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Proton Pump Inhibitor to Treat an Eosinophilic Duodenal Ulcer with Esophageal Involvement: A Pediatric Case

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Eosinophilic gastrointestinal disorders are diseases that cause inflammation and dysfunction due to infiltration of eosinophils into various regions of the gastrointestinal tract. Symptoms and treatment vary depending on lesion severity. We describe the first pediatric case of an eosinophilic duodenal ulcer with esophageal involvement that was effectively treated using proton pump inhibitor monotherapy. A 12-year-old boy with no relevant family or medical history presented with a one-month history of epigastric pain. Laboratory test results were as follows: white blood cell count, 4,700/μL; eosinophil count, 150/μL (3.2%); and total IgE, 151.6 IU/L; and IgG antibodies for *Helicobacter pylori* were absent. Esophagogastroduodenoscopy revealed longitudinal linear furrows in the esophagus, indicating eosinophilic esophagitis with an A1 ulcer from the duodenal bulb to the descending duodenum. The patient was diagnosed with an eosinophilic duodenal ulcer with esophageal involvement based on pathological findings. Esomeprazole, a common proton pump inhibitor, was orally administered, after which the symptoms promptly improved. After two months, the esophagogastroduodenoscopy and pathological examination results showed improvement in both the esophagus and duodenum. There have been no previous reports of an eosinophilic duodenal ulcer with esophageal involvement without post-duodenal involvement at the time of diagnosis. The possibility of eosinophilic gastrointestinal disorders should be investigated in patients with duodenal ulcers by means of active biopsy, and patients should be investigated for other types of gastrointestinal lesions. Proton pump inhibitor monotherapy may be considered a first-line treatment for eosinophilic duodenal ulcers with esophageal involvement, depending on lesion severity.

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Introduction

Eosinophilic gastrointestinal disorders (EGIDs) cause various gastrointestinal symptoms, such as abdominal pain and diarrhea. These symptoms are due to infiltration of eosinophils into the gastrointestinal tract. Symptoms vary depending on the area of the gastrointestinal tract that has been infiltrated. Treatment depends on lesion severity within the gastrointestinal tract. We describe the first pediatric case of an eosinophilic duodenal ulcer with esophageal involvement that was effectively treated using proton pump inhibitor (PPI) monotherapy.

Case Presentation

A 12-year-old boy with no relevant family or medical history presented with a one-month history of epigastric pain. The results of his laboratory tests were as follows: white blood cell count, 4,700/μL; eosinophil count, 150/μL (3.2%); albumin level, 4.5 g/dL; C-reactive protein level, < 0.01 mg/dL; and total IgE, 151.6 IU/L. IgE antibody levels in relation to the following antigens were tested: egg white, 0.41 IU/L; milk, 0.37 IU/L; wheat, 0.25 IU/L; soy, < 0.10 IU/L; peanut, 0.16 IU/L; and salmon, < 0.10 IU/L. Additionally, thymus and activation-regulated chemokine

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levels were 522 pg/mL, and IgG antibodies for *Helicobacter pylori* were absent. Abdominal ultrasonography showed no abnormal findings such as ascites. Esophagogastroduodenoscopy revealed longitudinal linear furrows in the esophagus, indicating eosinophilic esophagitis with an A1 ulcer from the duodenal bulb to the descending duodenum, and no abnormal findings in the stomach (Fig. 1A, B). A rapid urease test result was negative. Colonoscopy and balloon-assisted enteroscopy revealed no abnormalities in the ileum and colon. Pathological examination results showed eosinophilic infiltration of 60 per high-power field (/HPF) in the esophagus and > 100/HPF in the duodenum (Fig. 2A, B), and no eosinophilic infiltration in the ileum and colon. The patient was diagnosed with an eosinophilic duodenal ulcer with esophageal involvement.

Esomeprazole was orally administered, after which his symptoms promptly improved. After two months, the esophagogastroduodenoscopy (Fig. 1C, D) and pathological examination (Fig. 2C, D) results showed improvement in both the esophagus and duodenum. Esomeprazole treatment was discontinued and, over a year later, the symptoms had not recurred. A follow-up endoscopy cannot be performed without parental consent. Written informed consent was obtained from the patient's parents.

Discussion

In this case presentation, we report the first pediatric case of an eosinophilic duodenal ulcer with esophageal involvement that was effectively treated by PPI monotherapy. EGIDs comprise eosinophilic esophagitis (EoE) and eosinophilic gastroenteritis (EGE) (Kinoshita et al. 2013). One classification stratifies EGIDs into EoE and non-EoE EGIDs (Yamamoto et al. 2021). These classifications consider cases of no eosinophilic inflammation in the gastrointestinal tract below the esophagus to be EoE. One Japanese study reported that the rate of EGE with esophageal involvement was 9% (Kinoshita et al. 2013). Yamamoto et al. (2021) also reported that eosinophilic enteritis and eosinophilic colitis had no esophageal lesions, but 49% of patients with EGE had esophageal lesions. At the time of diagnosis, there had been no previous reports of an eosinophilic duodenal ulcer with esophageal involvement but without post-duodenal involvement.

We summarized cases of EGIDs presenting with duodenal ulcers in Table 1 (Russell and Evangelou 1965; Deslandres et al. 1997; Markowitz et al. 2000; Tee et al. 2009; Issa et al. 2011; Nakamura et al. 2014; Yamazaki et al. 2015; Riggle et al. 2015; Chen et al. 2017; Kubo et al.

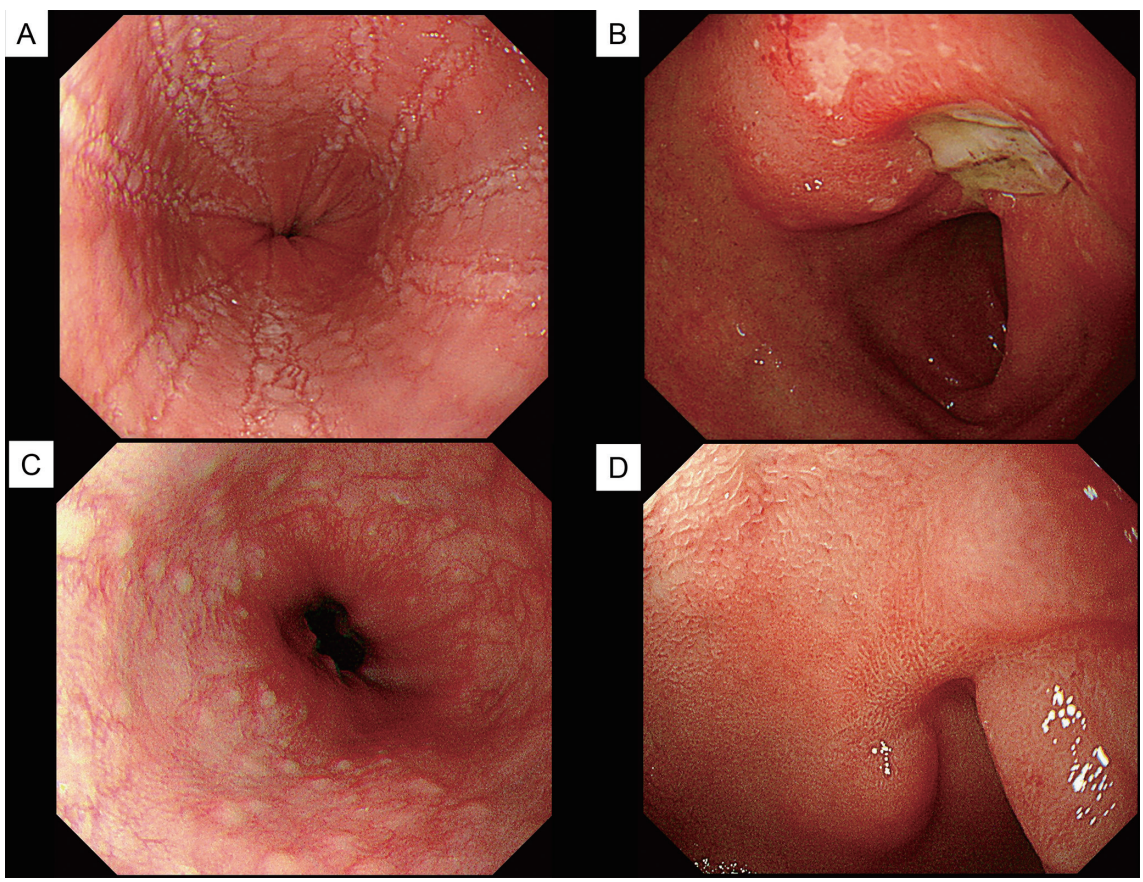

Fig. 1. Esophagogastroduodenoscopy images.
Esophagogastroduodenoscopy showed longitudinal linear furrows in the esophagus (A) and a stage A1 ulcer from the duodenal bulb to the descending duodenum (B). These findings improved two months after treatment with esomeprazole (C, D).

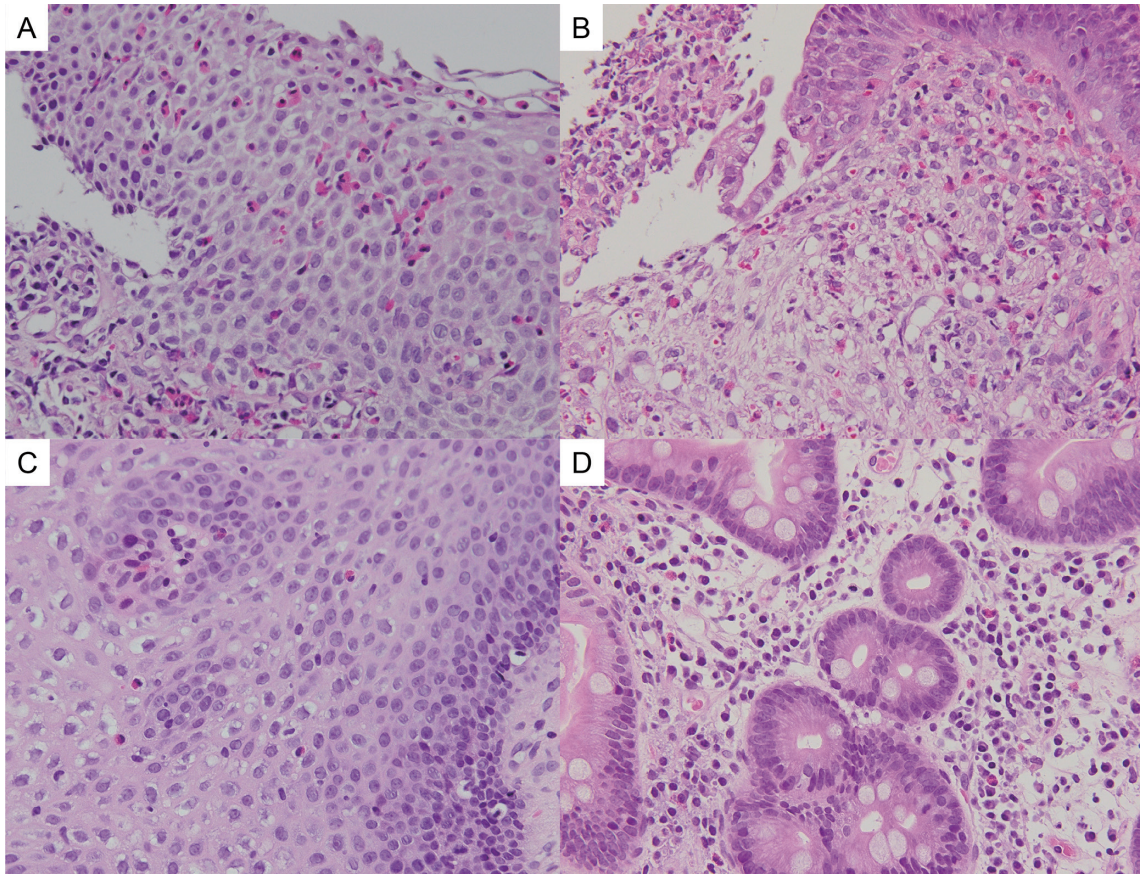

Fig. 2. Pathological findings of the biopsy tissue of esophagus and duodenum (hematoxylin and eosin staining). Pathological examination results showed eosinophilic infiltration of 60 high-power field (/HPF) in the esophagus (A) and > 100/HPF in the duodenum (B). The eosinophilic infiltration improved to 3/HPF in the esophagus (C) and 10/HPF in the duodenum (D) two months after initiation of treatment with esomeprazole (A-D, original magnification, × 400).

2020; Peck et al. 2020; Priyadarshni et al. 2020; Fujita et al. 2022). These studies involved many young people overall, and > 50% were children. Previously, we reported a pediatric patient who had been diagnosed with an eosinophilic duodenal ulcer that was complicated with *Helicobacter pylori* infection (Fujita et al. 2022). The possibility of EGIDs should be investigated in patients with duodenal ulcers by means of an active biopsy, and patients should be investigated for other types of gastrointestinal lesions (Kinoshita et al. 2013; Yamamoto et al. 2021).

A definitive treatment protocol for eosinophilic duodenal ulcers with esophageal involvement remains to be determined. Although PPIs are recommended as first-line treatment for EoE (Lucendo et al. 2017; Dellon et al. 2018), their effectiveness in cases with esophageal involvement in non-EoE EGIDs has not been investigated. EGE may often require various treatments, such as leukotriene receptor inhibitors (LTRA), systemic corticosteroids, and diet therapy. Recently a case in which crushed budesonide was effective was also reported (Kubo et al. 2020); however, the effectiveness of PPIs for EGE, including eosinophilic duodenal ulcers, remains to be determined. A few case studies have reported on the effectiveness of PPIs for eosinophilic duodenal ulcers (Tee et al. 2009). In our previous case report of a patient with eosinophilic duodenal ulcers, LTRA was the most effective, but a PPI appears to have been partially effective (Fujita et al. 2022). PPIs reduce duodenal eosinophilia in patients with functional dyspepsia (Wauters et al. 2021). Further studies are needed to determine the effectiveness of PPIs for EGE, especially duodenal lesions. Systemic glucocorticoids, which are associated with various side effects, especially in children, are more often indicated in non-EoE EGIDs than in EoE (Kinoshita et al. 2013; Yamamoto et al. 2021). In contrast, PPIs have fewer side effects and can be used safely. There have been no previous reports of improvement using PPI monotherapy in relation to both eosinophilic duodenal ulcers and esophageal involvement. In conclusion, PPI monotherapy may be considered as a first-line treatment for eosinophilic duodenal ulcers with esophageal involvement, depending on the severity.

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Author Contributions

Dr. Fujita collected and analyzed the data and drafted

Table 1. Previous reported cases of eosinophilic duodenal ulcer.

Case number	Age (years)	Sex	Symptoms	Peripheral eosinophil count (/μL)	Allergic diseases	H.pylori	Endoscopic findings	Treatment	Reference
1	11	M	epigastric pain	574	none	negative	deformed pylorus with erythema of the antrum and prepyloric area, and an edematous and hyperemic duodenal bulb with a scar noted in the duodenal bulb"	corticotherapy cimetidine diet therapy	Deslandres et al. 1997
2	11	F	nausea, epigastric pain	1,254	environmental allergies and asthma	negative	a large ulcer in the duodenal bulb	omeprazole sucralfate methylprednisolone	Markowitz et al. 2000
3	14	M	epigastric pain	1,666	bronchial asthma and allergic rhinitis	positive	multiple ulcers in the duodenal bulb	histamine 1 receptor antagonist proton pump inhibitor montelukast	Fujita, et al. 2022
4	early teens	M	hematemesis, tarry stools	ND	bronchial asthma	negative	an ulcer with a thickened, white, moss-like appearance in the duodenal wall at the superior duodenal angulus	proton pump inhibitor prednisolone	Yamazaki et al. 2015
5	15	M	epigastric pain, nausea	455	allergic rhinitis	negative	two A2-stage duodenal ulcers on the anterior wall and greater curvature of the duodenal bulb	esomeprazole crushed budesonide	Kubo et al. 2020
6	16	M	epigastric pain	normal	none	negative	a perforated ulcer in the first portion of the duodenum	diet therapy	Riggle et al. 2015
7	16	M	abdominal pain, etc	1,000	none	negative	duodenal ulcer, located proximal to the ampulla of Vater	sucralfate lansoprazole diet therapy swallowed fluticasone thrapy	Peck et al. 2020
8	late adolescence	F	epigastric pain, vomiting, inappetence	860	allergy to pollen	negative	an ulcer scar in the duodenal bulb	proton pump inhibitor	Nakamura et al. 2014
9	26	M	vomiting	ND	ND	ND	a duodenal ulcer with stenosis	pantoprazole prednisolone	Issa et al. 2011
10	28	M	dizziness	ND	allergy to peanuts	ND	high-grade duodenal stenosis, severe pyloroduodenal deformity and a duodenal ulcer with a visible vessel	pantoprazole prednisone coiling and embolization by interventional radiology service	Priyadarshni et al. 2020
11	31	M	abdominal pain	6,800	ND	ND	duodenal ulceration	proton pump inhibitor	Tee et al. 2009
12	45	M	abdominal pain, vomiting	ND	contact dermatitis	ND	a large perforation of a huge peptic ulcer in the first part of the duodenum	death after surgical treatment	Russell and Evangelou 1965
13	54	M	periumbilical pain, melena	261	allergy to trimethoprim	ND	multiple ulcers in the duodenum	protom pump inhitibor methylprednisolone montelukast	Chen et al. 2017
our case	12	M	epigastric pain	150	none	negative	an A1 ulcer from the duodenal bulb to the descending duodenum	esomeprazole	

M, male; F, female; ND, no data.

and revised the initial manuscript. Dr. Tominaga, Prof. Ishida, Dr. Masuyama, and Prof. Yoshihara interpreted all the data and critically revised the manuscript for important intellectual content. All the authors approved the final manuscript and agreed to be accountable for all aspects of the work.

Conflict of Interest

The authors declare no conflict of interest.

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