# Sentinel Node Navigation Surgery for Early Malignant Tumor of the Duodenum

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#### ABSTRACT

Introduction : Pancreaticoduodenectomy is a standard operation for duodenal malignant tumor but is associated with a high incidence of postoperative morbidity and impaired quality of life. We report on patients who successfully underwent limited surgery for early duodenal tumors using sentinel node navigation surgery and infrared ray observation.

Methods: Indocyanine green (ICG) was injected submucosally around the tumor through an endoscope. An infrared ray laparoscopy system was used to identify sentinel nodes. These nodes were stained with hematoxylin and eosin intraoperatively or with cytokeratin immunohisto-chemical staining postoperatively and examined for evidence of metastasis.

Results : In case 1, 1 retropancreatic lymph node (No. 13, Japanese classification) and 1 prepancreatic lymph node (No. 17) were ICG-positive. In case 2, 1 right gastroepiploic lymph nodes (No. 6) and 2 No. 13 lymph nodes were ICG-positive. In case 3, 1 right gastroepiploic lymph node (No. 6) was ICG-positive. These lymph nodes showed no metastasis on frozen-section examination. In case 1, wedge resection of the second part of duodenum and jejunal patch operation were performed, and in cases 2 and 3, wedge resection of the duodenal bulb was performed.

Conclusion : Sentinel lymph nodes in cases of early duodenal cancer could be easily detected with an infrared ray laparoscopy system, which seems to be useful for limited surgery for duodenal malignancy. (Jikeikai Med J 2009; 56: 11-7)

Key words: sentinel node navigation surgery, malignant duodenal tumor

### INTRODUCTION

Pancreaticoduodenectomy is a standard operation for duodenal malignant tumor but is associated with a high incidence of postoperative morbidity and impaired quality of life. We report patients who successfully underwent limited surgery for early duodenal tumors using sentinel node navigation surgery (SNNS) with infrared ray observation.

## METHODS AND PATIENTS

SNNS with infrared ray observation was performed in 3 patients with early duodenal tumors. Indocyanine green (ICG, 5 mg/ml, Diagnogreen®, Daiichi Pharmaceutical Co. Ltd., Tokyo, Japan) was injected submucosally (0.5 ml per injection) with a 23-gauge endoscopic puncture needle through an endoscope at 4 quadrants around the tumor. Because the duodenal wall was thin, physiological saline was injected into the submucosal layer before ICG was injected.

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Fig. 1. Endoscopic findings (case 1). a. Early cancer in the second part of the duodenum. b. Intraoperative endoscopy after ICG injection.



Fig. 2. SNNS (case 1). a. Observation with white light. ICG (+) LNs could not be detected. \*; pancreas <sup>†</sup>; duodenum (primary lesion). b. Observation with IRLS. ICG (+) lymphatic vessels and LNs were confirmed. Narrow arrows indicate ICG (+) lymphatic vessels. The thick arrow indicates an ICG (+) LN. c. Sentinel LNs. They could not be recognized as green nodes with the naked eye. d. Sentinel nodes. The ICG (+) LNs appeared as black nodes with IRLS.

Twenty minutes after the ICG injection, an infrared ray laparoscopy system (IRLS; Olympus Medical Systems Co., Tokyo, Japan) was used to identify ICGpositive [ICG (+)] lymphatic vessels and LNs through examination of the fatty tissue on the serosa of the duodenum and pancreas. We defined ICG (+) LNs as sentinel nodes. After observation, lymphatic basin dissection was performed. Thereafter, ICG (+) LNs



c. HE 100×

Fig. 3. Surgical specimen and pathological findings (case 1). a. Macroscopic appearance of surgical specimen of a duodenal tumor. b, c. Microscopic examination of the duodenal tumors showed well-differentiated adenocarcinoma in adenoma (b : hematoxylin and eosin,  $20 \times$ ; c : hematoxylin and eosin,  $100 \times$ ).

were preserved by freezing, subjected to hematoxylin and eosin staining or with cytokeratin immunohistochemical staining (CAM5.2; BD Biosciences, San Jose, CA, USA), and examined for evidence of metastasis.

Case 1: The patient was a 65-year-old woman with a  $50 \times 30$ -mm tumor of the second part of the duodenum (coIIa) pathologically diagnosed as well-differentiated adenocarcinoma in adenoma (Fig. 1 and 3).

Case 2: The patient was an 81-year-old woman with a 10-mm-diameter carcinoid of the anterior wall of the duodenal bulb (Fig. 4a). Endoscopic ultrasonography revealed that the carcinoid had reached the submucosa (Fig. 4b).

Case 3: The patient was a 59-year-old man with a 10-mm-diameter carcinoid of the anterior wall of

the duodenal bulb. Endoscopic ultrasonography revealed that the carcinoid had reached the submucosa.

b. HE  $20 \times$ 

#### RESULTS

Case 1: One retropancreatic LN (No. 13) and 1 prepancreatic LN (No. 17) were ICG (+) (Fig. 2). Although ICG (+) LNs could not be identified with the naked eye (Fig. 2a), such ICG (+) No. 13 LNs appeared black on IRLS (Fig. 2b). The ICG (+) LNs, which were about 5 mm in diameter, were removed (Fig. 2c, d). Intraoperative frozen-section examination revealed no LN metastasis. Wedge resection of the duodenum and jejunal patch reconstruction were performed. Pathological examination showed that the cancer was confined to the mucosa and measured  $43 \times$ 



Fig. 4. Endoscopic findings (case 2). a. Duodenal carcinoid in the anterior wall of the bulb. b. Endoscopic ultrasonography. The tumor was confined to the submucosal layer. c. Intraoperative endoscopy after ICG injection.

#### 30 mm (Fig. 3).

Case 2: Although conventional observation failed to identify any ICG (+) LNs (Fig. 5a), 1 ICG (+) right gastroepiploic LN (Fig. 5b) and 2 No. 13 ICG (+) LNs were detected with IRLS and then removed. Intraoperative examination of frozen sections demonstrated no LN metastasis. Wedge resection of the duodenal bulb was performed. Pathological examination showed that the carcinoid was confined to the submucosa and measured  $8 \times 7$  mm (Fig. 6).

Case 3: One ICG (+) No. 6 LN was detected with IRLS, whereas conventional observation failed to identify any ICG (+) LNs. Intraoperative examination of frozen sections demonstrated no LN metastasis. Wedge resection of the duodenal bulb was performed. Pathological examination showed that the carcinoid was confined to the submucosa and was 5 mm in diameter.

Preoperative abdominal computer tomography of

these 3 cases revealed no LNs around the duodenum. The 3 patients are alive without recurrence.

Lymph node (LN) stations were modified from those of the Japanese Classification of Gastric Carcinoma<sup>1</sup>.

#### DISCUSSION

Duodenal tumors are extremely rare in the gastrointestinal tract. Yokoyama et al. have reported that from 1985 through 1991 duodenal adenomas accounted for 0.04% (17 of 39,169 tumors) of gastrointestinal tumors at the National Cancer Center, Japan, and that primary duodenal cancers, excluding cancers of the papilla of Vater, accounted for only 0.01% of tumors (3 of 39,169 tumors)<sup>2</sup>. Primary duodenal carcinoids account for only 2.6% of all carcinoid tumors<sup>3</sup>. Because of the rarity of duodenal cancers and carcinoids, to our knowledge the incidence of LN metas-



Fig. 5. SNNS (case 2). a. Observation with white light. ICG (+) LNs could not be detected. \*, pancreas; \*, duodenum (primary lesion). b. Observation with IRLS. ICG (+) lymphatic vessels and LNs could be clearly detected. Narrow arrows indicate ICG (+) lymphatic vessels. The thick arrows indicate ICG (+) LNs. c. Sentinel nodes. These could not be recognized as green nodes with the naked eye. d. Sentinel nodes. These ICG (+) LNs could be recognized as black nodes on infrared ray observation.

tasis of early duodenal cancers has not been reported. A previous report from Japan found that 13% of small (less than 1 cm) duodenal carcinoid tumors are associated with regional LN metastasis<sup>4</sup>. In the United States, Burke et al. have reported that 16 of 77 carcinoid tumors (21%) of the duodenum had LN metastases<sup>5</sup>. Features associated with an increased risk of LN metastasis include involvement of the muscularis propria, size greater than 2 cm, and the presence of mitotic figures. Nevertheless, Mullen et al. have reported that LN metastases were identified in surgical specimen from 7 of 13 patients (54%), including specimens from 2 patients with tumors smaller than 1 cm and confined to the submucosa<sup>3</sup>. Therefore, endoscopic resection alone is inadequate for the treatment of duodenal carcinoids. Moreover, a largediameter duodenal mucosal cancer, like that in case 1, is difficult to treat with only endoscopic mucosal resection. However, because pancreaticoduodenectomy is major surgery with high rates of morbidity and mortality<sup>6</sup>, accurate intraoperative diagnosis of LN metastasis with SNNS would allow a less-invasive operation, such as wedge resection of the duodenum.

Since reported by Morton et al. in 1992, the concept of sentinel lymph nodes in melanoma and breast cancer has been validated, and SNNS is now widely performed<sup>7,8</sup>. Recently, several reports of SNNS for gastric cancer and colonic cancer have been published<sup>9–16</sup>. Since May 2000, we have been using our own technique, IRLS, for gastric cancer; we have obtained excellent results and have reported that SNNS with IRLS is useful for limited gastric surgery for early gastric cancer without compromising curability<sup>17,18</sup>.

In conclusion, IRLS can be used to detect sentinel LNs in early duodenal malignant tumors, and SNNS is useful for limited duodenal resection.



Fig. 6. Surgical specimen and pathological findings. a. Macroscopic appearance of a resected surgical specimen, which contained a yellowish submucosal tumor. b. Microscopic findings of the duodenal carcinoid tumor of the submucosal layer (hematoxylin and eosin,  $20 \times$ ). c. Histological examination showed small, round cells that were characteristic of carcinoid (hematoxylin and eosin,  $100 \times$ ).

#### References

- International and Japanese Gastric Cancer Association. Japanese Classification of Gastric Carcinoma - 2nd English Edition. Gastric Cancer 1998; 1: 10-24.
- Yokoyama T, Saito D, Kondo H, Kido M, Hosokawa K, Shirao K, et al. Endoscopic diagnosis of malignant lesions of the duodenum (in Japanese with English abstract). Stomach and Intestine (Tokyo) 1993; 28: 641-9.
- Mullen JT, Wang H, Yao JC, Lee JH, Perrier ND, Pisters PWT, et al. Carcinoid tumors of the duodenum. Surgery 2005; 138: 971-8.
- Soga J. Endocrinocarcinomas (carcinoids and their variants) of the duodenum : an evaluation of 927 cases. J Exp Clin Cancer Res 2003 ; 22 : 349-63.
- Burke AP, Sobin LH, Federspiel BH, Shekitka KM, Helwig EB. Carcinoid tumors of the duodenum: a clinicopathologic study of 99 cases. Arch Pathol Lab

Med 1990; 114: 700-4.

- Yang YM, Tian XD, Zhuang Y, Wang WM, Wan YL, Huang YT. Risk factors of pancreatic leakage after pancreaticoduodenectomy. World J Gastroenterol 2005; 11: 2456-61.
- Morton DL, Wen DR, Wong JH, Economou JS, Cagle LA, Storm FK, et al. Technical details of intraoperative lymphatic mapping for early stage melanoma. Arch Surg 1992; 127: 392-9.
- Velonesi U, Paganelli G, Galimberti V, Viale G, Zurrida S, Bedoni M, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. Lancet 1997; 349: 1864-7.
- Hiratsuka M, Miyashiro I, Ishikawa O, Furukawa H, Motomura K, Ohigashi H, et al. Application of sentinel node biopsy to gastric cancer surgery. Surgery 2001; 129: 335-40.
- Kitagawa Y, Fujii H, Mukai M, Kubota T, Otani Y, Kitajima M. Radio-guided sentinel node detection for

March, 2009

gastric cancer. Br J Surg 2002; 89: 604-8.

- Hayashi H, Ochiai T, Mori M, Karube T, Suzuki T, Gunji Y, et al. Sentinel lymph node mapping for gastric cancer using a dual procedure with dye- and gamma probe-guided techniques. J Am Coll Surg 2003; 196: 68-74.
- Miwa K, Kinami S, Taniguchi K, Fushida S, Fujimura T, Nonomura A. Mapping sentinel nodes in patients with early-stage gastric carcinoma. Br J Surg 2003; 90: 178-82.
- Kim MC, Kim HH, Jung GJ, Lee JH, Choi SR, Kang DY, et al. Lymphatic mapping and sentinel node biopsy using 99mTc tin colloid in gastric cancer. Ann Surg 2004; 239: 383-7.
- Aikou T, Kitagawa Y, Kitajima M, Uenosono Y, Bilchik AJ, Martinez SR, et al. Sentinel lymph node mapping with GI cancer. Cancer Metastasis Rev 2006; 25: 269– 77.

- Saikawa Y, Otani Y, Kitagawa Y, Yoshida M, Wada N, Kubota T, et al. Interim results of sentinel node biopsy during laparoscopic gastrectomy : possible role in function-preserving surgery for early cancer. World J Surg 2006; 30: 1962–8.
- Saha S, Dan AG, Viehl CT, Zuber M, Wiese D. Sentinel lymph node mapping in colon and rectal cancer: its impact on staging, limitations, and pitfalls. Cancer Treat Res 2005; 127: 105–22.
- Nimura H, Narimiya N, Mitsumori N, Yamazaki Y, Yanaga K, Urashima M. Infrared ray electronic endoscopy combined with indocyanine green injection of sentinel nodes of patients with gastric cancer. Br J Surg 2004; 91: 575-9.
- Odaira H, Nimura H, Mitsumori N, Kashiwaqgi H, Yanaga K. Validity of modified gastrectomy combined with sentinel node navigation surgery for early gastric cancer. Gastric Cancer 2007; 10: 117-22.