Eosinophilic Esophagitis:
A Clinician’s Guide to Diagnosis and Management

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Sheraton Overland Park

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Disclosures:
None
On November 10th...

- 1871 – H. M. Stanley locates missing explorer and missionary, Dr David Livingstone near Lake Tanganyika: “Dr Livingstone, I presume?”
- 1969 – National Education Television debuts “Sesame Street”
- 1975 – The wreck of the Edmund Fitzgerald in Lake Superior
- 1983 – Bill Gates introduces Windows 1.0
- 1989 – Germans begin to tear down the Berlin Wall
- 2018 – St Luke’s Annual Gastroenterology Conference
Profound changes in the field of GI since I started (1982)...

- Discovery of Helicobacter pylori
- Endoscopic management of varices
- Treatment of Hepatitis C virus
- Acid suppression
- Treatment for Irritable Bowel Syndrome (IBS)
- Treatment for Inflammatory Bowel Disease (IBD)
- Recognition and description of Eosinophilic Esophagitis

Case

- 50 y/o hospital employee
- Long history of intermittent solid food dysphagia
- Reports seasonal allergies
- March 2011
  - EGD: “whitish furrows in the esophagus”
  - Biopsy: “marked increased intraepithelial eosinophils, microabscesses”
  - Treated with daily PPI
- March 2015
  - Recurrent symptoms of dysphagia, chest “spasms”; treated with fluticasone swallows
- April 2018
  - “hot dog” impaction, hematemesis, contained esophageal perforation on imaging, hospitalized (4 d)
- October 2018
  - EGD: “trachealization” of esophagus, unable to pass diagnostic EGD scope

Next step?
Objectives

- Review the history and recognition of Eosinophilic Esophagitis (EoE)
- Understand the definition of EoE
- Describe the incidence, prevalence, genetic & environmental factors
- Examine the pathophysiology
- Detail features that assist with the diagnosis
- Explore treatment options
- Consider future directions

Eosinophilic Esophagitis (EoE)
History of EoE

• First case report in 1977
  • “Eosinophilic gastroenteritis with esophageal involvement.”
    *(Gastro 1977;72:1312-16)*
• Case series in early to mid 1990’s
• First consensus recommendations published in 2007

Eosinophilic Esophagitis (EoE): The Clinician’s Perspective

• What is it?
• How do I approach it?
  • What should be done to diagnose this condition?
  • What are the treatment options?
  • How important is it to diagnose and treat?
• Where are we headed?
Eosinophilic Esophagitis (EoE)

- Chronic allergic/immune-mediated
- Esophageal dysfunction
- Eosinophilic infiltration
  - > 15 eosinophils/high power field
  - No secondary causes for eosinophilia

Esophageal Eosinophilia: Other Causes

- Gastroesophageal reflux disease (GERD)
- Eosinophilic GI diseases
- Celiac disease
- Crohn’s disease
- Infectious esophagitis
- Pill-induced esophagitis
- Hypereosinophilic syndrome
- Achalasia
- Drug hypersensitivity
- Vasculitis
- Pemphigus
- Connective Tissue Diseases
- Graft versus host disease (GVHD)

GERD and EoE

- Complex interaction
- EoE can cause secondary reflux
  - Decreased esophageal compliance and dysmotility
- Acid exposure from GERD may cause epithelial damage
  - Penetration of allergic antigens triggering an eosinophilic response
- Use of the proton pump inhibitor (PPI) trial
  - Eliminate EoE if a response to the PPI

Updated International Consensus
Diagnostic Criteria for Eosinophilic Esophagitis:
Proceedings of the AGREE Conference

- Symptoms of esophageal dysfunction
- At least 15 eosinophils/hpf (60 eos/mm2) on esophageal biopsy
- After comprehensive assessment of non-EoE disorders that could cause or potentially contribute to esophageal eosinophilia

*(PPIs are better classified as a treatment for esophageal eosinophilia that may be due to EoE than as a diagnostic criterion)*

*Gastroenterology 2018;155:1022-33*
Epidemiology

• Incidence
  • Increasing cause of morbidity
  • Growing health problem

• Prevalence
  • 1 in 2000
  • Usually 20-40 yrs (but affects all ages)
  • EoE now the most common cause of esophageal food bolus impaction
    • Rate of food bolus impactions correlate with higher daily pollen counts
      (ACG Poster, October 2018, Clarkston et al)

• Genetics
  • Male to female – 3:1
  • Familial association

Risk Factors and Associated Disorders

• Aeroallergens
• Food allergens
• Helicobacter pylori – inversely associated with EoE
• Infections (HSV, mycoplasma)
• Oral/sublingual immunotherapy
• PPI use — induce IgE antibodies to certain foods
• Cold or arid climates (less in temperate or tropical zones)
• Population density (increased as population density decreases)
• Early life factors (atb use, C-section, preterm delivery)
• Connective tissue disorders (Ehlers Danlos, Marfan, Loes-Dietz)
• Celiac disease
• Autoimmune disorders (IBD, RA, IgA deficiency, MS, Hashimoto's)

Contributing Factors to the Development of EoE

O'Shea et al. Gastroenterology 2018;154:333-345

Pathophysiology

O'Shea et al. Gastroenterology 2018;154:333-345
Clinical Features

Feeding Problems
Vomiting
Abdominal Pain
Dysphagia
Food Impaction

EoE Subtypes

- Variable response to treatment
- Disease is heterogeneous
- Cross sectional study
- Three types
  - Mild
  - Inflammatory
  - Fibrostenotic
- Endphenotyping may help
  - Guide management
  - Improve patient outcome

*Shoda et al. Lancet Gastro Hep 2018;3(7):477*

Diagnosis

- History
  - History of atopy, seasonal allergies, pyrosis, chest pain, dysphagia, eating patterns
- Physical Exam
- Skin testing
  - Poor correlation to disease activity
- Barium Swallow
  - Multiple rings
  - Long segments of narrowing
- Endoscopic
  - Visual - Edema, rings, exudates, furrows, strictures
  - Histologic – eosinophils, mucosal changes
Diagnosis - symptoms

- **Children**
  - Failure to thrive
  - Feeding difficulties
  - Nausea and vomiting
  - Abdominal pain
  - Heartburn
  - Picky eating

- **Adults**
  - Dysphagia
  - Eating slowly
  - Solid food avoidance
  - Avoidance of social eating
  - Chest pain
  - Heartburn

*Straumann, Gastroenterology 2018;154:346*

Diagnosis – Symptom Scoring Systems

- “EoE Activity Index” – primarily for dysphagia
  - Patient reported outcome instrument
  - Frequency, intensity, duration
  - Time required to eat a meal
  - Pain with eating
- Mayo Dysphagia Questionnaire
- Cumbersome in clinical practice
- ? Correlation with histologic response
Diagnosis

- History
- Physical Exam
- Barium Swallow
  - Multiple rings
  - Long segments of narrowing
- Endoscopic
**Diagnosis – Endoscopy**

- Visual changes
  - Edema
  - Rings
  - Exudates
  - Furrows
  - Strictures
- Histology
  - 6-8 biopsies distal and proximal
  - Eosinophil count of >15 in high power field (hpf)
  - ? Need to stain for products of eosinophil degranulation
  - Spongiosis (dilatation of intercellular space)
  - Increased number of mast cells and lymphocytes
  - Basal-zone hyperplasia
  - “Scoring System” (eos density, basal zone hyperplasia, eos abscesses, eos surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells and lamina propria fibrosis)

**Diagnosis – Newer methods**

- Transnasal endoscopy
- Esophageal impedance
- Impedance planimetry
- Cytosponge collection of tissue
- Esophageal string
- Blood markers
- Urine markers

*Straumann A, Kratska DA. Gastroenterology 2018;154:346-59*
Treatment

Infancy → Medical/Dietary Therapy → Adulthood

Medical/Dietary Therapy

- Medical
  - PPIs – usually start at bid
  - Topical corticosteroids – fluticasone, budesonide
- Dietary
  - Elemental formulas
  - Elimination
- Endoscopic
  - Dilation

What is the Endpoint of Therapy?
Treatment - Medical

- Proton pump inhibitors
  - Start at bid dosing
- Topical steroids
  - Fluticasone
  - Budesonide
Treatment - Dietary

- No potential side effects
- Meta analysis (Arias et al, Gastroenterology 2014;146:1639)
  - Elimination diet (67.2%)
  - Topical steroid therapy (63.3%)
  - Quality of life is an issue
  - EGD biopsies necessary for follow up assessment

- Reduce or eliminate allergen exposure
- Challenges
  - Cost
  - Adherence
  - Avoid nutritional deficiencies
- Elemental diet (amino-acid based formulae)
  - Not well studied in adults
  - Not well tolerated (high drop out rate)
- 6 Food Elimination diet (6ED)
  - Wheat (other gluten containing grains OK)
  - Milk (cow)
  - Soy
  - Egg
  - Nuts
  - Seafood
- 4 Food Elimination diet (4ED)
  - Milk, soy, egg, wheat
  - Should be supervised by a Registered Dietitian
Treatment – Dietary: reverse fibrosis

- Historical cohort study
- Children with EoE
  - Dietary restrictions
  - Topical steroids
- Post treatment
  - Symptom resolution
  - Decrease intraepithelial eosinophils
- Conclusion:
  - Dietary restrictions alone reverses fibrosis

Lieberman, Allergy 2012; 67:1299

Treatment - Endoscopic

- Dilatation
  - Determine starting diameter
  - Bougienage preferred over balloon
  - “rule of threes”
- Risk
  - Early reports: concern regarding greater risk of perforation
  - Meta analysis: similar to other etiologies
Treatment Endpoints

- Esophageal eosinophilia
  - Total elimination of eos in the tissue achieved in few
  - Reduce eos/hpf (? 5, 10, 15)
- Control of symptoms
  - Medical therapy
    - Consider prior to dilatation in less severe cases of dysphagia
  - Dilatation
    - Alleviate dysphagia
    - Eliminate food impactions
- Prevention/reverse esophageal remodeling
  - Steroids and dietary treatment reduce remodeling

Clinical Overview

*O’Shea et al. Gastroenterology 2018;154:333-345*
Treatment – My Approach:

- EGD **early on** if EoE suspected
  - Biopsies (proximal, distal, ? mid) important
  - Dilate if needed
- Simultaneously...
  - Start PPI therapy
  - Dietitian consultation
- Follow-up in 6-8 weeks
- Topical steroids if needed
- Consider f/u EGD with biopsies
- Follow up in six months and ? annually

Future Directions

- Becoming more common place - greater awareness
- Newer diagnostic tests
- Newer therapies
  - Short term
  - Chronic maintenance
- Easier means to assess response
Case

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Next step?

Summary

- Reviewed the history of Eosinophilic Esophagitis (EoE)
- Achieved a better understanding of the definition of EoE
- Detailed the incidence, prevalence, genetic & environmental factors
- Examined the pathophysiology
- Established the diagnostic features (emphasis on early diagnosis)
- Outlined treatment options
- Discussed future directions
With Respect
Honor
and Gratitude
Thank You Veterans
Thank You!