

[ CASE REPORT ]

## Signet-ring Cell Carcinoma in Hyperplastic Polyp of the Stomach

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### 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

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### 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 Report

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).

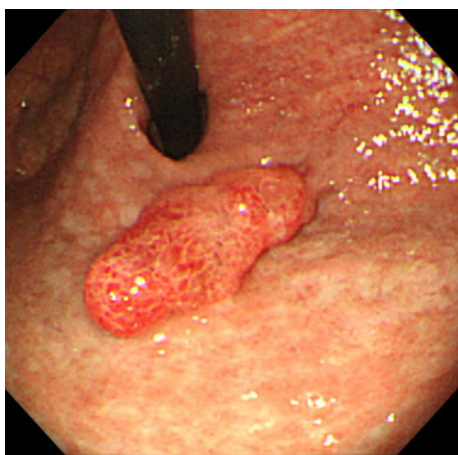
She had been diagnosed with *Helicobacter pylori* infection by another hospital and had received eradication therapy six years previously. Consequently, *H. pylori* antigen in her stool and *H. pylori* IgG antibody in serum were both negative now. The laboratory data did not show any significant abnormalities.

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-

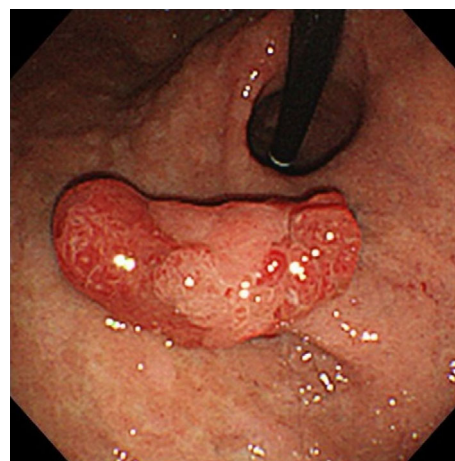
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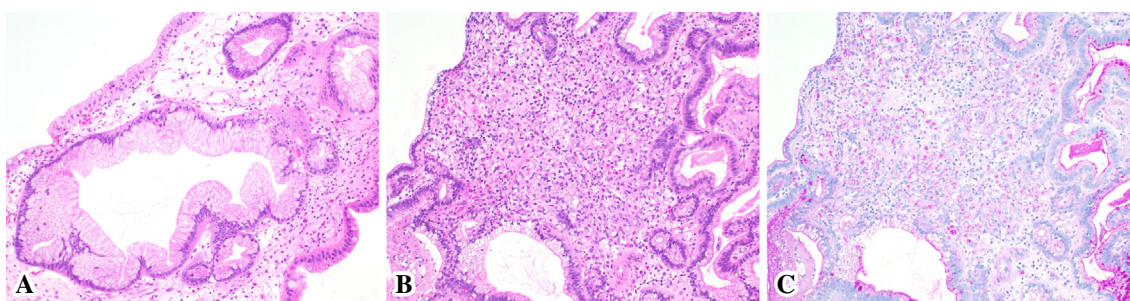
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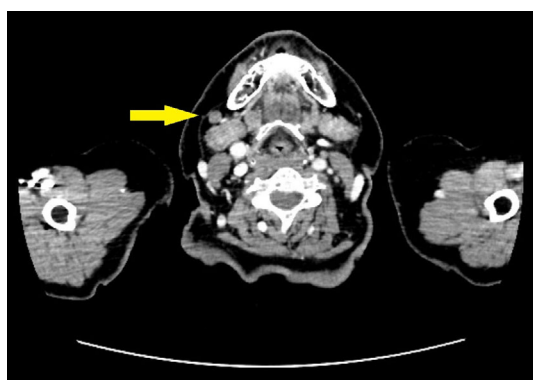
**Figure 1.** An endoscopic view of the hyperplastic polyp on the lesser curvature-anterior wall of the upper gastric body at the first examination in our hospital. The polyp has a pedunculated form, and almost the entire surface appears red.



**Figure 2.** An endoscopic view of the polyp at one year after the first examination. The polyp became slightly larger in size, and an area of faded color is evident.



**Figure 3.** (A) Biopsy specimen from the red region of the polyp [Hematoxylin and Eosin (H&E) staining,  $\times 200$ ]. Dilatated hyperplastic glands are seen. (B) Biopsy specimen from the faded color region of the polyp (H&E staining,  $\times 200$ ) revealing branching and dilatation of the glands with a large nucleus and signet-ring cells in the lamina propria. (C) Immunohistochemical expression on periodic acid-Schiff staining. Signet-ring cells in the faded color region of the polyp are stained positive.



**Figure 4.** Contrast CT image. Several cervical lymph nodes are swollen (pointed with an arrow). CT: computed tomography

active lymph follicular hyperplasia (Fig. 4).

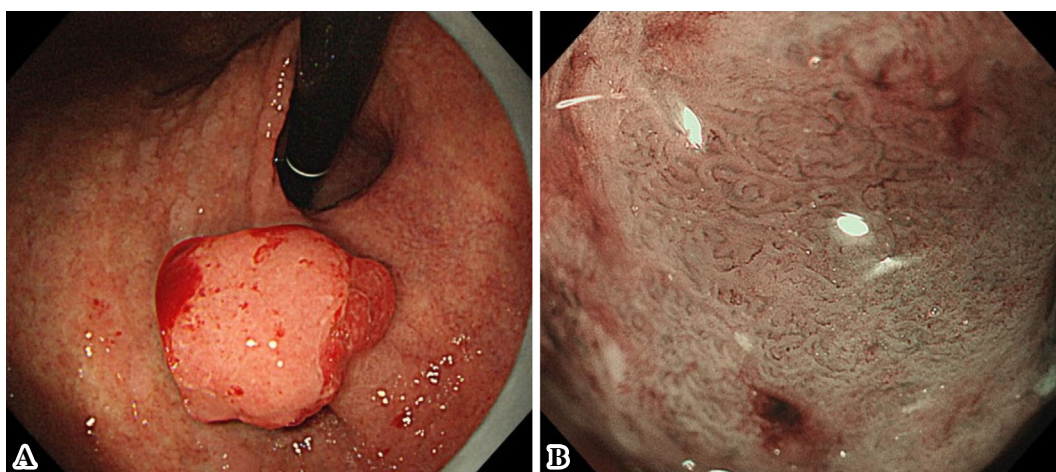
Approximately two months after the polyp had been diagnosed as carcinoma, magnifying endoscopy was performed. Severe atrophy, corresponding to O-3 in the Kimura-Takemoto classification, was noted in the gastric mucosa.

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  $20 \times 15 \times 20$  mm (tumor lesion:  $16 \times 10 \times 13$  mm) was resected completely with safe horizontal and vertical margins (Fig. 6).

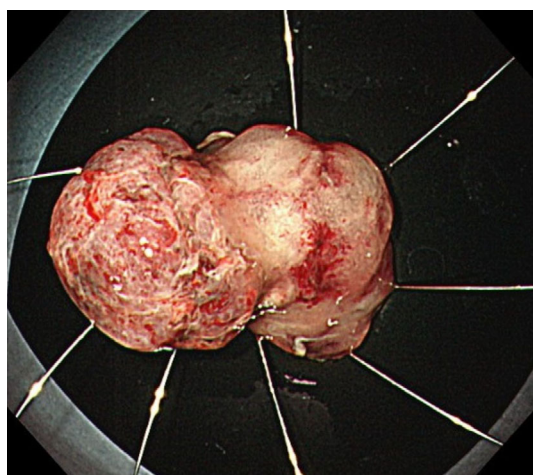
Histologically, the polyp consisted of hyperplastic columnar cells and several types of carcinoma cells. The cancerous lesion consisted of well-differentiated adenocarcinoma cells (tub1) and papillary adenocarcinoma cells (pap) mainly and signet-ring cell (sig) partially (Fig. 7).

Immunohistochemistry for the polyp was performed. The immunoreactivity to Ki-67 protein was higher in the 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



**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).

no evidence of recurrence.

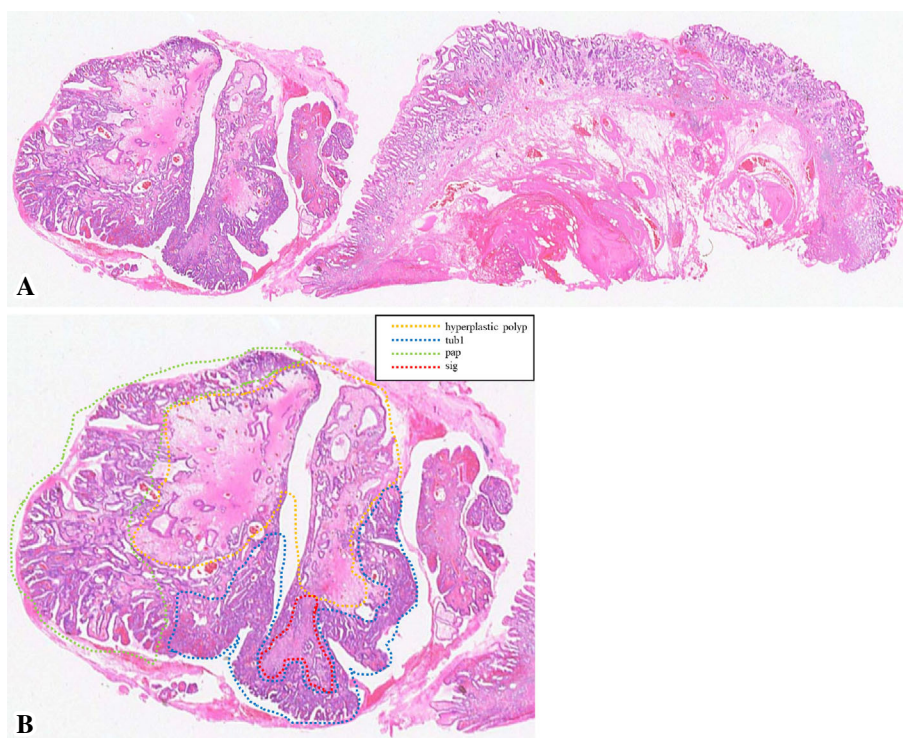
## Discussion

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.

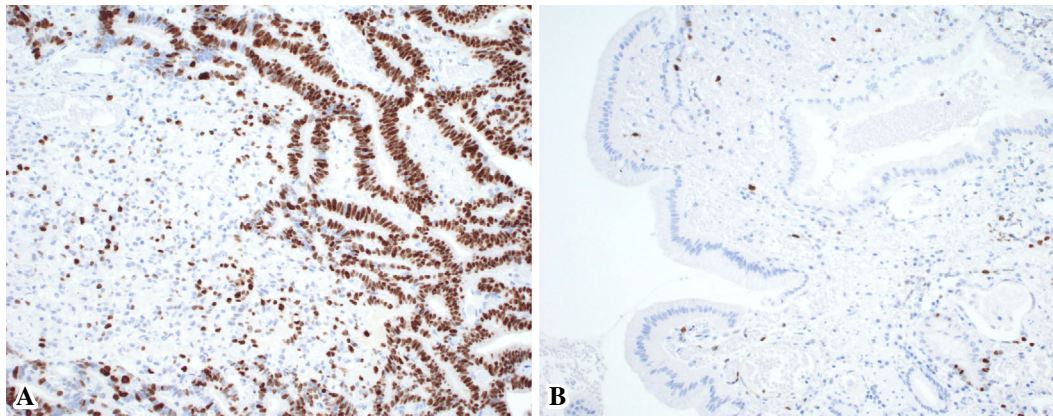
Although adenocarcinoma arising in gastric hyperplastic

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.

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 7.** (A) Resected specimen (Loupe image). The polyp showed invasion into the mucous membrane and was resected completely with safe lateral and vertical margins. (B) Resected specimens comprising several tissue components: hyperplastic polyp (yellow dotted line), tub1 (blue dotted line), pap (green dotted line), and sig (red dotted line).



**Figure 8.** Immunohistochemistry of the resected specimen ( $\times 200$ ). The immunoreactivity to Ki-67 protein is obviously higher in the cancer cells (A) than in the hyperplastic polyp (B).

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

**Table. Case Reports of Signet-ring Cell Carcinoma with Hyperplastic Polyp.**

Case	References	Year	Age	Sex	Part	Size(mm)	Macroscopic Type	Color	Histopathology	Treatment	Invasion Depth	Relapse
1	6	1995	68	W	Angulus	22	pedunculated	red	sig	polypectomy	mucosa	none (4 years)
2	7	2005	67	M	Antrum	35×40	pedunculated	unclear	sig	EMR	unclear	none (1 year)
3	8	2007	59	M	Antrum	48×38	pedunculated	unclear	por, sig	surgical operation	unclear	none (1 year)
4	2	2007	45	F	Body	6×5	0-IIa	red	sig	EMR	mucosa	unclear
5	9	2012	40	F	Body	35×32×18	0-I	red (mild)	tub1, tub2, por, sig	ESD	mucosa	none (22 months)
6	Our case	2019	76	F	Body	16×10×13	0-I	red and faded	tub1, pap, sig	ESD	mucosa	none (19 months)

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).**

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