Eosinophilic Esophagitis: New Disease

Special Presentation for ALGH

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AIMS

• Historical Background
• Definition
• Pathogenesis
• Symptoms
• Endoscopic Findings
• Comparison to Gastroesophageal Reflux
• Treatment
• Natural history of EoE
My first case
AJ

- 10 yrs old, boy
- Abdominal pain
- Features suggestive of FAP
- EGD – Eosinophils in the esophagus
Dillon

- 16 yrs
- Intermittent regurgitation
- No dysphagia
- Has eczema
- No improvement on PPI
- Esophageal biopsy - dense eosinophils
Esophagus

- Hollow, muscular organ
- From Epiglottis (C6) to GEJ (T11/12)
- 10 cm at birth - 25 cm adult
- Wall: mucosa, submucosa, muscularis propria, and adventitia (like rest of GI tract, but has no serosa)
Function of the Esophagus

- Function
- Peristalsis
- Saliva - 500 mls/day
- Liquids and solids

Dysphagia
Gastrointestinal Eosinophils

Normal values, per 400x microscopic field:

- Duodenum (20)
- Colon (Right-20; Left-10)
- Gastric antrum (10)
- Esophagus (0)

Average values obtained from several references
Historical Background

• Rare cases suggestive of eosinophilic esophagitis (EoE) were described over 30 years ago
• Appreciated as a distinct entity since 1995
• Over the last 10 years, the number of reported cases has increased worldwide
Distribution of EoE

- Canada
- United States
- Mexico
- Brazil
- Switzerland
- Spain
- Belgium
- England
- Netherlands
- Italy
- Germany
- France
- Germany
- Israel
- Australia
- Japan
Annual Incidence of EoE in Olten-County Switzerland

2.39 cases/year/100,000 (Range 0-11)
ACH- EoE Clinic

![Bar chart showing data from 2006 to 2013]
A Schematic Representation of the EoE Pathogenesis

EoE  *Consensus Statement 2007*

- Clinicopathologic diagnosis
  - Presence of clinical symptoms related to esophageal dysfunction
    - Dysphagia, Vomiting, Abdominal pain, Heartburn, Feeding difficulty, etc.
  - Isolated esophageal eosinophilia
    - > 15 eos per 40X HPF
    - Histology of remainder of GI tract normal
  - Exclusion of other GI disorders
    - Absence of pathologic GERD
      - Lack of response to PPI therapy or normal pH probe
    - Infection, Crohn’s disease, hypereosinophilic syndrome

Furuta, GT. et al; Gastroenterology 2007; 133:1342-63.
EoE-Revised Consensus Statement 2011-2013

- Chronic, immune/antigen mediated esophageal disease, characterized by symptoms related to eso. dysfunction & histological- eosinophil predominant inflammation
- Feeding Difficulty/ FTT
- GERD like- vomiting
- Abdominal Pain
- Dysphagia/ food impaction

Eosinophilic Esophagitis

Primary Presenting Complaint, by Age

Feeding Disorder 13%
Vomiting 26%
Abdominal Pain 26%
Dysphagia 27%
Food Impaction 7%

Noel RJ, Putnam PE, Rothenberg ME. Eosinophilic Esophagitis. NEJM 2004
Clinical Features

- Male predominance (about 3:1)
- Swallowing problem – adolescents and adults
  - Eating problem in children
- Association with food allergy and atopy
- Chronic condition in adults and children

Furuta, GT. Gastroenterology 2007; 133:1342.
Clinical Features

- Feeding difficulties
- Takes only pureed food
- Learned behavior

Furuta, GT. Gastroenterology 2007; 133:1342.
Coping with dysphagia

• Take long time to finish a meal
• Has a “chaser” with each swallow
• Jump up and down ‘to get food down”
• Cut food into small pieces
• Food impaction

Furuta, GT. Gastroenterology 2007; 133:1342.
Incidence of Atopic Symptoms

<table>
<thead>
<tr>
<th>Feature</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinoconjunctivitis</td>
<td>57.4</td>
</tr>
<tr>
<td>Wheezing</td>
<td>36.8</td>
</tr>
<tr>
<td>Food allergy*</td>
<td>46</td>
</tr>
<tr>
<td>FH atopy</td>
<td>73.5</td>
</tr>
<tr>
<td>FH eosinophilic esophagitis</td>
<td>6.8</td>
</tr>
</tbody>
</table>

* H/O positive skin-prick, RAST, or clinical response

Noel, P. N Engl J Med 2004; 351:940
Esophageal Furrowing
White Plaques
Esophageal Rings
Esophageal Fragility
Eosinophilic Esophagitis

Histology

Severe Eosinophilia

Superficial Layering

Eosinophilic Microabscess
EoE - Tests

- Blood Ig E levels- increased in 50-60% - not predictive of therapeutic response
- Peripheral Eosinophils- Increased > 350  40-50%

May correlate with tissue eosinophils
Direct Allergy testing for EoE
Systemic Corticosteroids
*Prednisone*

- Initial report in 1998 by Liacouras et al
- 20 patients treated with methylprednisolone 1.5 mg/kg/day for 4 weeks, weaned over next 6 weeks
- Clinical and histological resolutions noted in majority (34.2 eos/hpf at Week 0 to 1.5 eos/hpf at Week 4)
- Side effects need consideration
- ? *Incidence of relapse and duration to relapse*

Oral Viscous Budesonide (OVB)-EoE

- OVB 19   Placebo 9 = 3 months
- > 5’ = 2mg  < 5’  1 mg (all pts Lanso)
- EGD+ Bx  x 2
- Response: Responders: eos <6, partial 7-19 and non-responders >20 eos
- Responders   OVB 13 (81%) Placebo 0
- OVB-Pre and post Eos (mean) 66 and 4.8 Placebo pre/post 83/65
- Symptom and endoscopy score improved

Dohil R, et al Gastroenterology 2010;139:418-29
Budesonide is Effective in Adolescent and Adults with EoE

- Swallowed nebulized soln. budesonide 1mg BID x 15 days vs placebo

<table>
<thead>
<tr>
<th></th>
<th>Eos</th>
<th>Dysphagia</th>
<th>Furrows /white plaques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide</td>
<td>68.2/5.5</td>
<td>5.6</td>
<td>Improved</td>
</tr>
<tr>
<td>Placebo</td>
<td>62.3/56.5</td>
<td>2.2</td>
<td>No</td>
</tr>
</tbody>
</table>

P<0.05

Straumann A et al Gastroenterology 2010;139:1526-37
Effect of Anti-IL5 on Esophageal Eosinophil Number


B

Mean

Eosinophils/hpt

Before

After

P<0.05

Dietary Therapy for EoE - Types

• Selective Diet
  – Directed Diet ~ 50%
  – Empiric Diet 6 Food ~ 70%
  – 4 Food ~ 60%

• Total Elimination Diet
  – Amino-Acid based formula ~ 90%
Empiric Elimination Diet

• Six food elimination diet (SFED)
• 1st described by Kagalwalla
• Initiated due to lack of available allergists
• Removal of milk, soy, wheat, egg, peanut/nut and fish/seafood
• Monitor symptoms and histology

TEAM – It Works
EoE – Complications

- Food impaction
- Esophageal narrowing; short or long segment
- Secondary GERD
- Infections; candida or Herpes simplex
- Perforations- Boerhaave’s
- Procedure related complications
- Treatment related complications
Dissociation Between Symptoms and Histologic Severity in Pediatric EoE

• N=49 Age 3-18, Eos >24, Symptom score (PEESS)
• Symptom score lower in 34 treated subjects
• Rx: Elemental diet, elimination, fluticosone or combo, or none for the newly diagnosed
• Mean symptom score for treated subjects in histologic remission was same for Rx group vs. treated subjects with active EoE regardless of Rx type
• 20/34 subjects in histologic remission, continued to report symptoms
• 3 subjects with active EoE had no symptoms
• Abdominal pain was common symptom (69%)
• Conclusion; dissociation between symptoms and histology in pediatric EoE

EoE Clinic Advocate Children’s- Park Ridge

- ~ 200 patients
- Grouped as per CS 2011
- Dysphagia and Abdo Pain - ~ 60 each
- Standard Rx- D / D
- S/S entered into 2 step cluster analysis
- Discriminant function analysis
- III group of patients with FAP
- Cluster 1 – EoE – all pts AP and FAP+ 8 Dys
- Cluster 2- 57 pts with dysphagia + no others
## EoE

<table>
<thead>
<tr>
<th></th>
<th>Worsened</th>
<th>Stable</th>
<th>Improved</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>EoE- Dysphagia</td>
<td>2</td>
<td>16</td>
<td>49</td>
<td>67</td>
</tr>
<tr>
<td>EoE- Abdo Pain</td>
<td>16</td>
<td>15</td>
<td>33</td>
<td>64</td>
</tr>
<tr>
<td>FAP</td>
<td>3</td>
<td>10</td>
<td>48</td>
<td>61</td>
</tr>
</tbody>
</table>
Complex Interaction Between GERD and EoE

• Separating the 2 disorders into distinct diseases may be too simplistic

• Possible relationships
  – GERD causes esophageal injury with eosinophilia
  – GERD and EoE coexist, but are unrelated
  – EoE causes or contributes to secondary GERD
  – GERD causes or contributes to EoE

• A trial of proton pump inhibitors (PPIs), even when diagnosis of EoE is clear-cut, is recommended

Five Blind Men and the Elephant
Complex Interaction Between GERD and EoE

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Natural History- EoE –New Disease

• May resolve spontaneously after a certain time with permanent resolution
• May enter temporary remission with subsequent relapse
• May progress to a fixed stable state
• May follow relentless progression
Natural History- EoE –New Disease

• Case reports
• Case series
• Database analyses
• Placebo-group analyses
• Cohort studies- with controls


Natural History

• In a prospective case series of 30 adults with EoE
• Followed for a mean of 7.2 years
  – 29/30 persistent dysphagia
  – 11/30 underwent at least one dilatation procedure
  – Deeper biopsy tissue was available in 7, and 6 exhibited evidence of fibrosis in the lamina propria
  – Waxing and waning

Natural History- EoE – New Disease

- Does not seem to limit life expectancy
- Impairs QOL
- Disease restricted to Esophagus
- Leads to remodeling of esophagus- fibrosis

Is it in all patients?

? Cancer Risk
Conclusions

Six Steps
- I- Diagnose and classify

- II - Allergy evaluation

- III- Allergy Positive – Oligo-allergen and Poly-allergen
  Allergy Negative

- IV- Diet – Directed
  - Empiric
  - Elemental

- V – Drugs – topical vs systemic

- VI- Follow up and validate the diagnosis
Eosinophilic Esophagitis

THANK YOU
### Long Term Budesonide Maintenance

- 28 adults: 0.5 mg neb-14. Bud; Placebo-14; 50 wks

<table>
<thead>
<tr>
<th></th>
<th>Eos</th>
<th>Sympt.Score</th>
<th>Fibrosis</th>
<th>Blood Eos</th>
<th>EUS Mucosal vs Epithelium</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bud</strong></td>
<td>0.4/31.8</td>
<td>0.79/2.29</td>
<td>2.17/2.26</td>
<td>175/243</td>
<td>M 0.75-0.45mm E 261-277um</td>
</tr>
<tr>
<td><strong>Placebo</strong></td>
<td>0.7/65.0</td>
<td>0.71/4.0</td>
<td>1.94/2.1</td>
<td>133/283</td>
<td></td>
</tr>
</tbody>
</table>

|       | p<0.01 | NS  | NS  | NS  | p<0.04 |

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Straumann A et al Clin Gastroenterol Hepatol 2011;9:400-09
Conclusions

• EoE is a **chronic disease** which requires (?) long-term maintenance therapy

• Current evidence suggests that present treatment may not alter the natural history of EoE but it may prevent complications. There is no single, specific therapy that should be used in every pediatric/adult patient diagnosed with EoE.

• Several therapies have been shown to provide variable success in treatment; these therapies should be tailored to each individual patient.

• Should treatment be geared toward “histologic normalcy”?

• **Four subtypes**; abdominal pain and eos. in the esophagus should be carefully evaluated.

• Remember the **two cardinal** requirements for diagnosis of EoE.
Dietary Management
Amino Acid–Based Formula

- 172 Patients (128 nasogastric tube, 32 oral, 4 failed, 8 noncompliant)
- Patients evaluated 4-6 weeks after instituting diet

<table>
<thead>
<tr>
<th>160 Patients</th>
<th>Pre-diet</th>
<th>Post-diet</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eosinophils per HPF</td>
<td>38.7 ± 10.3</td>
<td>1.1 ± 0.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>30</td>
<td>1</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>GERD symptoms</td>
<td>134</td>
<td>3</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Selective Elimination Diet

• Removal of a limited number of foods

• Types of dietary restriction
  – Empiric (based on history of the most likely foods)
    • “The usual suspects”
    • Milk, soy, egg, peanut, wheat, fish, meats
  – Directed (based on allergy testing or clinical symptoms)
    • Clinical history
    • Allergy testing (skin prick tests, atopy patch tests)
Five Blind Men and the Elephant

Do these men know what is this animal?