**CASE REPORT**

## Signet-ring Cell Carcinoma in Hyperplastic Polyp of the Stomach: A Case Report

Kenta Yoshida\(^1\), Tatsuya Mikami\(^3\), Takao Oyama\(^1,2\), Yuki Sato\(^1\), Taro Saito\(^1\), Takaumi Mikami\(^1\), Chieko Itabashi\(^4\), Yasushi Soma\(^1\) and Shinsaku Fukuda\(^1\)

### Abstract:

Signet-ring cell carcinoma rarely occurs in gastric hyperplastic polyps, with only a few such cases reported. We treated a 76-year-old woman with a signet-ring cell carcinoma arising from a hyperplastic polyp. She had been diagnosed with a gastric hyperplastic polyp four years previously. A follow-up endoscopic examination revealed the lesion in the polyp. A biopsy showed signet-ring cell carcinoma. Hybrid endoscopic submucosal dissection with snaring and a histological examination revealed signet-ring cell carcinoma in a hyperplastic polyp. The polyp was completely excised, with no evidence of recurrence one year later. A hyperplastic polyp of the stomach may transform into adenocarcinoma of an undifferentiated type.

**Key words:** Signet-ring cell carcinoma, hyperplastic polyp, ESD, endoscopic submucosal dissection

(Intern Med Advance Publication)  
(DOI: 10.2169/internalmedicine.2860-19)

### Introduction

Hyperplastic polyps of the stomach are associated with chronic gastritis. Although hyperplastic polyps are typically treated as benign polyps, a small percentage (<2%-3%) of them, particularly the larger ones, show features of focal intraepithelial neoplasia or cancer (1). Most cases of cancer originating from hyperplastic polyps are differentiated-type adenocarcinoma, and signet-ring cell carcinoma rarely occurs in gastric hyperplastic polyps, with few such cases reported (2).

We herein report a rare case of a Japanese woman diagnosed with signet-ring cell carcinoma in a hyperplastic polyp treated by endoscopic submucosal dissection with snaring (hybrid ESD).

### Case Presentation

A 76-year-old woman visited our hospital for a follow-up study of a gastric polyp. She had been diagnosed with gastric hyperplastic polyp on the lesser curvature of the upper gastric body four years previously in another hospital and one year previously in our hospital (Fig. 1). Esophagogastroduodenoscopy (EGD) revealed that the polyp had grown slightly compared with one year ago. The center of the polyp was slightly depressed, and the red surface color was faded (Fig. 2). The biopsy specimen obtained from the faded area showed signet-ring cell carcinoma, and the red area showed the hyperplastic polyp (Fig. 3).

She had been diagnosed with *Helicobacter pylori* infection by another hospital and had received eradication therapy six years previously. Consequently, *H. pylori* antigen in her stool and *H. pylori* IgG antibody in serum were both negative now. The laboratory data did not show any significant abnormalities.

A physical examination and contrast-enhanced computed tomography (CT) revealed swollen lymph nodes in the cervical region, submandibular region, and mediastinum. A biopsy from the mediastinum under general anesthesia was initially considered, but it proved too stressful for the patient. After holding several discussions with the health team, a biopsy of the cervical lymph node was ultimately performed to eliminate the possibility of metastasis, which revealed re-
active lymph follicular hyperplasia (Fig. 4).

Approximately two months after the polyp had been diagnosed as carcinoma, magnifying endoscopy was performed. Severe atrophy, corresponding to O-3 in the Kimura-Takemoto classification, was noted in the gastric mucosa.

The region of the polyp with faded color had obviously expanded, and both irregular microvascular and irregular microsurface patterns were found (Fig. 5). An endoscopic examination as well as gastric roentgenography and CT showed no invasive finding beyond the submucosa. Hybrid ESD was performed to resect the polyp completely. A specimen measuring 20×15×20 mm (tumor lesion: 16×10×13 mm) was resected completely with safe horizontal and vertical margins (Fig. 6).

Histologically, the polyp consisted of hyperplastic columnar cells and several types of carcinoma cells. The cancerous lesion consisted of well-differentiated adenocarcinoma cells (tub1) and papillary adenocarcinoma cells (pap) mainly and signet-ring cell (sig) partially (Fig. 7).

Immunohistochemistry for the polyp was performed. The immunoreactivity to Ki-67 protein was slightly higher in cancer cells than in the hyperplastic polyp (Fig. 8). The immunoreactivity to p53 protein was slightly higher in cancer cells than in the hyperplastic polyp.

The patient was followed for one year with EGD and CT, and she remained in a good general clinical condition with
In the present case, adenocarcinoma existed mainly in the head and the hyperplastic polyp was found in the stalk up to the base, the adenocarcinoma probably originated from the hyperplastic polyp. How adenocarcinoma had come to coexist with the hyperplastic polyp was unclear. A pedunculated form and upper location of such polyps might be risk factors for adenocarcinoma, as they easily receive stimulation from food and gastric peristalsis.

Larger hyperplastic polyps have a particularly high potential for malignant transformation (10). The hyperplastic polyp in the present case grew over time. In addition, it showed only a red color component initially, but after adenocarcinoma arose, a faded color component appeared, which grew within a short period of time. Magnifying endoscopy of this faded color region showed irregular microvascular and microsurface patterns. The endoscopic pattern indicated a merger of gastric cancer. However, the endoscopic diagnosis of the histologic type was difficult due to instability while holding the scope and the presence of hemorrhagic features. Hyperplastic polyps tend to appear red because of inflammation or angiogenesis. In contrast, undifferentiated-type adenocarcinoma, including signet-ring cell carcinoma ...

Figure 5. (A) An endoscopic view on white-light imaging of the polyp during ESD. The polyp grew in size, particularly in the faded color region. The surface showed not only red areas but also areas of faded color. ESD: endoscopic submucosal dissection, (B) An endoscopic view on magnifying narrow-band imaging of the polyp during ESD. Both irregular microvascular and microsurface patterns are positive in the faded color region. ESD: endoscopic submucosal dissection

Figure 6. Endoscopically resected polyp, measuring approximately 20×15×20 mm (tumor lesion: 16×10×13 mm).

Discussion

We treated a 76-year-old woman diagnosed with signet-ring cell carcinoma arising from a hyperplastic polyp. Hyperplastic polyps are the most frequent (28.3%) type of gastric polyps (3). However, only approximately 2.1% of hyperplastic polyps transform into adenocarcinoma (4). Nakamura reported the following criteria for hyperplastic polyp transformation into adenocarcinoma (5): [1] the coexistence of benign and malignant areas in the same polyp, [2] the existence of sufficient evidence that the benign area had been a benign polyp, and [3] the existence of sufficient cellular and structural atypia in the malignant area. The adenocarcinoma in the present case met these criteria.

Although adenocarcinoma arising in gastric hyperplastic polyps tends to be of the differentiated type, the present case had an undifferentiated type (signet-ring cell carcinoma). A review of case reports of signet-ring cell carcinoma with hyperplastic polyp is shown in Table (2, 6-9). These cases were obtained through a search of PubMed from 1946 to 2018 using the following search terms: either “adenocarcinoma” and “hyperplastic polyp,” or “signet ring cell carcinoma” and “hyperplastic polyp” (some cases with unclear details were not included). Only six cases have been reported, and three had several cancerous structures. In the present case, the tumor had multiple structures, including tubular adenocarcinoma, signet-ring cell carcinoma, papillary adenocarcinoma, and hyperplastic polyp. Because the adenocarcinoma existed mainly in the head and the hyperplastic polyp was found in the stalk up to the base, the adenocarcinoma probably originated from the hyperplastic polyp. How adenocarcinoma had come to coexist with the hyperplastic polyp was unclear. A pedunculated form and upper location of such polyps might be risk factors for adenocarcinoma, as they easily receive stimulation from food and gastric peristalsis.
tends to show a faded color due to a relative lack of inflammation or angiogenesis. Adenocarcinoma in hyperplastic polyps tends to be composed of red-color lobes with a white coat on their surface (11).

In the present case, the adenocarcinoma was smaller than a 20-mm pedunculated polyp. Moreover, 92% of pedunculated adenocarcinomas (type 0-I; superficial polypoid) <20 mm are limited to the mucosal layer (12). Endoscopic surgery is less stressful than open surgical operation. Therefore, we performed endoscopic submucosal dissection after obtaining informed consent from the patient. It was reported that early signet-ring cell carcinoma (not extending beyond the submucosa) removed by endoscopic surgery has a better prognosis than non-signet-ring cell carcinoma (13).

The present case emphasizes the possibility that hyperplastic polyp of the stomach may transform into adenocarcinoma, and in a few cases, such as in the current one, it can be an undifferentiated type. In our case, the patient had been diagnosed with H. pylori infection and had received eradication therapy. Generally, H. pylori infection increases the risk of gastric cancer. Despite the patient’s history of H. pylori eradication, there was a possibility of adenocarcinoma. After eradication therapy for H. pylori, the relative risk of gastric cancer is 0.66 (95% confidence interval: 0.46-0.95) (14). At
the endoscopic examination of the hyperplastic polyps, the careful observation of the size, color, and structure of the polyp components is required. If a slight change is observed, further examinations, such as chromoendoscopy with indigo carmine, image-enhanced endoscopy, magnifying endoscopy, and a biopsy, should be performed aggressively.

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

Acknowledgement

I would like to thank clinical technologist Yasuyoshi Shikama for his helpful advice concerning the histopathological examination.

References

1. Markowski AR, Markowska A, Guzinska-Ustymowicz K. Pathophysiological and clinical aspects of gastric hyperplastic polyp. World J Gastroenterol 22: 8883-8891, 2016.
2. Hirano H. Minute signet-ring cell carcinoma occurring in gastric hyperplastic polyp. World J Gastroenterol 13: 5779-5780, 2007.
3. Stolte M, Sticht T, Eidt S, Ebert D, Finkenzeller G. Frequency, location, and age and sex distribution of various types of gastric polyp. Endoscopy 26: 659-665, 1994.
4. Daibo M, Itabashi M, Hirota T. Malignant transformation of gastric hyperplastic polyps. Am J Gastroenterol 82: 1016-1025, 1987.
5. Nakamura T. Malignant change of gastric polypl, with special reference to histopathological classification. I to Cho (Stomach and Intestine) 3: 737-747, 1968 (in Japanese).
6. Zea-Iriarte WL, Itsuno M, Makiyama K, Hara K, Haraguchi M, Ajioka Y. Signet ring cell carcinoma in hyperplastic polypl. Scand J Gastroenterol 30: 604-608, 1995.
7. Fry LC, Lazenby AJ, Lee DH, Mönkemüller K. Signet-ring-cell adenocarcinoma arising from a hyperplastic polypl in the stomach. Gastrointest Endosc 61: 493-495, 2005.
8. Hirano H, Yoshida T, Yoshimura H, et al. Poorly differentiated adenocarcinoma with signet-ring cell carcinoma in a hyperplastic polypl of the stomach: report of a case. Surg Today 37: 901-904, 2007.
9. Kim HS, Hwang EJ, Jang JY, Lee J, Kim YW. Multifocal adeno-carcinomas arising within a gastric inverted hyperplastic polypl. Korean J Pathol 11: 1374-1384, 2013.
10. Tone K, Moriuchi A, Tanimura K. Malignant transformation of hyperplastic polypl of the stomach. ENDOSCOPIC FORUM for Digestive Disease 12: 193-199, 1996 (in Japanese).
11. Ono H, Yoshida S. Endoscopic diagnosis of the depth of cancer invasion for gastric cancer. I to Cho (Stomach and Intestine) 36: 334-340, 2001 (in Japanese).
12. Ha TK, An JY, Youn HK, Noh JH, Sohn TS, Kin S. Indication for endoscopic mucosal resection in early signet-ring cell gastric cancer. Ann Surg Oncol 15: 508-513, 2008.
13. Ford AC, Forman D, Hunt RH, Yuan Y, Oayyedi P. Helicobacter pylori eradication therapy to prevent gastric cancer in healthy asymptomatic infected individuals: systematic review and meta-analysis of randomized controlled trials. BMJ 348: g3174, 2014.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (https://creativecommons.org/licenses/by-nc-nd/4.0/).

© The Japanese Society of Internal Medicine