

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

A case of eosinophilic gastroenteritis with high PET-CT accumulation treated by P-CAB ☆,☆☆,★

Noriaki Manabe, M.D.Ph.D.^{a,*}, Erika Todo, M.D.^b, Ken Haruma, M.D.Ph.D.^c, Maki Ayaki, M.D.^a, Jun Nakamura, M.D.^a, Minoru Fujita, M.D.Ph.D.^a, Yasumasa Monobe, M.D.Ph.D.^d, Katsuya Kato, M.D.Ph.D.^e, Tomoari Kamada, M.D.Ph.D.^f, Yoshihiko Handa, M.D.^g, Masaki Matsubara, M.D.^h, Tomoki Yamatsuji, M.D.Ph.D.^h, Yoshio Naomoto, M.D.Ph.D.^h

^a Division of Endoscopy and Ultrasonography, Department of Clinical Pathology and Laboratory Medicine, Kawasaki Medical School, 2-6-1 Nakasange, Kita-ku, Okayama, 700-8505, Japan

^b Clinical Education and Training Center, Kawasaki General Medical Center, Kawasaki Medical School, Okayama, Japan

^c Department of General Internal Medicine 2, Kawasaki Medical School, Okayama, Japan

^d Department of Pathology, Kawasaki Medical School, Okayama, Japan

^e Department of Diagnostic Radiology, Kawasaki Medical School, Okayama, Japan

^f Department of Health Care Medicine, Kawasaki Medical School, Okayama, Japan

^g Department of Surgery, Handa Central Hospital, Aioi, Japan

^h Department of General Surgery, Kawasaki Medical School, Okayama, Japan

ARTICLE INFO

Article history:

Received 10 April 2021

Revised 12 May 2021

Accepted 12 May 2021

Keywords:

Eosinophilic gastroenteritis

Positron emission tomography

Potassium-competitive acid blocker

Ultrasonography

Upper gastrointestinal endoscopy

ABSTRACT

Eosinophilic gastroenteritis (EGE) can present findings on computed tomography (CT) images that resemble malignant tumors. EGE is generally treated with systemic oral steroid administration, which is reportedly effective in relieving symptoms at least temporarily. Here, we report a case of EGE that mimicked malignant lymphoma in a gastroduodenal lesion, in which treatment with a potassium-competitive acid blocker without systemic oral steroid administration relieved the symptoms and reversed the initial image findings. A 56-year-old woman became aware of discomfort in her epigastric region, which gradually worsened. This case showed antroduodenal wall thickness, which mimicked a malignant lymphoma with increased F-18 fluorodeoxyglucose (FDG) uptake by positron emission tomography/computed tomography (PET/CT). An upper gastrointestinal endoscopy revealed protruding erosions in the antrum and severe edematous changes in the duodenum. Exten-

☆ Acknowledgements: We thank J. Iacona, Ph.D., and H. Nikki March, Ph.D., from Edanz Group (<https://jp.edanz.com/ac>) for editing a draft of this manuscript.

☆☆ Competing Interest: The authors declare that they have no links of interest.

* Patient Consent: We conducted this study in compliance with the principles of the Declaration of Helsinki. This study was reviewed and approved by the Institutional Ethics Committee of Kawasaki Medical School (IRB permission number: 5176-00). Written informed consent was obtained from the patient.

* Corresponding author.

E-mail address: n_manabe@med.kawasaki-m.ac.jp (N. Manabe).

<https://doi.org/10.1016/j.radcr.2021.05.039>

1930-0433/© 2021 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

sibility of the normal gastric wall by insufflation also occurred. However, an abdominal ultrasound indicated wall thickening with a preserved wall structure. Histological examinations showed a large amount of eosinophil infiltration, mainly in the gastroduodenal mucosa, without malignant cells. Thus, we made a final diagnosis of EGE. The patient was then administered 20 mg vonoprazan fumarate per day because she refused steroid treatment and because the pathological lesion was also localized from the duodenum to the antrum. After 3 weeks of potassium-competitive acid blocker treatment, her symptoms were alleviated, and the degree and extent of thickening of the gastroduodenal wall in upper gastrointestinal endoscopy and ultrasonographic image findings had remarkably improved.

© 2021 The Authors. Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

Eosinophilic gastroenteritis (EGE) is a rare disease characterized by eosinophil cell infiltration in the gastrointestinal (GI) tract [1-3]. Because EGE lacks specific symptoms and sometimes presents image findings that resemble malignant tumors, there have been several reports of surgeries performed in patients because malignant tumors were suspected [4-6]. EGE is generally treated with systemic oral steroid administration. Here, we report a case of EGE showing diffuse wall thickening in gastroduodenal lesions with increased F-18 fluorodeoxyglucose (FDG) uptake by positron emission tomography/computed tomography (PET/CT), mimicking malignant lymphoma. This patient was treated with a potassium-competitive acid blocker (P-CAB).

We conducted this study in compliance with the principles of the Declaration of Helsinki. This study was reviewed and approved by the institutional ethics committee of Kawasaki Medical School (IRB permission number: 5176-00). Written informed consent was obtained from the patient.

Case report

A 56-year-old woman became aware of discomfort in her epigastric region, which gradually worsened and was accompa-

nied by chest tightness. After she became unable to sleep because of this severe epigastric pain, she visited a nearby hospital 2 weeks after onset. An abdominal CT scan revealed swelling in the gastroduodenal wall with lymphadenopathy. The patient was referred to our hospital for an appropriate course of treatment on the basis of the detailed findings of examinations performed 5 days after visiting the nearby hospital.

At the time of referral to our hospital, physical findings showed she had a soft and flat abdomen, with tenderness in the epigastric region. Although blood tests showed that C-reactive protein was mildly elevated to 1.75 mg/dL, carcinoembryonic antigen (CEA) (< 1.0 ng/mL) and carbohydrate antigen (CA) 19-9 (< 37.0 U/mL) levels were within the normal range. A subsequent upper GI endoscopy revealed hyperemia of the gastric corpus, protruding erosions in the antrum, and severe edematous changes in the duodenum (Fig. 1A). The initial abdominal CT conducted at our hospital revealed circumferential wall thickening around the antroduodenal lesions, with thickening of the surrounding fatty tissue and lymphadenopathy (Fig. 2A). FDG-PET showed a high degree of FDG accumulation in the antroduodenal lesion [standardized uptake value (SUV)_{max}: 7.09], suspicious of malignant lymphoma (Fig. 2B), and the lymphadenopathy was not FDG avid. Histopathological examination of a biopsy specimen obtained during upper GI endoscopy indicated a large amount of eosinophil infiltration [14–21 cells/high power field (HPF)] in the duodenal mucosa without any malignant cells (Fig. 4),

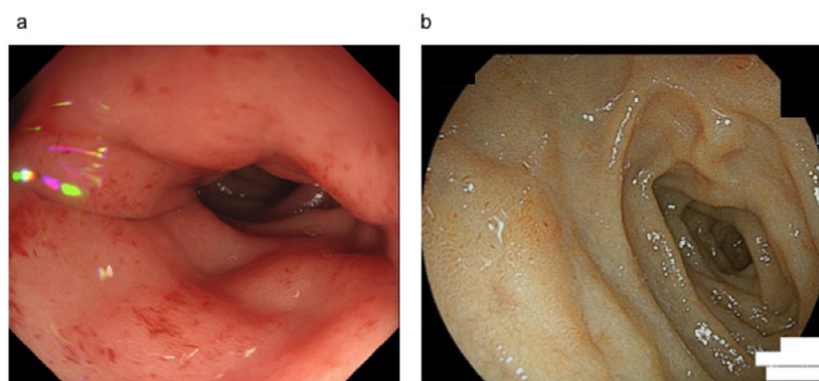


Fig. 1 – Upper gastrointestinal endoscopy. (A) An initial upper gastrointestinal endoscopic image showed marked mucosal edema with redness in the duodenal wall. (B) The degree and extent of thickening of the duodenal wall was improved after 3 weeks of vonoprazan fumarate treatment. (Color version of figure is available online).

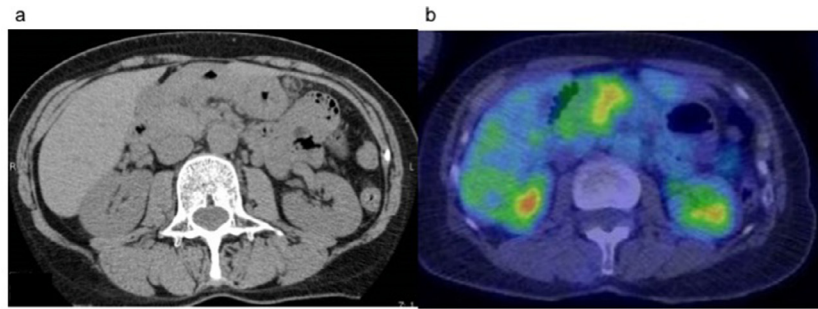


Fig. 2 – Abdominal computed tomography and positron emission tomography/computed tomography (PET/CT) findings. (A) Abdominal computed tomography showed circumferential wall thickening around the antroduodenal lesions with an increase in the concentration of the surrounding fatty tissues after the initial upper gastrointestinal endoscopic examination. (B) Positron emission tomography/computed tomography (PET/CT) showed a high degree of F-18 fluorodeoxyglucose (FDG) accumulation in the antroduodenal lesions [standardized uptake value (SUV)_{max}: 7.09].

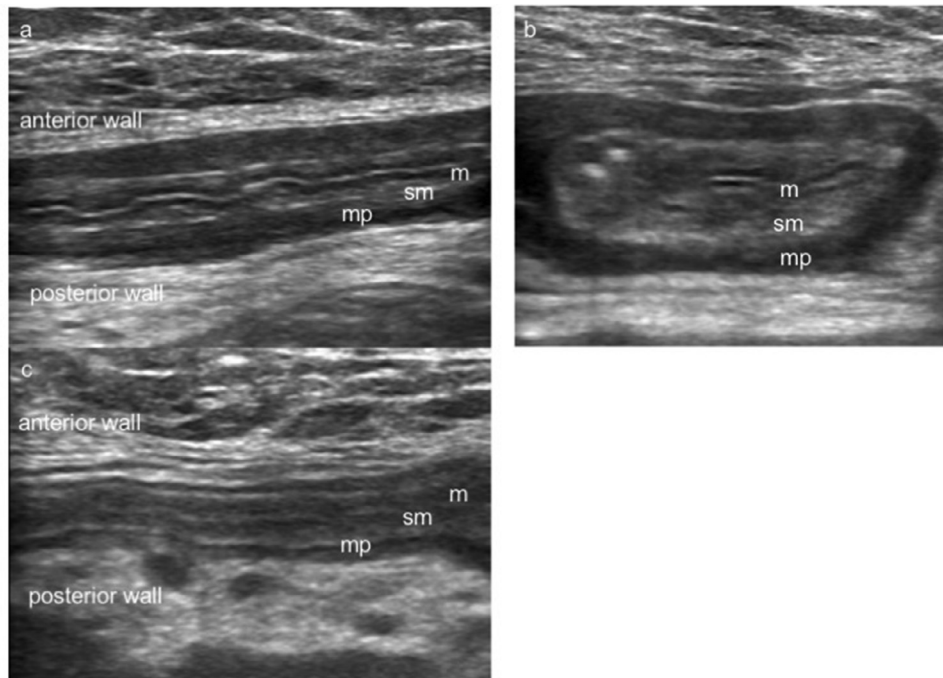


Fig. 3 – Abdominal ultrasonography findings. (A) Abdominal ultrasonographic images. Circumferential wall thickening around the duodenal lesions accompanied by thickening of the surrounding fat tissues was observed after PET/CT examination. (B) Circumferential wall thickening around the antral lesions was observed. (C) Circumferential wall thickening around the duodenal lesions improved after 3 weeks of vonoprazan fumarate treatment. m: mucosa, sm: submucosa, mp: muscularis propria.

as well as a high proportion of eosinophil infiltration (20 cells/HPF) in the antral mucosa. There were no endoscopic findings indicative of eosinophilic esophagitis identified in the esophageal mucosa of this patient. Thus, a blind biopsy was performed and no significant eosinophil infiltration in the esophageal epithelium was observed in the biopsy tissue. We followed the clinical practice guidelines of EGE in Japan, clarifying that, in EGE, eosinophilic infiltration is present in the gastric, small intestine, or large intestine mucosa, and meets the following conditions: (1) eosinophil infiltration of 20 cells/HPF or higher; (2) biopsy should be performed at

several sites; and (3) it is necessary to exclude other inflammatory intestinal diseases, parasite diseases, and systemic diseases [7]. A subsequent abdominal ultrasound (US) showed circumferential wall thickening with preserved wall stratification around the antroduodenal lesions, accompanied by an increased concentration of surrounding fatty tissues (Fig 3A,B). According to the abovementioned findings, including preserved gastric wall stratification, we considered EGE to be the diagnosis rather than malignant lymphoma. First, 20 mg vonoprazan fumarate/day was administered because the patient refused steroid treatment and the pathological le-

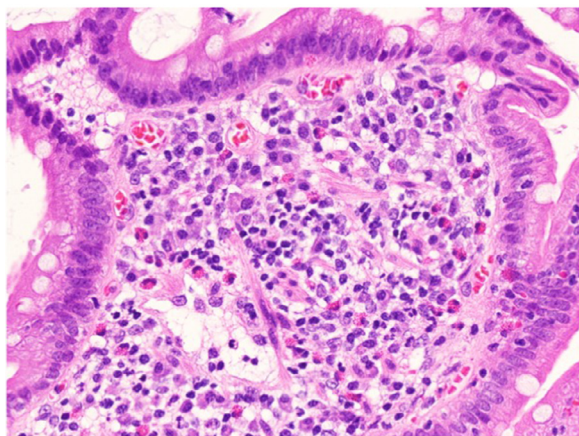


Fig. 4 – Histology. Histopathological findings of the biopsy specimen showed a large amount of eosinophil infiltration [14–21 cells/ high power field (HPF)] in the duodenal mucosa at the initial upper gastrointestinal endoscopic examination.

sion was localized from the duodenum to the antrum. After 3 weeks of treatment, her symptoms were alleviated, and the degree and extent of the gastroduodenal wall thickening in both upper GI endoscopy (Fig. 1B) and US image findings had remarkably improved (Fig. 3C). The patient was then administered 20 mg esomeprazole/day as a maintenance therapy for acid secretion suppression. She was feeling well with no recurrence of her symptoms. She underwent CT examination twice and US three times during the 6-month follow-up period, but the lymphadenopathy remained improved and no recurrence was observed.

Discussion

To the best of our knowledge, this is the first case report showing increased FDG uptake by PET/CT in thickened antroduodenal lesions in an EGE patient. To date, several studies have reported surgeries undertaken in EGE patients because of suspected malignant GI disease [4–6]. In this case, malignant lymphoma was initially considered because notable wall thickening around the antroduodenal lesion with increased FDG uptake was observed, in parallel with upper gastrointestinal endoscopic findings. FDG PET is often used to determine the metastatic status of malignant diseases, but in recent years, FDG uptake in the gastrointestinal tract has also been significantly associated with inflammation of this lesion [8]. FDG-avid in the esophageal wall has been reported in eosinophilic esophagitis [9], although the affected organ was not gastroduodenal, as in this case, but in the esophagus. Its pathogenesis is considered similar to that of EGE in that eosinophils infiltrate the target organ, suggesting that FDG-avid EGE is a rare but not one-off event. A previous study demonstrated that evaluation of FDG uptake was a non-invasive process and a highly predictive biomarker of eosinophilic airway inflammation and its functional effects. Accordingly, the authors con-

cluded that FDG PET/CT might serve to assist the understanding of allergic inflammation and in the testing of the therapeutic effectiveness of novel drugs or treatments [10]. We suspect that the accumulation of FDG in our case will also improve after treatment, although this could not be assessed because the patient did not give her consent. Considering studies in other fields, including allergic respiratory disease, FDG accumulation may be used for determining the disease treatment course. However, further studies are necessary to confirm this.

EGE is generally treated with systemic oral steroid administration, which is reportedly effective in temporarily relieving symptoms at least [11]. However, there have been no randomized controlled studies of EGE treatment, and there is no proven therapy with sufficient evidence [12]. A recent study showed a lack of universal response to corticosteroids in a cohort of EGE patients, bringing into question the clinical usefulness of this medication on the basis of high-level research results, especially considering its potential adverse side effects. This may also suggest that non-allergic or non-immune-mediated pathogenic mechanisms are at play in some patients [13]. A recent interesting case report showed that proton pump inhibitor (PPI) treatment decreased duodenal and esophageal eosinophilia in a patient with EGE [14]. Several studies have shown that PPIs have acid-independent anti-inflammatory effects, which may improve EGE. Furthermore, inflammatory cells have H⁺/K⁺ adenosine triphosphatases (proton pumps), which pump protons into the extracellular space or into intracellular organelles such as lysosomes [15]. In neutrophils and monocytes, PPIs can inhibit the oxidative burst and cell migration by inhibiting proton pumps [16,17]. To our knowledge, anti-inflammatory properties have not been reported for vonoprazan fumarate thus far. However, vonoprazan fumarate may also have anti-inflammatory effects because it can inhibit proton pumps more strongly than PPIs [18,19], although further studies are necessary to confirm this point. In the current case, vonoprazan fumarate treatment alone relieved the subjective symptoms and reversed the initial endoscopic and ultrasonographic findings.

In conclusion, our case indicates that EGE should be considered as a differential diagnosis of abnormal accumulation of FDG uptake in the GI wall. Treatment with a P-CAB is a potential alternative approach to systemic oral steroid administration therapy in patients with EGE.

Compliance with Ethical Standards

This article does not contain any studies involving human participants performed by any of the authors.

REFERENCES

- [1] Klein NC, Hargrove RL, Sleisenger MH, Jeffries GH. Eosinophilic gastroenteritis. *Medicine* 1970;49:299–319.
- [2] Ingle SB, Hinge Ingle CR. Eosinophilic gastroenteritis: an unusual type of gastroenteritis. *World J Gastroenterol* 2013;19:5061–6.

- [3] Ranjzad F, Mahban A, Shemirani AI, Mahmoudi T, Vahedi M, Nikzamir A, et al. Influence of gene variants related to calcium homeostasis on biochemical parameters of women with polycystic ovary syndrome. *J Assist Reprod Genet* 2011;28:225–32.
- [4] Madhotra R, Eloubeidi MA, Cunningham JT, Lewin D, Hoffman B. Eosinophilic gastroenteritis masquerading as ampullary adenoma. *J Clin Gastroenterol* 2002;34:240–2.
- [5] Kotru M, Aggarwal S, Sharma S, Usha Rani Singh UR. Eosinophilic gastritis masquerading as gastric carcinoma. *Indian J Pathol Microbiol* 2010;53:380–2.
- [6] Bori R, Cserni G. Eosinophilic gastritis simulating gastric carcinoma. *Orv Hetil* 2003;144:529–31.
- [7] Kinoshita Y, Ishihara S, Amano Y, et al. Diagnosis and treatment of eosinophilic gastroenteritis. *Gastroenterol Endosc* 2012;54:1797–805.
- [8] Kitajima K, Nakajo M, Kaida H, Minamimoto R, Hirata K, Tsurusaki M, et al. Present and future roles of FDG-PET/CT imaging in the management of gastrointestinal cancer: an update. *Nagoya J Med Sci* 2017;79:527–43.
- [9] Dong A, Wang Y, Zuo C. FDG PET/CT in eosinophilic esophagitis. *Clin Nucl Med* 2014;39:540–3.
- [10] Harris RS, Venegas JG, Wongviriyawong C, Winkler T, Kone M, Musch G, et al. 18F-FDG uptake rate is a biomarker of eosinophilic inflammation and airway response in asthma. *J Nucl Med* 2011;52:1713–20.
- [11] Kinoshita Y, Furuta K, Ishimaura N, Ishihara S, Sato S, Maruyama R, et al. Clinical characteristics of Japanese patients with eosinophilic esophagitis and eosinophilic gastroenteritis. *J Gastroenterol* 2013;48:333e9.
- [12] Méndez-Sánchez N, Chaávez-Tapia NC, Vazquez-Elizondo G, et al. Eosinophilic gastroenteritis: a review. *Dig Dis Sci* 2007;52:2904–11.
- [13] Reed C, Woosley JT, Dellon ES. Clinical characteristics, treatment outcomes, and resource utilization in children and adults with eosinophilic gastroenteritis. *Dig Liver Dis* 2015;47:197–201.
- [14] Yamada Y, Toki F, Yamamoto H, et al. Proton pump inhibitor treatment decreased duodenal and esophageal eosinophilia in a case of eosinophilic gastroenteritis. *Allergol Int* 2015;64:S83–5 Suppl.
- [15] Lafourcade C, Sobo K, Kieffer-Jaquinod S, et al. Regulation of the V-ATPase along the endocytic pathway occurs through reversible subunit association and membrane localization. *PLoS ONE* 2008;3:e2758.
- [16] Suzuki M, Mori M, Miura S, et al. Omeprazole attenuates oxygen-derived free radical production from human neutrophils. *Free Radic Biol Med* 1996;21:727–31.
- [17] Handa O, Yoshida N, Fujita N, et al. Molecular mechanisms involved in anti-inflammatory effects of proton pump inhibitors. *Inflamm Res* 2006;55:476–80.
- [18] Sakurai Y, Mori Y, Okamoto H, et al. Acid-inhibitory effects of vonoprazan 20 mg compared with esomeprazole 20 mg or rabeprazole 10 mg in healthy adult male subjects—a randomised open-label cross-over study. *Aliment Pharmacol Ther* 2015;42:719–30.
- [19] Ishimura N, Kinoshita Y. Eosinophilic Esophagitis in Japan: Focus on Response to Acid Suppressive Therapy. *J Gastroenterol Hepatol* 2018;33:1016–22.