

Utility of X-ray and indocyanine green fluorescence imaging in detecting hepatocellular carcinoma dissemination on laparoscopic surgery: A case report

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Abstract. Indocyanine green (ICG) fluorescence imaging is useful for the intraoperative detection of the peritoneal dissemination of hepatocellular carcinoma (HCC). However, in laparoscopic surgery, disseminations cannot be accurately identified unless the camera lens is positioned close to the lesion. The present study describes a case of HCC dissemination in which the lesions were accurately identified by combining intraoperative fluoroscopy with ICG fluorescence imaging. A 76-year-old male was diagnosed with HCC dissemination. Computed tomography revealed a 9-mm disseminated nodule near the gallbladder. Although transarterial chemoembolization had also been used to treat this lesion, chemoembolization was technically difficult to perform. Therefore, a coil was placed around the lesion to serve as an intraoperative landmark for later laparoscopic resection. Given the potential difficulty of detecting the lesion during laparoscopic surgery, ICG fluorescence imaging was used to determine the approximate location of the dissemination. The lesion exhibited strong fluorescence, which facilitated its complete resection.

Introduction

Indocyanine green (ICG) fluorescence imaging is used intraoperatively to detect the disseminated recurrences of hepatocellular carcinoma (HCC) (1). However, as the tissue penetration of near-infrared light is limited, detecting tumors in deeper sites using this approach is difficult. At our department, a case of minor peritoneal dissemination of HCC was

encountered, in which the lesions were able to be accurately identified and located by combining intraoperative fluoroscopy with ICG fluorescence imaging during laparoscopic surgery.

Case report

A 76-year-old male was diagnosed with HCC caused by alcoholic liver cirrhosis. The patient had received percutaneous ethanol injection therapy for S2 and S5 HCC 13 years previously, radiofrequency ablation for S4/5 HCC 6 years ago and S6 HCC 3 years previously.

At one year prior to presentation, computed tomography revealed tumor dissemination on the surface of S6 and transcatheter arterial chemoembolization was performed. It also revealed a 9-mm disseminated nodule near the gallbladder (Fig. 1). Since intrahepatic lesions were well controlled and there was only one recurrent lesion, surgical treatment was suggested to the patient. However, the patient requested a less invasive treatment and thus, initiation of the treatment with transcatheter arterial chemoembolization was first planned. A disseminated nodule was identified by selective imaging of the ileal artery, which branches off from the superior mesenteric artery (Fig. 2A). Chemoembolization was attempted but impaired blood flow to the ileum was a concern. Since it was technically difficult to treat the lesion with chemoembolization, laparoscopic surgical resection was opted for to remove the lesion. A coil was placed in the artery that supplies the ileum near the disseminated nodule to serve as an intraoperative marker (Fig. 2B).

Given the difficulty of identifying small, disseminated lesions during laparoscopic surgery, ICG fluorescence imaging with intraoperative fluoroscopy was used to facilitate identification. ICG (0.5 mg/kg) was injected intravenously into the patient 24 h prior to the operation.

With the coil as a landmark, intraoperative fluoroscopy was used to gauge the disseminated nodule's approximate position (Fig. 2C), which was beneath the adipose tissue (Fig. 3A). The Stryker 1588 AIM camera system was utilized for this. ICG fluorescence imaging confirmed the exact position of the lesion (Fig. 3B), which exhibited strong fluorescence. Therefore, it was completely resected laparoscopically. In addition, two

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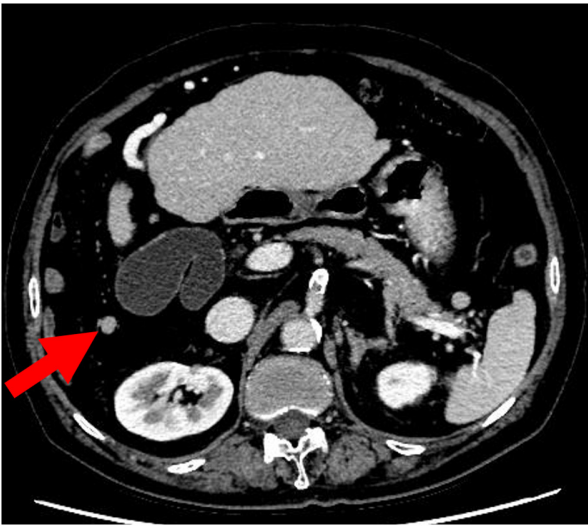


Figure 1. Dissemination of the hepatocellular carcinoma. Computed tomography indicated a 9-mm disseminated nodule around the gallbladder (red arrow).

small lesions on the right diaphragm (Fig. 3C and D) and one small lesion on the liver surface were also detected by fluorography and all were resected. The patient's postoperative course was uneventful and he was discharged on postoperative day 4. Pathologically, all four lesions were diagnosed as HCC disseminations (Fig. 4). At the time of writing this case study, 10 months had passed since the operation and the patient has been alive without any recurrence.

Discussion

Molecular targeted drug therapy is the standard treatment for advanced HCC with extrahepatic lesions (2,3). However, if intrahepatic lesions are absent or well-controlled, resection of the disseminations may be beneficial. A previous study reported that the cumulative 1-, 3- and 5-year overall survival rates after resection of thoracoabdominal implants were 71, 44 and 39%, respectively, with a median survival time of 34.5 months (4).

ICG fluorescence imaging has been used in various fields of surgery. In breast cancer surgery, the identification of sentinel lymph nodes using ICG fluorescence imaging has been standardized (5). ICG fluorescence imaging is also used to determine the excision range of non-occlusive mesenteric ischemia (6-8) and evaluate the blood flow at the anastomotic site in colorectal cancer surgery (9). In the field of lung surgery, thoracoscopic lung segment resection using ICG fluorescence imaging has also been performed (10). Nishino *et al* (11) reported that ICG fluorescence imaging is useful for evaluating arterial blood flow to the stomach in distal pancreatectomy with celiac axis resection. In HCC surgery, ICG fluorescence imaging provides anatomical information during laparotomy and laparoscopic surgery (12,13). Previous studies have reported that ICG fluorescence imaging is a convenient method for intraoperatively detecting extrahepatic HCC metastases (14,15). The uptake of ICG by HCC cells in extrahepatic metastases is similar to that observed in hepatocytes and intrahepatic HCC cells (16). According to Satou *et al* (1), of the 33 lesions (lung, adrenal gland, lymph node and peritoneum)



Figure 2. (A) The disseminated nodule was identified by selective imaging from the ileal artery. (B) A coil is placed in the artery near the lesion. (C) Intraoperative fluoroscopy. The lesion is indicated by a red arrow.

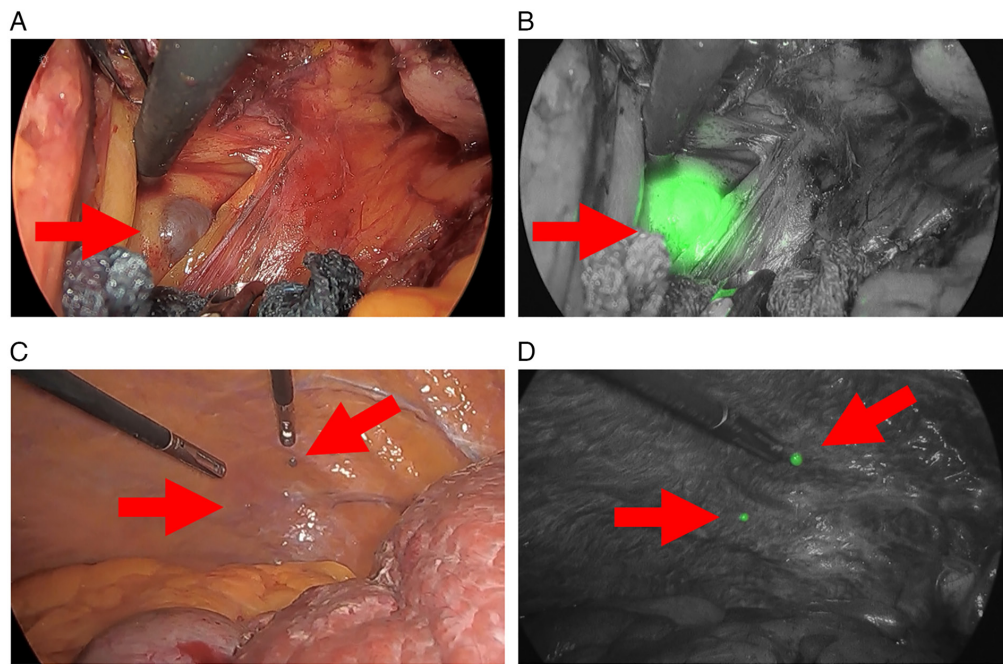


Figure 3. Intraoperative images. (A) Tumor located beneath the adipose tissue. (B) The lesion from A exhibited strong fluorography in ICG mode. (C) Two small lesions, which were not able to be identified preoperatively, were detected on the right diaphragm. (D) The lesions from C exhibited strong fluorography in ICG mode. The lesion is indicated by red arrows.

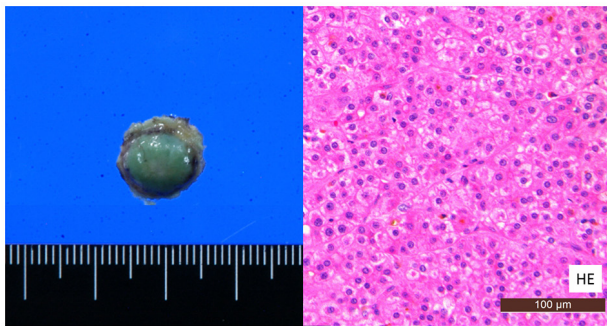


Figure 4. Pathological examination indicated that the resected lesions were disseminations of hepatocellular carcinoma. Left: Image of resected lesion (~1 cm); right: Histology image with HE staining (scale bar, 100 μm).

suspected to be extrahepatic metastases of HCC, 26 exhibited fluorescence on ICG and all were metastases of HCC. Of the seven lesions that did not exhibit any fluorescence, one was a metastasis of HCC and six were benign (1).

Ishizawa and Saiura (17) proposed that in patients with intrahepatic HCC, ICG at a dose of 0.5 mg/kg body weight should be administered within 2 weeks prior to surgery. In addition, they advised against the administration of ICG 1 day prior to surgery to decrease the possibility of false-positive nodules. In patients with extrahepatic HCC, the currently recommended interval ranges from 1 to 5 days (1). However, the duration of ICG retention in extrahepatic HCC may be longer than expected and ICG administration immediately prior to surgery may be permissible due to the lack of uptake by the background tissue (18). In the present case, ICG 0.5 mg/kg was administered intravenously 24 h prior to surgery.

Small metastatic nodules are difficult to recognize with the naked eye or on standard laparoscopic view. For extrahepatic

HCC metastases, ICG fluorescence imaging has a positive predictive value of 100% and a sensitivity of 92% (1). However, as the tissue penetration of near-infrared light is limited to 5-10 mm (19), detecting tumors in deeper sites, such as the dorsal site of adipose tissue, using this approach is difficult. To identify deep-seated lesions, a coil may be placed in the artery near the lesion and intraoperative fluoroscopy with ICG fluorescence may be used to facilitate detection. In the present case, the disseminated lesion was able to be identified laparoscopically using this method. Placing a marker, such as a coil, around a tumor may be considered if the tumor is difficult to detect with ICG fluorescence imaging alone. Furthermore, disseminated lesions that cannot be identified preoperatively may be identified using ICG fluorescence imaging.

ICG contains iodine, and there are reports of occasional anaphylactic shock due to administration (20,21). Therefore, it is necessary to be aware of the patient's history of allergies.

In conclusion, the combination of intraoperative ICG fluorescence imaging and fluoroscopy is useful for identifying small, disseminated HCC lesions laparoscopically.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

SS drafted the manuscript. MT revised the manuscript. YM and SN contributed to preoperative checks and diagnoses. SS, MT and TH performed the surgery. YM and SN followed up the patient. SI diagnosed the disease as a pathologist. MT and SS checked and confirmed the authenticity of the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report.

Competing interests

The authors declare that they have no competing interests.

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