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ORIGINAL ARTICLE

Value of microarray allergen assay in the management of eosinophilic oesophagitis

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Abstract
Background: Eosinophilic oesophagitis (EoE) is a disorder characterised by oesophageal dysfunction and, histologically, by eosinophilic inflammation. Although treatment, which includes dilatations, oral corticosteroids and restrictive diets, is often effective, choosing the foods to be eliminated from the diet is difficult.
Objective: Component resolved diagnostic by microarray allergen assay may be useful in detecting allergens that might be involved in the inflammatory process.
Methods: We studied 67 patients with EoE, diagnosed clinically and histologically by endoscopic biopsy. CRD analysis with microarray technology was carried out in the 67 EoE patients, 50 patients with pollen allergy without digestive symptoms, and 50 healthy controls.
Results: Allergies were not detected by microarray in only seven of the 67 patients with EoE. Controls with pollen allergy showed sensitisation to different groups of pollen proteins without significant differences. In EoE patients with response to some allergens, the predominant allergens were grasses group 1 and, in particular, nCyn d 1 (*Cynodon dactylon*) or Bermuda grass pollen in 59.5%, followed by lipid transfer proteins (LTP) of peach (19.40%), hazelnut (17.91%) and Artemisia (19.40%).

Abbreviations: EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; SFED, Six-Food Elimination Diet; Pol. Group 1,4,5,6, groups 1, 4, 5 and 6 of pollens; nCyn d 1, group 1 of *Cynodon dactylon* (Bermuda grass pollen); nDer p1 and Der p2, cysteine-proteases of *Dermathophagoides pteronyssinus* and farinae respectively; R Alt a 1, acidic glycoprotein of *Alternaria alternata*; nApi m1, phospolypase A2 of apis venom; Ves v5, phospolypase A2 of yellow jacket venom; rAni s 1, serine-protease inhibitor of Anisakis simplex; nPrup3, peach lipid transfer protein; rCor a 8, hazelnut lipid transfer protein; nArt v3, mugwort lipid transfer protein; Prof T, tree pollen profilin; Prof G, grasses pollen profilin; Prol T, tree pollen polcalcin; Prof G, grasses pollen polcalcin; CCD, cross-reactivity carbohydrate determinants; CRD, component resolved diagnostics; PPI, proton pump inhibitor.

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Conclusions: In patients with EoE, sensitisation to plant foods and pollen is important. The proteins most frequently involved are nCyn d 1 and lipid transfer proteins, hazelnuts and walnuts. After one year of an array-guided exclusion diet and pollen-specific immunotherapy in the case of high levels of response, patients with EoE showed preliminary significant improvements.

Introduction

Eosinophilic oesophagitis (EoE) is an atopic disease of the oesophagus whose diagnosis has been increasing over the last decade. Accumulating animal and human data have provided evidence that EoE appears to be an antigen-driven immunologic process that involves multiple pathogenic pathways; so a conceptual definition is proposed highlighting that EoE represents a chronic, immune/antigen-mediated disease characterised clinically by symptoms related to oesophageal dysfunction and histologically by eosinophil-predominant inflammation.[1]

EoE occurs in both children and adults worldwide. It affects 1 in 2500 people in both USA and EU, but its incidence is increasing. The diagnosis is based on clinical symptoms and histological findings (predominantly eosinophilic inflammation).[1–5] Apart from severe choking, inflammation of the oesophagus may have severe systemic and emotional repercussions for patients and their families. Some patients exhibited histological remission after proton pump inhibitor (PPI) treatment.[6] Unlike gastro-oesophageal reflux disease (GERD), whose symptoms overlap with oesophagitis, EoE is often due to allergen hypersensitivity that may be improved with diet control if the food implicated is clearly known.[6,7]

There are results for different therapeutic options, which, although not providing a definitive cure for the disease, are effective in providing and maintaining disease remission. However, to date, no reliable, risk-free diagnostic technique for EoE has yet been found.

Symptomatic treatments of EoE include the Six-Food Elimination Diet (SFED),[2–5] oral corticosteroids, leukotriene modifiers and palliative measures such as mechanical dilation of the oesophagus. Empirical elimination of foods has so far been the most effective therapeutic measure but requires multiple control endoscopies and can significantly hinder quality of life. A definitive aetiological diagnosis would be fundamental in determining the specific allergens which cause eosinophilic inflammation of the oesophageal mucosa and which foods should be avoided.

There have been no randomised studies designed to find the real causes and specific measures required to prevent EoE.[8–12] Routine allergic techniques (prick tests) and determination of IgE have a poor predictive value for food allergens in EoE.[13]

Although the international consensus document for diagnosis or therapeutic management of EoE[1] establishes demonstration of disease recrudescence after food reintroduction, provocation techniques with foods are very hard in EoE, especially in multi-sensitised patients.[14,15]

According to consensus guidelines for managing EoE in children and adults, allergy test results by themselves cannot be used to make a diagnosis of EoE food triggers, which only can be achieved after documented disease remission upon food restriction and recrudescence when reintroduction. As a result, restrictions in diets should not be recommended to EoE patients exclusively on the basis of positive test results.

Nevertheless, it is difficult to choose what foods should be excluded from diet and a restrictive diet of six principal foods is complicated to follow for a long time.

Recently, it has become possible to measure IgE antibodies to specific allergen molecules, a method called ''component resolved diagnostics'' (CRD). For aeroallergens, CRD has shown a good correlation with classic IgE assays in multi-sensitised patients and allows 112 IgE measures to be obtained with a very small volume of sera.

It would be of interest to complete diagnostic tests with molecular analysis of all the proteins involved in hypersensitivity to allow better-targeted dietary restrictions or, when this is not possible, to try a specific, safe hyposensitising treatment. We used the microarray technique, based on micro-immunoassays, which, in the case of the Thermofisher® panel, allow testing of 112 allergenic native and recombinant components, to obtain a more specific and complete profile of sensitisation to food allergen hypersensitivity.[16,17] In addition to foods, the panel includes environmental allergens that have not been tested in EoE patients, but could prove to be important, since many allergens, such as pollen, are swallowed after reaching the oropharynx.

The general aim of our study was to evaluate IgE-mediated allergic hypersensitivity to various food and environmental allergens (native and recombinant) in EoE affected population.

The specific objectives were as follows:

1. To evaluate the incidence of the IgE-mediated response to foods and aeroallergens in patients with EoE, patients with pollen allergy, and healthy controls.
2. Evaluate the value of CRD analysis by microarrays in the management of EoE.

Patients and methods

This was a cross-sectional study. Patients were included and the analyses made between 15 November 2011 and May 2013. We randomly selected 67 consecutive patients attending the hospital's facilities diagnosed with EoE by the Department of Gastroenterology, Hospital Universitario Rio Hortega (HURH). These patients were recruited over two years avoiding the pollination period (May–July in our area).