EOSINOPHILIC ESOPHAGITIS: ENDOSCOPY AND MANAGEMENT

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Increasing awareness of EGID

During the last two decades the annual number of papers has been exponentially increasing.

**EGID** is of multidisciplinary interest, the papers emanating from the following specialties (decreasing order):

- **Gastroenterology**
- Pathology
- Allergy / Immunology
- ENT and Surgery

The eosinophil cell

- Described in peripheral blood by Paul Ehrlich in 1879. Considered "a good guy" and a positive prognostic sign: "the dawn of healing"
- Developes in bone marrow in about 8 days
- Colonize peripheral tissue in about 8 hours

EOSINOPHILS IN THE GASTROINTESTINAL MUCOSA

- Transcription factors: IL-5, IL-13, GATA-1
- Lamina propria
- Cecum and Appendix
- Gastrointestinal homeostasis: antimicrobial effects

Eosinophil contain:

- major basic protein (MBP)-1/2
- eosinophil cationic protein (ECP)
- eosinophil-derived neurotoxin (EDN)
- eosinophil peroxidase (EPO)

Inflammatory Bowel Disease
- Celiac Disease
- Helicobacter infection
- Food Allergy
- Gastrointestinal Eosinophilic Diseases
- adhesion molecules
- vascular permeability
- mucus secretion
- smooth muscle contraction

Padigel UM, Infect Immunol 2006
Eosinophilic Esophagitis

History

  - Esophageal intraepithelial eosinophils correlated with reflux on pH probe
  - Number of eosinophils found during study were low (<10 per 400x microscopic field)
  - Reflux becomes the assumed diagnosis when eosinophils found in esophageal biopsies
Eosinophilic Esophagitis

History

  - Comparison of a series of adults with esophageal eosinophilia to patients with gastroesophageal reflux

  - Reported 13 males with eosinophilic esophagitis and their response to oral corticosteroids
Eosinophilic Esophagitis

History

1982: Esophageal eosinophils are a diagnostic criterion for gastroesophageal reflux disease

1995: Esophageal eosinophils suggest food allergy as a cause of refractory reflux symptoms
“MODERN” DEFINITION

- **EoE** is a chronic inflammatory disorder of the oesophagus characterised by the proton pump inhibitor-refractory accumulation of EoE in eophageal epithelium (15/hpf)

- Dysphagia, vomiting, chest pain, food impaction

- Variable with age

Furuta GT, Gastroenterology 2007
EoE is the only eosinophil-associated gastro-intestinal disorder (EGID) with well-defined and established diagnostic criteria:

- Symptoms related to esophageal dysfunction
- Eosinophil-predominant inflammation on esophageal biopsy, characteristically consisting of a peak value of ≥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 (Table 2)
- A response to treatment (dietary elimination; topical corticosteroids) supports, but is not required for, diagnosis. (Strong recommendation, low evidence)

*Am J Gastroenterol* advance online publication, 9 April 2013; doi:10.1038/ajg.2013.71
EPIDEMIOLOGY

- Reported from all continents except Africa
  - 76 % males (age 14-89 years, mean 38)
  - Hereditary predisposition?  

- **Prevalence**
  - Children: 1/10000 ("The Kalixanda Study")
  - 6.5% of patients undergoing UEGD-endoscopy

- **Incidence**
  - About 10 per 100 000
  - Accelerating togheter with food allergy

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Ronkainen J et al. Gut 2007 May;56(5):615-20


Clinical Case

Salvatore, 11 years old

- Allergic asthma
- Parietaria
- Immunotherapy
- **8 years**: admission for suspected meat bolus
- moderate dysphagia to solids
- **10 years**: admission for meat bolus with necessity of endoscopic extraction
- therapy with IPP
- It’s better, but sometimes **dysphagia**
DIAGNOSIS?

SMALL CALIBER ESOPHAGUS

Langdon DE, AJG 2000
STRICTURES AND EoS

- Isolated Esophageal Strictures

- Straumann\(^1\) in longest follow-up (11.5 yrs) for 30 pts with EoS demonstrated strictures in 70% of cases

Straumann A, Gastroenterology 2003
> 1/3 of patients with bolus obstruction has EoE

41 patients undergoing endoscopy due to bolus obstruction

12 patients - no biopsy

29 patients - biopsy taken

14 patients with EoE

ENDOSCOPY ASSESSMENT

- **ADULT**: endoscopic findings with sensitivities of 50-90%
- **CHILDREN**: sensitivities 50-70%
- no specific findings
- 7-10% of EoE with normal appearance
- Crepe Paper Esophagus
- Narrow Calibre Esophagus

Moy N, Gastroenterology 2011
OESOPHAGEAL FEATURES

Interobserver agreement

- limited consensus on how best to characterise the endoscopically-identified oesophageal features

- lack of standardised terminology and grading criteria of EoE

- **7-10%** of EoE with normal endoscopy

- Kim HP et al, meta-analysis of 100 studies reporting EoE findings in **4700** pts with sensibility, specificity and predictive value positive
ATLAS: FURROWS VERTICAL LINE

- FELINE ESOPHAGUS
- TRANSIENT Plication or ring-like
- Disappears upon adequate distension

NO SUGGESTIVE TO EoE

Mild: Subtle circumferential ridges seen on esophageal distension

Moderate: Distinct rings that do not occlude passage of diagnostic endoscope

Severe: Distinct rings that do not permit passage of diagnostic endoscope

GRADE 1
GRADE 2
GRADE 3

Kwiatek MA, Gastroenterology 2011
ATLAS : FIXED ESOPHAGUS RING

56-81% of agreement

Mild: Vertical lines without visible depth
GRADE 1

Severe: Vertical lines with clear depth (indentation) into the mucosa
GRADE 2

NARROW CALIBER ESOPHAGUS

ATLAS : EXUDATES PLAQUES

- Poor agreement for endoscopic diagnosis
- Not improve with narrow band imaging
- 56-85% of agreement

Mild: White lesions occupying < 10% of the esophageal surface area

Severe: White lesions involving ≥ 10% of surface area of esophagus

Peery AF, Clin Gastroenterol Hepatol 2011
- MUCOSAL FRAGILITY OF ESOPHAGUS

- LACERATION UPON PASSAGE OF DIAGNOSTIC ENDOSCOPY

Endoscopically-detected oesophageal features of Eosinophilic Oesophagitis

NEW CLASSIFICATION

Major features
- Fixed rings (also referred to as concentric rings, corrugated oesophagus, corrugated rings, ringed oesophagus, trachealisation)
  - Grade 0: none
  - Grade 1: mild (subtle circumferential ridges)
  - Grade 2: moderate (distinct rings that do not impair passage of a standard diagnostic adult endoscope (outer diameter 8–9.5 mm))
  - Grade 3: severe (distinct rings that do not permit passage of a diagnostic endoscope)
- Exudates (also referred to as white spots, plaques)
  - Grade 0: none
  - Grade 1: mild (lesions involving <10% of the oesophageal surface area)
  - Grade 2: severe (lesions involving >10% of the oesophageal surface area)
- Furrows (also referred to as vertical lines, longitudinal furrows)
  - Grade 0: absent
  - Grade 1: present
- Oedema (also referred to as decreased vascular markings, mucosal pallor)
  - Grade 0: absent (distinct vascularity present)
  - Grade 1: loss of clarity or absence of vascular markings
- Stricture
  - Grade 0: absent
  - Grade 1: present

Minor features
- Crepe paper oesophagus (mucosal fragility or laceration upon passage of diagnostic endoscope but not after oesophageal dilation)
  - Grade 0: absent
  - Grade 1: present

Multiple biopsies (≥ 3) from various levels (1 biopsy 55 % sensitivity, 5 biopsies ≈ 100 %)

- Biopsies from stomach and duodenum

Disposable biopsy-forceps with spike

1: Duodenum
2: Fundus ventriculi
3: Esophagus lower 1/3
4: Esophagus middle 1/3
5: Esophagus upper 1/3

Cherian  S, Arch Dis Child 2006
Markowitz, JPGN 2011
Esophageal Histology

**Normal:**
- Basal layer ~15% of epithelial height
- Papillary length ~40%
- Minimal (<5) lymphocytes

**Reflux esophagitis:**
- Basal layer 30% of epithelial height
- Papillary length ~90%
- Increased lymphocytes

**Eosinophilic esophagitis:**
- Numerous eosinophils
- Eosinophilic abscess
- Basal cell proliferation (BCP)

S. Mueller, Histopathology 2008
Fibrosis

- little is known about natural history
- it is unclear if the stenosing phenotype is preceded by inflammatory phenotype
- Schoepfer et al, a retrospective analysis of 44 pts

<table>
<thead>
<tr>
<th>DURATION DISEASE</th>
<th>STENOSIS RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 yrs</td>
<td>0</td>
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<tr>
<td>4-6 yrs</td>
<td>37%</td>
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<tr>
<td>5-10 yrs</td>
<td>67%</td>
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</tbody>
</table>

Gastroenterology 2012
Dilation Approach

- Retrospective case series
- Multiple stenosis: Savary bougies
- Better tactile assessment of lumen narrowing
- TTs balloons: better control of radial dilating forces
- Cumbersome and need repositioning for multiple strictures
- Area maximum narrowing and dilation 15-18 mm (severe < 9 mm)

Schoepfer AM, Am J Gastroenterol 2010
Bohm M, Dis Esophagus 2010
Dellon E, Clin Endosc 2010
Safety and potential complications

- esophageal mucosal tears in most cases and rare the perforation
- chest pain or odynophagia
- 14 cases correlated to endoscopy passage and Boerhaave’s syndrome

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient</th>
<th>Clinical scenario</th>
<th>Reason perforation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riou et al.\textsuperscript{a5}</td>
<td>26 y/o male with EoO</td>
<td>Progressive dysphagia with food impaction</td>
<td>Boerhaave’s syndrome</td>
</tr>
<tr>
<td>Kaplan et al.\textsuperscript{a6}</td>
<td>Adult with EoO</td>
<td>N/A</td>
<td>Perforation with passage endoscope</td>
</tr>
<tr>
<td>Prasad and Arora\textsuperscript{a7}</td>
<td>54 y/o male</td>
<td>Chest pain; diagnosed with EoO</td>
<td>Boerhaave’s syndrome</td>
</tr>
<tr>
<td>Eisenbach et al.\textsuperscript{a44}</td>
<td>17 y/o female hx congenital oesophageal stenosis, EoO</td>
<td>Progressive dysphagia</td>
<td>Perforation during dilation</td>
</tr>
<tr>
<td>Liguori et al.\textsuperscript{a48}</td>
<td>32 y/o male with EoO</td>
<td>Total dysphagia with food impaction</td>
<td>Perforation with passage endoscope</td>
</tr>
<tr>
<td>Cohen et al.\textsuperscript{a49}</td>
<td>4 patients</td>
<td>N/A</td>
<td>3 perforations unclear precipitant; 1 Boerhaave’s syndrome</td>
</tr>
<tr>
<td>Straumann et al.\textsuperscript{a50}</td>
<td>17 y/o male, 37 y/o female, 28 y/o female</td>
<td>Food impaction; complete dysphagia; chest pain, hematemesis</td>
<td>(i) and (ii): perforations during removal of food impaction by ENT with rigid scope; (iii): Boerhaave’s syndrome</td>
</tr>
<tr>
<td>Giles et al.\textsuperscript{a51}</td>
<td>12 y/o male</td>
<td>Solid food dysphagia</td>
<td>Boerhaave’s syndrome</td>
</tr>
<tr>
<td>Robles-Medranda et al.\textsuperscript{a52}</td>
<td>9 y/o female</td>
<td>Chest pain and fever; diagnosed with EoO</td>
<td>Boerhaave’s syndrome</td>
</tr>
<tr>
<td>Quiroga et al.\textsuperscript{a53}</td>
<td>24 y/o male with EoO</td>
<td>Severe chest pain</td>
<td>Boerhaave’s syndrome</td>
</tr>
</tbody>
</table>
PATIENT-CENTRED GOAL

- **Oesophageal dilation** has proven effective treatment with relieve patient’s symptoms

- **Head to head trial:**
  
  a) comparision dilation vs steroid therapy with 1-2 yrs of follow-up ?
  
  b) bougies vs TTS balloon dilation ?
  
  c) combination therapy with steroids before or after dilation ? or with PPI ?

Kwiatek MA, Gastroenterology 2011
EVOLUTION OF EoE: PATHOGENESIS

GERD

Dietary or airborne allergens

Eosinophilic oesophagitis with chronic inflammation

Early

Fibrosis

Late

Rings diffuse scarring

Children

Erosive Esophagitis

Adults

EVOLUTION OF EoE: DIAGNOSIS

Eosophageal eosinophilia on biopsy

Assess for all causes of esophageal eosinophilia

Isolated esophageal eosinophilia

PPI trial followed by repeat endoscopy and biopsy

PPI-non-responsive (persistent eosinophilia and symptoms)

PPI-responsive (eosinophilia and symptoms resolved)

EoE (immune-mediated)

Non-GERD PPI-REE (mechanism yet unknown)

GERD with eosinophils (acid-mediated)

Erosive Esophagitis

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The voyage of discovery is not in seeking new landscapes but in having new eyes

Marcel Proust