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CASE REPORT

Proton-pump inhibitor-induced fundic gland polyps with hematemesis

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Abstract

Fundic gland polyps (FGPs) are generally considered benign. Proton-pump inhibitors (PPIs) are used worldwide as first-line therapy for gastroesophageal reflux disease and nonsteroidal anti-inflammatory drug-induced ulcer treatment. Long-term use of PPIs increases the risk of FGP development. We report an extremely rare case of PPI-induced FGPs with hematemesis. A 37-year-old woman taking daily rabeprazole presented to the hospital with a complaint of hematemesis and tarry stools. Esophagogastroduodenoscopy (EGD) revealed > 20 pedunculated polyps in the gastric body and fundus. Histological examination showed multiple fragments of fundic gland mucosa with dilated glands. Based on these findings and the clinical history, FGPs were diagnosed. Rabeprazole use was discontinued. Repeat EGD performed 9 months later showed a significant decrease in the number and size of the polyps. FGPs are small polyps typically located in the gastric corpus and fundus. They are commonly reported in patients in their 60s and predominantly in females. We conclude that PPI use is a risk factor for the development of FGPs and hematemesis.

Keywords Fundic gland polyps (FGPs) · Proton-pump inhibitors (PPIs) · Gastroesophageal reflux disease (GERD) · Esophagogastroduodenoscopy (EGD)

Abbreviations

FGPs	Fundic gland polyps
PPIs	Proton-pump inhibitors
GERD	Gastroesophageal reflux disease
EGD	Esophagogastroduodenoscopy

Introduction

Fundic gland polyps (FGPs) are generally considered benign. The reported prevalence in patients undergoing esophagogastroduodenoscopy (EGD) is 0.8–1.9% [1]. Proton-pump inhibitors (PPIs) are used worldwide as first-line therapy for gastroesophageal reflux disease and nonsteroidal anti-inflammatory drug-induced ulcer treatment. Long-term PPI use increases the risk of FGP development [2]. We report an extremely rare case of PPI-induced FGPs with hematemesis.

Case report

A 37-year-old woman presented to the hospital complaining of hematemesis and tarry stools. She had been taking 10 mg of rabeprazole daily for the past year for gastroesophageal reflux disease (GERD). The serum anti-*Helicobacter pylori* antibody level was within normal range, but the serum gastrin level was high (290 pg/ml). EGD revealed reddish, hemorrhagic polyps in the gastric body and fundus. Coagulum was observed in the stomach but bleeding had already stopped (Fig. 1a). The next day, EGD revealed > 20 pedunculated polyps. The antrum was normal. The polyps measured between 0.5 cm and 2.0 cm (Fig. 1b). Multiple biopsies of the polyps were taken. Histological examination showed multiple fragments of fundic gland mucosa with dilated glands. The dilated gastric glands were lined by mucous neck and ballooned parietal cells. No mucosal inflammation, dysplasia, or evidence of *H. pylori infection* was observed

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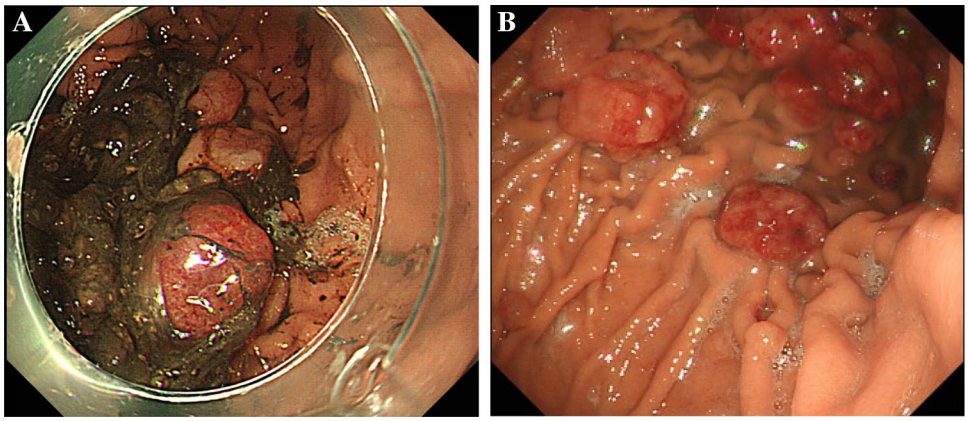

Fig. 1 Esophagogastroduodenoscopy findings. **a** Esophagogastroduodenoscopy revealed reddish, hemorrhagic polyps in the corpus. Coagulum was observed in the stomach. **b** Multiple white edematous polyps in the corpus were thought to be fundic gland polyps, as determined on endoscopy before admission

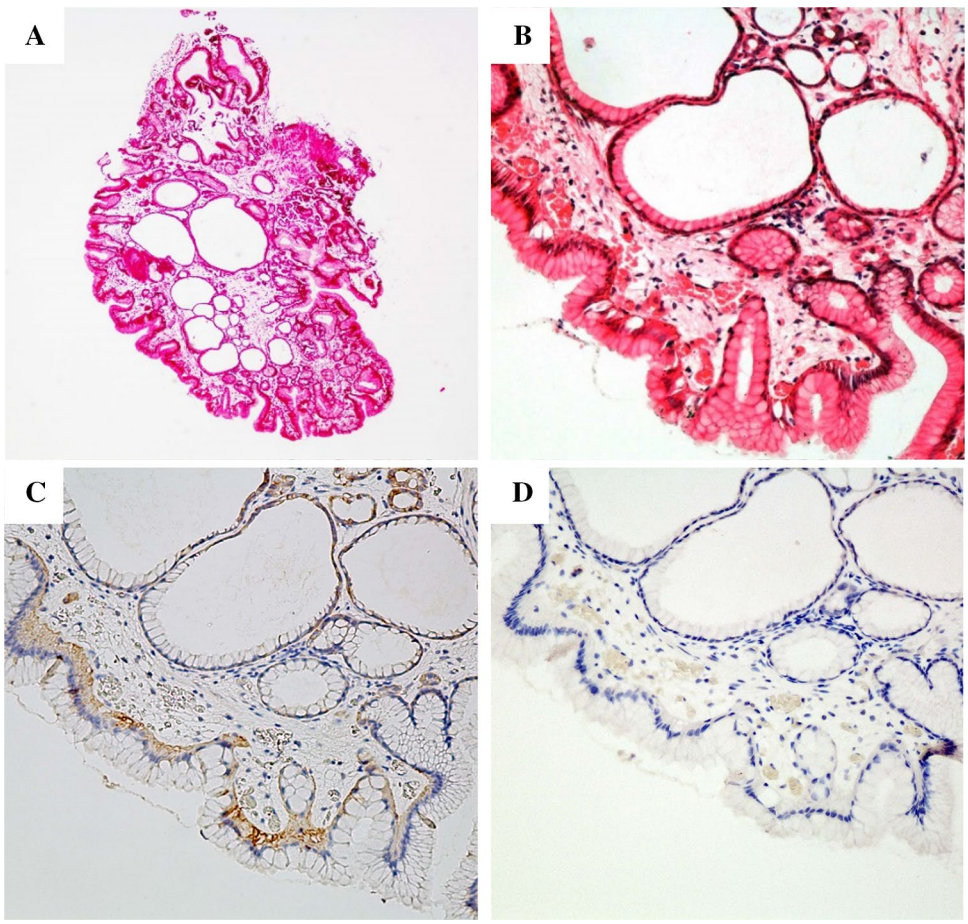

Fig. 2 Histological findings. **a, b** Histological examination showed multiple fragments of fundic gland mucosa with dilated glands. (hematoxylin–eosin stain, **a** ×40, **b** ×200). **c, d** Immunohistochemical study showed that cells in FGPs were β-catenin positive and CDX2 negative (**c** ×200, **d** ×200)

(Fig. 2a, b). Immunohistochemical analysis was negative for β-catenin and CDX2 (Fig. 2c, d). Colonoscopy did not reveal any abnormalities. Abdominal computed tomography was negative for hemorrhage or infarction.

Rabeprazole use was discontinued. EGD revealed a significant decrease in the number and size of polyps 9 months after discharge (Fig. 3). The serum gastrin level after PPI withdrawal remained within normal range (110 pg/ml).

Discussion

Bleeding gastric polyps are rare but some cases have been reported. Gastric polyps were revealed as the cause of bleeding in 14 of 5000 patients (0.28%) who presented with upper gastrointestinal hemorrhage [3]. The polyps are mostly hyperplastic or inflammatory fibroid polyps. Bleeding from FGPs is very rare.

Fig. 3 Esophagogastroduodenoscopy findings 9 months after discontinuing PPI. The size of the FGPs decreased significantly

FGPs are small polyps typically located in the gastric corpus and fundus. They are commonly reported in patients in their 60s and predominantly in females. Bertoni et al. reported that PPI therapy longer than 1 year is associated with a fourfold increased risk of FGP development [4]. FGPs were found in 13.6% of patients on long-term PPI use [5]. The mechanism remains unknown.

Long-term PPI use is associated with a large cystic area and parietal cell hyperplasia. A high level of serum gastrin suggests profound acid suppression that causes enlargement of parietal cells [6]. In the present case, the gastrin level decreased after PPI withdrawal. Hypergastrinemia appears to play an important role in polyp development.

Infection with *H. pylori* may inhibit FGPs [7], as their development during long-term PPI therapy is strongly associated with the absence of *H. pylori* [5]. *H. pylori* was not detected in this case.

The histopathological changes most commonly observed with long-term PPI therapy are parietal cell hyperplasia, stromal edema, and cystic dilatation of the fundic gland ducts. Hyperplasia of parietal cells has also been reported [8]. In this case, parietal cell hyperplasia, stromal edema, and extended fundic glands were observed (Fig. 2a, b).

Genetic studies have shown that FGPs are linked to somatic mutations in the β-catenin gene [1]. The β-catenin mutations in FGPs indicate a neoplastic nature, but it is known that FGPs have very limited malignant potential [9]. The presence of CDX 2 in FGPs has been correlated with β-catenin expression. However, β-catenin and CDX 2 tested negative in this case (Fig. 2c, d).

In the present case, a significant decrease in multiple gastric polyps was observed on EGD 9 months after PPI withdrawal. This strongly suggests an association between PPIs and gastric polyp development. PPI administration for a year or more increases the risk of polyp development and bleeding from the polyps.

Author contributions Mamoru Tanaka was the major contributor in writing the manuscript; Hiromi Kataoka was involved in drafting, writing and editing the manuscript, and reviewed the manuscript as corresponding author; Takashi Yagi and Takashi Joh edited the manuscript; all authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethics approval Not applicable.

Informed consent Informed written consent was obtained from the patient at the time of the endoscopic procedure.

Availability of data and materials All data generated or analyzed during this study are included in this published article (Additional file 1).

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