Eosinophilic Esophagitis
“New kid on the block”

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Eosinophilic Esophagitis

Topics

• History
• Incidence
• Symptoms
• Definition
• Diagnosis
• Therapy
• Natural history
Eosinophilic Esophagitis

History

• Attwood 1993 (Dig Dis Sci 1993; 38: 109-16)
  - 12 patients with dysphagia, no GERD (endoscopy/pH-testing)
  - Intra-epithelial eosinophils (>20 eos/hpf), squamous intra-epithelial hyperplasia

• Straumann 1994 (Schweiz Med Wochenschr 1994;124: 1419-29)
  - 10 patients with intra-epith. eos and dysphagia
  - Endoscopic abnormalities in the esophagus:
    “white structures, partly finely reticular or plaque-like in 9/10 patients, one had a web and another a ring.”

• In the following years a discussion started on the overlap between EoE, GERD and an “intermediate” condition, PPI-REE
Eosinophilic Esophagitis

Incidence

- Netherlands
  - 674 pats (538 adults) with EoE identified in the PALGA database

EoE incidence highest in 20-29 yr old males (3.23/100,000 persons)

EoE incidence 1.31/100,000 persons in 2010

Eosinophilic Esophagitis
Symptoms

• Dysphagia (80-90%)

• Food impaction (33-54%)

• Heartburn, chest pain, upper abdominal pain

• Atopy:
  • Rhino-conjunctivitis (57%)
  • Asthma (37%)
  • Food allergy (46%)
  • Atopic dermatitis
Esophageal Eosinophilia
Differential diagnosis

- GERD
- Eosinophilic gastrointestinal diseases
- Hypereosinophilic syndrome
- Celiac disease
- Crohn’s disease
- Infection (parasites)
- Achalasia
- Drug hypersensitivity
- Vasculitis
- Graft vs. host disease
- PPI use
### Esophageal Eosinophilia

#### Overlap EoE with GERD

<table>
<thead>
<tr>
<th>Factors</th>
<th>EoE</th>
<th>GERD</th>
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<tbody>
<tr>
<td><strong>Dominant symptom</strong></td>
<td><strong>Dysphagia</strong></td>
<td><strong>Heartburn Regurgitation</strong></td>
</tr>
<tr>
<td>Food impaction</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Gender</td>
<td>&gt;&gt; Male</td>
<td>Male = female</td>
</tr>
<tr>
<td>Age</td>
<td>Children, young adults</td>
<td>Middle-age</td>
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</tbody>
</table>

Eosinophilic Esophagitis
Definition

EoE is defined by:

- Symptoms related to **esophageal dysfunction**
- Eosinophil-predominant inflammation on esophageal biopsy, characteristically consisting of a peak value of $\geq 15$ eosinophils per high-power field (eos/hpf)
- Mucosal eosinophilia is isolated to the esophagus and persists after a **PPI trial**
- **Secondary causes** of esophageal eosinophilia excluded
- Response to treatment (dietary elimination, topical steroids) supports, but is not required for the diagnosis
1. Clinical characteristics
   • Typical patient: atopic non-Hispanic white male (m:f ratio: 3:1) presenting in childhood or during the 3rd or 4th decade
   • Symptoms: dysphagia, food bolus obstruction

2. Endoscopy
Eosinophilic Esophagitis
Endoscopic findings

Eosinophilic Esophagitis
Endoscopic classification and grading

Endoscopic assessment of the oesophageal features of eosinophilic oesophagitis: validation of a novel classification and grading system

Ikuo Hirano,¹ Nelson Moy,¹ Michael G Heckman,² Colleen S Thomas,² Nirmala Gonsalves,¹ Sami R Achem³


- Endoscopic videos from 25 EoE patients and controls reviewed by 21 gastroenterologists
- Proposed system included the grading of
  - 5 major features: rings, furrows, exudates, edema, stricture
  - 3 additional features: narrow calibre esophagus, feline esophagus and crepe paper esophagus
Eosinophilic Esophagitis
Endoscopic classification and grading

(F) Transient oesophageal rings (feline oesophagus)

Time 0

Time 1 (with insufflation)

Hirano et al. Gut 2013; 62: 489-95
Eosinophilic Esophagitis
Endoscopic classification and grading

<table>
<thead>
<tr>
<th>Endoscopic abnormality</th>
<th>N (%) of pairwise agreement (N = 5250)</th>
<th>k (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed rings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw score</td>
<td>2933 (56%)</td>
<td>0.40 (0.29 to 0.54)</td>
</tr>
<tr>
<td>Mild/moderate collapsed</td>
<td>3707 (71%)</td>
<td><strong>0.50 (0.35 to 0.64)</strong></td>
</tr>
<tr>
<td>Exudates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw score</td>
<td>3396 (65%)</td>
<td>0.46 (0.33 to 0.58)</td>
</tr>
<tr>
<td>Mild/severe collapsed</td>
<td>4006 (76%)</td>
<td><strong>0.51 (0.37 to 0.67)</strong></td>
</tr>
<tr>
<td>Furrows</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw score</td>
<td>3198 (61%)</td>
<td>0.38 (0.28 to 0.50)</td>
</tr>
<tr>
<td>Mild/severe collapsed</td>
<td>4216 (80%)</td>
<td><strong>0.54 (0.37 to 0.70)</strong></td>
</tr>
<tr>
<td>Oedema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw score</td>
<td>2682 (51%)</td>
<td>0.23 (0.13 to 0.35)</td>
</tr>
<tr>
<td>Mild/severe collapsed</td>
<td>4278 (81%)</td>
<td><strong>0.43 (0.19 to 0.59)</strong></td>
</tr>
<tr>
<td>Stricture</td>
<td>4168 (79%)</td>
<td></td>
</tr>
<tr>
<td>Feline oesophagus</td>
<td>3578 (68%)</td>
<td>0.15 (0.03 to 0.33)</td>
</tr>
<tr>
<td>Narrow calibre oesophagus</td>
<td>3896 (74%)</td>
<td>0.30 (0.20 to 0.41)</td>
</tr>
<tr>
<td>Crepe paper oesophagus</td>
<td>4852 (92%)</td>
<td><strong>0.58 (0.05 to 0.77)</strong></td>
</tr>
</tbody>
</table>
1. Clinical characteristics
   • Typical patient: atopic non-Hispanic white male (m:f ratio: 3:1) presenting in childhood or during the 3rd or 4th decade
   • Symptoms: dysphagia, food bolus obstruction

2. Endoscopy
   • Endoscopic EREFS Score system

3. Esophageal biopsies
   • 2-4 biopsies taken from prox. and dist. esophagus (≥15 eos/hpf)
   • Additional biopsies from antrum and duodenum in pats. with gastric or small intestinal symptoms
4. Diagnostic challenge
   • 2-months course of PPIs followed by endoscopy + biopsies to exclude PPI-Responsive Esophageal Eosinophilia (PPI-REE)
   • Symptomatic and histologic response to PPIs (30-50%)
   • PPI-REE does not establish a diagnosis of GERD!!!
Eosinophilic Esophagitis
Diagnostic algorithm

Eosinophilic Esophagitis
Treatment

1) Pharmacologic treatment
   - Topical steroids:
     • Fluticasone propionate 500 µg BID
     • Budesonide 1 mg BID (viscous formulation)

   ➔ Initial duration of treatment with topical steroids: 8 wks.
   ➔ Avoid eating or drinking for 30-60 min. after intake
   ➔ Candida esophagitis in 5-30% of pats.

   - Systemic prednisone if topical steroids not effective or if rapid improvement of symptoms is required

   - Alternatively: longer course or higher dose of topical steroids

2) Dietary treatment
   a) **Total elimination** of all food allergens with elemental or amino-acid based formula
   b) **Targeted elimination diet** guided by allergy testing, typically skin prick testing or patch testing
   c) **Empiric six-food elimination diet** removing 6 most common known foods: soy, egg, milk, wheat, nuts, and seafood

=> Drawback total elimination diet: elemental diets costly (feeding tubes) and impact QoL
=> Empiric diet: resolution in 74% of pats.
=> Wheat (60%) and milk (50%) most common triggers
3) Endoscopic treatment
   • Dilation for focal strictures and narrow-caliber esophagus
   • Dilation should be combined with medical or dietary treatment
   • Dilation technique
     - Method of dilation: balloon or bougie dilation?

Dilation

radial + longitudinal force

radial force
Eosinophilic Esophagitis Treatment

3) Endoscopic treatment
   • Dilation for focal strictures and narrow-caliber esophagus
   • Dilation should be combined with medical or dietary treatment
   • Dilation technique
     - Method of dilation: bougie dilation (??)
     - Start dilation at a diameter slightly larger than size of endoscope
     - Maximum progression in diameter: max. 3 mm
     - Ultimate target of dilation 16-18 mm
   • Complications: post-procedural chest pain (75%), perforation (0.3%) and bleeding (1%)

• EoE is a **chronic disease**, with no evidence for progression to hypereosinophilic syndrome or malignancy

• A subgroup of patients may progress from an inflammatory to a **fibrotic process** (optimize medical treatment!)

• **EoE recurs** almost always after withdrawal of treatment (limited studies)

• **Maintenance treatment** should be considered:
  - Topic steroids and/or dietary restrictions
  - Intermittent esophageal dilation ("on demand")

*Straumann and Schoepfer. Gut 2014; 63: 1355-63*
Eosinophilic Esophagitis

Conclusions

• GERD, PPI-REE and EoE are the three most common conditions when esophageal eosinophilia is detected

• A PPI trial is important for distinguishing EoE from PPI-REE

• The first-line treatment of EoE includes swallowed topical steroids or dietary elimination

• Endoscopic dilation is an effective treatment for strictures and narrow-caliber esophagus in EoE

• Maintenance treatment (medication, diet, dilation) indicated in EoE patients