Esophageal Eosinophilia and Eosinophilic Esophagitis
Case 1

- 61 yo male
- No upper-GI symptoms
- Gastroscopy vor bariatric Operation
- Lesion: Papilloma
- Histology of the surrounding mucosa: 20 Eosinophils / HPF

• How would you characterize this finding
Definitions: esophageal eosinophilia

Esophageal eosinophilia: the finding of (any) eosinophils in the squamous epithelium of the esophagus

Lewis JT, Oxentenko AS: Gastrointestinal Pathology: Case Studies, The Mayo Clinic
Causes of esophageal eosinophilia
Causes of esophageal eosinophilia

- Eosinophilic Esophagitis
- PPI-REE
- GERD
  - Eosinophilic gastrointestinal diseases
  - Celiac disease
  - Crohn’s disease
  - Infection
  - Hypereosinophilic syndrome
  - Achalasia
  - Drug hypersensitivity
  - Vasculitis
  - Pemphigus
  - Connective tissue diseases
  - Graft vs. host disease
Case 2

- 32 yo male with intermittent dysphagia for 9 months
- Upper endoscopy: unremarkable, no biopsies, 8 weeks PPI
- Persistence of symptoms, follow-up endoscopy on PPI: unremarkable
- 4 biopsies in the distal and 4 in the proximal esophagus
- **Diagnosis?**
Eosinophilic esophagitis: Definition and diagnostic criteria
Eosinophilic esophagitis: Definition and diagnostic criteria

- Symptoms related to esophageal dysfunction
- Eosinophil-predominant inflammation. Peak value of ≥ 15 eos/hpf
- Eosinophilia isolated to the esophagus
- Persists after a PPI trial
- Secondary causes of eosinophilia excluded

*Response to treatment (dietary elimination; topical corticosteroids)

Lewis JT, Oxentenko AS: Gastrointestinal Pathology: Case Studies, The Mayo Clinic
Case 3

- 28 yo male with food bolus impaction
- Recurrent spontaneously resolving episodes in the last 2 years
- Endoscopy: no Bolus (see Image)
- Immediate next step?
Biopsies for diagnosis of eosinophilic esophagitis

- At least 2-4 in the **proximal and distal esophagus**
  - in separate pathology jars
  - target the areas with abnormal findings
- **antrum ± duodenum** to rule out other causes of esophageal eosinophilia
  - in all children and
  - adults with gastric or small intestinal symptoms or endoscopic abnormalities.
Epidemiology of EoE

- Typical EoE patient: atopic male (♀:♂ = 3:1) who presents in childhood or during the third or fourth decade of life
- EoE occurs in most racial and ethnic groups,
- Predominance in non-Hispanic Whites
- Rising incidence: 3.7/100000 person years
- 10% of patients presenting with dysphagia
Etiology of EoE
Etiology of EoE

- Allergic basis
- Aberrant “antigenic” or “immune” response associated with consistent clinical and histologic abnormalities
- Triggering antigens probably food and air particles
Clinical features of EoE
Clinical features of EoE

• Feeding difficulties

• Vomiting
• Pain
• Other atopic diatheses (food allergy, asthma, eczema, chronic rhinitis, environmental allergies)

• Solid food dysphagia
• Food impaction necessitating endoscopic bolus removal occurs in (33 – 54 %)
• Chest pain, heartburn, and upper abdominal pain
Endoscopic finding in EoE
Endoscopic finding in EoE

- Fixed esophageal rings
- Diffuse narrowing
Endoscopic finding in EoE

- Fixed esophageal rings
- Diffuse narrowing
- Lacerations induced by passage of the endoscope
Endoscopic finding in EoE

• Fixed esophageal rings
• Diffuse narrowing
• Lacerations induced by passage of the endoscope
• Edema
Endoscopic finding in EoE

- Fixed esophageal rings
- Diffuse narrowing
- Lacerations induced by passage of the endoscope
- Edema
- Exudates or plaques
Endoscopic finding in EoE

- Fixed esophageal rings
- Diffuse narrowing
- Lacerations induced by passage of the endoscope
- Edema
- Exudates or plaques
- Longitudinal furrows
Endoscopic finding in EoE

- Fixed esophageal rings
- Diffuse narrowing
- Lacerations induced by passage of the endoscope
- Edema
- Exudates or plaques
- Longitudinal furrows
- 10 – 25 % normal findings
## Endoscopic Reference Score (EREFS)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Edema</th>
<th>Fixed rings</th>
<th>Exudates</th>
<th>Furrows</th>
<th>Stricture</th>
<th>Mucosal fragility</th>
<th>Narrow-caliber esophagus</th>
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<tbody>
<tr>
<td>Grade 0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Grade 1</td>
<td>Loss of vascularity</td>
<td>Mild: subtle circumferential ridges</td>
<td>&lt; 10 % surface</td>
<td>Vertical lines present</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
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<tr>
<td>Grade 2</td>
<td>Moderate: do not impair passage</td>
<td>&gt;10 % surface area</td>
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<tr>
<td>Grade 3</td>
<td>Severe: impair passage of a diagnostic endoscope</td>
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</tbody>
</table>

Case 4

• 24 yo female with bolus impaction
• Upper endoscopy: fixed rings, Histology: >25 eos/hpf
• Repeat endoscopy on PPI: regression of endoscopic findings. Histology eos < 5/hpf

• Diagnosis
• Expected findings in an 24h impedance study?
PPI-RE

Definition

• Esophageal symptoms
• Histologic findings of eosinophilia
• Clinical and histologic response to PPI

Important notes

- Histologic response to PPI 30-50% in EoE
- If typical GERD symptoms and endoscopic findings – it is GERD
- Response alone does not establish GERD. Consider Impedance/PH testing
- Long term course unclear, overlap with EoE reported.
Case 5

• 22 yo male with bolus impaction
• Endoscopic signs of EoE
• Histology max 95 eos/hpf
• 8 weeks dd PPI without resolution
• Begin oral budesonide
• Consultation in 2 months: almost complete resolution of symptoms
• Immediate next step?
Treatment goals in EoE
Treatment goals in EoE

• Symptom resolution / improvement
• Histologic resolution / improvement

Problems
Treatment goals in EoE

• Symptom resolution / improvement
• Histologic resolution / improvement

Problems

• Symptoms alone neither specific nor sensitive
  • Lack of concrete endpoints
  • Compensatory mechanisms (e.g. softer diet)
  • Structural problems (e.g. strictures)
  • Poor correlation with histology
• Histologic resolution
  • Lack of concrete endpoints
Pharmacologic treatment
Pharmacologic treatment

1. Topical steroids
   - Budesonid 2mg/d: 1 mg / 2 ml (inh) mixed with 5 gm of sucralose 1-0-1
   - Fluticasone 880 – 1760 mcg/day: 250mcg Dosisaeros. 3-0-3
     - Avoid oral intake for 30 Min
     - Candida esophagitis in 5 – 30 % of cases

2. Systemic steroids
   - if topical steroids are not effective or in patients who require rapid improvement in symptoms.
     - More systemic adverse effects.
Dietary treatments
Dietary treatments

1. Elemental diet
2. Empiric elimination diets
3. Allergy test guided elimination
Elemental Diet

+ Strongest evidence in children (95-98% resolution in 4 weeks) and adults
+ No additional testing required

- High cost of elemental formulas
- Low tolerability, enteric feeding often required
- Suitable for highly motivated patients in resource rich settings
Empiric elimination diets
Empiric elimination diets

• the six-food elimination diet: milk, wheat, soy, egg, nuts, and seafood
Empiric elimination diets

• the six-food elimination diet: **milk, wheat, soy, egg, nuts**, and seafood

+ Low cost
+ High response rates
+ No additional testing needed

- Follow up and reintroduction process unclear
Allergy test guided elimination
Allergy test guided elimination

• Identification of triggering allergen though:
  • Skin prick test
  • Immunoassays for serum food-specific IgE
  • Atopy patch testing

+ Assessment of comorbid allergic diseases
- Best testing modality unknown
- RCT: Skin prick test only 13% predictive
  - Expensive and time consuming, suitable for resource rich settings
Endoscopic therapy
Endoscopic therapy

Indications
• Symptomatic stenosis or low caliber esophagus that do not respond to treatment
• Severe stenosis with dysphagia or bolus impaction prior to treatment

Methods
• Balloon = Bougies
• More conservative compared to that of peptic strictures (friability)
• Goal 15 – 18 mm
Endoscopic therapy

+ Lasting symptom relief (> 1 year)
+ High patient satisfaction
+ Complication rates comparable to other benign stenoses (Perf 0.3%)

- Multiple sessions required
- Post procedural pain (70%)
Maintenance therapy
Maintenance therapy

• Recurrence of EoE is almost universal after withdrawal of any treatment modality
• Time to recurrence varies

Indications
• Considered in every EoE patient
• Highly recommended for those with severe initial symptoms or rapid relapse

Modalities
• Topical steroids
• Elimination diets
• *Intermittent dilatation*
Maintenance therapy

Low dose maintenance therapy is safe and effective

- Budesonid 0.25mg 1-0-1
- Prospective, randomized, double blind, placebo controlled, 50w follow-up
- Significantly better symptomatic and histologic outcomes

Management algorithm

Suspicion of EoE: EGD + Biopsies

Confirmation of eosinophilia: exclude DD

dd PPI 8w + EGD + Biopsies

EoE
- Topical Steroids
- Elimination diets
- Consider allergy testing
- Endoscopic therapy as needed

PPI-REE
- PPI
- Endoscopic therapy as needed
- Consider GERD: functional testing

GERD
- PPI vs surgery
- Endoscopic therapy as needed
- Consider functional testing

Control resolution of symptoms and histology
Recent developments

Is PPI-RE a subset of EoE?

• PPI-RE patients have similar 24h impedance-PH tests with EoE patients
• Similar atopy testing profiles, endoscopic scores, gene expression
• 24-50% of EoE patients respond to PPI

PPI trial should be reserved only for patients with typical GERD features

Recent developments

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Recent developments

Is PPI-RE a subset of EoE?

- PPI-RE patients have similar 24h impedance-PH tests with EoE patients
- Similar atopy testing profiles, endoscopic scores, gene expression
- 24-50% of EoE patients respond to PPI
- Eosinophilia may recur on PPI (other modalities have no better long term results)
- Long term complications on PPI unknown
Case 6

- 25yo male with dysphagia for 2 years
- Endoscopy: low caliber esophagus, exudates, friability
- Histology: 85 eos/hpf
- PPI trial: persistence
- Budesonid 1mg 2x/d for 8 Weeks
- Limited relief of dysphagia
- Next step?
Recent developments

EndoFLIP
- strictures discovered in 39% of patients with a diagnostic delay of over 8 years and 70% with a delay of greater than 20 years
- EndoFLIP emerges as a diagnostic tool in the early identification
- Possible role in follow-up
Recent developments

Elimination diets

- **4food elimination diet:** milk, soy/legumes, egg, and wheat
- **2food elimination diet:** milk, wheat
Recent developments

Elimination diets

• **6food elimination diet:** milk, wheat, soy, egg, nuts, and seafood

• **4food elimination diet:** milk, wheat, soy, egg

• **2food elimination diet:** milk, wheat
Recent developments

Long term results of topical steroids:

- Loss of response (clinical) 50% by 18.5 m, 75% by 29.6 m
- 58% (histology) at 24 week

Long term results of elimination diet

- 1 study (n=15) 100% response in 2 years
- Loss of response (clinical) 50% in 2 years
- Even lower in other studies
- Compliance?
Recent developments

Novel treatment targets

- Mepolizumab (anti-IL-5)
- QAX576 (anti-IL-13)
- RPC4046 (anti-IL-13)
Recent developments

Novel treatment targets

• Mepolizumab (anti-IL-5)
• QAX576 (anti-IL-13)
• RPC4046 (anti-IL-13)

• Dupilumab (anti-IL-4, anti-IL-13) ongoing
Recent developments

Disease monitoring

• Esophageal string test with measurement of eos derived proteins
• Cytosponge (Medtronic)
  - *Assess activity, not structural changes*
• EndoFLIP
Thank you for your attention