Eosinophilic Esophagitis: A Relevant Entity for the Otolaryngologist

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Received 15 May 2015; accepted 3 June 2015

KEYWORDS
Dysphagia; Deglutition disorders; Esophagitis; Eosinophilia; Food impaction; Transnasal esophagoscopy; Atopy

Abstract  Eosinophilic esophagitis (EE) is a recently recognised pathologic entity whose prevalence has risen significantly since it was first described. Its diagnosis represents a challenge for different medical specialties, among which ENT specialists play an important role. Clinical suspicion in a patient with recurrent food impaction or a child with eating disorders and history of hypersensitivity constitutes the first warning sign of a possible EE.

The purpose of this review is to highlight EE as a possible differential diagnosis in patients with deglutition disorders and describe the possible clinical symptoms that should alert the ENT specialist to perform appropriate diagnostic tests and procedures. The transnasal esophagoscopy, performed in-office by the ENT, is ideal for reducing possible underdiagnosed cases.

Given the fact that an ENT specialist will evaluate a great many patients with deglutition disorders, it is paramount for possible EE cases to be suspected and recognised so that a correct multidisciplinary approach involving not only ENT specialists but also paediatricians, gastroenterologists, allergologists and pathologists can be established. Identifying the dietary component responsible for the esophageal inflammation and removing that food from the patient’s diet is the key in the treatment of this immune-mediated disease.

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Introduction

The association of dysphagia with infiltration of eosinophils in the oesophagus was first reported in 1978 by Landres et al. In 1993 Attwood et al. observed an increase in eosinophils in oesophageal mucosa in patients with dysphagia and normal pH, and described a different clinical pathological syndrome called eosinophilic oesophagitis (EoE) with dysphagia. Initial consensus regarding the disease was published in 2007, distinguishing it from gastroesophageal reflux disease (GERD). However, after a series of patients with EoE who responded to treatment with proton-pump inhibitors (PPI), a new separate entity of EoE, called PPI respondent EoE was reported.

20 years after its initial description, the latest consensus in 2011 and 2013 defined this disease as an immuno-allergic based, chronic inflammatory condition, characterised by an inflammation of the oesophageal wall, predominantly eosinophilic, which does not respond to treatment with PPI and which appears with symptoms relating to the corresponding oesophageal dysfunction.

Its incidence or recognition has increased since then, both in children and adults, with a similar prevalence to Crohn’s disease in developed countries. There has been an increased number of publications due to the interest aroused by this disease, particularly in the last 4 years.

The EOE patient type is usually a young Caucasian, male aged approximately 35 with a history of allergy or atopia, whose symptoms may present from infancy, as a consequence of the progressive alteration of the oesophagus which may begin as an initial inflammatory phenotype and develop into a fibrostenotic one.

In small children the predominant symptoms are anorexia, vomiting and abdominal pain, whilst in adolescents and adults symptoms are dysphagia and food impaction. Since patients usually alter their eating habits, it is possible that they do not request medical attention until complications arise, which delays diagnosis.

This disease is confined to the oesophagus, where unlike in the remainder of the gastrointestinal tract, there should be no presence of eosinophils, and it must be differentiated from general gastrointestinal eosinophilic infiltration.

Diagnostic criteria of EoE require the presence of over 15 eosinophils per high power field in one or more biopsies of the oesophagus, after ruling out other possible causes of oesophageal eosinophilia, and in particular GERD.

The increase of EoE appears to be due to a combination of several factors: a real rise in the number of cases and an increase of its acceptance by the medical community, which has in turn been facilitated by the increased number of biopsies of the oesophagus performed.

This disease is of major relevance to the ENT specialist for several reasons:

1. It is the primary cause of dysphagia and oesophageal impaction in children and young adults.
2. It is the second most common cause of oesophagitis after GERD.
3. It is probably the final stage of many cases of oesophageal stenosis normally treated with dilatations, which could have been avoided with early diagnosis and treatment of this disease.
4. It has similar symptoms to GERD and laryngopharyngeal reflux, especially in patients with GERD symptoms who do not respond to PPI.
5. Frequent symptoms such as coughing, croaking, or dysphonia may be initial signs of EoE.
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0.35 per 100 000 inhabitants in 1991 to 43–100 per 100 000 inhabitants in 2014.7,10–12
Lucendo et al. reported that the prevalence of EoE in Spain is approximately 45 patients per 100 000 inhabitants,13
and calculated that 23 500 people suffer from this disease (Congress of chronic patients of the Sociedad Española de
Médicos de Atención Primaria [SEMGERDN], March 2015) (AEDESEO: Asociación Española de Esófagitis Eosinofílica.
www.aedeseo.org).

Epidemiology

Prevalence of EoE in Europe and U.S.A. has increased by

According to the above study, diagnosis in Spain is
delayed over 4.5 years in adults and 2.3 years in children.

With regard to incidence, the majority of publications
state there are from 6 to 13 cases per 100 000 inhabitants.
In Spain it is 6.4 (Table 1).

These figures are probably higher if we consider that
many patients do not seek medical attention. Recent studies
show that the percentage of patients may be around 1%,14
in a population of 1000 randomly selected patients.

The Dellon12 study confirms this, where 23% of patients
treated with digestive endoscopy for dysphagia presented
with EoE. It is of note that 2% of patients who did not com-
plain of dysphagia but who were treated with endoscopy
for other reasons, also suffered from an EoE.50% of patients
treated with food deimpaction presented with EoE.15–18

EoE has increased 35 times19 in the last 2 decades, along-
side allergic diseases. Outside of this parallelism, it has been
observed that 50%–80% of patients with EoE also present
allergic diseases, and it has been suggested therefore that
a shared pathogenic mechanism exists.

There are several hypotheses regarding the increase of
EoE incidence:

1. Increase in the recognition of the disease, the number of
endoscopies and biopsies of the oesophagus.21,22
2. Lower exposure to environmental antigens in developed
countries, in the last 20 years,23 together with other
allergic diseases.

Table 1 Clinical Characteristics of EoE in Patients Included
in the Spanish Register.

<table>
<thead>
<tr>
<th>Characteristic No.: 705 patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age in years (DE), range</strong></td>
</tr>
<tr>
<td>Gender: male:female</td>
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<tr>
<td><strong>Background of allergies</strong></td>
</tr>
<tr>
<td>Rhinoconjuntivitis</td>
</tr>
<tr>
<td>Drug allergy</td>
</tr>
<tr>
<td>Bronchial asthma</td>
</tr>
<tr>
<td>Food allergy</td>
</tr>
<tr>
<td>Family history of atopy</td>
</tr>
<tr>
<td>Evolution of symptoms in months</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
</tr>
<tr>
<td>Dysphagia</td>
</tr>
<tr>
<td>Food impaction</td>
</tr>
<tr>
<td>Pyrosis</td>
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<tr>
<td>Chest pain</td>
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<tr>
<td>Vomiting</td>
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<tr>
<td>Weight loss</td>
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<tr>
<td><strong>Endoscopy</strong></td>
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<tr>
<td>Oesophageal rings</td>
</tr>
<tr>
<td>Mucosa of standard appearance</td>
</tr>
<tr>
<td>Hiatus hernia</td>
</tr>
<tr>
<td>Oesophageal stenosis</td>
</tr>
<tr>
<td>Mean of eosinophils found</td>
</tr>
</tbody>
</table>

Source: Lucendo et al., 2013.13

3. Involvement of allergenic environmental factors,24,25
including several foods.26,27

4. The eradication of the Helicobacter pylori (H. pylori)
which alters immunity to a lower allergenic tolerance,
to the extent that an inverse relationship between the
rate of H. pylori and the presence of eosinophilia has
been demonstrated.28

5. Correlation between the use of antibiotics in the first few
years of life and the increase in allergic and inflammatory
diseases, specifically EoE.29,30

6. Association between EoE, connective tissue diseases and
other auto-immune diseases.31

Physiopathology

Eosinophilic tissue infiltration is the common characteris-
tic of allergic inflammatory diseases such as asthma, atopic
dermatitis, allergic rhinitis, anaphylaxis to foods or gastroin-
testinal eosinophils. EoE is characterised by an infiltration
of eosinophils in the oesophagus, the only organ in the
gastrointestinal tract devoid of these cells. Although its
aetiology is not completely known, the participation of
external food and air-borne allergens, with a genetic base, is
recognised.

This was the suspected view because elimination of
food allergens with elemental diets leads to up to 90.8%32
remission of the disease and because new cases have been
detected after immunotherapy to egg and milk33,34 and
in times of higher pollen density.35–36 This confirms that
airborne allergens are potential inducers of EoE and are
responsible for the disease remaining in patients who do not respond to diets which exclude 6 foods. It has been speculated that genetic modifications to foodstuffs and crops which were initiated in the 90s or the changes in food processing has contributed to the development of this new allergic disease. \(^\text{12}\)

EoE is the result of a reaction of hypersensitivity to food antigens. In EoE, the patient develops the disease when they no longer tolerate food or environmental allergens, which they previously had no reaction to. The loss of this tolerance is measured by the T-helper 2 lymphocytes and activated in the oesophagus by both IgE mediated and IgE non-mediated pathways.

The antigen forms a union with the specific IgE antibody and produces a rapid degranulation of mast cell and basophil preformed mediators where histamine is predominant and may be responsible for the increase of oesophageal contractility in EoE.

This rapid initial phase is followed by a slow one in which there is infiltration or inflammation by cells, including eosinophils.

80% of patients with EoE present this type of IgE mediated reactions to food allergens, which is confirmed by testing specific IgE levels to a food or by prick tests. However, only 15% would suffer from anaphylaxis reactions to these foods. This suggests that it is possible that inflammation of IgE-mediated eosinophils only presents in the oesophagus, as occurs in the oral allergy syndrome, and as a result no general symptoms occur.

In non IgE mediated or delayed reaction allergic hypersensitivity, antigens stimulate the T-helper 2 cells, which engage inflammatory cells with an increase of IL-4, IL-5 and IL-13 interleukins. IL-13 increases the production of eotaxin-3 which causes the migration of eosinophils to the oesophagus, a critical stage in its remodelling and fibrosis. It also causes the migration of TGF-beta which increases the production of collagen, fibronectin and other extracellular matrix proteins, leading to fibrosis and hypertrophy of the smooth muscle, which in turn lead to symptoms of dysphagia and impactions.

These alterations cause the following histopathological changes: hyperplasia of the basal layer of the epithelium, fibrosis of the plate from the increase in collagen deposits, hyperplasia of smooth muscle tissue and increased vascularisation (Fig. 1). This histological remodelling of the oesophagus correlates with the symptoms observed in patients affected by EoE.

**Natural History**

EoE is a chronic, progressive disease which if left untreated leads to irreversible structural damage to the oesophagus. This risk doubles every ten years of the disease if left untreated. \(^\text{8}\)

Inflammation is the initial stage of the disease seen in children who present with GERD symptoms, whilst in teenagers and adults, the most predominant symptoms are dysphagia and impactions and these indicate a more advanced stage caused by the resulting progressive fibrosis (Fig. 2).

Damage to the oesophagus or stenosis reported in 30%-80% of cases and the limitation of the oesophagus wall compliance present in 70% of cases are the underlying causes of dysphagia and impactions.

In this advanced stage patients have great difficulty swallowing and repeatedly attend the emergency services for impaction with a risk of perforation when endoscopy is used as a therapy, due to the fragility of the oesophagus. \(^\text{17}\) The patient’s quality of life progressively lowers and there is a risk of malnutrition due to the restriction of foods for fear of impactions. \(^\text{38}\)

**Clinical Presentation**

EoE symptoms vary with age. In children under 2 the most characteristic symptom is difficulty in feeding which leads to lack of growth and typical reflux symptoms. In contrast, school age children are more likely to present with vomiting, abdominal pain and regurgitation. Otteson et al. \(^\text{39}\) reported that the most common symptom in 92 children with EoE was coughing (46%), followed by dysphonia (38%) and croaking (28%), which are standard symptoms in an ENT unit. Dysphagia and food impaction are prevalent symptoms in teenagers and adults (Table 2).

Chronic sinusitis, dysfunction of the Eustachian tube, sleep alterations, dysphonia and subglottic stenosis were present in patients with EoE, which suggests that they are another sign of a systemic inflammatory disease. \(^\text{40,41}\) It is of note that over 30% of children with EoE require ENT surgery. \(^\text{41}\) Comorbidities with allergic diseases, with which they share a physiopathological mechanism, range from 50% to 80%. We should suspect an EoE in those children who take a long time eating and whose parents say “they make the food into balls”. In adults, the typical symptom is
that of a young person with repeated impactions caused by small volume, non sharp foods (rice, pills and bread), many of which are spontaneously resolved. Patients usually improve the act of swallowing with carbonated drinks and avoid crumbly foods. They also develop compensatory food and postural mechanisms to prevent impactions and avoid social events for fear of impaction. One adaptation into Spanish of the quality of life questionnaire shows that fear of food impaction is what most concerns those affected\(^\text{43}\) and reflects the genuine social impact of this condition.

### Diagnosis

This disease necessitates a multidisciplinary approach involving ENT specialists, gastroenterologists, allergologists, paediatricians and pathologists (Fig. 3).

There may also be a large variety of endoscopic findings in EoE patients, with the following 2 phenotypes as outstanding: inflammatory (longitudinal folds, exudate or whitish platelets, loss of vascularisation or paleness, crepe mucosa

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**Table 2** Predominant Symptoms According to Patient Age With EoE.

<table>
<thead>
<tr>
<th>Children&lt;2</th>
<th>Children between 2 and 11</th>
<th>Children&gt;12 years old and adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reject food</td>
<td>Vomiting</td>
<td>Dysphagia</td>
</tr>
<tr>
<td>Dribbling</td>
<td>Abdominal pain</td>
<td>Pharyngeal pouch</td>
</tr>
<tr>
<td>No weight gain</td>
<td>Pyrosis</td>
<td>Food impactions</td>
</tr>
<tr>
<td>GERD symptoms that do not respond to treatment</td>
<td>Regurgitation</td>
<td>Increased salivation</td>
</tr>
<tr>
<td></td>
<td>Very slow feeding</td>
<td>Slow feeding</td>
</tr>
<tr>
<td></td>
<td>Anorexia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Early satiety</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increased salivation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cough</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dysphonia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Croaking</td>
<td></td>
</tr>
</tbody>
</table>

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**Figure 2** Natural, clinical endoscopic evolution, of the EoE with no treatment.

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**Figure 3** Multidisciplinary team involved in EoE patient management.
which lacerates easily when an endoscopy is performed, and normal appearance in 17%) and stenotic (fixed or temporary concentric rings, stenosis, narrowing)\textsuperscript{44,45} (Fig. 4). Hirano et al.\textsuperscript{44} created an endoscopic classification system which groups major and minor characteristics together (Table 3).

Diagnosis of the disease is based on a graded procedure which begins with carrying out oesophageal biopsies in patients who present compatible clinical symptoms. According to the latest consensuses,\textsuperscript{3} biopsy of the oesophagus is recommended for all patients who present with dysphagia with no clear oropharyngeal cause. This is particularly relevant for ENT specialists who frequently attend patients with this symptom. Normally these examinations are carried out in the digestive endoscopy services, which involves patient referral and loading to a different service to the one which made the suspected diagnosis and it also involves sedation with its consequential morbidity. We now suggest that the role of the ENT specialist in carrying out these biopsies with transnasal oesophagoscopy be performed in-office under local anaesthesia with a subsequently lower consumption of resources and less morbidity for the patient. In the clinical trials conducted by our group (clinical trial 298, 07/04/2014) we attempted to compare the reliability of oesophageal brush cytology to biopsy in the follow-up of EoE, aimed at minimising the most serious adverse effects (risk of perforation).

If 15 or more eosinophils per high power field are found in the biopsy, other causes of oesophageal eosinophilia must be ruled out (Table 4).

Biopsies will be carried out regardless of the appearance of the oesophagus, since a normal appearance does not rule out the disease, although if its appearance has changed this is highly specific (90\%–95\%). EoE is very patchy, which means that at least 2–4 biopsies in 2 different locations are recommended, usually proximal and distal.\textsuperscript{3} A sample from pathological looking regions are intended for biopsy. With 6–9 biopsies sensitivity is approximately 100\%.\textsuperscript{44,46}

In the case of oesophageal eosinophilia, it is recommended that at least one biopsy be taken by the Gastronenterology Service, of the antrum and duodenum, to exclude other possible causes of oesophageal eosinophilia such as celiac disease or gastrointestinal eosinophilias.\textsuperscript{44,45}

Less invasive tests than oesophageal biopsy are being developed. Among them is the string test, an adaptation of the enterocol test which consists of a gelatine capsule that is eliminated from the body in one hour\textsuperscript{37} and the cytosponge, which is a gelatine capsule which is left in the gastric cardia and which collects a sample of oesophageal mucosa. This is currently used in the diagnosis of Barret’s oesophagus.\textsuperscript{48}

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**Figure 4** Endoscopic appearance of most frequent findings of the EoE. (A) and (B) accumulation of eosinophils in the upper layers of the oesophagus; (C) circular rings; (D) oesophageal impaction with food ball; (E) after deimpeaction, oesophageal stenosis is visible; (F) longitudinal furrows; (G) oesophageal trachealisation; (H) tears; (I) longitudinal furrow.
Eosinophilic Esophagitis: A Relevant Entity

Table 3 Endoscopic Classification of EoE.

<table>
<thead>
<tr>
<th>Major criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Trachealisation</strong></td>
</tr>
<tr>
<td>Grade 0: none</td>
</tr>
<tr>
<td>Grade 1: slight (subtle circumferential edges)</td>
</tr>
<tr>
<td>Grade 2: moderate (different rings which do not prevent the passage of the standard adult endoscopy)</td>
</tr>
<tr>
<td>Grade 3: severe (marked rings which prevent the passage of the standard adult endoscopy)</td>
</tr>
<tr>
<td><strong>B. Exudate</strong></td>
</tr>
<tr>
<td>Grade 0: none</td>
</tr>
<tr>
<td>Grade 1: slight (&lt;10% of the oesophageal surface area)</td>
</tr>
<tr>
<td>Grade 2: severe (&gt;10% of the oesophageal surface area)</td>
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<tr>
<td><strong>C. Furrows</strong></td>
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<tr>
<td>Grade 0: absent</td>
</tr>
<tr>
<td>Grade 1: present</td>
</tr>
<tr>
<td><strong>D. Oedema (loss of vascularisation)</strong></td>
</tr>
<tr>
<td>Grade 0: absent</td>
</tr>
<tr>
<td>Grade 1: present</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Minor criteria</th>
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</thead>
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<tr>
<td><strong>A. Oesophagus with mucosa in crepe paper (fragility)</strong></td>
</tr>
<tr>
<td>Grade 0: absent</td>
</tr>
<tr>
<td>Grade 1: present</td>
</tr>
</tbody>
</table>

Source: Hirano et al. 44

Table 4 Diseases Which May Cause Oesophageal Eosinophilia.

<table>
<thead>
<tr>
<th>Causes of oesophageal eosinophilia</th>
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<tbody>
<tr>
<td>Eosinophilic oesophagitis which responds to PPI</td>
</tr>
<tr>
<td>Eosinophilic gastroenteritis</td>
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<tr>
<td>Celiac disease</td>
</tr>
<tr>
<td>Crohn's disease</td>
</tr>
<tr>
<td>Infections</td>
</tr>
<tr>
<td>Hypereosinophilic syndrome</td>
</tr>
<tr>
<td>Acalasia</td>
</tr>
<tr>
<td>Hypersensibility to drugs</td>
</tr>
<tr>
<td>Pemphigus</td>
</tr>
<tr>
<td>Connective tissue disease</td>
</tr>
<tr>
<td>Graft-versus-host disease</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
</tr>
</tbody>
</table>

Differential Diagnosis

Differential diagnosis of EoE is mainly carried out with PPI respondent oesophageal eosinophilia, 49,50 recently reported as a separate entity, corresponding to over 30% of cases 51 (Fig. 5). For this reason, an 8 week treatment with high dose PPI is administered. Of those patients who histologically and clinically improve, approximately 70% correspond to the classical GERD, confirmed by compatible pH impedancemetry (GERD with oesophageal eosinophilia) and the remaining 30% with the entity called non GERD PPI respondent oesophageal eosinophilia. 52 EoE and GERD are not exclusive diseases and their interactions may be complex.

This appears to be due to the fact that the PPI are not just inhibitors of gastric acid production but also present anti-inflammatory effects and probably due to this action, achieve improvement in both entities. The eosinophilia presenting in GERD is moderate, with under 7 eosinophils per high power field. These are usually located in the distal region of the oesophagus. The presence of acid in the oesophagus stimulates chemotaxis of the eosinophils by

![Figure 5] Diagnostic algorithm of the oesophageal eosinophil.
complex mechanisms which are still fairly unknown. Both entities may be made stronger. The eosinophils may lead to GERD on avoidance of normal clarification of the oesophagus. Acid in the oesophagus may include the engagement of inflammatory cells such as mast cells and its mediators.

The new PPI respondent EoE entity which does not show up GERD by pH-metry is considered as a previous step towards EoE, in which the PPI do not act against acid but against the inflammation present in the oesophagus and therefore improve the patient’s symptoms and resolve the eosinophilia. The contact of the acid and pepsin in the oesophagus seems to increase its permeability to molecules over 90 kDa, which are all food allergens.

Remote exposure to PPI in infancy may initiate food allergy which leads to EoE and which may later respond to the anti-inflammatory effect of the previously described PPI.

**Treatment**

The aim of treatment is threefold: to improve clinical symptoms, eliminate eosinophilia from the oesophagus and prevent complications of stenosis or impaction. The symptoms themselves cannot be considered as a disease improvement marker or as success of treatment administered. This is due to the fact that the patient may compensate for their symptoms by changing their diet, their eating habits and their lifestyle. Published symptom improvement questionnaires correlating with histological improvements have therefore not yet been validated.

The reduction of eosinophils of between 0 and 6 eosinophils/field, the reduction of eosinophils of over 90% or the presence of baseline hyperplasia is considered to be the histological response.

Treatment is based on 3 pillars: corticosteroids, diet and oesophageal dilations. Corticosteroids and diet are first line treatment and recommended to equal degree. The choice of one or the other must be discussed with the patient and will depend on age, the severity of the disease, lifestyle and the ability of the patient and their family to adhere to a diet which may be complicated, or on the long-term secondary effects of the corticosteroids.

**Medical Treatment: Corticosteroids**

Topical swallowed steroids are the only drugs which have proven to be effective in both children and adults, with cure rates of between 50% and 80%. However, to our knowledge and up until now, they have not yet received approval from the FDA. Presentations used are aerosols or nasal drops used in asthma and in rhinoconjunctivitis, which are swallowed to cover the oesophagus and produce a topical effect. There is a clinical and histopathological response when using them for between 1 and 3 months of approximately 75% in children and 62% in adults, although no significant improvement in symptoms has been appreciated in adults.

Both fluticasone (88–440 μg/day in children; 880–1760 μg/day in adults) and budesonide (1 mg/day in children and 2 mg/day in adults) have proven to be effective. The patient is instructed to put the dose of the aerosol in their mouth, then swallow and not to eat for 30–60 min. Budesonide aqueous (1 mg/2 ml) may be mixed with 5 mg of sucralse to create a consistency called ‘viscous budesonide’ which is more agreeable to swallow and is used in both children and adults.

New effervescent capsules are being developed to provide better adherence to the oesophagus, preventing fast elimination through oesophageal motility.

From 5% to 30% of patients will present with the complication of oesophageal candidiasis, although the figure may be greater as often this is found in asymptomatic patients when oesophageal endoscopy is performed.

Treatment with systemic corticosteroids is reserved for occasional situations in which the patient requires fast relief from their symptoms and has not responded to topical corticosteroids. Research into these new anti-eosinophilic drugs is currently very active and promising results may develop.

**Treatment by Diet**

It is known that EoE is a chronic inflammatory, immunomediated disease triggered by allergens in food for the majority of patients. Treatment must be aimed at identifying the food allergen which is causing the oesophagitis, the exclusion of which improves the histology and clinical symptoms of the patient and maintains this over time. Therapy with dietary treatment is as effective as corticosteroids and prevents any side effects of long-term corticosteroid treatment. There are 3 dietary treatment strategies with different outcome rates. Selecting one or other of these will depend on the patient’s age, the risk of malnutrition by a restrictive diet and finally the possibility, skill and acceptance of one type of diet. In accordance with the latest consensuses, confirmation that one type of food is the cause of the EoE is based on the fact that histologically the disease recurs when the said food is re-introduced, after improvement from having avoided it for 4–8 weeks (Table 5).

**Elemental Diet With Amino Acids**

In this diet proteins are eliminated and the source of nitrogen is administered in the form of amino acids, thereby eliminating all antigens from the diet. The main disadvantage of this diet is that it is very difficult to accept socially, the taste is unpleasant and children will usually require nasogastric tube feeding. It is also expensive and not normally financed.

**Empirical Diet With Elimination of Common Allergens**

The aim of this diet is to avoid the impracticality of the elemental diet and the low specificity and sensitivity of diets
guided by allergy tests. Foods which most frequently lead to allergies are milk, followed by wheat, egg, pulses, nuts, fish and seafood. There may be more than one food that causes EoE.

There are other more restrictive diets where all cereals are eliminated and pseudocereals are allowed: quinoa, amaranth and buckwheat. This diet is similar to the elemental one with the difference that, despite being very restrictive, meats, vegetables and fruit are allowed. Nutritional assessment by a dietician is recommended in order to avoid nutritional deficiencies. One of the most popular diets is the one where 6 goods groups are avoided (egg, milk, wheat, pulses, nuts, fish and seafood). No unanimously agreed protocol exists for reintroduction of foods. In general, this will depend on clinical suspicion and family dietary habits and will be agreed to with the patient or family member.

Elimination diets of suspicious foods last between 4 and 8 weeks, which is considered sufficient time for the elimination of eosinophils from the oesophagus. After this, histological confirmation is required by means of multiple oesophageal biopsies, every 6 or 8 weeks, with a total of 5–10 digestive endoscopies, which until now have been performed by gastroenterologists. After finding the food which is responsible for the condition and confirming that its reintroduction leads to recurrence of the disease, this particular food must be avoided indefinitely. The need for such a high repetition of endoscopies limits this dietary intervention and the possibility is being studied for performing histological studies which would not require digestive endoscopy. A study is being conducted to discover whether biopsies performed in the ENT office would be as valid as those performed by gastroenterologists and also whether brush cytology could produce an equally valid outcome, minimising the complications of a biopsy of a very fragile oesophagus. This would be particularly useful in follow-up of these patients.

In one study with children, just by eliminating milk, which is the most frequent cause of EoE, a 65% improvement was obtained.64 Highly hydrolysed cow’s milk formulas have proven to be successful alternatives for patients where milk is the cause of allergy.65

**Elimination Diet Based on Allergy Tests**

Foods are eliminated from these diets after completing tests for allergies: immunoassays for specific food IgE, prick tests and atopy patch test. Diets resulting from these have not proven to have a high improvement rate, which is around 45%, partly due to the lack of uniformity in the various studies. It has also been postulated that allergy to foods does not necessarily correspond to known and tested food antigens. Multicentric studies are needed and at present this diet is recommended in centres with advanced allergology. However, the role of the allergologist is necessary due to the frequent concurrence of other allergic diseases and, in particular, IgE allergy measured by other foods which requires the avoidance of certain foods and instructions for the case of a possible anaphylaxis. In many centres it is the allergologists who coordinate the management of these patients.

**Oesophageal Diations**

Dilations are the treatment used to alleviate dysphagia, but they do not act on the underlying inflammation and should be reserved for patients who do not respond to medical treatment. The desired diameter of the oesophagus is from 15 mm to 18 mm.65 Topical corticosteroids will be administered in addition to dilation to reduce oesophageal inflammation. Dilations should be performed with the greatest of care and a recommended depth of under 3 mm per session. Patients may present with chest pain in 75% of cases.65 There is a 2% risk of perforation.

The suspected diagnosis of patients presenting at the emergencies services with non sharp food impactions should be EoE. Deimpaction should be carefully carried out and is generally performed in the majority of centres by a gastroenterologist (flexible endoscopy). In the case of rigid oesophagoscopy, precautions must be extreme since the oesophagus may be greatly weakened, stenotic and very easily eroded.

All cases, even if resolved in the emergency services, must later be referred for biopsies of the oesophagus to rule our EoE.

Spontaneous resolution of impaction may be supported by calming down the patient, manoeuvres involving posture, advice on diet and speech therapy.

**Conclusions**

EoE is a chronic allergic disease with symptoms of oesophageal dysfunction, from the infiltration of eosinophils in its wall. There are more than 15 eosinophils per field. After ruling out other causes of eosinophilia, EoE responds particularly well to PPI. EoE affects both children and adults, with a natural evolution from a reversible inflammatory phenotype to a permanent stenotic phenotype. The incidence of this disease is exponentially increasing and it has been suggested that the general increase in allergies is the parallel cause. 80% of patients will present with concomitant allergic diseases (asthma, rhinitis, atopia and food allergies). Prevalence is as high as in other diseases such as Crohn’s disease.

The clinical symptoms most suggestive of this disease are anorexia and vomiting in children under 2, abdominal pain and vomiting in children under 11 and impactions and dysphagia in adolescents and adults. Adults suffer most frequently from food impactions. Over half of patients with dysphagia with no clear oropharyngeal cause will present with an EoE. 80.9% of cases are resolved with an elemental diet in which the food antigens were eliminated. Food allergies do not necessarily correspond with known food antigens. For this reason, there is not necessarily any correlation with allergy tests. The effect of the allergy compared with airborne allergens may be the cause of no improvement in elimination diets and of seasonal decline. Diagnosis requires a total of 4–8 biopsies of the regions which are proximal, medial and distal to the oesophagus after ruling out other causes of oesophageal eosinophilia. Of those patients who respond to PPI, 70% will correspond to GERD and another 30% to the non acid dependent PPI respondent EoE.
The coincidence of the high incidence of EoE in pediatric patients who present with an inflammatory disease in the ORL area is conducive to ENT specialists considering this disease.

EoE treatment is based on 3 pillars: corticosteroids which are swallowed, exclusion diets and oesophageal dilations in cases presenting with stenosis. Empirical exclusion diets have a 72% success rate on eliminating the most antigenic foods: milk, wheat, egg, pulses, nuts, fish and seafood. Multiple confirmatory biopsies responding to treatment hinder this therapeutic focus both on an institutional level and a personal level for the patient. Milk is responsible in 65% of cases, and therefore to begin with a diet which eliminates milk is a valid alternative.

ENT specialists must acknowledge this disease because it is the cause of dysphagia, impactions and probably because it justifies cases of laryngitis, dysphonias and chronic coughing which does not respond to treatment that includes PPI. Transnasal oesoscopy and the familiarity of the ENT specialists with brush biopsy procedures results in a diagnosis and follow-up which may be more cost-effective and with lower morbidity.

Conflict of Interests

The authors have no conflict of interests to declare.

References

Eosinophilic Esophagitis: A Relevant Entity


