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Single Case

Proton Pump Inhibitor-Associated Large Hyperplastic Polyp in Non-*Helicobacter pylori*-Infected Stomach

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Keywords
Hyperplastic polyp · Linked color imaging · Proton pump inhibitor · *Helicobacter pylori*-negative status

Abstract
A proton pump inhibitor (PPI)-associated hyperplastic polyp (HP) in the non-*Helicobacter pylori*-infected stomach is rare, and its endoscopic features remain poorly described. A 42-year-old man with tarry stool was referred to our hospital for examination and treatment. He had taken PPI for 14 years and was confirmed to be *H. pylori*-negative. Transnasal endoscopy revealed bleeding from a 20-mm, reddish pedunculated polyp with a nodular surface, located in the greater curvature of the upper gastric body. Endoscopic mucosal resection was performed, and the lesion was diagnosed as an HP. To our knowledge, this report represents a valuable addition to the HP literature describing a rare case of PPI-associated large HP in the non-*H. pylori*-infected stomach.

Introduction

Hyperplastic polyps (HPs) are among the most common gastric polyps. A 5-year survey of gastric polyps reported that HPs, fundic gland polyps, and adenomatous polyps accounted for 71.3, 16.3, and 12.4%, respectively [1]. HPs are histopathologically characterized as elongated, distorted, branching, and dilated hyperplastic foveolae lying in an edematous stroma rich in vasculature, and small distributed smooth muscle bundles with varying degrees of chronic and active inflammation [2]. HPs are shown to be associated with chronic (*Helicobacter pylori*) gastritis in most cases [3] and disappear or shrink following the eradication of *H. pylori* [4]. Recently, however, cases of proton pump inhibitor (PPI)-associated HPs have been

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Case Reports in Gastroenterology
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reported in normal (non-*H. pylori*-infected) gastric mucosa [5, 6], while they are rare, and their endoscopic features remain poorly described. We herein report a case of PPI-associated large HP in the non-*H. pylori*-infected stomach.

Case Report/Case Presentation

A 42-year-old man with tarry stool was referred to our hospital for examination and treatment. He had a history of systemic lupus erythematosus and had taken prednisolone, ethyl icosapentate, beraprost sodium, and the PPI rabeprazole (10 mg) for 14 years. Laboratory data revealed slight anemia (Hb, 13.4 g/dL), hypergastrinemia (gastrin, 1,060 pg/mL), and negativity for serum IgG antibody and fecal antigen to *H. pylori*. Transnasal endoscopy revealed bleeding from a 20-mm, reddish, pedunculated polyp with a nodular surface, located in the greater curvature of the upper gastric body (Fig. 1), and colonoscopy findings were normal. He was diagnosed with a special type of hemorrhagic polyp and was treated endoscopically the next day. Esophagogastroduodenoscopy revealed the same polyp on white light imaging (Fig. 2a). On linked color imaging, the lesion was highlighted as a purple-colored polyp, which was in part pale-colored (Fig. 2b). Endoscopic mucosal resection was thus performed on the lesion.

A histological examination showed dilated, elongated, and tortuous foveolae, which led to the diagnosis of HP (Fig. 3a). A tissue biopsy from the gastric body showed parietal cell protrusions and dilated oxyntic glands (Fig. 3b), thus establishing the lesion as a PPI-associated HP.

A follow-up esophagogastroduodenoscopy examination revealed no signs of recurrence for 2 years. His anemia improved, and his serum gastrin level decreased to 80 pg/mL after switching from rabeprazole to esomeprazole.

Discussion/Conclusion

Our case has 2 important clinical implications. First, a large HP may occur in the non-*H. pylori*-infected stomach. A PPI-associated large HP in the non-*H. pylori*-infected stomach is rare, and its endoscopic features remain poorly described in the literature.

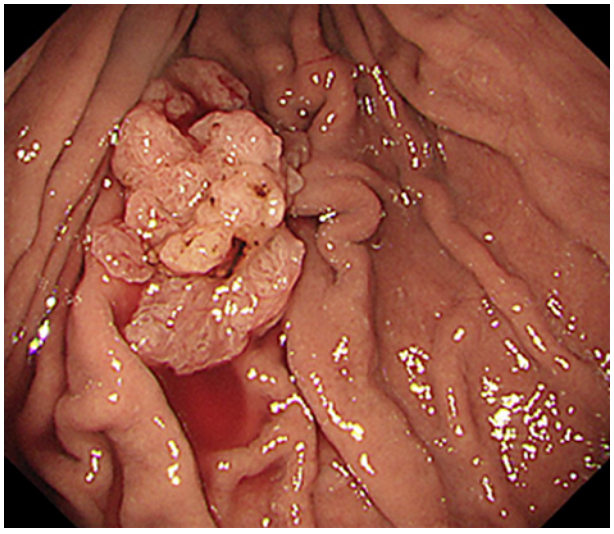

Fig. 1. Transnasal endoscopy. Bleeding was observed from a 20-mm, reddish, pedunculated polyp with a nodular surface, located in the greater curvature of the upper gastric body.

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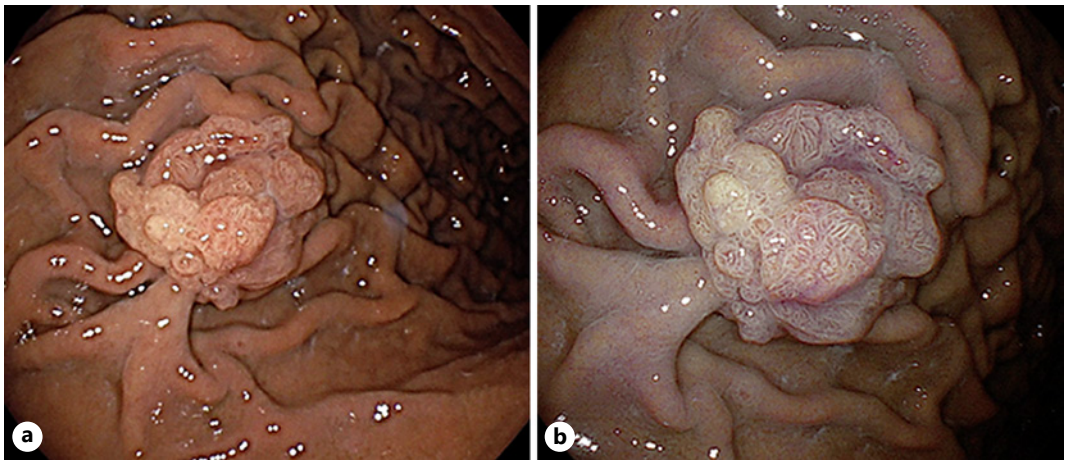

Fig. 2. EGD. **a** The same polyp was shown on WLI. **b** On LCI, the lesion was highlighted as a purple-colored polyp, which was in part pale-colored. EGD, esophagogastroduodenoscopy; WLI, white light imaging; LCI, linked color imaging.

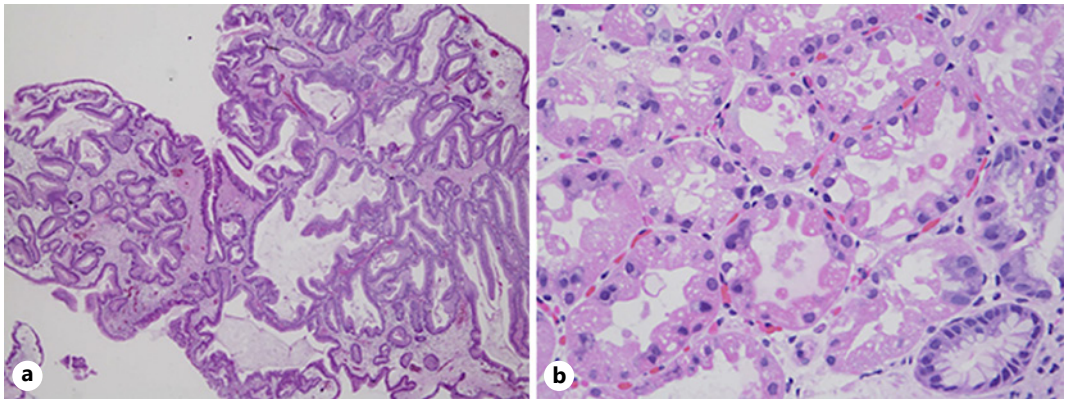

Fig. 3. Histopathologic examination. **a** Pathological findings showed dilated, elongated, and tortuous foveolae, which led to the diagnosis of an HP (×100). **b** A tissue biopsy from the gastric body showed parietal cell protrusions and dilated oxyntic glands (×200). HP, hyperplastic polyp.

The long-term use of PPI has been reported to be strongly associated with fundic gland polyp formation [7–9]. In a prospective study, Hongo et al. [10] reported that HP had also occurred in long-term users of PPI, especially in *H. pylori*-positive patients. In contrast, PPI-associated HPs in *H. pylori*-negative patients are extremely rare, with only 2 cases of PPI-associated HPs in the non-*H. pylori*-infected stomach reported, to date, in males who had received PPI for 4 years, one occurring in the antrum and the other in the gastric body (Table 1) [5, 6]. Endoscopic findings included reddish, smooth, dome-shaped polyps of <10 mm in diameter in both cases. Both were found to be similar in endoscopic features to those of HPs previously characterized as being multiple, smooth, and dome-shaped [2] and those of the PPI-associated HP previously characterized as being <10 mm in diameter [10]. However, unlike these 2 cases, the present case was found to be unusual in that it was a single, large, pedunculated polyp with a nodular surface, measuring 20 mm in diameter.

The other implication was that large HP may be caused by hypergastrinemia associated with long-term PPI administration. Gastrin exerts trophic effects on the entire gastrointestinal tract tissue, including both parietal and enterochromaffin-like cells distributed

Table 1. Cases reported to date of PPI-associated HPs in non-*H. pylori*-infected stomach

No.	Reference	Year	Age, years	Sex	PPI, mg	Duration of PPI administration, years	SGL, pg/mL	Location	Lesion number	Size (maximum), mm	Endoscopic findings	Treatment
1	[5]	2010	30	M	Esomeprazole 20	4	(–)	Antrum	Multiple	10	Reddish, smooth, and dome-shaped polyp	PPI discontinuation
2	[6]	2017	56	M	Omeprazole 20	4	529	Gastric body	Multiple	10	Reddish, smooth, and dome-shaped polyp	PPI discontinuation
3	Our case	2021	42	M	Rabeprazole 10	14	1,060	Greater curvature of the upper gastric body	Single	20	Reddish, pedunculated polyp with a nodular surface	EMR

PPI, proton pump inhibitor; SGL, serum gastrin level; EMR, endoscopic mucosal dissection.

throughout the oxyntic mucosa [11]. Suppression of gastric acid secretion by long-term PPI administration has been reported to increase serum gastrin levels [12], causing histopathological changes, such as parietal cell protrusions and dilated oxyntic glands [13]. In addition, it is speculated that hypergastrinemia causes HPs due to hyperplasia of the gastric foveolar epithelium [14]. In the present case, after 14 years of PPI therapy, there was not only evidence of hypergastrinemia (gastrin, 1,060 pg/mL) but a histological examination also revealed parietal cell protrusions and dilated oxyntic glands, which appeared to support the hypothesis that this case constituted one of PPI-associated HPs. In conclusion, PPI-associated HPs may occur in the non-*H. pylori*-infected stomach, possibly due to hypergastrinemia associated with long-term PPI administration.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose in association with this study.

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Author Contributions

K.K., N.K., N.M., S.M., M.T., T.M., and M.K. contributed equally to the study as well as to the preparation of the manuscript for publication.

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