Laparoscopic repeat hepatectomy with indocyanine green fluorescence navigation: A case report

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Abstract

The indocyanine green (ICG) fluorescence method is reportedly useful for intraoperative visualization of hepatocellular carcinoma and metastatic liver cancer. Herein, we report the case of a 73-year-old man who underwent laparoscopic hepatectomy using an ICG fluorescence navigation system. The patient had a surgical history of two laparotomies for hepatocellular carcinoma resection. During follow-up at our hospital, abdominal computed tomography revealed recurrence of hepatocellular carcinoma in the lateral area of the liver, and so the patient was hospitalized for surgery. Because of his surgical history, adhesions within the abdominal cavity were predicted. We scheduled laparoscopic repeat hepatectomy (LRH) using an ICG fluorescence method in which the ICG was injected intravenously 2 days before surgery. The ICG fluorescence was easily detected intraoperatively. The advantages of the present approach were: 1) inducing pneumoperitoneum and using laparoscopic magnification enabled good visualization of the surgical field for LRH; 2) use of the ICG fluorescence technique enabled clear intraoperative identification of the tumor, thus facilitating LRH. Laparoscopic partial resection of the liver (S3) was successfully performed, with an operation time of 197 minutes and a bleeding volume of 30 mL. The patient had an uneventful postoperative course and was discharged on postoperative day 10.

Key words: laparoscopic repeat hepatectomy, indocyanine green (ICG) fluorescence navigation
Introduction

Laparoscopic liver resection (LLR) is now being performed much more frequently, with several modifications. Furthermore, we now perform many laparoscopic repeat hepatectomy (LRH) procedures for patients who have previously undergone upper abdominal laparotomy procedures, including hepatectomy. For the safe completion of LRH, it is mandatory for the surgeon to recognize post-resection liver deformities and accurately locate the tumor. In addition, the degree of surgical difficulty in LRH can be high because of the limited utility of intraoperative ultrasound and the presence of adhesions around the liver.

An indocyanine green (ICG) fluorescence navigation system in combination with preoperative three-dimensional simulation has been introduced for LRH. Recently, the intraoperative usefulness of injecting intravenous ICG 2 days before surgery has been reported in various fields, including liver surgery\(^1,2\). The specific distribution of ICG over time can yield visualization of blood flow, the hepatic parenchyma, and the biliary tract. In patients with cirrhosis of the liver or those who have previously undergone transcatheter arterial chemoembolization or surgery (especially hepatectomy), the boundary between the tumor and non-tumorous parenchyma can be unclear, making it difficult to determine the required range of resection. Thus, the ICG fluorescence technique might be able to clearly identify tumor tissue in such cases.

Herein, we report the successful performance of LRH in a patient who had undergone two previous hepatectomies.
Case report

A 73-year-old man with nonalcoholic steatohepatitis (negative for hepatitis B surface antigen and hepatitis C virus antibody) and diabetic nephropathy was followed-up at our outpatient clinic. The patient had undergone an anterior segmentectomy of the liver for hepatocellular carcinoma (HCC) at 65 years of age, and a hepatic caudate partial resection for HCC recurrence at 68 years of age. Follow-up abdominal computed tomography (CT) detected recurrent suspected liver cancer in the lateral area of the liver. The patient was admitted to our hospital for further investigation and treatment.

His physical status on admission was unremarkable. Preoperative hematologic and blood biochemical tests, including testing for the tumor markers α-fetoprotein and PIVKA II, showed only hyperglycemia and mild renal dysfunction. Abdominal ultrasonography revealed a low echoic mass lesion in segment 3 (S3) of the liver. Abdominal contrast CT indicated that the tumor was a recurrent HCC with a diameter of 1.5 cm. The tumor was intensively stained with a contrast agent early in the arterial phase and washed out in the venous phase (Fig. 1). On the basis of these findings, a diagnosis of a single recurrence of HCC in liver S3 was made, indicating the need for partial laparoscopic resection of the segment. As the patient had previously undergone two open hepatectomies, we predicted that there would be adhesions in the abdominal cavity and that the accurate identification of the tumor location would be difficult. Nevertheless, we selected to perform a laparoscopic operation because of the minimal invasiveness and the magnification provided by the laparoscope. The ICG fluorescence navigation method was also planned to enable easier identification of the tumor. ICG reagent (0.5 mg/kg) was injected intravenously 2 days before surgery.

Surgical procedure

The use of intravenous ICG injection for intraoperative navigation was approved by the ethics committee of our institute.

Although our patient had previously undergone upper abdominal laparotomy and had a surgical
scar at the umbilicus, a 3 cm incision was created at the umbilicus, and a Lap Protector™ (Hakko, Nagano, Japan) was attached. A 12 mm port for a camera and two 5 mm ports for the multiaccess port system (EZ Access®; Hakko, Nagano, Japan) were also constructed (Fig. 2). In LRH, the location and number of additional ports are decided in accordance with patient factors such as adhesions in the abdominal cavity. In the present case, an additional 12 mm port was inserted in the right upper abdominal quadrant, and a 5 mm port was inserted in each of the right lower and left upper quadrants (Fig. 3). In LRH cases, the previous upper abdominal surgery has often resulted in strong adhesions followed by shortening deformities of the hepatic duodenal ligament, which prevents the use of the Pringle method.

Preoperative three-dimensional CT imaging indicated that the tumor was located on the dorsal side of the liver (Fig. 4a, 4b). Therefore, adhesions were detached or divided as much as necessary to create the surgical field for the planned hepatectomy. Adhesions from the abdominal wall, transverse colon, omentum, lateral extrahepatic area, and stomach were sufficiently detached to enable partial resection of liver S3, while adhesions that were not in the required surgical field were left intact (Fig. 5a–5c). As the tumor was located on the dorsal side of the liver, the adhesions that could be used to lift the liver were left in situ. When the liver surface on which the tumor was predicted was exposed, the camera was switched to ICG fluorescence mode, enabling visualization of the tumor as a clearly demarcated region of green fluorescence (Fig. 6a, 6b). An ultrasonically activated scalpel was used to dissect the superficial layer, while the deep layer was dissected using a Cavitron ultrasonic surgical aspirator (Valley lab; Medtronic, Minneapolis, MN, USA). The appropriate vessels in the liver were clipped and dissected, and partial resection of liver S3 was performed in accordance with the preoperative simulation (Fig. 6c, 6d). The operative time was 197 minutes, and the bleeding volume was 30 mL. The postoperative course was uneventful, and the patient was discharged 10 days postoperatively.
Discussion

With improvements in the outcomes of treatment of HCC and liver metastases from colorectal cancer, repeat hepatectomy is becoming more frequently indicated. Additionally, the development and evolution of surgical instruments and improvements in the reliability and safety of surgical techniques have enabled the safe and effective implementation of minimally invasive LLR.

In LRH, there are limitations on securing an adequate visual field as a result of adhesions, liver displacement, and deformation from previous surgery. As it is sometimes difficult to achieve adequate resection in LRH, the established indications for LRH have not been conclusively established. However, laparoscopic surgery has been reported to be a feasible and effective option for repeat hepatectomy\(^4\),\(^5\). In our institute, we have performed LRH in 24 patients, and these experiences have shown the safety and feasibility of LRH. The adhesions encountered during LRH can be managed with the aid of the good visual field provided by the induction of pneumoperitoneum, while the magnification provided by the laparoscopic approach facilitates surgical success in a small operative field. Access to the lesion and excision is often possible with minimal management of adhesions in LRH, which results in less bleeding and short operation times, as in the present patient. In contrast, conventional re-operative laparotomy requires the creation of the same sized surgical field as in the previous laparotomy, thus necessitating a wider range of adhesion detachment. In conventional LLR, intraoperative ultrasonic assessment is indispensable for confirmation of the tumor location and extent. However, in patients undergoing LRH, ultrasound probe movement may be limited by adhesions. In addition, residual liver displacement and deformation can make it difficult to visualize the tumor, and it is often hard to distinguish the borderline between normal liver and tumor in a patient with an impaired liver.

ICG fluorescence techniques are used in various fields for intraoperative identification of lymph nodes, vessels, and tumors. ICG is a water-soluble compound with a molecular weight of 77,460 Da that rapidly binds with plasma lipoproteins, most of which are taken up by liver parenchymal cells and excreted in bile without being metabolized\(^6\), enabling its wide use for preliminary
evaluation of the liver. ICG fluorescence techniques have also been applied to identify target areas of the liver during anatomical hepatic resection\(^7\), and for the detection of bile leakage to reduce the incidence of postoperative biliary fistula formation after hepatectomy\(^8\). A camera with a charge coupled device can be used to observe the near-infrared wavelength of ICG fluorescence to a depth of 10 mm from the body surface\(^9,10\). ICG emits a fluorescent color upon binding with \(\alpha\)-1 lipoprotein\(^11\). HCC exhibits fluorescence because well-differentiated HCC produces bile; however, the excretion of bile is delayed. It is also speculated that normal liver parenchyma surrounding HCC has impaired ability to excrete bile\(^10\).

As mentioned above, it can be difficult to locate tumors by using ultrasound examination in patients undergoing repeat hepatectomy. However, the identification of tumor tissue is made easier using the ICG fluorescence navigation method. ICG fluorescence navigation enables the identification of approximately 100% of gross HCC, and of 40% of microscopic lesions that were not detected preoperatively\(^4\). For these reasons, we use an ICG fluorescence navigation system when performing LRH.

One of the limitations of the ICG fluorescence technique is that it can produce false positives, as precancerous lesions and regenerative nodules also reportedly fluoresce in patients with liver cirrhosis. Therefore, the combined use of ultrasound examination using Sonazoid\(^12\) (Diichi-Sankyo, Tokyo, Japan) and an ICG fluorescence technique could provide superior results, particularly when identifying tumors during LRH where the operative field for liver resection is narrow.

In the present patient, the outcomes of LRH with ICG fluorescence navigation were good in terms of operation time, bleeding volume, and duration of hospital stay. Overall, we believe that implementing ICG fluorescence navigation when performing LRH is feasible and useful in improving safety and convenience.

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Conflict of Interest: The authors declare that they have no conflict of interest.
References

1) Liberale G, Bourgeois P, Larsimont D, Moreau M, Donckier V, Ishizawa T. Indocyanine green fluorescence-guided surgery after IV injection in metastatic colorectal cancer: A systematic review. Eur J Surg Oncol 2017; 43: 1656-1667.

2) Terasawa M, Ishizawa T, Mise Y, Inoue Y, Ito H, Takahashi Y, Saiura A. Applications of fusion-fluorescence imaging using indocyanine green in laparoscopic hepatectomy. Surg Endosc 2017; 31: 5111-5118.

3) Kim YI, Kitano S. Segment VIII resection of the cirrhotic liver under continuous Pringle maneuver with in situ cooling followed by temporary portal decompression. Am J Surg 1999; 177: 244-246.

4) Hu M, Zhao G, Xu D, Liu R. Laparoscopic repeat resection of recurrent hepatocellular carcinoma. World J Surg 2011; 35: 648-655.

5) Shafaezi Z1, Kazaryan AM, Marvin MR, Cannon R, Buell JF, Edwin B, Gayet B. Is laparoscopic repeat hepatectomy feasible? A tri institutional analysis. J Am Coll Surg 2011; 212: 171-179.

6) Wada T, Kawada K, Takahashi R, Yoshitomi M, Hida K, Hasegawa S, Sakai Y. ICG fluorescence imaging for quantitative evaluation of colonic perfusion in laparoscopic colorectal surgery. Surg Endosc 2017; 31: 1061-1069.

7) Aoki T, Yasuda D, Shimizu Y, Odaira M, Niiya T, Kusano T, Mitamura K, Hayashi K, Murai N, Koizumi T, Kato H, Enami Y, Miwa M, Kusano M. Image-guided liver mapping using fluorescence navigation system with indocyanine green for anatomical hepatic resection. World J Surg 2008; 32: 1763-1767.

8) Kaibori M1, Ishizaki M, Matsui K, Kwon AH. Intraoperative indocyanine green fluorescent imaging for prevention of bile leakage after hepatic resection. Surgery 2011; 150: 91-98.

9) Gotoh K, Yamada T, Ishikawa O, Takahashi H, Eguchi H, Yano M, Ohigashi H, Tomita Y, Miyamoto Y, Imaoka S. A novel image guided surgery of hepatocellular carcinoma by indocyanine green fluorescence imaging navigation. J Surg Oncol 2009; 100: 75-79.

10) Ishizawa T, Fukushima N, Shibahara J, Masuda K, Tamura S, Aoki T, Hasegawa K, Beck Y,
Fukayama M, Kokudo N. Real-time identification of liver cancers by using indocyanine green fluorescent imaging. Cancer 2009; 115: 2491-2504.

11) Baker KJ. Binding of sulfobromophthalein (BSP) sodium and indocyanine green (ICG) by plasma α₁ lipoproteins. Oroc Soc Exp Biol Med 1966; 122: 957-963.

12) Uchiyama K, Ueno M, Ozawa S, Kiriyama S, Shigekawa Y, Yamaue H. Combined use of contrast enhanced intraoperative ultrasonography and a fluorescence navigation system for identifying hepatic metastases. World J Surg 2010; 34: 2953-2959.
Computed tomography image demonstrating a 1.5 cm tumor in liver S3 (white arrow) with wash-out in the late contrast phase, indicating hepatocellular carcinoma.
A 3 cm incision has been made at the umbilicus. Adhesions under the umbilicus and in the surroundings have been identified. A multiaccess port system (EZ access; Hakko Medical, Nagano Japan) with one 12 mm and two 5 mm ports is being used.
Postoperative photograph showing the surgical wound sites. A 12 mm port was inserted in the right upper abdominal quadrant, and 5 mm ports were inserted in the right lower and left upper quadrants.
(a, b) Three-dimensional computed tomography simulation showing the tumor located on the dorsal side of the liver S3.
Intraoperative photographs. The transverse colon and omentum are adherent to the peritoneum, consistent with the previous laparotomies, restricting the visual field of the upper abdomen.

Adhesion in the left upper abdominal cavity.
The outer lateral area of the liver is adherent to the abdominal wall, enabling a good field of view from the dorsal side as was required for resection of the tumor.
Intraoperative photographs. (a) After switching to an indocyanine green (ICG) fluorescence camera, the tumor area is visualized by its emission of fluorescent green light. (b) With the aid of an ICG fluorescence camera, the liver surface is marked to indicate the required area of resection encompassing the tumor.
Intraoperative photographs. (c) The required liver resection can be performed in a limited space with a good field of view. (d) The required hepatic resection has been achieved in the left upper abdomen; a drain has been left in place.