Successful Endoscopic Resection in a Case of Ectopic and Metachronous Quintuple Gastric Cancers

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A 71-year-old man was referred to us from another hospital for endoscopic treatment of a IIc lesion at the anterior wall of the lower body of the stomach. In November 2008, he underwent resection of this lesion with endoscopic submucosal dissection (ESD). Follow-up endoscopy revealed a IIc lesion in the posterior wall of the lower body of the stomach, and ESD was again performed in February 2009. At the same time, *Helicobacter pylori* was detected, and successful first-line eradication therapy was verified in May 2009. Subsequent follow-up endoscopy detected multiple ectopic and metachronous gastric cancers at three sites, all of which were endoscopically resected (quintuple gastric cancer). Although ectopic and metachronous recurrence of gastric cancer was detected immediately after *H. pylori* eradication, recurrence of gastric cancer has not been detected in the 5 years since eradication. Future directions include determining the time point at which the preventative effects of *H. pylori* eradication therapy appear against gastric cancer recurrence. We report our findings herein, along with a review of the related literature.

Key words: gastric cancer recurrence, *H. pylori* eradication, ESD, ectopic and metachronous gastric cancers

INTRODUCTION

The prevalence of *Helicobacter pylori* infection has been decreasing in recent years in Japan [1] and, perhaps due to this, gastric cancer mortality rate has also been tending to decrease. In June 2010, *H. pylori* eradication therapy became eligible for national insurance coverage in cases of early gastric cancer that had previously been treated endoscopically. Since then, aggressive eradication treatments have been performed and a decrease in the number of gastric cancer patients in Japan is anticipated in the future. We encountered a case in which a patient underwent endoscopic mucosal resection to treat ectopic and metachronous quintuple gastric cancer and during that time underwent *H. pylori* eradication therapy. This patient is presently relapse-free. Our observations are reported herein.

CASE REPORT

A 71-year-old man was referred to us from another hospital for endoscopic treatment of a IIc lesion at the anterior wall of the lower body of the stomach. In November 2008, the patient underwent resection of this lesion with endoscopic submucosal dissection (ESD) (Fig. 1a, b). At follow-up endoscopy, a IIc lesion was discovered in the posterior wall of the lower body of the stomach, and the patient underwent ESD in February 2009 (Fig. 2a, b). At the same time, *H. pylori* was detected, and successful first-line eradication therapy was verified in May 2009. At a subsequent follow-up endoscopy, a IIc lesion was discovered at the posterior wall of the mid-body of stomach, and the patient underwent ESD in June 2010 (Fig. 3a, b). Endoscopy performed to confirm ulcer healing after ESD revealed a IIc lesion at the lesser curvature of the cardia, and the patient underwent another ESD in August 2010 (Fig. 4a, b). Further endoscopy was performed to verify ulcer healing after this ESD, and a IIc lesion was observed at the posterior wall of the mid-body of the stomach. The patient subsequently underwent ESD again in November 2010 (Fig. 5a, b). Endoscopy of the upper digestive tract has since been performed every 6 months, but no ectopic or metachronous recurrences of gastric cancer have been detected.

DISCUSSION

Metachronous gastric cancer first occurred in our patient more than 3 months after the initial endoscopic eradication. Although the patient immediately received successful *H. pylori* eradication therapy after second eradication, multiple ectopic and metachronous gastric cancers were subsequently detected at three sites. Some reports have mentioned that rates of gastric cancer after endoscopic resection of 2.70–14.0% [2–8]. Boda *et al*. [9] reported that the incidence of metachronous gastric tumors was significantly greater among male patients than among female patients. Baek *et al*. [10] reported that the clinicopathological characteristics of patients with multiple sites of gastric epithelial dysplasia showed some similarities in terms of morphological type, location, and macroscopic shape compared to primary lesions. Lim *et al*. [11] concluded that the risk factors for synchronous or metachronous gastric neoplasms were location in the antrum with intestinal metaplasia regardless of *H. pylori* status, and Kato *et*

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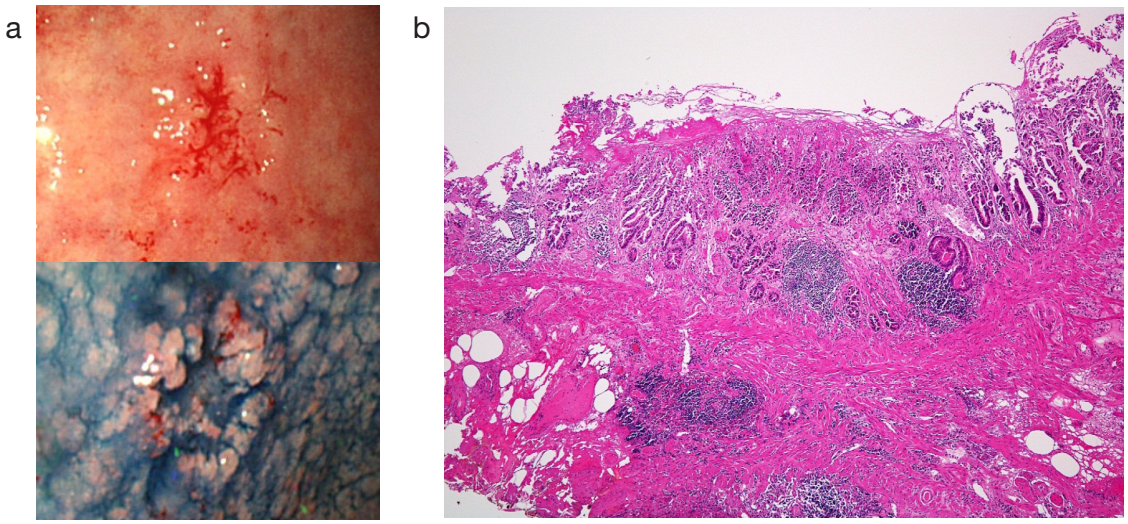

Fig. 1 a) A IIc lesion at the anterior wall of the lower body of the stomach.
b) A section of the gastric mucosa showing invasive proliferation of atypical epithelial cells arranged in irregular tubular or fused glandular structures in the mucosa and focally involving the muscularis mucosa. Resection margins are free from malignancy.

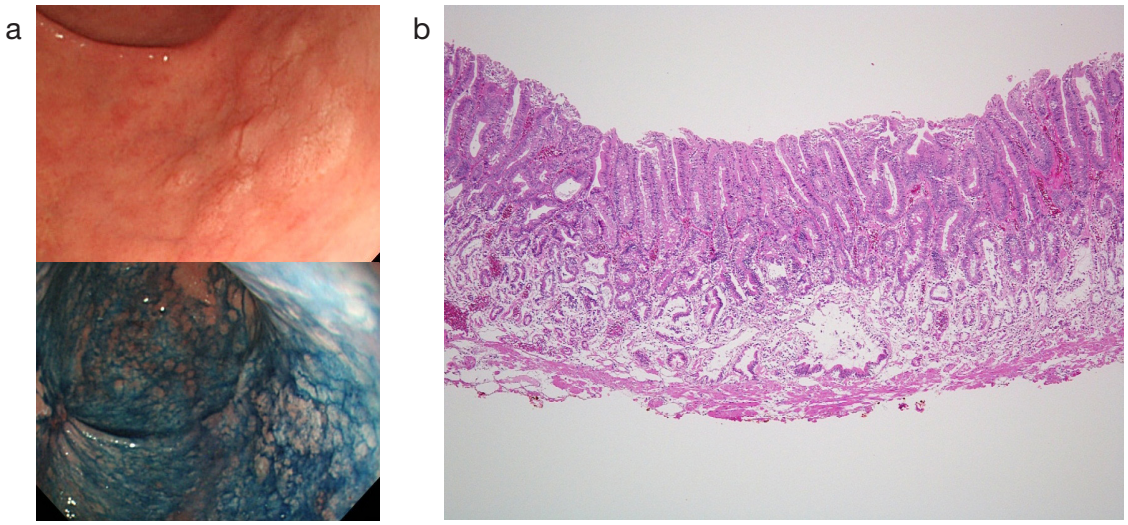

Fig. 2 a) A IIc lesion at the posterior wall of the lower body of the stomach.
b) A section of the gastric mucosa showing invasive proliferation of atypical epithelial cells arranged in irregular tubular structures. Tumor invasion is localized in the mucosal layer. Resection margins are free from malignancy.

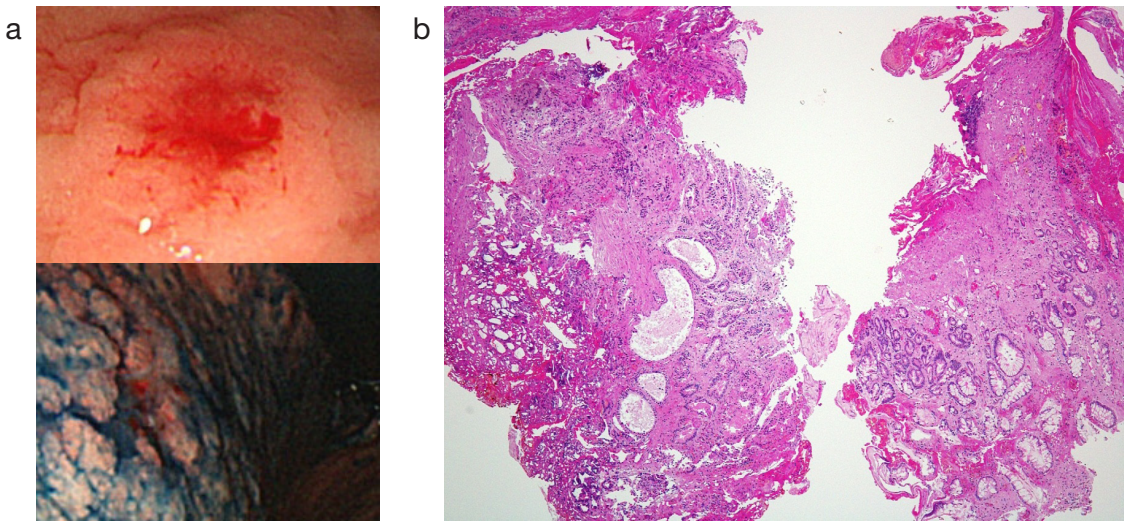

Fig. 3 a) A IIc lesion at the posterior wall of the mid-body of the stomach.
b) A section of the gastric mucosa showing invasive nets of adenocarcinoma arranged in irregular tubular structures.

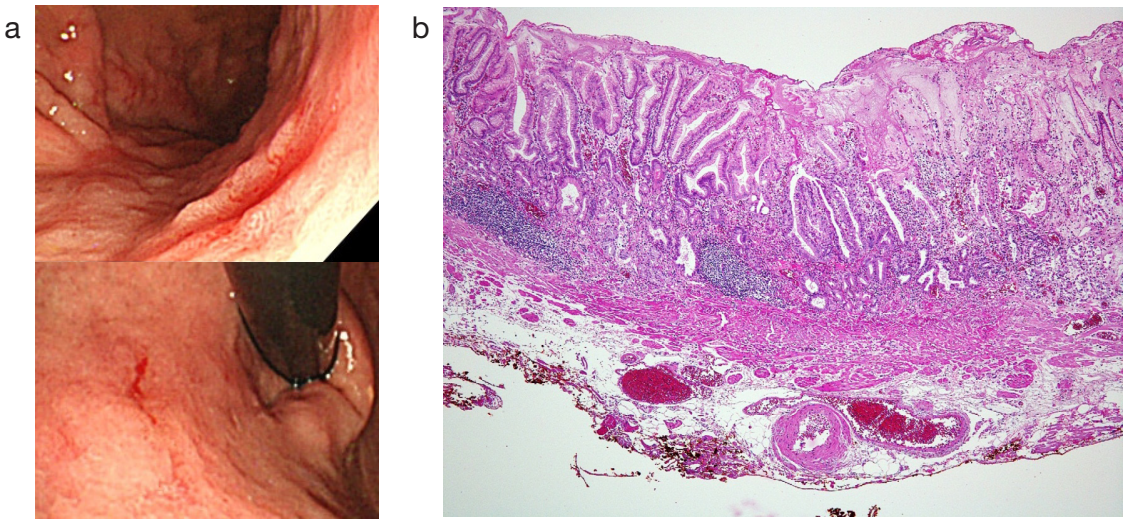

Fig. 4 a) A IIc lesion at the lesser curvature of the cardia of the stomach.
b) A section of the gastric mucosa showing invasive nets of adenocarcinoma arranged in irregular tubular structures. Non-tumorous mucosa reveals moderate inflammation and marked intestinal metaplasia.

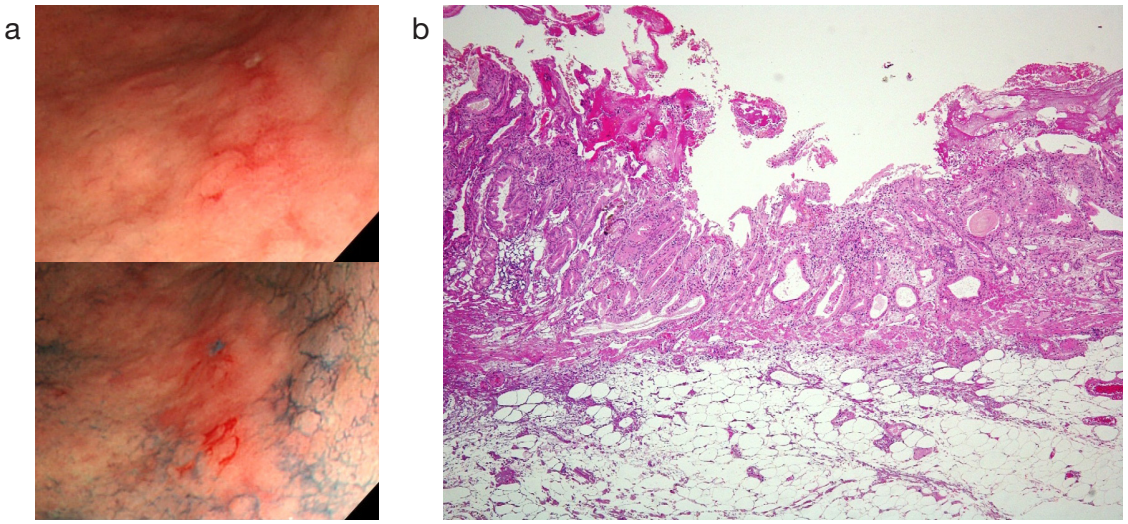

Fig. 5 a) A IIc lesion at the posterior wall of the mid-body of the stomach.
b) A section of the gastric mucosa showing invasive nets of adenocarcinoma arranged in irregular tubular structures. Tumor cell nets are localized in the mucosal layer. Resection margins are free of tumor cell invasion.

al. [12] reported that multiple gastric cancers were not decreased by *H. pylori* eradication. Some reports have indicated that the risk of metachronous recurrence is lower in *H. pylori*-negative groups than in *H. pylori* eradicated and noneradicated groups [13, 14].

In Japan, the prevalence of *H. pylori* infection has been steadily decreasing. Within a few decades, individuals who are currently in the age group with a low *H. pylori* infection rate will reach the age at which cancer is prevalent, and this cancer may thus become relatively rare. In June 2010, *H. pylori* eradication therapy became eligible for national insurance coverage in cases of early gastric cancer that have been treated endoscopically, and this is predicted to result in a decrease in the recurrence rate of ectopic and metachronous gastric cancers. Furthermore, in February 2013, *H. pylori* eradication therapy became covered under insurance for atrophic gastritis, a condition that is also known to represent an origin of gastric cancer. This development is considered likely to further accelerate the decrease in gastric cancer incidence. In the present case, since the patient was referred from a reliable gastroenterologist, we may have misjudged the presence of synchronous multiple ectopic gastric cancers at the initial consultation after referral. However, all subsequent endoscopic examinations were performed with extreme care (examinations were always performed by noting the potential for gastric cancer to be present at other sites), and metachronous and ectopic gastric cancers appeared to have developed during this period (past endoscopic findings have been re-examined several times). In the present case, endoscopic resection was performed over an approximately 2-year period for ectopic and metachronous recurrences immediately after *H. pylori* eradication therapy. However, subsequent semi-annual follow-up examinations have not revealed any recurrences of gastric cancer. This indicates that, while the evidence relates to only one case, *H. pylori*

eradication therapy may exhibit preventative effects against gastric cancer recurrence after approximately 2 years. In the present case, we had obtained informed consent from the patient to perform total gastrectomy after detecting the recurrence of ectopic and metachronous gastric cancers following *H. pylori* eradication therapy, but this surgical procedure was ultimately able to be avoided, since medical *H. pylori* eradication therapy was successful. In Japan, the recurrence of gastric cancer after endoscopic treatment has been previously assessed based on whether *H. pylori* eradication therapy was performed [15, 16], and it is therefore fully reasonable that *H. pylori* eradication therapy after endoscopic treatment of early gastric cancer can be performed under national insurance. However, up to what age patients should be eligible for *H. pylori* eradication therapy in our aging society remains to be determined, along with whether endoscopic follow-up is necessary (aging of gastric cancer morbidity). The accumulation of further evidence is thus eagerly awaited. The interval until suppression of gastric cancer recurrence after successful *H. pylori* eradication therapy is another topic in need of investigation. In the present case, the recurrence of metachronous and ectopic gastric cancers was suppressed after approximately 2 years following the completion of *H. pylori* eradication therapy. Nonetheless, intervals may vary depending on the histological type and morphology of gastric cancer, and this information will presumably be elucidated through investigations of cases from various facilities or multicenter data in the future.

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