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New method of indocyanine green fluorescence sentinel node mapping for early gastric cancer

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HIGHLIGHTS

- ICG fluorescence SN mapping for early gastric cancer using PINPOINT® is described.
- ICG positive nodes were able to be observed in all the patients.
- The mean of ICG positive lymph nodes was 8.6.
- One patient had a metastatic lymph node in SN.
- PINPOINT® make identification of SNs easy and simple for gastric cancer surgey.

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ABSTRACT

Background: The present study describes the retrospective feasibility study of ICG fluorescence SN mapping in back-table for early gastric cancer using PINPOINT®.

Method: SN mapping were performed as following; the day before surgery, 0.5 ml ICG was injected endoscopically in four quadrants of the submucosa surrounding the gastric cancer using an endoscopic puncture. Intraoperatively, the gastrocolic ligament was divided to visualize all possible directions of lymphatic flow from the stomach. PINPOINT® (NOVADAQ, Canada) was used to illuminate regional lymph nodes from the serosal side. Positive staining was confirmed by at least 3 surgeons and an endoscopist during surgery (Figure 1). Lymph node dissection and gastrectomy were performed according to the criteria of gastric cancer treatment guidelines of JGCA.

Result: All 6 patients had gastrectomy with laparoscopic approach. ICG positive lymphatic flow and lymph nodes were able to be observed in all the patients. Final pathological diagnosis was all StageI and curative resection.

All the patients had ICG positive lymphatic area in left gastric artery (LGA) area.

Two patients with tumor located in L area had ICG positive flow to right gastroepipoloic artery (RGEA) area. The mean of ICG positive lymph nodes was 8.6. One patient had a metastatic lymph node in station No.4, which was positive for ICG.

Conclusion: Our method made identification of ICG positive lymph nodes easy in SN mapping in back-table under room light. Although further accumulation and analysis are necessary, we may be able to apply this method for intraoperative SN mapping of laparoscopic gastric cancer surgey.

1. Introduction

Gastrectomy with D2 dissection has been a standard surgical procedure for resectable gastric cancer in the treatment guidelines of the Japanese Gastric Cancer Association (JGCA) [1,2]. These recommendations are based on the large amounts of data obtained from patients who had undergone gastrectomy in Japan.

However, some studies from western countries reported that patients with gastric cancer treated by D2 dissection had a significantly higher rate of complications, a higher postoperative

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mortality rate and a longer hospital stay than those who had D1 dissection [3]. More attention should be payed to the improvement of postoperative quality of life without impairing long term outcome. Gastrectomy with D2 seems to be an overly invasive surgery for patients with pN0 gastric cancer.

According to this background, sentinel node concept has been introduced for early gastric cancer surgery. In fact, Several successful single-institution studies for sentinel node (SN) mapping in gastric cancer have been reported [4–8].

However, the indications and the procedures applied for SN mapping in these previous reports varied. Kitagawa et al. conducted prospective multicenter trial for sentinel node mapping using the dual tracer method with technetium 99 m–labeled tin colloid and 1% isosulfan blue dye [9]. In several institutions, indocyanine green fluorescence SN mapping has been performed [8,14].

Recently, PINPOINT® (NOVADAQ, Canada) has developed for ICG fluorescence guided surgery [10–12]. Evaluations of the blood supply for reconstructed organ and anastomosis in gastrointestinal surgery has been reported. In our institute, PINPOINT has been applied for gastric cancer surgery to identify lymphatic flows and SNs.

The present study describes the retrospective feasibility study of ICG fluorescence SN mapping in back-table for early gastric cancer using PINPOINT.

2. Patients and methods

The protocol was approved by the Ethics Committee for Biomedical Research of the International University of Health and Welfare Hospital, and all patients provided informed consent.

Nine patients diagnosed as early gastric cancer with no obvious metastasis were admitted to our hospital between September and December in 2015. In this study, six patients with cT1N0 or cT2N0 gastric cancer were enrolled and evaluated retrospectively.

Injection of the tracer was performed according to Kitagawa's dual tracer method [4,9]. The day before surgery, ICG (ICG: Diagnogreen®; Dai-Ichi Sankyo Pharm, Tokyo, Japan) was injected in four quadrants of the submucosal layer of the primary lesion by using an endoscopic puncture needle (Fig. 1). As a preliminary trial, for five case each 50.0 μg/ml of the ICG was injected. During the course of this trial, quality of camera scope for ICG fluorescence imaging was fixed and improved, and the number of ICG positive lymph node increased too much. Therefore, we decrease the concentration of ICG to 33.3 μg/ml for last case.

Intraoperatively, surgical field was made to visualize all possible directions of lymphatic flow. For ICG fluorescence imaging, PINPOINT® was used and illuminated regional lymph nodes from the serosal side with three modes (Pinpoint mode, spy mode, colorized mode) (Fig. 2). Positive staining was confirmed by at least 3 surgeons during surgery.

Lymph node dissection and gastrectomy were performed according to the criteria of gastric cancer treatment guidelines of JGCA regardless of intraoperative SN result. Range for the node dissection and gastrectomy depended on the preoperative diagnosis of the depth and location. This is because SN biopsy has established false negative rates and has not been incorporated into standard work-up as per oncological surgery guidelines (such as NCCN).

Postoperatively, back-table observation of staining nodes and pathological examination with haematoxylin and eosin staining was performed (Fig. 3). Findings of macroscopy and pathology were described according to the Japanese classification of gastric carcinoma (3rd English edition) [3].

Injection of the ICG and laparoscopic gastrectomy were performed by two surgeons (Hironori Ohdaira and Masashi Yoshida). Pathological examination were done by one pathologist (Shinya Okada).

3. Results

No allergic reaction were observed after ICG injection.

All the six patients' characteristics are listed in Table 1. All the patients had gastrectomy with laparoscopic approach. Case⑤ patient was suspected that the depth of tumor was muscularis propria. We judged that this clinical T2 patient had no lymph

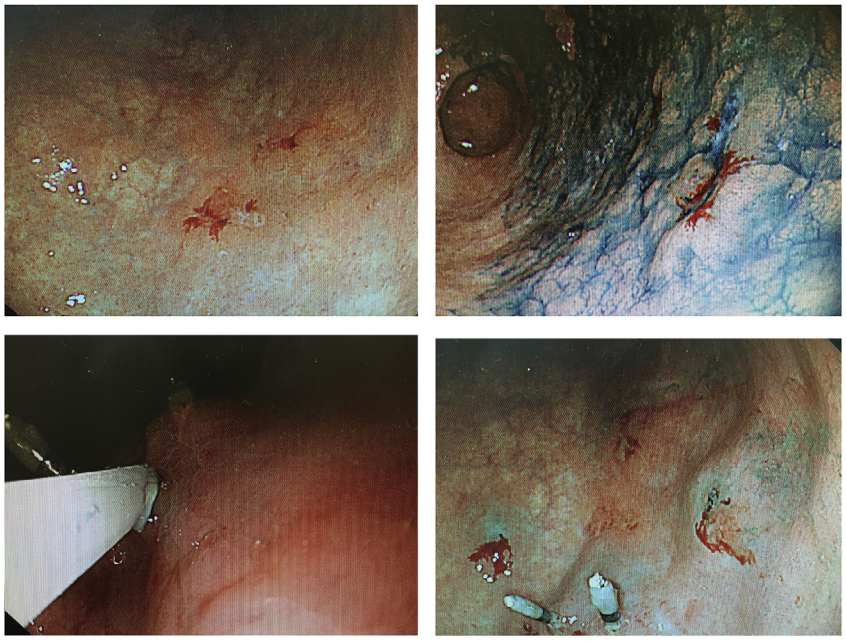

Fig. 1. Injection of the tracer. The day before surgery, ICG was injected in four quadrants of the submucosal layer of the primary lesion by using an endoscopic puncture needle.