) and rhinoconjunctivitis (52%) was significantly higher in the bird-sensitized patients than in the control group (19%). Similarly, sensitivity to common inhalants was observed more frequently in the bird-allergic group (78%) than in the control group (42%), although when each inhalant was individually analyzed, only the presence of fungal sensitivity (29% in the patients and 5% in the controls) was relevant.

We found no significant differences in the presence of other concomitant food allergy (milk, fish, nuts, shellfish,

and vegetables) in subjects with bird allergy (63%) and in the control group (47%).

Clinical characteristics of egg allergy in both groups of patients are presented in Table 2. There were no significant differences between subjects with or without bird sensitization regarding the age of appearance of egg allergy. Cutaneous symptoms (urticaria, angioedema, flare, and pruritus) within a few minutes following egg ingestion were present in all control patients and they were the only manifestation in more than 60%; 37% experienced digestive symptoms (abdominal pain, vomiting, and/or diarrhea) and no patient from this group presented egg ingestion-related respiratory symptoms (rhinoconjunctivitis, cough, breathing difficulty, and/or asthma). By contrast, not all bird-sensitized patients displayed cutaneous symptoms (89%), 78% had immediate digestive symptoms after egg ingestion, and more than 37% of these patients had respiratory symptoms. All these differences were statistically significant when compared with the control group.

After 4 years of follow-up and despite having a slightly higher average age, only 15% of children with bird sensitization achieved tolerance to egg ingestion, compared with 58% of patients in the control group; these differences were also statistically significant.

Mean age of egg tolerance in patients with bird sensitization was 8.7 years (range 5 to 14). In the control group, it was 5.2 years (range 2 to 8). At the end of the follow-up period, the mean duration of egg allergy among the patients with persisting egg hypersensitivity was 9.1 years (SD = 3.8) in those sensitized to birds and 4.9 years (SD = 2.3) in controls (*P* < .001).

We found significant differences (*P* < .05) between the two groups when direct contact with birds was analyzed. Eighty-one percent of bird-sensitized patients and 47% of the controls reported contact with birds (mainly chickens and canaries). Despite this, none of the control patients presented

Table 1. Epidemiologic Data of Children with Egg Allergy

	Sensitized to Birds n = 27	Controls n = 19
Mean age, yr	5 $\pm$ 3.8	3.3 $\pm$ 2.1
Males/females	20/7	14/5
Family atopy	16	8
Atopic dermatitis	13	13
Rhinoconjunctivitis	14*	2
Asthma	23*	2
Allergy to other foods	17	9
Allergy to inhalants	21†	8
Mold sensitization	8†	1

* *P* < .001 and, † *P* < .05.

Table 2. Clinical Data of Patients with Egg Allergy

	Sensitized to birds n = 27	Controls n = 19
Onset of egg allergy, months	20.5 ± 25.8	14.9 ± 15.3
Symptoms after egg ingestion		
Urticaria/angioedema	24	19
Gastrointestinal	21*	7
Respiratory	10†	0
Resolved egg hypersensitivity	4*	11
Mean age of egg tolerance, yr	8.7 (5–14)*	5.2 (2–8)
Mean duration of egg allergy, yr	9.1 ± 3.8‡	4.9 ± 2.2
Exposure to birds	22‡	9
Bird-related symptoms	7	0
Chicken meat related symptoms	6	0

* $P < .01$, † $P < .001$, and ‡ $P < .05$.

direct symptoms in presence of birds, while 26% ($P < .01$) of the studied patients reported respiratory symptoms (rhinoconjunctivitis and/or asthma) when in contact with birds.

Twenty-two percent of bird-sensitized patients reported symptoms after ingestion of chicken meat (angioedema, vomiting, asthma, urticaria, perioral syndrome, cough, or contact urticaria). All controls tolerated chicken meat.

In vitro analysis showed higher levels of total serum IgE in the bird-sensitized group (mean 887 KU/L at start and 1203 KU/L at follow-up) than in the control group (mean 186 KU/L at start and 473 KU/L at follow-up), with

significant differences ($P < .01$ and $P < .05$ respectively).

Table 3 shows the results of the allergic study of patients at the start and after 4 years follow-up. Initially, all patients in both groups had positive prick tests or CAP to egg white proteins, and all except one patient from the bird-sensitized patients had positive prick test or CAP to egg yolk. At this moment, there were no significant differences between both groups in regard to the presence or degree of sensitization to egg white and egg yolk.

At the end of the 4-year follow-up period, all patients who had not yet acquired egg tolerance (23 bird-sensitized patients and 8 controls) had sen-

sitization to egg white proteins. Egg yolk sensitization was observed in all 23 members of the study group and in seven of the eight controls. At this moment, mean specific IgE values for egg white were 38.9 (0.8 to 100) KU/L in bird sensitized patients compared with 12.7 (1 to 70) KU/L in the controls ($P < .001$). The mean value of specific IgE to egg yolk was 51.5 (1.9 to 100) KU/L in the bird-sensitized children compared with 2.7 (0 to 10) KU/L in the controls ($P < .001$).

DISCUSSION

Egg is one of the most frequent causes of food hypersensitivity in children.^{1,7} Typically, egg allergy appears before the age of 2 years. The incidence tends to subside with age and usually disappears after 2 to 5 years. Although in allergic patients egg ingestion may induce anaphylaxis and gastrointestinal or respiratory symptoms,^{7,8} the most frequent symptoms are cutaneous (urticaria, angioedema, pruritus, and flare). It has been stated⁷ that those patients who experience egg allergy for a longer period suffer more frequent respiratory symptoms and their IgE tends to remain high. Although egg yolk has several proteins, egg white contains the major allergens for egg-allergic patients. Ovalbumin is the most plentiful protein and the main allergen.^{8,9}

Recently, a group of egg-allergic patients has been described^{2–6} in which egg allergy is secondary to a previous sensitivity to bird proteins (feathers, meat, droppings, and serum). In these patients, egg yolk sensitivity predominates over egg white sensitization; it appears mainly in adult women and frequently affects several target organs. This bird-egg syndrome is the result of sensitization to serum albumin present in bird products and in egg yolk. Serum albumin has been identified with the alpha-livetins from egg yolk.^{3,6,10} The appearance of sensitization to bird proteins secondary to previous allergy to egg (egg-bird syndrome) also has been previously described by several authors.^{3,4}

Table 3. Diagnostic Data of Patients with Egg Allergy

	Sensitized to birds n = 27	Controls n = 19
At the start of the study		
Positive prick to egg white	27	19
Positive prick to egg yolk	26	19
Mean IgE to egg white (KU/L)	23.6	9.6
Mean IgE to egg yolk (KU/L)	12.5*	0.8
Egg-challenge†	8/8	5/5
Chicken meat challenge†	2/2	0/0
At 4 years follow-up		
Patients with persisting egg allergy	23	8
Positive prick to egg white	23	8
Positive prick to egg yolk	23	7
Mean IgE to egg white (KU/L)	38.9*	12.7
Mean IgE to egg yolk (KU/L)	51.4*	2.7
Egg challenged†	9/5	13/2
Chicken meat challenge†	4/0	0/0

* $P < .001$ and † done/positive.

Only one of our patients was definitely diagnosed with bird-egg syndrome.¹¹ In those patients who had had asthma prior to the onset of egg allergy we cannot entirely exclude the presence of bird-egg syndrome, since, initially, a study of this disease was not carried out. Nevertheless, apart from the above-mentioned case,¹¹ our patients have an egg-bird syndrome; this could explain the peculiar characteristics of egg allergy in these children. Thus, the sex, the family atopy, the presence of atopic dermatitis, the sensitivity to other foods, the age at onset of egg allergy and the occurrence of cutaneous symptoms after egg ingestion are all similar when compared with controls; however, in patients sensitized to avian proteins, associated asthma is more prevalent and digestive and respiratory symptoms occur more frequently in response to egg ingestion. In this group, egg allergy tends to persist with age and the tolerance to egg is less frequent and develops later. Total IgE is usually higher. Initially there was no difference regarding sensitization (positive skin tests and serum specific-IgE) to egg white nor to egg yolk between the groups, although the egg-yolk specific IgE levels were significantly higher in the bird-sensitized patients. At the end of the follow-up period, egg white sensitization persisted in both groups, but specific IgE to egg yolk had increased significantly more in the bird-sensitive patients. In these patients, sensitization to egg yolk was even more intense than to egg

white. We believe these differences could be the result of the sensitization to avian proteins.

Only 20% of patients with bird sensitization had allergic symptoms after exposure to bird antigens. Continuous contact with birds may be the responsible factor for the persistent and increased egg yolk sensitization due to cross-reactivity between proteins from birds and egg yolk.

Finally, we believe that in cases of egg allergy it is necessary to rule out bird protein sensitization, mainly in patients with associated respiratory or digestive symptoms after egg ingestion, in those patients whose egg allergy persists over a long period, and in cases with intense yolk hypersensitivity. We believe that patients with both egg and bird allergy should avoid contact with birds and eliminate from their diet not only egg, but also all bird-related products. Although further studies are needed, this may lead to a shorter duration of egg allergy.

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