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

Kathryn A. Peterson MD1, Robert M. Genta MD2, Henrik S. Rasmussen MD PhD3, Bradford A. Youngblood PhD1, Amol P. Kamboj MD3

1University of Utah, Salt Lake City, UT, 2Baylor College of Medicine, Houston, TX, 3Allakos, Inc., Redwood City, CA

BACKGROUND

- Eosinophilic gastrointestinal (GI) disorders are chronic inflammatory conditions characterized by the aberrant localized accumulation and activation of eosinophils and mast cells1,2
- 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

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 been included as a control group (‘EoE’) were evaluated at initial work-up and blocks were cut for H&E staining and assessment by an independent, blinded GI pathologist skilled in eosinophilic (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
  - EG and/or EoD patients met histologic criteria for EG and/or EoD
  - EoE-S patients met histologic criteria for EoD
- EG±EoD EoE+S patients had peak eosinophil counts of 58 ± 14 in the stomach
- 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

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Symptomatic (EoE+S)</th>
<th>Asymptomatic (EoE-S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>34.3±10.1</td>
<td>40.4±15.4</td>
</tr>
<tr>
<td>Male sex</td>
<td>49%</td>
<td>67%</td>
</tr>
<tr>
<td>Initial gastric pathology</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>62%</td>
<td>83%</td>
</tr>
<tr>
<td>Nonspecific inflammation</td>
<td>38%</td>
<td>17%</td>
</tr>
<tr>
<td>Initial duodenal pathology</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>91%</td>
<td>100%</td>
</tr>
<tr>
<td>Nonspecific inflammation</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Types of additional tests performed</td>
<td>5 ± 2</td>
<td>0</td>
</tr>
<tr>
<td>Final diagnosis</td>
<td>Eosinophilic gastritis (EG)</td>
<td>19%</td>
</tr>
<tr>
<td>Eosinophilic duodenitis (EoD)</td>
<td>51%</td>
<td>4%</td>
</tr>
<tr>
<td>EG and EoD</td>
<td>14%</td>
<td>0%</td>
</tr>
<tr>
<td>Peak esophageal eosinophils</td>
<td>41.1±36.2</td>
<td>51.7±128.6</td>
</tr>
<tr>
<td>Peak gastric eosinophils</td>
<td>25.9±27.1</td>
<td>17.5±45.8</td>
</tr>
<tr>
<td>Peak duodenal eosinophils</td>
<td>43.1±20.8</td>
<td>35.2±27.2</td>
</tr>
</tbody>
</table>

Figure 1. Pathogenesis of Eosinophilic GI Disorders

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

CONCLUSIONS/DISCUSSION

- In patients with EoE and extra-esophageal G1 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