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Original article

Eosinophil infiltration in the upper gastrointestinal tract of patients with bronchial asthma

Hiroyuki Imaeda [a, *], Minoru Yamaoka [a], Hideki Ohgo [a], Kazuaki Yoneno [a], Takehito Kobayashi [a], Toru Noguchi [a], Yoshitaka Uchida [b], Tomoyuki Soma [b], Hidekazu Kayano [c], Minoru Kanazawa [b], Hidetomo Nakamoto [a], Makoto Nagata [b]

[a] Department of General Internal Medicine, Saitama Medical University, Saitama, Japan
[b] Department of Respiratory Medicine, Saitama Medical University, Saitama, Japan
[c] Department of Pathology, Saitama Medical University, Saitama, Japan

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Abbreviations:
GI, gastrointestinal; PPIs, proton pump inhibitors; EGE, eosinophilic gastroenteritis; EoE, eosinophilic esophagitis; BA, bronchial asthma;
EGD, esophagogastroduodenoscopy;
EGPA, eosinophilic granulomatosis with polyangiitis

ABSTRACT

Background: Eosinophilic esophagitis (EoE) is related to allergic diseases such as bronchial asthma (BA), atopic dermatitis, and allergic rhinitis. The aim of this study was to examine the eosinophil infiltration in the upper gastrointestinal (GI) tract in patients with BA using esophagogastroduodenoscopy.
Methods: Patients with BA who had upper GI tract symptoms were enrolled. Patients who received systemically administered steroids were excluded. Eosinophil infiltrations in the esophagus, stomach, and duodenum were examined with regard to the endoscopic findings and pathological findings of biopsy specimens (UMIN000010132).
Results: Ninety patients were enrolled from October in 2012 to September in 2014. Thirty-six were male, 54 were female, and the mean age was 57.5 years. Eighty-one (90%) used inhaled corticosteroids. Fourteen patients (15.6%) had reflux esophagitis, 8 of whom had grade A and 6 had grade B. No patient with EoE was observed. One female patient who had marked eosinophil infiltration in the esophagus, stomach, and duodenum was diagnosed as having eosinophilic gastroenteritis, but endoscopy showed only mucosal edema in the antrum. Another female patient who had marked eosinophil infiltration in the esophagus, stomach, and duodenum was diagnosed as having eosinophilic granulomatosis with polyangiitis, and endoscopy showed erosions in the antrum and the duodenum. Three patients had eosinophil infiltration in the stomach, but none of them had severe symptoms.
Conclusions: Patients with asthma who had upper gastrointestinal symptoms rarely had eosinophilic gastrointestinal disorders. Biopsy specimens are of high importance in the diagnosis of eosinophilic gastrointestinal disorders even if there is no remarkable endoscopic finding.
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Introduction

Eosinophilic esophagitis (EoE) and eosinophilic gastroenteritis (EGE) are rare pathological conditions characterized by dense infiltration of eosinophils in esophagogastrointestinal mucosa.[1,2] When eosinophil infiltration is demonstrated only in the esophageal epithelial layer, the pathological condition is called EoE. On the other hand, when it is found in gastric and/or intestinal/colonic mucosa irrespective of esophageal involvement, it is called EGE. Affected patients develop esophageal fibrostenotic complications after chronic inflammation and often suffer from dysphagia, swallowing discomfort, and heartburn.[3–5] Patients with EGE have abdominal pain and diarrhea, high peripheral eosinophil counts, and gastrointestinal wall thickening identifiable in CT images. The prevalence of EoE has been reported to be increasing rapidly in Western countries.[6–9] Straumann *et al.*[1] reported that in Switzerland it increased from 2/100,000 in 1989 to 23/100,000 in 2004. Similarly, Prasad *et al.*[9] found that in the US it was 55/100,000 in 2006 and that the incidence of clinically diagnosed EoE has increased markedly over the last 3 decades, whereas the prevalence and incidence of EGE have not been fully clarified. The prevalence of EoE was calculated to be 17.1/100,000 in the Japanese population,[10]

* Corresponding author. Department of General Internal Medicine, Saitama Medical University, 38 Morohongo, Moroyama-machi, Iruma-gun, Saitama 350-0495, Japan.
E-mail address: imaedahi@yahoo.co.jp (H. Imaeda).
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and EGE is more prevalent than EoE.[11] The prevalence of EoE in endoscopy-examined cases was recently reported in the USA to be 6.5%.[12] EoE cases are frequently associated with allergic diseases such as bronchial asthma (BA), atopic dermatitis, allergic rhinitis, and various food or drug allergies. Approximately 30–50% of individuals with EoE have asthma, whereas only 10% of the general population does.[13,14] Similarly, 50–75% have allergic rhinitis, and only 39% of healthy children do. In addition, 10–20% of children with EoE have IgE-mediated food allergies (urticaria and anaphylaxis), whereas only 1–5% of normal children does.[5,13,14] These rates of atopy (asthma, allergic rhinitis, and atopic dermatitis) are approximately three times higher than what is expected in the general population. Also, approximately 30–50% of individuals with EGE have allergic diseases like EoE.[15,16]

This study was to examine the eosinophil infiltration in the upper gastrointestinal (GI) tract in patients with BA by using esophagogastroduodenoscopy (EGD).

Methods

Ninety patients (36 male and 54 female) with BA who had upper GI symptoms and underwent EGD in our hospital were enrolled in this study. Patients treated with systemically administered steroids were excluded, but those taking only inhaled steroids were not. Their ages ranged from 16 to 78 years, and the mean age was 57.5 years. Eighty-one patients (90.0%) took inhaled corticosteroids, 14 (15.6%) took proton pump inhibitors, and 2 (2.2%) took H_2 receptor antagonists. Twenty-nine patients (32.2%) had allergic rhinitis, 8 (8.9%) had atopic dermatitis, and 5 (5.6%) had food allergies (Table 1).

Upper GI symptoms were examined using a frequency scale for symptoms of gastroesophageal disease (F-scale).[17] EGD was conducted, and hiatal hernia was assessed using Makuuchi's classification[18] and reflux esophagitis was assessed using the Los Angeles classification.[19] A circular ring, longitudinal furrow, white exudate, or stenosis in the esophagus was observed as a characteristic finding in EoE. Moreover, edema, marked redness, erosion, or ulcer in the stomach was observed as an endoscopic finding in EGE, although those were not specific for EGE. Biopsy specimens were taken at the upper, middle, and lower body of the esophagus and at the gastric body and antrum and at the bulbus of the duodenum. Eosinophilic infiltration was histologically diagnosed as more than 15 eosinophils in a high-power field.

The study protocol was in accordance with the tenets of the revised Declaration of Helsinki (1989) and was approved by the institutional review boards at our institutions. Written informed consent was obtained from all the patients. This study was registered with the UMIN Clinical Trials Registry (UMIN000010132).

Results

The questionnaire of upper GI symptoms was examined in 72 patients (80%).

Table 1
Clinical characteristics of patients.

Male/Female	36/54
Mean age	57.5 (16–78)
Inpatients/Outpatients	6/84
Medication	
Inhalant corticosteroids	81 (90.0%)
Proton pump inhibitor	14 (15.5%)
H_2 receptor antagonist	2 (2.2%)
Allergic disease	
Allergic rhinitis	29 (32.2%)
Atopic dermatitis	8 (8.9%)
Food allergy	5 (5.6%)

Table 2
Upper gastrointestinal symptoms.

Heart burn	62 (86.1%)
Bloating	63 (87.5%)
Feeling heavy after meals	65 (90.3%)
Subconsciously rubbing your chest	43 (60.9%)
Feeling sick after meals	21 (29.2%)
Heart burn after meals	20 (27.8%)
Unusual sensation in your throat	25 (34.7%)
Feeling full while eating meals	23 (31.9%)
Stucking when you swallow	25 (34.7%)
Bitter liquid coming up into your throat	61 (84.7%)
Burping a lot	62 (86.1%)
Heart burn when you bend over	18 (25.0%)
Epigastralgia	13 (18.1%)

Sixty-two patients (89.9%) had heartburn, 63 patients (87.5%) had bloating, 65 patients (90.3%) had a heavy feeling after meals, 43 patients (59.7%) subconsciously rubbed their chest, 61 patients (84.7%) had bitter liquid coming up into the throat, and 62 patients (86.1%) had a lot of burping. Twenty-five patients (34.7%) had food sticking when swallowing. Only thirteen patients (18.1%) had epigastralgia (Table 2). The mean F-scale score was 9.0 (1–34), and 32 patients (44.4%) had an F-scale score greater than 8.

Eighty patients (88.9%) had hiatal hernia, 14 of whom had grade A, 65 of whom had grade B, and one had grade C. Fourteen patients (15.6%) had reflux esophagitis, 8 of whom had grade A and 6 of whom had grade B, however, all had mild reflux esophagitis. A circular ring, longitudinal furrow, white exudate, or stenosis in the esophagus was not observed in any patient. Edema in the stomach was observed in one patient, marked redness was observed in one patient, and erosions were observed in one patient.

One patient, a 69-year-old female was diagnosed as having EGE because she had severe epigastralgia, eosinophilia (1,825/μL) and BA, which was treated with inhaled corticosteroids. EGD showed no abnormal findings in the esophagus and the duodenum and showed mild edema in the gastric antrum (Fig. 1). The pathological findings in any location, however, showed eosinophil infiltration (Fig. 2a, b). She has been improved by administration of oral corticosteroids.

Another patient, a 16-year-old female who had precedent BA that was treated with inhaled corticosteroids was diagnosed as

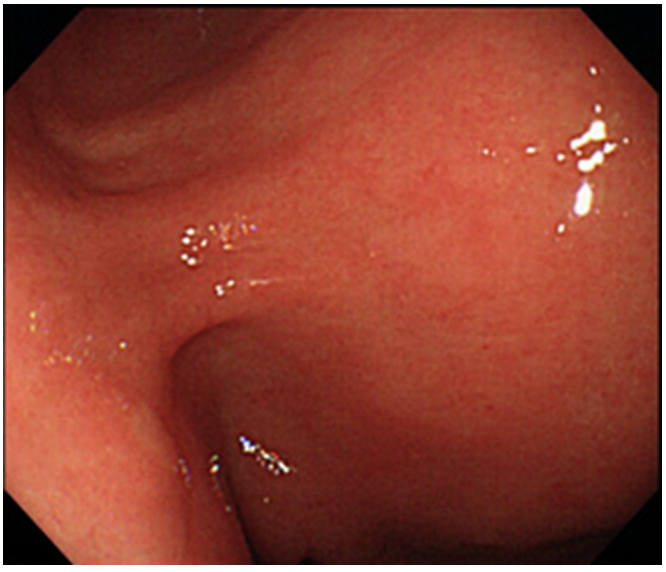

Fig. 1. Mild edema in the antrum.

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