

Eosinophilic gastroenteritis associated with multiple gastric cancer

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Eosinophilic gastroenteritis (EG) is an inflammation of the digestive tract that is characterized by eosinophilic infiltration. There are no specific symptoms, and are related to the layer in which eosinophilic infiltration is observed. A 69-year-old Japanese man presented to our hospital with a history of general malaise, diarrhea, and dysgeusia. Esophagogastroduodenoscopy showed reddish elevated lesions that were edematous all over the gastric mucosa. In addition, three tumors were also observed. The biopsies of the reddish elevated mucosa revealed eosinophilic infiltration and tubular adenocarcinoma from the tumors. Colonoscopy showed abnormal reddish elevated mucosa. The biopsies from the reddish elevated mucosa showed eosinophilic infiltration. From the abdominal contrast computed tomography scan, tumor stain was seen in the anterior wall of the gastric body. No ascites, intestinal wall thickening, or lymph node swelling were found. A slight elevation in the serum immunoglobulin E (IgE), 480 IU/ml, was found from the laboratory test results; other laboratory results were within normal limits including the number of peripheral eosinophils. No specific allergen was found from the multiple antigen simultaneous test and from the skin patch test.

The parasitic immunodiagnosis was negative. He was diagnosed with EG associated with gastric cancer and underwent total gastrectomy, regional lymph node dissection with reconstruction by a Roux-en-Y method. He was prescribed prednisolone after the operation and showed a good clinical response. There are many case reports on EG, but none of them were associated with cancer. We encountered a case of EG associated with multiple gastric cancer; the patient underwent total gastrectomy. *Eur J Gastroenterol Hepatol* 24:727–730 © 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins.

European Journal of Gastroenterology & Hepatology 2012, 24:727–730

Keywords: eosinophilic colitis, eosinophilic gastroenteritis, eosinophilic gastrointestinal disorders, gastrectomy, multiple gastric cancer

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Received 15 January 2012 Accepted 10 February 2012

Introduction

Eosinophilic gastrointestinal disorders (EGIDs) are a group of inflammatory diseases of unknown origin, whose common histological characteristic is related to the eosinophilic leukocytes affecting different layers and sections of the digestive tract without any known causes of eosinophilia. Therefore, the long-term prognosis for EGIDs is usually good. To the best of our knowledge, there have been no case of EGIDs associated with cancer, but there may be a relationship between EGIDs and gastric cancer.

Case report

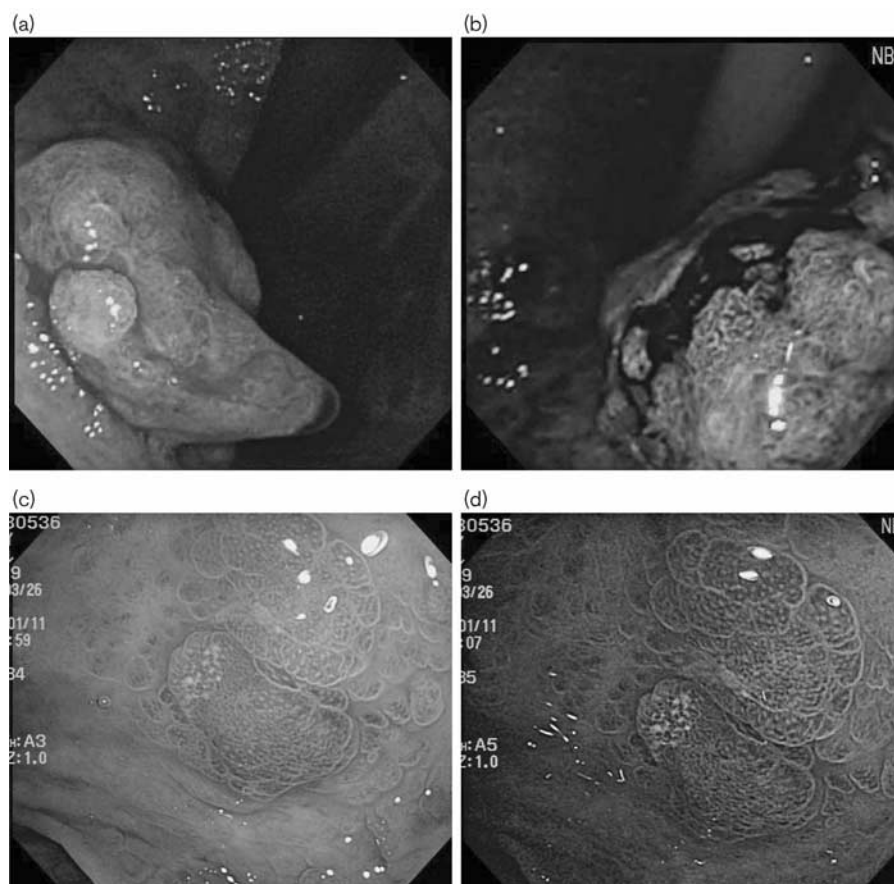
A 69-year-old Japanese man presented to our hospital with a history of general malaise, diarrhea, and dysgeusia. Physical examination revealed no abnormal findings. He had no personal history or family history of atopy, asthma, and allergies.

Esophagogastroduodenoscopy showed reddish elevated lesions that were edematous all over the gastric mucosa. Type 1 tumors were observed in the lesser curvature of

the antrum and the anterior wall of the gastric body. Narrow band imaging examination showed an irregular pit pattern and obscuration on some parts of the surface (Fig. 1a and b). A type 0-I tumor was observed in the posterior wall of the gastric body. Biopsies of the reddish elevated mucosa revealed an eosinophilic infiltration and tubular adenocarcinoma from the tumors (Fig. 2a and b). No specific changes were observed in the esophagus. Colonoscopy showed abnormal reddish elevated mucosa throughout the colon, but there were no mucosal changes in the small intestine. Narrow band imaging examination of the colon surface was sharply defined and showed a regular pit pattern (Fig. 1c and d). The biopsies were taken from the reddish elevated mucosa and showed eosinophilic infiltration (Fig. 2c and d). Therefore, the diagnosis of EG-associated multiple gastric cancer was confirmed.

From the abdominal contrast computed tomography scan, tumor stain was seen in the anterior wall of the gastric body. No ascites, intestinal wall thickening, or lymph node swelling were found.

Fig. 1



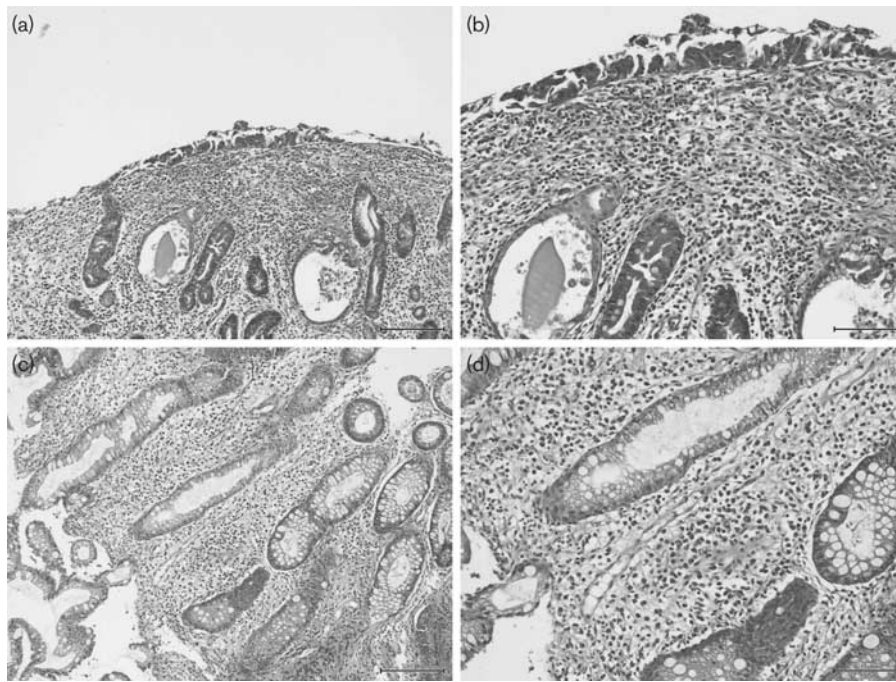
Esophagogastroduodenoscopy of the stomach showed reddish elevated lesions that were edematous all over the gastric mucosa. Narrow band imaging (NBI) examination showed an irregular pit pattern and obscuration on some parts of the surface (a, b). Colonoscopy of the large intestine showed abnormal reddish elevated mucosa throughout the colon, but there were no mucosal changes in the small intestine. NBI examination of the colon surface was sharply defined and showed a regular pit pattern (c, d).

The laboratory test results were within normal limits, except for a slight elevation in serum IgE: 480 IU/ml. The other laboratory data were as follows: white blood cell $8100/\text{mm}^3$, peripheral eosinophil $160/\text{mm}^3$, carcinoembryonic antigen 1.5 ng/ml, and carbohydrate antigen 19-9 4.5 U/ml. No specific allergen was found from the multiple antigen simultaneous test, and the parasitic immunodiagnosis was negative. He was subjected to a standard and metallic skin patch test, but the results were negative.

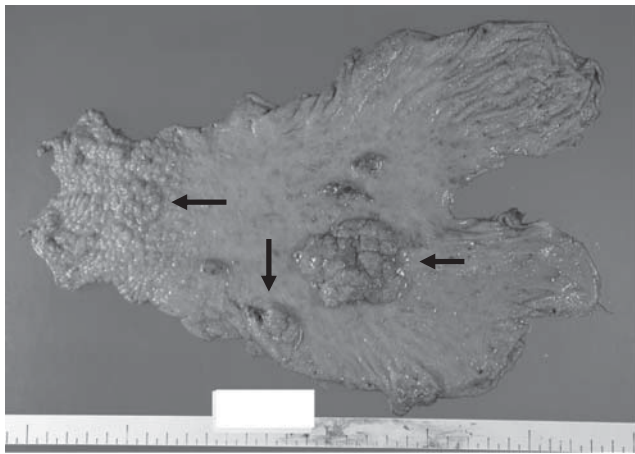
He underwent total gastrectomy and regional lymph node dissection with reconstruction by the Roux-en-Y method. There were no specific macroscopic changes in the stomach and intestine, such as wall thickening or sclerosis. No swelling of the lymph nodes and ascites were observed. The pathological findings showed an eosinophilic infiltration in the mucosal layer, but no eosinophilic infiltration was observed in the peritoneal wash (Figs 3 and 4). Three gastric cancers and hyperplastic polyps were

also observed. The eosinophilic infiltration was also observed in the tissue of the cancer and the hyperplastic polyps. According to the Japanese Classification of Gastric Cancer, the histopathological diagnosis was pT2(3), INFa, ly1, v1, pN0, pPM0, pDM0, sM0, sP0, pCY0, sH0, fstageIB, and R0 and no adjuvant chemotherapy was performed.

Diarrhea was still observed after the operation and he was prescribed olopatadine hydrochloride 20 mg per day. After a month of treatment with olopatadine hydrochloride, a colonic fiberscope was performed. Reddish elevated mucosa was still observed, but the range of redness had improved. There was no difference in the serum IgE level and the frequency of diarrhea. Therefore, he was prescribed prednisolone 40 mg per day and the dose was gradually reduced. Prednisolone induced a very good clinical response and the findings of the colonic fiberscope improved markedly. Although eosinophilic infiltration was still seen in the mucosa, reddish elevated

Fig. 2

Histopathological findings showed eosinophilic infiltration in the noncancerous lesions of the stomach [hematoxylin–eosin: (a) $\times 100$, (b) $\times 200$] and the colon [hematoxylin–eosin: (c) $\times 100$, (d) $\times 200$].

Fig. 3

Macroscopic findings of the resected specimen. Multiple gastric carcinoma (black arrows) were seen in the stomach.

mucosa and the range of redness was only seen in a limited area.

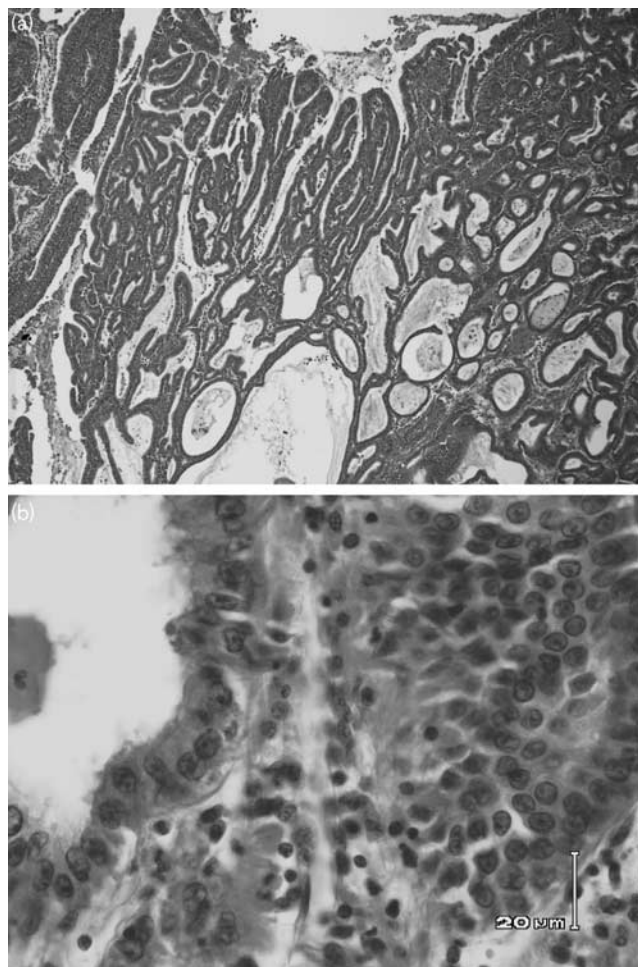
Discussion

EGIDs are classified into three groups on the basis of the location of the eosinophilic infiltration, although their

symptoms, prognosis, and treatment vary. Eosinophilic esophagitis is the most common disorder in this group and eosinophilic infiltration is observed in the esophagus. Eosinophilic gastroenteritis (EG) is a rare disorder involving the stomach and the small bowel. In certain cases, it also involves the esophagus or the colon. Eosinophilic colitis is considered as a specific non-IgE-mediated allergy to food protein and is usually observed in children.

A case report of EG was first reported by Kaijser in 1937 [1]. The current generally accepted criteria are as follows: (a) presence of recurrent gastrointestinal symptoms, (b) biopsies with a histopathology showing predominant eosinophilic infiltration with sheets of eosinophils, and (c) absence of parasitic or extraintestinal diseases that may cause eosinophilia [2].

EG involves tissue eosinophilia of any layer or layers of the gut wall, stomach, or small bowel. The symptoms are linked to the layer in which eosinophilic infiltration is observed and are classified into three major types. The predominant mucosal layer disease is the most common, and presents with nonspecific symptoms such as abdominal pain, nausea, vomiting, and diarrhea. The predominant muscle layer diseases are often observed with intestinal obstruction such as thickening or sclerosis of the bowel wall, ileus, and perforation of the bowel wall. The predominant subserosal layer disease presents with eosinophilic ascites.

Fig. 4

Microscopic findings of the tumor. Eosinophilic infiltration was seen in the type 1 tumor [hematoxylin–eosin: (a) $\times 40$, (b) $\times 200$].

It occurs mainly in the third and fourth decades of life, is more common in men, and occurs mostly in the Caucasian population [3]. Elevation in the peripheral eosinophilia is found in up to 80% of patients [4]. In the mucosal and serosal types of the disease, a history of atopy is common and does not occur in the muscular types [5]. A history of drug and food allergies is common in all types, but commonly available allergy tests have a low sensitivity and high rates of false-positive results [3]. Steroid therapy is a highly effective treatment with a rapid clinical response and combination with another therapy leads to a higher response [3].

In our patient, there was no past history of allergies and the peripheral eosinophilia was normal. However, a slight elevation in the serum IgE suggested allergic disorders, parasitic disorders, and lymphoma. The possibility of parasitic disorders and abdominal lymphoma were excluded because of the history of the present illness, physical findings, and the laboratory results.

To avoid the side-effects of systemic steroids, topical steroids such as fluticasone propionate and budesonide solution are used widely. In some case reports, the clinical usefulness of anti-inflammatory steroid drugs such as ketotifen, sodium cromoglicate, and montelukast sodium has been reported. We chose olopatadine hydrochloride because it is known to suppress eosinophilic infiltration.

There are some reports of EG in which an operation has been conducted. The most common reason for the operation was intestinal obstruction such as thickening or sclerosis of the bowel wall. These symptoms are caused by eosinophilic infiltration in the predominant subserosal layer, and is sometimes misdiagnosed as cancer. To the best of our knowledge, there are no reports associated with gastric cancer.

There are several risk factors for multiple gastric cancer such as intestinal metaplasia of the gastric mucosa, atrophic changes in the gastric mucosa, and the presence of *Helicobacter pylori*. In our patient, the presence of *H. pylori* was confirmed and the eosinophilic infiltration was seen in the mucosal layer and also in the tissue of the cancer and the hyperplastic polyps. As a case of EG associated with gastric cancer is very rare, we need to accumulate reports to determine the relationship between EG and multiple gastric cancers.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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