Internal Medicine

【 CASE REPORT 】

Eosinophilic Gastroenteritis in Which Obstructive Jaundice Developed due to Invagination of the Duodenal Wall

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Abstract:

A 63-year-old woman was admitted with epigastric pain, eosinophilia, and elevated hepatobiliary enzyme levels. An upper gastrointestinal endoscopic examination showed that the mucosa of the gastroduodenal wall was edematous. Eosinophilic gastroenteritis (EGE) was diagnosed based on eosinophilic infiltration of the gastroduodenal mucosa. Computed tomography showed invagination of the duodenal wall into the common bile duct. The invagination of the duodenal wall improved after conservative therapy, while bile duct drainage was impossible due to the narrowing of the duodenal lumen. EGE was successfully treated without recurrence with steroids and antiallergic therapy. We herein report a rare case of EGE with obstructive jaundice.

Key words: eosinophilic gastroenteritis, obstructive jaundice

Introduction

Eosinophilic gastroenteritis (EGE) is a relatively rare disease that was first reported by Kaijser et al. in 1937 (1). It is characterized by peripheral blood eosinophilia and eosinophilic infiltration of the gastrointestinal wall. Although EGE causes various clinical symptoms-depending on the depth of eosinophilic infiltration-obstructive jaundice is a rare symptom of EGE. In this report, we present a rare case of EGE in which obstructive jaundice developed due to invagination of the duodenal wall.

Case Report

A 63-year-old woman presented to her family doctor with a high fever and epigastric pain of 3 months' duration. An upper gastrointestinal endoscopic examination revealed edematous thickening of the gastroduodenal mucosa. She was transferred to our hospital to undergo a further examination. A physical examination on admission to our hospital revealed a body temperature of 38.3℃. She had mild tenderness in the epigastric region but no jaundice in the bulbar conjunctiva. The laboratory data on admission showed

eosinophilia (white blood cell count, 8,430/μL with 2,613/μL eosinophils) and elevated hepatobiliary enzyme levels [aspartate aminotransferase (AST), 200 IU/L; alanine aminotransferase (ALT), 210 IU/L; alkaline phosphatase, 888 IU/L; total bilirubin (T-Bil), 0.6 mg/dL]. As shown in Table 1, the other laboratory findings were as follows: elevated C-reactive protein (CRP, 6.22 mg/dL), amylase (239 IU/L), immunoglobulin E (IgE, 1,060 IU/mL). Tests for viral hepatitis, antibodies for autoimmune diseases, and specific anti-parasite antibodies, including the anti-anisakis antibodies IgG and IgA, were negative. A microscopic test of a stool sample for parasites was also negative. No parasitic worms were confirmed on capsule endoscopy. No abnormalities were detected in the eosinophilic morphology, and the patient's bone marrow was negative for the FIP1L1-PDGFRα fusion gene. Other diseases that might have caused eosinophilia, such as parasite infection or hypereosinophilic syndrome, were excluded. She had no history of allergic disease and was not taking any medicine. Before her epigastric pain appeared, her daily alcohol intake had been 40 g (converted to pure ethanol). An upper gastrointestinal endoscopic examination showed that the mucosa of the stomach and duodenum was thickened and edematous (Fig. 1). The descending part of the duodenum was edema-

Table 1.   The Laboratory Data on Admission.

Peripheral blood		Biochemistry			
WBC	**8,430 /μL**	**TP**	**6.6 g/dL**	IgG	997 mg/dL
Stab	0.5 %	**Alb**	**3.5 g/dL**	IgG4	63.1 mg/dL
Seg	59.5 %	BUN	10 mg/dL	**IgE**	**1,060 IU/mL**
Lymph	6.5 %	Cre	0.66 mg/dL	IgA	273 mg/dL
Mono	1.5 %	T-Bil	0.6 mg/dL	RF	<5.0 U/mL
Eosino	**31 %**	D-Bil	0.2 mg/dL	ANA	1:40
Baso	1 %	**AST**	**200 IU/L**	MPO-ANCA	<1.0 U/mL
RBC	434×10⁴ /μL	**ALT**	**210 IU/L**	PR3-ANCA	<1.0 U/mL
Hb	13.4 g/dL	**LDH**	**342 IU/L**	**Prealbumin**	**7.6 mg/dL**
Hct	39 %	**γ-GTP**	**201 IU/L**	**Transferrin**	**171 mg/dL**
Plt	24.6×10⁴ /μL	**ALP**	**888 IU/L**	**Retinol-binding protein**	**0.8 mg/dL**
		AMY	**239 IU/L**	**Soluble interleukin-2 receptor**	**1,619 U/mL**
Coagulation				**Interleukin-5**	**4.8 pg/mL**
PT	88 %	Na	138 mEq/L	Specific anti-parasite antibody	Negative
PT-INR	1.07	K	4 mEq/L	IgE-MAST33	Shrimp (class 1)
		Cl	104 mEq/L	Anti-Anisakis antibodies IgG and IgA	Negative
Tumor marker		**CRP**	**6.22 mg/dL**		
CEA	1 ng/mL			Bone marrow	
CA19-9	10.4 U/mL			FIP1L1-PDGFRα fusion gene	Negative

MPO: Myeroperoxidase, ANCA: antineutrophil cytoplasmic antibody, PR3: Proteinase 3, MAST: Multiple antigen simultaneous test, FIP1L1: Fip1-like 1, PDGFR: platelet-derived growth factor receptor
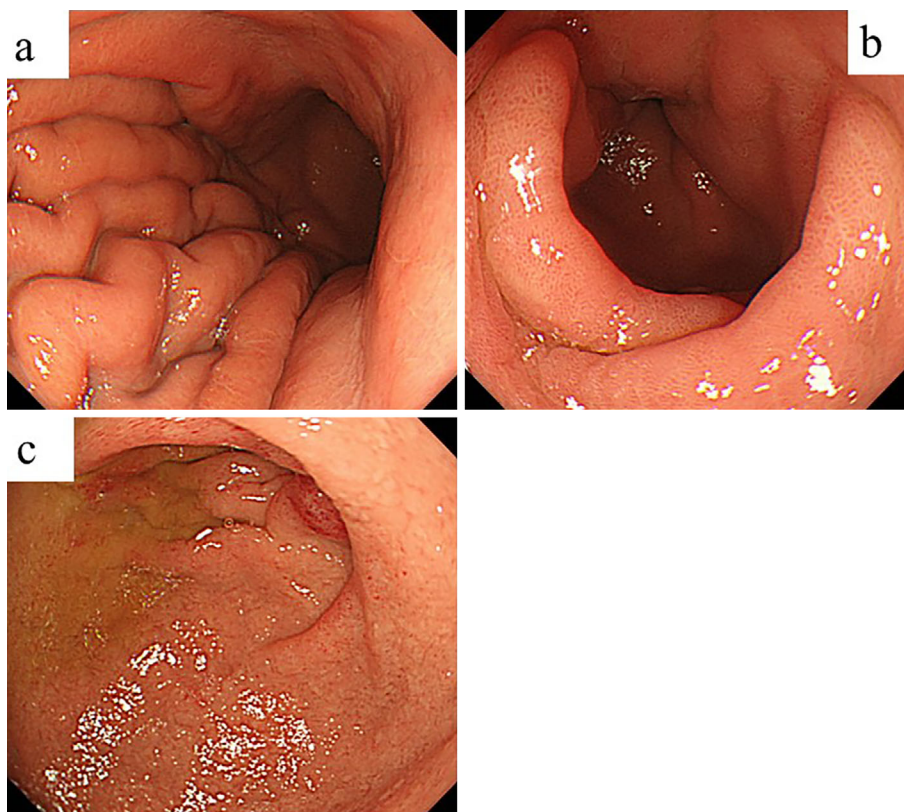

Figure 1.   An upper gastrointestinal endoscopic examination before treatment showed that the mucosa of the stomach and duodenum was edematous and thickened; (a) the gastric body, (b) the antrum and (c) the duodenal bulb.

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tous (Fig. 2f), so the papilla of the ampulla of Vater was not detected. Endoscopic ultrasound (EUS) of the duodenum revealed extreme thickening of the mucosal and muscular wall (Fig. 2d). Capsule endoscopy showed that the jejunum was thickened and edematous. The esophagus, ileum and colon showed no abnormal endoscopic findings. The histopa-
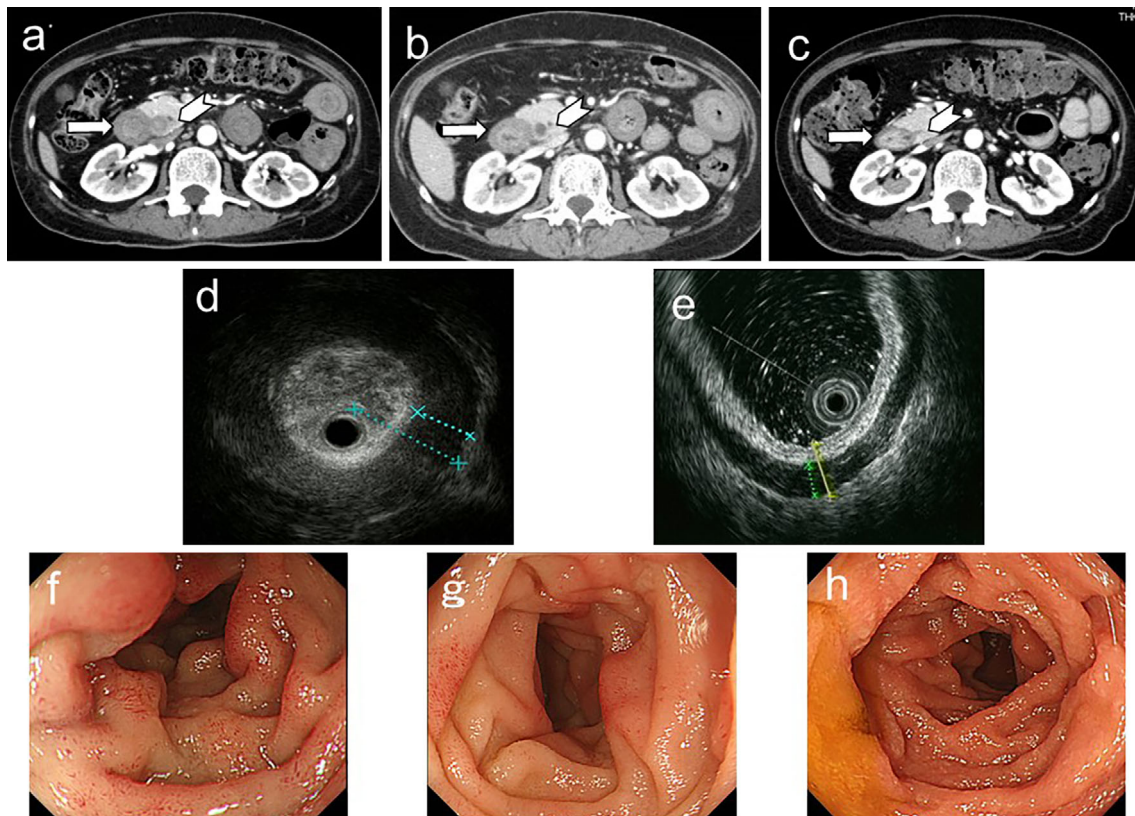
Figure 2. Contrast-enhanced computed tomography (CT) findings (a-c) and endoscopic ultrasound (EUS) findings of the duodenum (d-e), upper gastrointestinal endoscopic examination findings (f-h). (a) CT revealed the thickening of the gastroduodenal mucosal wall (arrow), and (d) EUS of the duodenum revealed extreme thickening of the mucosal and muscular walls. (c) (e) Both findings were improved after steroid therapy. In contrast, (b) dilation of the bile duct (arrow head) and (g) narrowing of the lumen of the second part of duodenum diminished before steroid therapy. (a) (d) (f) On admission, (b) (g) five days before steroid administration and (c) (e) (h) two weeks after steroid administration.
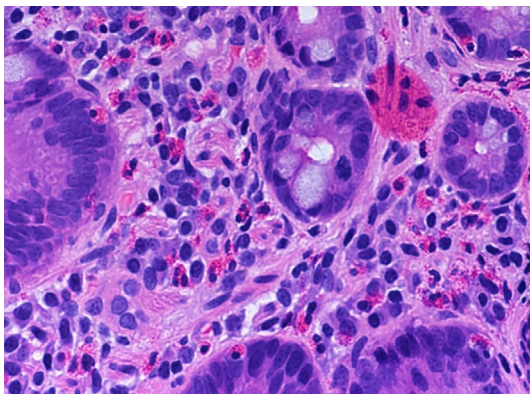

Figure 3. The histological examination of the duodenal mucosa. Hematoxylin and Eosin staining (magnification×400): Eosinophilic infiltration ≥100 per high-power field (HPF) was observed in the duodenal mucosa.

thological examination of a biopsy specimen of the stomach and duodenum mucosa revealed significant eosinophilic infiltration (Fig. 3). A histopathological examination of biopsy specimens of the esophagus, colon and ileum end appeared normal, with eosinophilic infiltration <20 per high-power field (HPF).

We diagnosed our patient to have mixed-type (both mucosal and muscular type) EGE, based on the symptoms as well as the imaging and pathological findings. Jaundice occurred during the clinical course after admission. Abdominal contrast-enhanced computed tomography (CT) showed the marked thickening of the gastrointestinal wall (Fig. 2a), liver abscesses in the left lobe of the liver (Fig. 4a and b) and biliary dilatation. Regarding magnetic resonance imaging (MRI), the abscesses showed a positive signal on diffusion-weighted imaging (Fig. 4c), findings that were compatible with abscesses. The diameter of the common bile duct had expanded to 15 mm, and the diameter of the main pancreatic duct was 2.8 mm. Furthermore, invagination of the duodenal wall to the common bile duct was confirmed (Fig. 4d). Magnetic resonance cholangiopancreatography (MRCP) also showed invagination of the duodenal wall into the common bile duct (Fig. 5a). Other causes of obstruction of the bile duct were not observed by either of these imaging modalities. A liver biopsy was performed to exclude eosinophilic cholangitis at day 30 after admission. A histo-
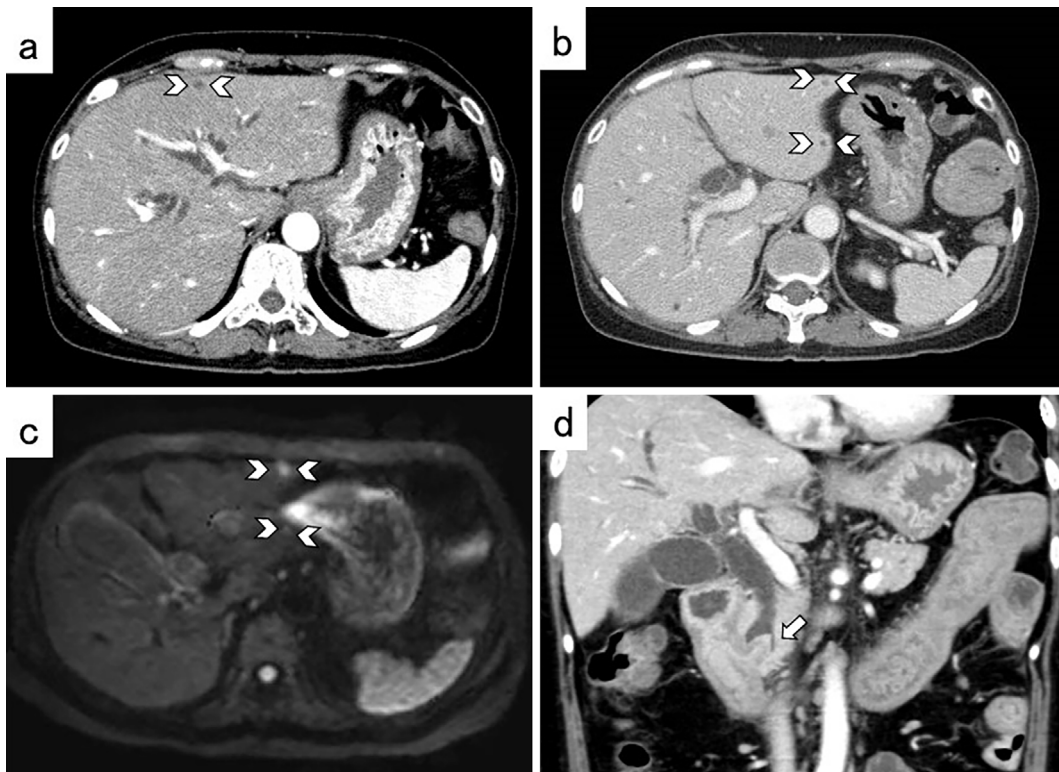
Figure 4. Abdominal contrast-enhanced computed tomography (CT) and dynamic contrast-enhanced magnetic resonance imaging (MRI) findings. (a) (b) CT showed the common bile duct dilatation and micro abscesses in the left lobe of the liver (arrowhead). (c) Regarding MRI, the abscesses showed a positive signal on diffusion-weighted imaging (arrowhead). (d) In the CT examination, invagination of the duodenal wall caused bile duct dilatation (arrow).
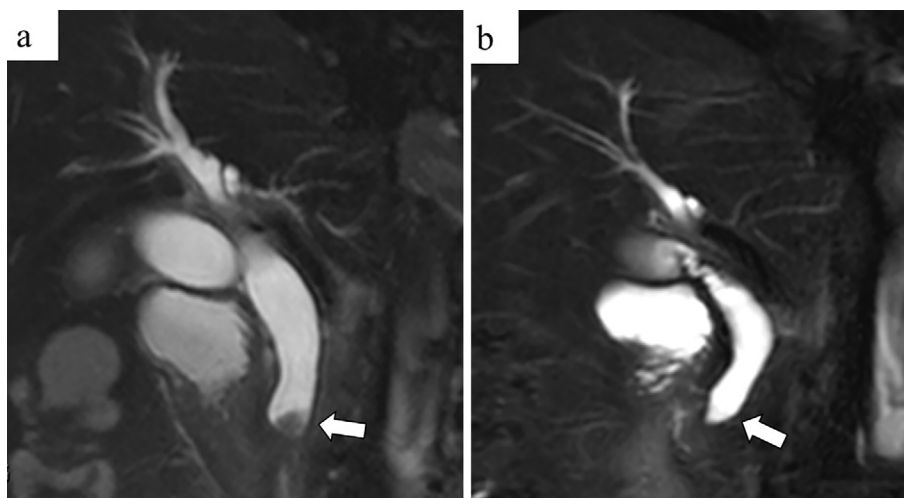

Figure 5. The change in the invagination of the duodenal wall during the clinical course. The changes were observed by magnetic resonance cholangiopancreatography. Before steroid therapy (a); after half a year of steroid therapy (b).

pathological examination of the liver biopsy specimen showed no eosinophilic infiltration in the portal lesion or the destruction of the interlobular bile duct, and therefore we ruled out eosinophilic cholangitis. Given these findings, the cholangitis and hepatic abscesses were presumed to have been caused by biliary obstruction induced by the invagination of the duodenal wall into the common bile duct. Endo-

scopic retrograde cholangiopancreatography (ERCP) was attempted to treat the patient's cholangitis; however, insertion of the duodenoscope into the second part of the duodenum was not possible due to the narrowing of the duodenal lumen.

We initiated antibiotic treatment and fasting to treat the patient's cholangitis and liver abscesses. Following the in-
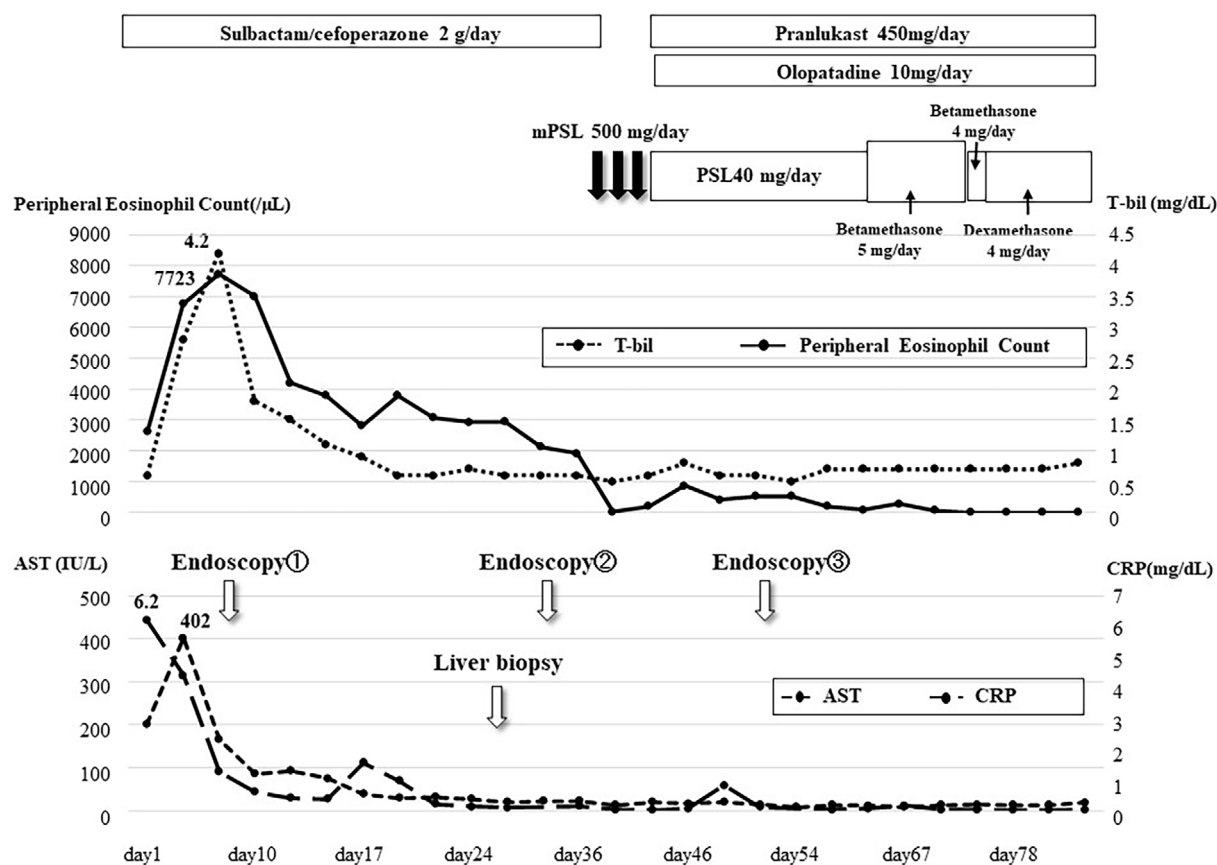
Figure 6.   The clinical course of the patient.

itiation of these conservative therapies, the patient's fever, inflammation-associated laboratory data, and hepatobiliary enzyme levels showed improvement. The liver abscesses, dilation of the bile duct, and narrowing of the lumen of the second part of duodenum also were improved after these conservative therapies (Fig. 2b and g). However, the patient's epigastric pain and eosinophilia persisted. Intravenous methylprednisolone was administered for three days to treat the clinical symptoms of EGE. Thereafter, oral prednisolone (PSL; 40 mg, daily) and antiallergic drug (pranlukast 450 mg daily and olopatadine 10 mg daily) were started. Her symptoms and eosinophilia improved following the initiation of steroids and antiallergic drugs (Fig. 6). The edematous thickening of the gastrointestinal wall disappeared after the initiation of the therapy (Fig. 2c and h). Although the dose of PSL was gradually tapered, erythema was observed all over the patient's body. A drug eruption due to steroids was diagnosed because lymphocyte stimulation tests for prednisolone and betamethasone were positive. The eruption improved after PSL was changed to dexamethasone. The dose of dexamethasone was gradually reduced and then maintained after discharge.

After six months of steroid treatment, MRCP revealed that the invagination of the duodenal wall into the common bile duct had disappeared (Fig. 5b) and that the diameters of both the bile duct and the pancreatic duct were normal. The patient is currently being followed as an outpatient. There has been no recurrence of EGE.

Discussion

We experienced a rare case of EGE in which obstructive jaundice developed. EGE is characterized by peripheral eosinophilia and the eosinophilic infiltration of the gastrointestinal mucosa. Although the etiology of EGE is unknown, 52% of patients with EGE have been reported to have allergic disease (2). Our patient also had drug allergies to PSL and betamethasone.

EGE causes various clinical symptoms, and abdominal pain and diarrhea are the chief complaints. The symptoms are related to the lesions of eosinophilic infiltration. Klein et al. classified EGE into three types according to the depth of eosinophilic infiltration: mucosal type, muscular type and serosal type (3). Patients with mucosal-type EGE usually present with diarrhea and malabsorption; those with muscular-type EGE present with symptoms of obstruction of the gastric outlet or small intestine; and those with serosal-type EGE present with eosinophilic ascites. We diagnosed our patient with combined-type (mucosal-type and muscular-type) based on the clinical symptoms and imaging findings.

Obstructive jaundice is a rare symptom of EGE. We searched the MEDLINE database for articles published from 1949 to 2016 using the keywords "eosinophilic gastroenteritis" and "jaundice" or "biliary obstruction." The search revealed nine reports, including our own case (4-11) (Table 2). Eosinophilic infiltration in the muscular layer of the duode-

Table 2. A Summary of the Nine Reported Cases of Eosinophilic Gastroenteritis with Obstructive Jaundice.

Case	Reference	Age	Sex	WBC (/μL)	Eosino (/μL)	T-Bil (mg/dL)	Depth of eosinophilic infiltration	Imaging findings of the biliary tract	Surgical procedure	Steroid therapy
1	4)	67	M	16,050	3,370	7.1	Mucosal and muscular layer	Bile duct and pancreatic duct dilatation	Gastrojejunostomy, choledochoduodenostomy	○
2	5)	60	M	12,800	2,944	1.5	Muscular and serosal layer	Bile duct dilatation	Gastrojejunostomy, cholecystojejunostomy	○
3	6)	15	M	ND	3,750	ND	Muscular and serosal layer	Bile duct and pancreatic duct dilatation	Exploratory laparotomy	○
4	7)	17	F	16,700	1,670	8.6	Muscular and serosal layer	Bile duct dilatation	Exploratory laparotomy	-
5	8)	47	M	15,600	>1,500	4.9	Muscular and serosal layer	Bile duct and pancreatic duct dilatation	Pylorus preserving pancreaticoduodenectomy	○
6	9)	59	F	14,100	3,102	ND	Mucosal layer (only biopsy)	Bile duct and pancreatic duct dilatation	-	○
7	10)	29	F	15,900	3,975	2.8	Muscular and serosal layer	Bile duct dilatation	Roux-en-y loop biliary disconnection	Lost to follow-up
8	11)	47	M	16,900	7,774	7.1	No description	Bile duct dilatation	Whipple procedure	○
9	Our case	63	F	12,660	7,722	4.2	Mucosal and muscular layer	Bile duct and pancreatic duct dilatation	-	○

WBC: white blood cells

num was histopathologically confirmed in all six cases in which surgery was performed. Dilatation of the bile duct and the main pancreatic duct was reported in five patients, including our own. We suspect that the infiltration of eosinophils into the mucosal and muscular layers of the duodenal wall caused reversible stenosis of the bile duct and pancreatic duct, which penetrated the wall. In addition, the invagination of the edematous duodenal wall was thought to have caused the biliary obstruction because both the patient's hepatobiliary enzyme levels and the degree of biliary dilation improved after the edematous duodenal mucosa around the ampulla of Vater was treated, and because the imaging findings revealed no other organic problems that could have caused obstruction of the bile duct.

Cholangitis was diagnosed based on the Tokyo guidelines for the management of acute cholangitis and cholecystitis (12). Cholangitis is usually caused by biliary obstruction. In addition, most liver abscesses are secondary to abdominal infections. Krige et al. reported that cholangitis due to biliary stones or stricture was the most common cause of liver abscesses (13). In our case, we suspect that the hepatic abscesses developed secondary from cholangitis, which had been caused by biliary obstruction due to the invagination of the duodenal wall. The hepatic abscesses diminished rapidly with the improvement in the inflammation-associated laboratory data and hepatobiliary enzyme levels by fasting and antibodies. A MEDLINE search with the keywords "eosinophilic gastroenteritis" and "hepatic abscess" or "liver abscess" from 1949 to 2016 turned up no reports. We therefore judged there to be no direct association between EGE and liver abscess.

In the present case, the invagination of the duodenal wall with thickening of the mucosal and muscular layers was a unique and interesting imaging finding. There are no previous reports of EGE with obstructive jaundice due to invagination of the duodenal wall; thus, the present case is very rare.

When patients with eosinophilia are diagnosed with EGE, the differential diagnosis should be considered before treatment. There was no clinical evidence of connective tissue disorder, parasitic infection, hypereosinophilic syndrome or malignancy. In cases such as ours, other diseases that are associated with elevated hepatobiliary enzyme levels, such as alcoholic hepatitis and eosinophilic cholangitis, should be ruled out. Alcoholic hepatitis was ruled out because the patient had hardly consumed any alcohol in the three months after epigastric pain appeared. Furthermore, her hepatobiliary enzyme levels were normal during the period in which she had been treated by her previous doctor. We also excluded the possibility of eosinophilic cholangitis based on a histopathological examination of the liver biopsy specimen. The liver biopsy was performed after the liver abscesses has diminished in size in order to avoid the spread of infection. Despite persistent eosinophilia, the liver biopsy specimen showed no eosinophilic infiltration into the portal lesion or the destruction of the interlobular bile ducts, both of which are needed to make a diagnosis of eosinophilic cholangitis (14). The typical imaging findings of eosinophilic cholangitis are reported to include multiple stenosis [such as primary sclerosing cholangitis (PSC)] or stenosis of the in-

trahepatic and extrahepatic bile duct (such as cholangiocarcinoma) (15). Among the three reported cases of eosinophilic cholangitis accompanied by EGE (16-18), PSC-like multiple stenosis was confirmed in two cases, while stenosis of the intrahepatic bile duct was confirmed in one case. In our case, we did not observe any irregularity or stenosis of the bile duct wall that was suspected to be eosinophilic cholangitis.

Steroids are the most commonly used treatment for EGE (19) and are considered to be effective in approximately 90% of EGE cases (20). In our case, we initially used antibiotic therapy and fasting to treat the patient's cholangitis and liver abscess; steroid therapy was administered after the antibiotics. Antibiotic therapy and fasting rapidly improved the patient's hepatobiliary enzyme levels according to the number of eosinophils in the peripheral blood. Furthermore, dilation of the bile duct and narrowing of the lumen of the second part of duodenum improved after these conservative therapies. These therapies might have improved the edematous thickening of the gastroduodenal wall, especially the mucosal layer, by reducing the patient's exposure to certain food antigens.

The clinical symptoms disappeared promptly after the initiation of steroid and antiallergic therapy. The efficacy of antiallergic drugs in the treatment of EGE has been reported (21, 22). Our patient's treatment started with a combination of PSL and antiallergic drugs after antibiotic therapy and fasting. Daikh et al. reported that montelukast reduced peripheral blood eosinophilia but not the eosinophilic infiltration of the gastrointestinal mucosa (21). In contrast, Melamed et al. reported that an H1 blocker reduced the eosinophilic infiltration of the gastrointestinal mucosa (22). We suspect that the antiallergic drugs and PSL synergistically improved our patient's clinical symptoms and the edematous thickening of the gastrointestinal wall, including the muscular layer. Her condition has been well-controlled without relapse after two years of steroid and antiallergic therapy.

In summary, we herein presented a rare case of EGE with obstructive jaundice. EGE should be considered in the differential diagnosis of patients with eosinophilia who present with obstructive jaundice. Invagination of the duodenal wall was the characteristic finding in this case, and conservative therapy was effective for treating the jaundice.

The authors state that they have no Conflict of Interest (COI).

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