

## Eosinophilic Esophagitis and Food Allergy: Is There an Established Relationship? Clinical Case

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**Received:** March 15, 2016; **Published:** May 11, 2016

### Abstract

**Introduction:** Eosinophilic esophagitis (EE) is an entity characterized by esophageal symptoms with the presence of dense eosinophilia, in the absence of reflux disease excluded by pHmetry or lack of response to treatment with proton pump inhibitor. Various guidelines try to establish diagnostic criteria.

**Clinical Case:** Teenager, 14 years old. A history of low birth weight from 19 months (p5) and asthma since age of 3. Started symptoms of intermittent dysphagia, being placed reflux disease hypothesis, he did prolonged treatment with PPI with no success. The patient was referred to the Digestive Pathology enquiry, because of persistence of complaints, now with dysphagia for solids and impact feeding episodes. In HDE the progression of the endoscope was not possible by the existence of stenosis, in a mucosa with traqueiform rings. A biopsy confirmed the diagnosis. Were performed allergens tests with positivity for food and inhalant allergens (hazelnut, wheat). Started fluticasone with slight improvement. Later, started eviction of food he had allergy, showing clinical improvement, which resulted in weight gain.

**Conclusion:** The pathogenesis of EE is related to atopy. The goal of treatment is to improve the quality of life of the patient. As illustrated by this case, the control of the disease with a dietary component led to greater clinical improvement.

**Keywords:** Eosinophilic esophagitis; Allergens; Esophagus; Endoscopy

### Introduction

The first case of eosinophilic esophagitis (EE) was described in 1977 and until 1990 the presence of eosinophilic infiltration was synonymous with gastroesophageal reflux disease (GERD). Only in 1993, EE was considered as a distinct clinical entity.

In fact the symptoms of EE are similar to those of GERD, hence constitute an important diagnostic difficulty. However, the pathological features and symptoms of EE don't improve with treatment of acid suppression. EE is a clinical condition characterized by: gastrointestinal symptoms, particularly esophageal, associated with the presence of dense eosinophilia ( $\geq 15$  intraepithelial eosinophils/high magnification field) in biopsy material, with hyperplasia of the squamous epithelium. The absence of GERD should be discarded by pH monitoring or, lack of clinical response after prolonged treatment with high dose ( $> 2$  mg/kg/day) of proton-pump inhibitor [1-4].

Esophageal eosinophilia is not exclusive of EE. It is also found in numerous pathologies such as GERD, infectious diseases, Connective Tissue disorders, drug hypersensitivity response, hyper eosinophilic syndrome, inflammatory bowel disease or eosinophilic gastroenteritis, among others. The EE more often affects males (3: 1 to 4: 1), not being clear any ethnic or racial relationship. Given the lack of mortality, the prevalence over time tends to increase even if the incidence continues similar [5].

There is evidence that EE has strong family association. There is a type of T helper response, with degranulation of eosinophils, which will cause immediate damage. Eosinophils are cells capable of initiating adaptive immune responses, as well as maintain and propa-

**Citation:** Monteiro Maria Ines., *et al.* "Eosinophilic Esophagitis and Food Allergy: Is There an Established Relationship? Clinical Case". *EC Gastroenterology and Digestive System* 1.1 (2016): 33-37.

gate inflammatory reactions. In vitro studies have shown that eosinophils have cytotoxic granules, leading to increased reactivity of the smooth muscle, leading to degranulation of mast cells and basophils. Eosinophils produce pro-inflammatory cytokines, leading to fibrosis and angiogenesis, loss of elasticity and luminal narrowing. Important to highlight the good response that occurs with environmental change [3,6-8].

Do not undervalue the importance of the clinic. Clinical manifestations of EE range from: food intolerance/aversion, GERD refractory to medical or surgical treatment, vomiting/regurgitation, food impact/foreign bodies, failure to thrive, epigastric abdominal pain or dysphagia. The diagnosis is based on important clinical suspicion, leading to accomplishment of upper gastrointestinal endoscopy and biopsy [9,10].

The changes found are: longitudinal grooves, more friable mucosa, edema, whitish exudates, esophageal tracheizao (rings), mucosa in cellophane, detachment of the mucosa with micro abscesses, lower motility and narrowing. Do not forget that macroscopically, the mucosa may be without visible changes. The pH measurement is normal in 90% - 100% of children, do not have diagnostic value.

The contrast study may be beneficial in children with vomiting, to exclude anatomical etiology (malrotation) and may be useful for subsequent endoscopy, for the decision of the endoscope gauge/need for expansion. The typical histology associated with IT is the presence of more than 15 intraepithelial eosinophils/HMF: is controversial whether it will be the sole criterion. Usually there are eosinophilic micro abscess (aggregates of 4 or more eosinophils), eosinophilic inflammatory infiltrate of superficial layers (top third to the middle third of the squamous epithelium), hyperplasia of the basal layer (when it occupies > 20% of the epithelium) and elongation of the papillae. None of these changes is pathognomonic. Shall hold up a considerable number of biopsies, most centers perform at least 6, since it is a focal disease. It must also be made at two levels, proximal and distal esophagus. Simultaneous gastric and duodenal biopsy is also advised to rule out other diseases, including eosinophilic gastroenteropathy. EE pathogenesis is directly related to atopy. It is certainly a chronic disease of the immune forum. Most patients have evidence of food hypersensitivity / air allergens / history of respiratory allergies, often associated with peripheral eosinophilia and increased IgE. Patients with EE in 50-80% of cases are atopic (allergic rhinitis / asthma / atopic dermatitis / allergic skin sensitization). Patients with allergic rhinitis have seasonal increases in esophageal eosinophils. Patients with EE also feature seasonal variations in their symptoms. Approximately 2/3 of the patients have a positive skin test to at least a food allergen [4,11].

The most commonly associated food are: peanut, egg, soybean, cow milk and wheat. The elimination of some food leads to 77% resolution histological changes. Still unknown is the impact of long-term treatment and the final disease damage [12]. Acid suppression with proton pump inhibitors are useful in diagnosis. We know that acid irritates the esophagus, already inflamed, so it is also an adjuvant therapy. Esophageal stricture dilation is critical to the patient's well-being. Dilation is indicated when symptoms occur secondary to stenosis. It increases risks of the procedure itself: perforation, laceration (mucosal tearing) and despite the success, 7-50% of patients have recurrence of symptoms and needs further expansion.

Systemic corticosteroid therapy provides clinical and histological improvement. It is useful on the need for rapid relief of symptoms (severe dysphagia, dehydration due to difficulty swallowing, weight loss, esophageal stricture). Not forgetting the side effects of this medication in children.

Topical corticosteroids have associated clinical and histological improvement. The most common adverse effects are esophageal candidiasis and sensation of "dry mouth". Among the most used fluticasone (220-440 ug 2x / day) dose inhaled; > 750 ug / day; although not yet approved for the treatment of EE has a 95% response at 3 months, fast response.

Do not forget that the incentives are maintained and therefore the disease tends to perpetuate itself. The leukotriene receptor antagonist promote relief of symptoms, but no beneficial effect on eosinophilia. The dietary treatment with removal of food antigens/specific foods (history + tests) control the symptoms and histopathological changes: it is still a controversial treatment. The use of empirical diet should be closely monitored by a nutritionist. Removal of 6 foods (milk, wheat, soy, nuts, egg) for 4- 6 weeks, followed by reintroduction

individually every 4-6 weeks. The diet guided by allergy tests (PRICK, PATCH) often associated with avoidance of milk seems to be better accepted by the patient. The use of amino acids formula is the gold standard for determining whether food antigens are responsible for EE. But they have low palatability, low adhesion and high cost [7,11-16]. Recent treatments with antibodies have still not proven efficiency [17,18].

**CLINICAL CASE**

D.T.C., male, 14 years of age.

**Personal history of relief**

Underweight since the nineteenth month (5th percentile up to 12 years without deceleration). Bronchial asthma diagnosed at 3 years. Family history was irrelevant. Teenager in Immuno allergology consultation since 2001. In 2006 there was the realization of Phadiatop, positive for atopy to inhalant allergens. In 2010 revealed: IgE 187 kU/l, atopy to inhalant allergens, positive for weeds, grass, cat dander atopy, positive for specific IgE to house dust mite and farinae (class 2). Search for food allergens was positive. Started unspecific symptoms of intermittent dysphagia, in 2010, hypothesized GERD. He made prolonged treatment with PPIs, although no improvement/improvement very mild of the symptoms.

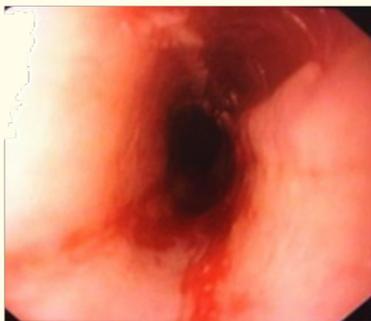
Thus, in 2011 he has been directed to Digestive Pathology consultation for more consistent complaints of dysphagia, now mainly for solid, with episodes of food impact, that the patient solved at home, without recurrence to the emergency service. Refers to ingest preferably liquid, high water intake and took longer to make meals, since chewed repeatedly each solid food. In January 2012, he held esophagus-gastro-duodenal transit that revealed discrete irregularities with spiculated outline of the wall of the proximal third of the esophagus compatible with esophagitis.



**Figure 1:** *Contrasted study esophagus-gastro-duodenal: discrete irregularities with spiculated outline of the wall of the proximal esophagus third, compatible with esophagitis.*

Later was performed endoscopy, which revealed stenosis at 30 cm, not allowing the passage of the endoscope. The mucosa had tracheiformes rings (Figure 2). Biopsies were made, compatible with marked eosinophilic esophagitis. He began treatment with fluticasone (250 2 puffs 2x/day - 8 weeks) with slight improvement of symptoms.

In October 2012 progressed in skin tests that revealed: positive for hazelnut and mixture of cereals mainly wheat. He linked to treatment, avoidance of these foods, which had allergy, showing marked clinical improvement, with translation in weight gain. Repeated endoscopy in February 2013: tracheiforme esophagus, now without stenosis. The biopsies remain with eosinophilic esophagitis, slight lower. He remains currently in outpatient follow-up and is clinically asymptomatic.



**Figure 2:** Endoscopic image: evident edema and friability of the esophageal mucosa, with longitudinal striations, whitish speckles or exudates and fixed circular mucosal rings (traqueiformes rings).

## Discussion/ Conclusion

Given the lack of mortality and prevalence of this disease, over time it tends to increase even if the incidence continues similarly [5,19]. No doubt, its pathogenesis is directly related to atopy: most patients present hypersensitivity evidence to food / inhalant allergens [4,11,12]. Control of the disease should include dietary component, such as this clinical case has showed. The removal of specific foods (medical history + Tests) led to a greater relief of symptoms. It is not clear, in this patient, the exact date of the EE framework. Fica por esclarecer, neste doente, a data exata de inicio do quadro de EE. The diagnosis is often delayed, mainly by similarity or GERD coexistence. At histological level, there is still unclear data to allow the pathologist to state the degree of eosinophilia [20].

It is important to reflect on the purpose of treatment. If we want a clinical improvement or histologic improvement (prevention of food impact, prevention fibrostenose, risk of HSV infections) [15,21]. What will be the biggest risk markers or markers of greater disease severity. Does stenosis translates more difficulty to control disease?

The major EE complications are remodeling and esophageal narrowing, that we should avoid. This requires strategies to monitor the disease. For now, follow-up of these patients is short. There is no evidence of association with malignancy. Do not forget the importance of biopsy to the diagnosis of this pathology, the 8 week treatment with PPI, not only inhibits acid secretion but also decreases cytokines (IL-5 e eotaxina 3) and subsequent repetition of EDA with biopsy. Only then we have some final conclusions and consider the need to further study [3,7,8]. It is a disease with a good clinical-histological correlation, thus questions on the need for repetitions of endoscopies and biopsies, in asymptomatic patient. Yet to be defined, in the global consensus, the timings for their achievement [21].

This article aims to highlight the importance of considering this diagnosis, to improve the patient's quality of life, risk reduction/impaction and prevention of irreversible damage (tissue remodeling). We must consider this etiology in cases of failure to thrive and feeding difficulties [5]. The therapy should be appropriate to the patient and in conjunction with the allergist opinion [7, 11, 12, 18].

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**Volume 1 Issue 1 May 2016**

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