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Authors: Kaoru Omori, Kanako Yoshida, Toshiaki Kamei, Masahiro Kan

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AUTHORS:
Kaoru Omori¹, Kanako Yoshida², Toshiaki Kamei³, Masahiro Kan⁴

AFFILIATIONS:
¹MD, PhD, Department of Gastroenterology and Hepatology, Sato Daiichi Hospital, 77-1 Hokyoji, Usa City, Oita 879-0454, Japan, meitokukai-omo@sato-d1.com
²MD, PhD, Department of Gastroenterology and Hepatology, Sato Daiichi Hospital, 77-1 Hokyoji, Usa City, Oita 879-0454, Japan, k-yoshida@sato-d1.com
³MD, PhD, Medical Director of Pathology & Cytology Center BML group PCL, 5-20-25 Matsushima, Fukuoka City, Fukuoka 813-0062, Japan, TK49913YK@bml.co.jp
⁴MD, PhD, Department of Gastroenterology and Hepatology, Sato Daiichi Hospital, 77-1 Hokyoji, Usa City, Oita 879-0454, Japan, meitokukai-kan@sato-d1.com

CORRESPONDING AUTHOR DETAILS
Masahiro Kan, MD, PhD
Department of Gastroenterology, Sato Daiichi Hospital, 77-1 Hokyoji, Usa City, Oita 879-0454, Japan.
Phone number: 81-978-32-2110
Email: meitokukai-kan@sato-d1.com
Fax: 81-978-32-4290

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TITLE: Safety and efficacy of endoscopic submucosal dissection for early gastric remnant cancers post-proximal gastrectomy with jejunal interposition

ABSTRACT

Introduction
Endoscopic submucosal dissection has been widely accepted as a standard treatment for early gastric cancers. However, endoscopic submucosal dissection for an early gastric remnant cancer post-proximal gastrectomy with jejunal interposition is not yet widespread.

Case Series
A large, flat, elevated lesion was detected in an 83-year-old man (Case 1), whereas two separate flat, elevated lesions were detected in a 75-year-old man (Case 2). Successful curative en bloc resection of these lesions by endoscopic submucosal dissection using the insulation-tipped diathermic knife-2 revealed well-differentiated adenocarcinoma confined to the mucosa. No postoperative bleeding nor perforation was observed in the present cases.

Conclusion
These cases underscore the importance of periodic upper gastrointestinal endoscopy follow-up and the value of endoscopic submucosal dissection using the insulation-tipped diathermic knife-2 for treating early gastric remnant cancers post-proximal gastrectomy in the presence of interposed jejunum, even when extensive removal is necessary.

Keywords: early gastric remnant cancer, endoscopic submucosal dissection, proximal gastrectomy, insulation-tipped diathermic knife-2
TITLE: Safety and efficacy of endoscopic submucosal dissection for early gastric remnant cancers post-proximal gastrectomy with jejunal interposition

INTRODUCTION

Total gastrectomy for gastric cancer located in the proximal third of the stomach has been widely performed as a standard procedure to achieve tumor free margins and complete lymph node dissection [1]. Recently, proximal gastrectomy (PG) for early stage proximal gastric cancer has been accepted to preserve the physiologic function of the gastric remnant. In a previous report, the incidence of gastric remnant cancer (GRC) post-PG was higher than that of GRC post-distal gastrectomy (DG) [2]. It was previously considered that radical surgical resection was the only therapeutic procedure for GRC post-PG. On the other hand, endoscopic submucosal dissection (ESD) has been widely accepted as a standard treatment for early gastric cancers. Several knives, such as the needle, insulation-tipped diathermic (IT) knife-2, hook, flex and flush knives, are currently used. Selection of the proper knife influences the quality of the ESD procedure and overall outcome because of its own merits and disadvantages. Although ESD for an early GRC post-DG has been reported [3], ESD for an early GRC post-PG with jejunal interposition has been rarely reported. Here we report three lesions in two cases that underwent successful ESD using the IT knife-2 for early GRCs post-PG with jejunal interposition. The importance of periodic upper gastrointestinal endoscopy follow-up for the detection of a small early GRC post-PG to facilitate ESD and the possible benefits of ESD using the IT knife-2, even for an early GRC post-PG for which extensive removal is necessary, are emphasized.

CASE SERIES

Case 1

An 83-year-old man had undergone PG with jejunal interposition for mucosal gastric cancer at another hospital (Figure 1a-1b). Approximately 2 years later, he requested to undergo his first follow-up upper gastrointestinal endoscopy. Physical examination and routine laboratory examinations revealed no abnormalities. Conventional
endoscopy and chromoendoscopy with indigo carmine dye showed a large, flat, elevated, soft lesion, approximately 40 mm in diameter, on the distal gastric remnant (Figure 1c-1e). This lesion was biopsied, revealing a well-differentiated adenocarcinoma. Endoscopic ultrasonography was performed to evaluate the invasion depth, and the cancer was classified to be an intramucosal carcinoma with negligible risk of lymph node metastasis. We explained to the patient that ESD is an investigational treatment for this lesion according to the expanded indication mentioned in the Japanese Gastric Cancer Treatment Guidelines [4], and he chose to undergo ESD instead of surgery. Curative en bloc resection of the lesion was successfully achieved by ESD using the IT knife-2 (KD-611 L; Olympus Medical Systems, Tokyo, Japan) and the transparent hood (F-030; TOP Co., Ltd., Tokyo, Japan) (Figure 2a-2e). The procedure time was 50 min. The resected specimen revealed well-differentiated adenocarcinoma confined to the mucosa without vessel infiltration (Figure 2f). The resection margins were negative. Neither recurrence nor metastasis of GRC has been detected at present, i.e., 2 years later.

Case 2
A 75-year-old man had undergone PG with jejunal pouch interposition for mucosal gastric cancer at another hospital, with resultant reflux esophagitis (Figure 3a-3b). Approximately 5 years later, he requested to undergo his first follow-up upper gastrointestinal endoscopy. Physical examination and routine laboratory examinations revealed no abnormalities. Conventional endoscopy and chromoendoscopy with indigo carmine dye showed two separate flat, elevated soft lesions on the distal gastric remnant (Figure 3c-3e). The lesion on the proximal side was approximately 25 mm in diameter. The lesion on the distal side was approximately 15 mm in diameter. Biopsy of these lesions revealed well-differentiated adenocarcinoma. Endoscopic ultrasonography was performed to evaluate the invasion depth, and both cancers were classified to be an intramucosal carcinoma with negligible risk of lymph node metastasis. He chose to undergo ESD in response to our explanations, which is similar to case 1. Curative en bloc resection of both lesions was successfully achieved by ESD using an IT knife-2 and a transparent hood (Figure 4a-4e). The procedure time was 150 min. The resected
specimen revealed well-differentiated adenocarcinoma confined to the mucosa without vessel infiltration (Figure 4f). The resection margins were negative. Neither recurrence nor metastasis of GRC has been detected at present, i.e., 2 years later.

**DISCUSSION**

We experienced three early GRCs in two cases of PG with jejunal interposition that were successfully treated with extensive en bloc resection during ESD. ESD for early gastric cancers with negligible risk of lymph node metastasis has been widely accepted as a standard treatment, while improving efficiency and safety of ESD. However, it is often more difficult to perform ESD in the remnant stomach than in the normal stomach because of a narrow working space in the gastric remnant, as well as the existence of fibrosis and staples under the suture line [5]. Post-PG endoscopic surveillance of the remnant stomach has been reported to be difficult because of the interposed jejunum [6]. Therefore, ESD for an early GRC, particularly post-PG with jejunal interposition, is not yet widespread.

In our cases, both ESD procedures were an investigational treatment for early GRCs post-PG according to the expanded indication mentioned in the Japanese Gastric Cancer Treatment Guidelines [4]. Therefore, we consider that ESD for early GRCs post-PG with negligible risk of lymph node metastasis should follow two independent indications for ESD mentioned in Japanese Gastric Cancer Treatment Guidelines [4]: the absolute indication for a standard treatment, and the expanded indication for an investigational treatment.

Selection of the proper knife from various knives, such as the needle, IT knife-2, hook, flex, and flush, influences the quality of the ESD procedure and overall outcome. One of the most important factors contributing to the safe completion of ESD for an early GRC post-PG with a narrow working space is careful dissection of the submucosal layer to prevent perforation. The IT knife-2 has a ceramic ball at the top of the incising needle knife to prevent perforation. Therefore, both ESD procedures were performed by technically qualified experts using the IT knife-2 in the present cases. The ESD procedure durations took longer than usual because of technical difficulties. Although the complications of ESD for GRCs post-DG have
been reported to be perforation and delayed bleeding [3], these complications were not observed in the present cases.

The incidence of early gastric cancer in the proximal third of the stomach has recently increased in Japan; PG has been accepted, considering the improvement of the quality of life after gastrectomy [7]. As a consequence, however, GRCs post-PG are now increasing [2]. Radical surgical resection was previously considered to be the only therapeutic procedure for curing GRCs post-PG. Recent advances in diagnostic techniques and endoscopic surveillance programs have increased the early detection of GRCs post-DG [8]. Similarly, early GRCs post-PG, even when extensive removal is necessary, may also be treatable by ESD, as demonstrated in our cases. Recently, favorable survival rates after endoscopic resection for early GRC have been reported [5]. ESD using the IT knife-2 for early GRCs post-PG in the presence of jejunal interposition was considered to be the safe and effective therapeutic procedure in the present cases. However, only highly skilled and experienced endoscopists should perform ESD for early GRCs post-PG with jejunal interposition because of technical difficulties, particularly when extensive removal is required, as observed in our cases.

CONCLUSION

Use of the IT knife-2 contributed to the safe and effective ESD for early GRCs post-PG with jejunal interposition, for which extensive removal was necessary. Our cases suggest that the indications of ESD for early GRCs post-PG with negligible risk of lymph node metastasis should follow the Japanese Gastric Cancer Treatment Guidelines

CONFLICT OF INTEREST

Authors declare no conflict of interest.

AUTHOR’S CONTRIBUTIONS

Kaoru Omori

Group 1- Conception and design, Acquisition of data, Analysis and interpretation of data
Group 2- Drafting the article, Critical revision of the article
Group 3- Final approval of the version to be published

Kanako Yoshida
Group 1- Conception and design, Acquisition of data, Analysis and interpretation of data
Group 2- Drafting the article, Critical revision of the article
Group 3- Final approval of the version to be published

Toshiaki Kamei
Group 1- Conception and design, Acquisition of data, Analysis and interpretation of data
Group 2- Drafting the article, Critical revision of the article
Group 3- Final approval of the version to be published

Masahiro Kan
Group 1- Conception and design, Acquisition of data, Analysis and interpretation of data
Group 2- Drafting the article, Critical revision of the article
Group 3- Final approval of the version to be published

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REFERENCES


FIGURE LEGENDS

Figure 1: (a) – Abdominal computed tomography showed anastomosed parts post-proximal gastrectomy with jejunal interposition (yellow arrows); (b) – Conventional view of the anastomosed part post-proximal gastrectomy with jejunal interposition; (c) – Conventional view of early gastric cancer (approximately 40 mm in diameter); (d) – Chromoendoscopic view of the distal side of early gastric cancer stained with indigo carmine; (e) – Chromoendoscopic view of the proximal side of early gastric cancer stained with indigo carmine.

Figure 2: (a) – Electrocautery marking around the target lesion; (b) – Submucosal injection of diluted epinephrine with indigo carmine and circumferential cutting of the lesion; (c) – Submucosal dissection using insulation-tipped diathermic knife-2 and a
transparent hood; (d) – Completion of resection; (e) – A mapping image of the resected specimens showing well-differentiated adenocarcinoma confined to the mucosa (yellow lines); (f) – Pathological finding of the resected lesion stained with hematoxylin and eosin revealed well-differentiated adenocarcinoma comprising intramucosal carcinoma without vessel infiltrations.

Figure 3: (a) – Abdominal computed tomography showed anastomosed parts post-proximal gastrectomy with jejunal pouch interposition (yellow arrows); (b) – Conventional view of the anastomosed part post-proximal gastrectomy with jejunal pouch interposition; (c) – Conventional view of early gastric cancer; (d) – Chromoendoscopic view of the cancer on the proximal side (approximately 25 mm in diameter) stained with indigo carmine; (e) – Chromoendoscopic view of the cancer on the distal side (approximately 15 mm in diameter) separated from the proximal side and stained with indigo carmine.

Figure 4: (a) – Electrocautery marking around the target lesion; (b) – Submucosal injection of diluted epinephrine with indigo carmine and circumferential cutting of the lesion; (c) – Submucosal dissection using insulation-tipped diathermic knife-2 and a transparent hood; (d) – Completion of resection; (e) – A mapping image of the resected specimens showing well-differentiated adenocarcinoma confined to the mucosa (yellow lines); (f) – Pathological finding of the resected lesion stained with hematoxylin and eosin revealed well-differentiated adenocarcinoma comprising intramucosal carcinoma without vessel infiltrations.
FIGURES

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