The 4th International Gastrointestinal Eosinophil Research Symposium (Tigers)

Pro/Con Debate:

SYMPTOMS

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Nothing to disclose financially regarding research funding, legal work, gifts, organizational work or other sources of funding.
EoE: Diagnosis

2011 Consensus Update

– “The diagnostic guidelines define EoE as an isolated chronic disorder of the esophagus diagnosed by the need of both clinical and pathological features.”

– “EoE should be diagnosed by clinicians, taking into consideration all clinical and pathological information; neither of the parameters should be interpreted in isolation.

Liacouras CA, et al JACI 2011;128:3-20
EoE: Monitoring Disease Activity

Assessment Tools

- Symptoms
  - Endoscopy with mucosal biopsies
    - Histological evidence of inflammation
The Discrepancy Issue

Mismatch between symptoms and histological evidence of inflammation

– Persistent symptoms, normal mucosa

– No symptoms, abnormal mucosa

Assa’ad AH, et al. Gastroenterol 2011;141:1593-1604
Spergel JM, et al. JACI 2012;129:456-463
Biopsy: Concerns

First do no harm...

- Invasive procedure
  - Requires anesthesia
  - Potential for complications
  - Often repeated multiple times
  - Source of anxiety for patients and their families

Eisenach JC. Anesthesia and Neurodevelopment in Children: Time for an Answer? Anesthesiology 2008;1097:57-761
Biopsy: Concerns

A penny saved is a penny earned...

- Expensive
  - Cost varies (~ $8,700)
  - Often repeated multiple times
- Can pose a financial burden
Biopsy: Concerns

Another instance where size really matters...

- Tiny tissue sample size (2-3mm)
- ~ 0.01% of esophageal surface area
Biopsy: Concerns

Just scratching the surface...

- Variable depth of biopsies
  - Remodeling of the lamina propria or the muscularis mucosa missed in mucosal pinch biopsies

Saffari H, et al. JACI 2012;130:798-800
Biopsy: Concerns

It’s all about location, location, location…

- EoE is a patchy disease
- Potential for sampling error
  - Overestimate disease
  - Underestimate disease

Biopsy: Concerns

Just a snapshot, not a movie, not even the full picture...

- View of only one point in time
- Potential effect of other variables
- Seasonality
- Inability to predict future stricture

Biopsy: Concerns

Diagnosing the entire forest after examining the leaves of one tree...

- EoE is a patchy disease
- Small biopsy tissue size
- Variable depth of biopsies
- Potential for sampling error
Symptoms: Strengths

First do no harm...

- Noninvasive history taking
- Easily assessed
- No anesthesia required
- Can be complicated, but almost no risk of complications
Symptoms: Strengths

A penny saved is a penny earned...

- Inexpensive
- Can easily be repeatedly assessed
  - Symptom remission or progression
Evidence for Correlation of Symptoms and Histology

- Most data derived from therapeutic intervention studies


- Correlation between symptoms measured with symptom-scoring tool (dysphagia and anorexia/early satiety) and histologic findings in 35 children with EoE.
Symptoms: Concerns

- Lack of validated clinical scoring system or patient-reported outcome tool specific for EoE

- Reliability of patient report of symptoms
  - Patient variability in symptom perception
  - Subconscious alteration of eating habits
  - Sporadic or seasonal symptoms

Symptoms versus Biopsy Findings

Correlations
- No symptoms, normal mucosa
- Symptoms, abnormal mucosa

Discrepancies
- Symptoms, normal mucosa
- No symptoms, abnormal mucosa
Symptom control is currently the preferable treatment endpoint

- Noninvasive
- Safer
- Cheaper
- Easy to obtain repeated assessments
- Reliable in many patients
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Pro/Con Debate Rebuttal:

SYMPTOMS

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Biopsy: Concerns

- Invasive procedure
  - Requires anesthesia
  - Potential for complications
- Costly
- Potential for sampling error
  - Tiny tissue sample size
    - Approximately 2-3 mm tissue sample
      (~ 0.01% of esophageal surface area)
  - Variable depth of biopsy
  - Patchy disease
EoE: 2011 Consensus Update

Major Unresolved Issues

Optimization of methodologies for histologic analysis of mucosal samples

1. Number of biopsy specimens
2. Proximal versus distal biopsy specimens
3. Number of hpfs that need to be examined
4. Effect of associated histologic features on diagnostic sensitivity

Liacouras CA, et al JACI 2011;128:3-20
Optimization of methodologies for histologic analysis of mucosal samples…cont’d

5. Mean versus peak number of eosinophils
6. Size of hpf used to quantitate eosinophils
7. Use of completely filled versus partially filled hpfs
8. Reporting eosinophil density as number per hpf versus number per unit area (mm²)
9. Eosinophil degranulation and optimal markers (MBP, EPO, and EDN)

Liacouras CA, et al JACI 2011;128:3-20
Major Unresolved Issues

- Optimal endpoints of treatment (symptom relief and histologic normalcy)

- Frequency of endoscopy in follow-up (Is it needed in asymptomatic patients?)

Liacouras CA, et al JACI 2011;128:3-20
Rebuttal: Symptoms

Summary: Symptom control is currently the preferable treatment endpoint.

–Safer, noninvasive, reliable in most patients, cheaper, easily repeated
Rebuttal: Symptoms

Most important reason:
The patient’s primary motivation for being seen is...

Symptom Control!!