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Prospective observational study on the characteristics of eosinophilic esophagitis in southeast Spain

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Abstract
Introduction: Eosinophilic esophagitis (EoE) is a chronic esophageal atopic disease because sensitization to aeroallergens and foods allergens is very common.
Objectives: This study is the first work that studies multiple characteristics of EoE in the southeast of Spain to know whether EoE in the patients of this region is similar to that of other regions of Spain in terms of demography, symptoms, and atopic characteristics.
Method: It is an observational prospective study of patients diagnosed with EoE at Granada (Spain). We recorded demographic data (age, sex, and personal history of atopy), clinical data (impaction and dysphagia), allergologic data (prick test and specific immunoglobulin E) to foods, aeroallergen, and pan-allergens, and other endoscopic-histologic data and comorbidities.
Results: The demographic, allergologic, and endoscopic characteristics of patients with EoE in Granada were similar to the rest of Spain, except the higher frequency of sensitization to olive pollen, food allergy, and anaphylaxis reactions.
Conclusions: The higher frequency of sensitization to olive pollen and food allergy with severe clinical manifestations (anaphylaxis) in patients with EoE in Granada could have a negative impact on patients' quality of life.

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Introduction

Eosinophilic esophagitis (EoE) is a chronic esophageal disease characterized clinically by symptoms of esophageal dysfunction, and histologically by eosinophilic inflammation.[1] Other systemic and local causes must be ruled out. Clinical manifestations and histopathology data should be interpreted jointly rather than separately.[2] EoE is currently considered an atopic disease, since sensitization to aeroallergens and foods allergens is quite common.[2,3]

Objective

The objective of this study was to determine the demographic, clinical, allergologic, analytic, endoscopic, and histologic characteristics and comorbidities in a series of patients with EoE.

Materials and Methods

We performed an observational prospective study of patients diagnosed with EoE[2] at Complejo Hospital ariode Granada (Spain) between November 2018 and May 2019. The hospital had a catchment population of 602,230 inhabitants.

We used an Excel spreadsheet to record demographic data (age, sex, and personal history of atopy), clinical data (impaction and dysphagia) and allergologic data (prick test and specific immunoglobulin E [sIgE] to the most frequently involved foods in EoE [milk, cereals, egg, nuts, legumes, and fish], aeroallergen and pan-allergens such as lipid transfer protein [LTP] and profilin). We also recorded laboratory data (eosinophilic cationic protein [ECP], total IgE [tIgE] and eosinophils in peripheral blood), endoscopic data, histologic data and comorbidities (atopic dermatitis, rhinoconjunctivitis, bronchial asthma, allergy to inhaled allergens, and allergy to foods [anaphylaxis, urticaria/angioedema, and oral allergy syndrome]).

The prick tests were performed using commercial extracts (Alk-Abelló, Madrid, Spain; Leti, Barcelona, Spain) according to the recommendations of the European Academy of Allergy and Clinical Immunology, with a positive histamine control (10 mg/mL) and a negative saline control. Results were considered positive if the wheal was ≥3 mm, eosinophil values > 0.55 × 10^3/Ml, and total white cells > 5.50% were considered high. Levels of tIgE and sIgE were determined using ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden); tIgE > 100 kU/L and sIgE > 0.34 kU/L were considered high. ECP > 10 ng/mL determined using enzyme-linked immunoassay (CUSABIO) was considered high.

Qualitative variables were reported as frequencies, and quantitative variables were reported as averages and standard deviations (SD). This study was approved by the Provincial Ethics Committee of Granada (Supplementary Figure S1).

Results (Table 1)

We recruited 31 patients. Most of them were young adult men, and more than a half of them had a history of atopy. The main symptom was food impaction, and not dysphagia, which was much less frequent.

More than 70% of patients were atopic. Sensitization to foods was high (two-thirds in the present series). LTP was the most prevalent food allergen in more than one-third of the series, closely followed by milk, legumes, and nuts. More than half of the patients were sensitized to aeroallergens, the most prevalent being olive pollen.

According to biomarkers, the average value of blood eosinophil count was high in more than a quarter of patients. The percentage of eosinophils and tIgE was high in more than half of patients, and ECP was high in >85% of patients.

Endoscopic study revealed a predominance of pseudo-rings. Histology revealed basal cell hyperplasia, eosinophilic granules, and dilatation of intercellular spaces in all patients.

Anaphylaxis was the most frequent comorbidity, very closely followed by rhinitis. More than one-third of the patients had bronchial asthma. Atopic dermatitis was the least frequent comorbidity.

Discussion

In this report, the average age and personal history of atopy were similar to those reported in other studies.[2,5] Male patients were more frequent in our series (2:1). It was slightly lower than reported in other studies because of low number of patients.[6-9] Food impaction was more common than found in other studies.[5] It could probably be due to the longer course of EoE.

Sensitization was more common to food allergens than to aeroallergens, in contrast to other studies with adult patients.[5-8] This result would justify the high rate of LTP sensitization and anaphylaxis in the present study.[10] Findings for the most prevalent food allergens—LTP, nuts, and legumes—were similar to those for Central Spain.[5-7] However, sensitization to cow's milk was more common in our patients than in the rest of Spain.[5-8] It is worth highlighting the sensitization to olive pollen in aeroallergens because it was notably more frequent than grass-pollen sensitization, even though other reports show the opposite.[6-8] This was due to the aerobiology of the living areas of the patients.

In laboratory, percentage of eosinophils was higher than reported in another study,[8] and ECP was also high in most of the patients. These findings could be related with the presence of concomitant atopic diseases in our patients.[5,8] Our histologic findings were similar to other findings,[6] although they were higher for basal cell hyperplasia.[8,9] The endoscopic findings of our patients were similar to those of other studies, but the presence of pseudo-rings was higher.[5,6,8] This shows a stenosing phenotype caused by the long-term EoE.

More than half of the patients in the present study were atopic.[1,2,5] The geographic distribution of allergy to LTP and cross-reactivity in areas of high pollen exposure[10] could explain secondary sensitization to nuts and legumes.[2,3,6] The high rate of anaphylaxis found could be due to food allergens and LTP sensitization in patients having EoE in Granada.[2,7] There was no evidence of involvement of LTP in EoE. Nevertheless, cow's milk was the most involved

Table 1 Demographic, clinical, endoscopic, histologic, and allergologic characteristics.

Demographic data	N	%
Age: mean (SD)	31	35.4 ± 12.7
Gender: Men–women (n, %)	31	21; 67.7%-10; 32.23%
Personal history of atopy (n, %)	31	21; 67.7%
Evaluation by the allergology department (n, %)	31	23; 74.2%
Clinical data		
Impaction (n, %)	29	19; 65.51%
Dysphagia (n, %)	29	2; 6.89%
Comorbidities		
Food allergy		
—Anaphylaxis	31	19; 61.3%
—OAS/urticaria	28	6; 21.43%
Rhinitis and/or conjunctivitis	28	16; 57.14%
Asthma	28	11; 39.28%
Atopic dermatitis	28	3; 10.71%
Laboratory parameters		
Mean (SD) eosinophil count	25	0.438 ± 0.25 ($\times 10^3$)
Mean (SD) eosinophil percentage	25	5.76 ± 3.05
Mean (SD) IgE level (kU/L)	12	177.08 ± 162.51
Mean (SD) ECP level (IU)	7	63.7 ± 37.9
Endoscopy findings		
Rings and/or trachealization	28	24; 85, 71%
Furrows or striae	28	10; 35, 71%
Stenosis	28	1; 3, 57%
Histology findings		
Microabscess	20	10; 50%
Hyperplasia	19	19; 100%
Granules	20	20; 100%
Fibrosis	9	6; 66.66%
Allergologic characteristics		

Sensitization to aeroallergens*	N	% (N = 23)	Sensitization to foods*	N	% (N = 23)
(n, %)	14	60.8695	(n, %)	17	73.9130%
Olive	12	52.17	Milk and fractions	7	30.4346%
Grasses	8	30.4346	Egg and fractions	6	26.0869%
Artemisia	6	26.0868	Cereals (wheat, corn)	5	21.7391%
Parietaria	4	17.3912			
Salsola	4	17.3912	Legumes (lentils, beans, peas)	7	30.4346%
Mites	3	13.0434	Nuts (peanut, hazelnut, walnut)	7	30.4346%
Alternaria	6	26.0868	Shellfish and fish	0	0
Cat	7	30.4346	Lipid transfer protein	8	34.7824%
Horse	3	13.0434	Profilin	3	13.0434%

ECP: eosinophilic cationic protein; IgE: immunoglobulin E; SD: standard deviation.
*Sensitization (TC and IgE).

food in this disease,[1,2] followed by wheat and legumes.[10] Bronchial asthma and especially rhinoconjunctivitis are frequent comorbidities in patients with EoE.[5] Besides, patients with EoE, especially children, are more likely to suffer from food and respiratory allergies.[5]

Our study was limited with low number of patients, non-randomized selection, and lack of studies from Andalucía. However, it provided new data from a Spanish region that was different from others in terms of pollination and allergy sensitization.

Conclusions

Overall, the demographic, allergologic, and endoscopic characteristics of patients with EoE in a sanitary district of Granada are similar to those found in the rest of Spain, except the higher frequency of sensitization to olive pollen and food allergy with severe clinical manifestations (anaphylaxis) and a slight predominance of the stenosing endoscopic phenotype. These differences could impact negatively patients' quality of life.

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Statement of Ethics

Subjects have given their written informed consent and the study protocol was approved by the Provincial Ethics Committee of Granada.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Author contributions

ACJ, FFL, JRV, and ALJ did consultation and diagnosis of patients. ACJ did recruitment of patients, study their characteristics, and carried out statistical work. RGG searched bibliography and translated the paper from Spanish to English. EGT did designing and writing of the manuscript. RGR did the general review of the study and checked its English language.

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