Gastroduodenal Eosinophilia Is Under-Appreciated In Eosinophilic Esophagitis (EoE) Patients With Functional Bowel Symptoms: A Real Life Experience

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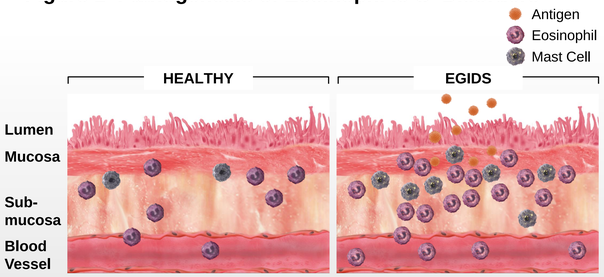
BACKGROUND

- Eosinophilic gastrointestinal (GI) disorders are chronic inflammatory conditions characterized by the aberrant localized accumulation and activation of eosinophils and mast cells[1,2]
- Eosinophilic esophagitis (EoE) is the best understood of these disorders, but there is evidence that eosinophilic gastritis and/or duodenitis (EG and/or EoD) are more prevalent than previously thought
- Many patients with EoE have extra-esophageal symptoms that are unlikely to be caused by inflammation limited to the esophagus
- These patients may have EG and/or EoD, which may be missed if systematic gastric and duodenal biopsies are not performed, and tissue is not evaluated for eosinophils

Figure 1. Pathogenesis of Eosinophilic GI Disorders



- EG and EoD is thought to affect 45,000 - 50,000 patients in the US, however, new evidence suggests it may be much more common
- Current treatment options such as diet restriction and corticosteroids have limited efficacy and/or are inappropriate for chronic use
- There is a significant unmet need for novel therapies

OBJECTIVE

- We evaluated gastric and duodenal biopsies from patients with EoE, with and without persistent non-esophageal GI symptoms, to determine the frequency of EG and/or EoD in these patients

METHODS

- EoE patients with previous EGD and gastroduodenal biopsies with pathology reported as normal / non-specific inflammation were recruited
- Patients were grouped by presence/absence of extra-esophageal symptoms:
  - 52 EoE patients with extra-esophageal GI symptoms (i.e. abdominal pain, nausea, bloating, irritable bowel) who had stomach and small bowel biopsies interpreted as non-specific inflammation or normal were identified ("EoE+S")
  - 15 EoE patients without extra-esophageal complaints who had were included as a control group ("EoE-S")
- Biopsies taken at initial work up were identified and blocks were cut for H&E staining and assessment by an independent, blinded GI pathologist skilled in eosinophil (eos) assessment
- Biopsies were evaluated for:
  - Eosinophil counts
  - Endoscopic findings
  - Histopathologic morphology
  - Functional gastrointestinal symptoms

RESULTS

- After exclusion for gastric/duodenal surgery, opiate dependence, systemic immunosuppression, H Pylori, and loss of tissue, a total of 45 EoE+S and 12 EoE-S patients were evaluated
- Common symptoms among EoE+S patients were abdominal pain, bloating, nausea, and "IBS"
- EoE+S patients had up to six additional types of tests to evaluate their extra-esophageal complaints
- All patients had prior pathology reports consistent with non-specific inflammation or normal tissue
- Upon blinded re-assessment
  - EoE+S patients met histologic criteria for EG and/or EoD
    - 8/45 (18%) with EG (≥30 eos/hpf in ≥5 gastric hpfs)
    - 23/45 (51%) EoD (≥30 eos/hpf in ≥3 duodenal hpfs)
    - 7/45 (16%) had concomitant EG+EoD
  - None of the EoE-S patients met histologic criteria for EG, 3/12 (25%) met histologic criteria for EoD
- EG±EoD EoE+S patients had peak eosinophil counts of 58 ± 14 in the stomach
- EoD ±EG EoE+S patients had peak eosinophil counts of 57± 19 in the duodenum
- EoE-S patients had peak counts of 11 ± 7 in the stomach and 35 ± 21 in the duodenum

Table 1. Baseline Characteristics of EoE Patients

Patient Characteristics	Symptomatic (EoE+S) n=45	Asymptomatic (EoE-S) n=12
Age, years	34.1 ±11.1	40.4 ±15.4
Male sex	49%	67%
Initial gastric pathology		
Normal	62%	83%
Nonspecific inflammation[a]	38%	17%
Initial duodenal pathology		
Normal	91%	100%
Nonspecific inflammation	9%	0%
Types of additional tests performed[b]	3 ±2	0
Final diagnosis		
Eosinophilic gastritis (EG)	18%[c]	0%
Eosinophilic duodenitis (EoD)	51%	25%
EG and EoD	16%	0%
Peak esophageal eosinophils	41.1 ±36.2	51.7 ±28.6
Peak gastric eosinophils	25.9 ±21.1	11.1 ±6.5
Peak duodenal eosinophils	43.1 ±20.8	35.2 ±21.0
EREFS	2.7 ±2.0	3.9 ±1.4

Values reported as mean ±standard deviation or proportion of patients
a Nonspecific inflammation includes reactive gastritis, chronic gastritis, focal inflammation, duodenitis, reactive epithelial changes
b Additional tests include additional EGDs with biopsies for pain, breath tests for bacterial overgrowth, colonoscopies, capsule endoscopies, exploratory laparoscopy, ultrasound, CT scan, single balloon enteroscopy, etc
c 7/8 were diagnosed with nonspecific inflammation of the stomach

Figure 2. Functional GI Symptoms Present in EoE Patients

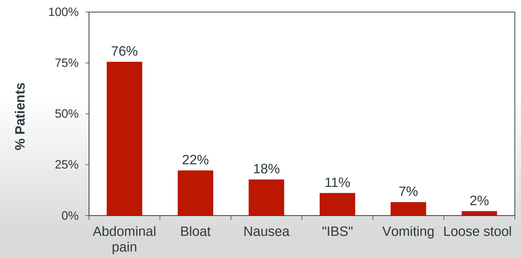


Figure 3. Gastric and Duodenal Morphology in EoE Patients With and Without GI Symptoms

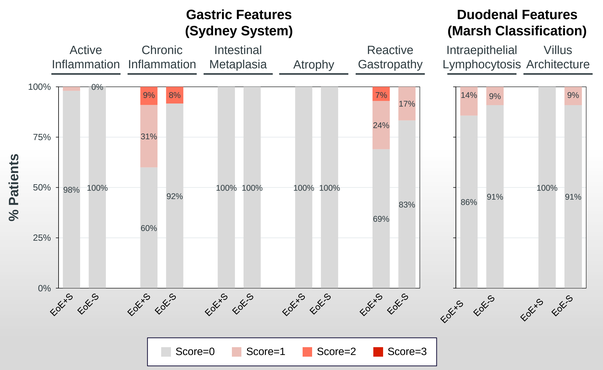
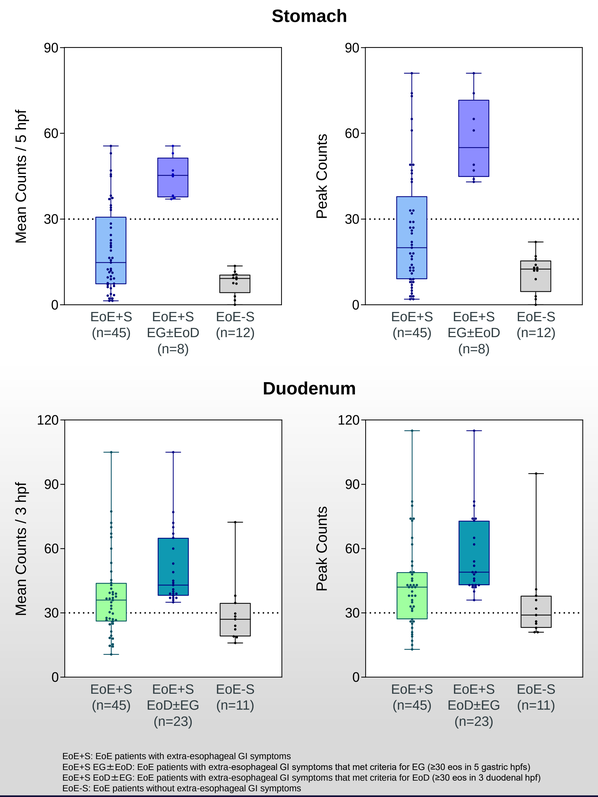


Figure 4. Mean and Peak Eosinophil Counts in EoE Patients With and Without GI Symptoms



EoE+S: EoE patients with extra-esophageal GI symptoms
EoE+S EG±EoD: EoE patients with extra-esophageal GI symptoms that met criteria for EG (≥30 eos in 5 gastric hpfs)
EoE+S EoD±EG: EoE patients with extra-esophageal GI symptoms that met criteria for EoD (≥30 eos in 3 duodenal hpf)
EoE-S: EoE patients without extra-esophageal GI symptoms

CONCLUSIONS/DISCUSSION

- In patients with EoE and extra-esophageal GI complaints, review of gastric and duodenal biopsies previously reported as normal or "non-specific inflammation" demonstrated a high discovery rate of gastroduodenal eosinophilia meeting criteria for EG and/or EoD
- These findings suggest that intentional evaluation of gastric and duodenal eos is indicated in patients with EoE and persistent non-esophageal GI symptoms
- Increased awareness of EG and/or EoD and consensus diagnostic criteria may lead to the identification of currently undiagnosed patients with EG and/or EoD
- Proper diagnosis of EG and/or EoD could lead to targeted treatment of gastric and/or duodenal inflammation and symptoms

Reference: (1) Caldwell JM, et al. J Allergy Clin Immunol. 2014.; (2) Youngblood BA, et al. Gastroenterology. 2019.

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