Laparoscopic Treatment of a Hepatoduodenal Ligament Schwannoma With Infrared Indocyanine Green Fluorescence

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Abstract. Schwannomas occurring in the hepatoduodenal ligament are extremely rare, with only four cases reported. Here, we describe a case of a 30-mm schwannoma that originated in the hepatoduodenal ligament of a 38-year-old female found during a periodic medical check-up. Magnetic resonance imaging demonstrated a tumor in the hepatoduodenal ligament. Following an ultrasound-guided microbiopsy, histological examination showed solitary fibrous tumor or schwannomas in the liver or originating from the hepatoduodenal ligament. The relationship between the tumor and associated organs was confirmed intraoperatively, and the tumor was removed safely in its entirety using indocyanine green. The postoperative histopathological examination revealed the presence of a schwannoma with typical characteristics. To our knowledge, this is the first case of hepatoduodenal ligament schwannoma treated by laparoscopic surgery using indocyanine green fluorescence imaging.

Schwannomas are neurogenic tumors originating from Schwann cells in nerve sheaths or cells in the peripheral nervous system (1). They appear in all ethnic groups, all

ages, and both sexes, worldwide (2). More than 90% of schwannomas are benign and composed of 5% of benign soft-tissue neoplasms (2, 3). Although they occur in most parts of the body, the head, neck, and flexor surfaces of the extremities are the most commonly affected sites. Schwannomas are mostly found in patients aged 20-50 years, with no significant predominance of either sex (4). Most schwannomas show either monosomy 22 or loss of 22q material (5). They can arise in all anatomical sites, with the most common ones being the head, neck, and extremities (4), whereas 10% originate from multiple locations (6). They rarely occur in the retroperitoneum (7, 8), including the ligaments (8), bowel mesentery (9), and abdominal organs, including the gallbladder (7), pancreas (10), and liver (11). The most common treatment for schwannomas is surgery, and long-term survival can be expected in the majority of cases (1). Interestingly, schwannomas occurring in the hepatoduodenal ligament are extremely rare, with only four cases reported in the literature to date (12-15) (Table I). Patients presenting with schwannomas in the hepatoduodenal ligament have no specific symptoms; thus, the preoperative diagnosis is considerably difficult and the tumors are found incidentally.

The present report describes the case of a hepatoduodenal ligament schwannoma in a 38-year-old female patient and includes a review of the existing literature. Although surgical resection is the standard treatment for the schwannoma, when it occurs in the hepatoduodenal ligament, as seen in the present case, it may be difficult to dissect or remove the tumor without injuring or damaging the surrounding organs because of its close contact with the bile duct and other important vessels. Furthermore, it is sometimes necessary to resect surrounding organs, which may cause excessive surgical

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Table I. Available reports of schwannomas in the hepatoduodenal ligament published in the literature.

Author	Year	Age	Gender	Country	Preoperative diagnosis	Treatment	Size (mm)	Follow-up (Months)
Nagafuchi <i>et al.</i> (12)	1993	62	Female	Japan	Mass in the hepatic hilus	Laparotomy, cholecystectomy	90*50*45	26
Pinto <i>et al.</i> (13)	2011	29	Male	Portugal	Spindle cell neoplasia or stromal tumor	Laparotomy	45*29	NA
Tao <i>et al.</i> (14)	2016	50	Male	China	Stromal tumor	Laparoscopic surgery	45*25*25	7
Xu <i>et al.</i> (15)	2016	43	Male	China	Abdominal tumor	Laparotomy	85*55*30	17
Present case	2019	38	Female	Japan	Spindle cell neoplasia	Laparoscopic surgery with ICG	30*28*17	14

NA: Not available; ICG: indocyanine green.

Figure 1. White arrow points to a tumor. (A) Abdominal mass detected using conventional ultrasound. (B) Color Doppler ultrasound showed no blood supply in the tumor mass. (C) Enhanced computed tomography demonstrated a hypodense tumor approximately 25 mm in diameter beside the portal vein. (D) Magnetic resonance imaging of the tumor; T1-weighted sequences. (E) Magnetic resonance imaging of the tumor; T2-weighted sequences.

stress. In the present case, the relationship between the tumor and the organs was confirmed intraoperatively, and the tumor was removed safely in its entirety using indocyanine green (ICG). ICG binds to serum proteins *in vivo* and expresses a fluorescent signal (16). ICG fluorescence imaging has previously clearly demarcated the liver segments of a liver tumor (17, 18) and is, thus, extremely useful in this case. Histopathological and immunohistological evaluation is generally needed to confirm the diagnosis of schwannomas. Two main tissue patterns are generally recognized in schwannomas, designated as: i) Antoni type A (interlacing and cellular fascicles) and ii) B tissues (less cellular and myxoid) regions (14). Immunohistochemically, schwannomas are

strongly positive for S-100 and negative for desmin, smooth muscle myosin, α -SMA, CD34, and CD117 (19).

To our knowledge, this is the first case of a patient who underwent laparoscopic surgery using infrared ICG fluorescence to visually distinguish the organs adjacent to the tumor, such as the liver, hepatic artery, portal vein, and common bile duct in the hepatic portal region, and to avoid a bile duct injury.

Case Report

A 38-year-old female with no symptoms was referred to our hospital for a detailed examination due to a liver tumor pointed

out during a periodic medical check-up. Laboratory testing revealed normal levels for all items, with serum tumor markers, including carcinoembryonic antigen, cancer antigen (CA) 19-9, alpha-fetoprotein (AFP), and squamous cell carcinoma antigen being within a normal range. Abdominal contrast-enhanced ultrasound (CEUS) using Sonazoid (perfluorobutane microbubbles; GE Healthcare, Chicago, IL, USA) revealed well-defined, noncalcified isoechoic lesions measuring 28×16 mm in the space between the liver and the gallbladder. No blood flow signal was found in the mass using color Doppler US (Figure 1). An enhanced abdominal computed tomography (CT) scan revealed a 20×15-mm, well-defined cystic and solid round mass with a ring enhancement behind the segment 4 of the liver, in the space between the porta hepatis and the stomach (Figure 1). Magnetic resonance imaging (MRI) showed a tumor in the hepatoduodenal ligament with a low signal intensity on T1-weighted images and a high signal intensity on T2-weighted images (Figure 1). Schwannomas manifest as well-defined, hypoattenuating masses on nonenhanced CT and show peripheral enhancement with an irregular pattern on contrast-enhanced CT. Delayed peripheral enhancement until the late venous phase reflects a fibrous capsule and an internal fibrillary element on CT (20). MRI composes another useful tool for determining the nature of tumors. On MRI, schwannomas are usually presented as masses with a low signal intensity on T1-weighted images and inhomogeneous high signal intensity on T2-weighted images (21). At this point, US-guided microbiopsy was performed. Morphological findings were obtained using Hematoxylin and eosin staining of 3μm formalin-fixed, paraffin-embedded sections, indicating a proliferation of nonatypical round-to-spindle-shaped cells without mitoses. Immunohistochemical investigation using the following antibodies: S-100 (Polyclonal Rabbit), α-SMA (1A4), desmin (D33), β-catenin (β-catenin-1), Vimentin (V9) (Dako, Agilent technologies, Glostrup, Denmark), CD34 (Nichirei Bioscience, Tokyo, Japan), CD117 (c-kit) (Ventana, Tucson, AZ, USA) showed that vimentin was positive, while S-100, CD34, desmin, CD117, and alpha smooth muscle actin (α-SMA) were negative. These findings suggest a solitary fibrous tumor or schwannoma in the liver or originating from the hepatoduodenal ligament. Accordingly, laparoscopic resection using ICG fluorescence imaging was planned, and liver resection and lymphadenectomy were also planned if any malignant potential was observed intraoperatively. During surgery, 2.5 mg of ICG (Diagnogreen; Daiichi Sankyo, Tokyo, Japan) was injected intravenously in one bolus. The PINPOINT Endoscopic Fluorescence Imaging System (Novadaq, Mississauga, ON, Canada) was used to visualize the liver and bile duct in a pseudo-color (green) in real time. Under the laparoscopic view, the tumor surrounded by a fibrous capsule was located in the hepatoduodenal ligament without invasion to the surrounding tissue and organs (Figure 2). ICG fluorescence imaging proved very useful for

Figure 2. Intraoperative findings. The encapsulated tumor (double white arrows) was found in the hepatoduodenal ligament, with no invasion of the common hepatic artery (white arrow) (A). After ICG injection, the tumor was divided from surrounding organs (liver, hepatic artery (white arrow) and bile duct (black arrow) are presented in a pseudo-color green) (B). The tumor was completely resected (C).

identifying the liver parenchyma and the common bile duct next to the tumor and confirmed the fact that the tumor did not originate in the liver, given the absence of near-infrared fluorescence (superimposed in a green pseudo-color) in the tumor. The tumor was completely resected (operation time was 208 min with a small amount of bleeding) and the gross specimen was described as a mass measuring 30×28×17 mm. Both the postoperative pathological examination using hematoxylin and eosin and the immunohistochemical staining revealed that the tumor mainly consisted of: i) spindle-shaped cells with no atypia, ii) a positive expression of S-100 protein, and iii) absence of CD34, α-SMA, desmin, and β-catenin

Figure 3. Tissue histology. (A) Histopathological examination revealed that the tumor was mainly composed of spindle cells (hematoxylin and eosin staining). (B) Tumor specimens were strongly positive for S-100.

expression. These results revealed the presence of a schwannoma with typical characteristics (Figure 3). In the present case, intraoperative ICG imaging and these histopathological examinations revealed that the tumor originated from the ligament rather than the liver parenchyma. The patient developed no complications after operation and was discharged on hospital day 5.

This study was approved by a suitably constituted Ethics Committee in our institution (approval number is 1754). A written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Discussion

In the present case, the tumor occurred in the hepatoduodenal ligament, and because of its contact with the liver surface, it was quite difficult to preoperatively evaluate the site of occurrence. Although the schwannomas are benign tumors, it needs to be distinguished from a liver malignant tumor, and surgical treatment seems to be appropriate. Preoperative image evaluation should be comprehensively and carefully evaluated by CT, MRI and US, and the tumor should be diagnosed and biopsy was considered if necessary. Although schwannomas are considered benign tumors, at least histologically (2, 3), considering of the possibility of pressure on adjacent organs due to the tumor growth and the risk of vascular occlusion, surgical treatment to remove the tumor with its surrounding capsule is desirable. When the tumor is located in the liver edge, it may be difficult to determine whether it is primarily affiliated with the liver or an adjacent organ. Although extrahepatic tumors often have a boundary with the liver parenchyma, preoperative diagnosis can be

difficult; this was true in the present case because the border was unclear. Here, while the tumor was intraoperatively thought to be benign because it was wrapped in a capsule, soft, and showed no tendency toward infiltrating the surroundings, limited minimal surgical resection was considered appropriate. A two-stage additional hepatectomy with lymphadenectomy of the hepatoduodenal ligament might be necessary when potential residual tumor cells are considered. Finally, a careful follow-up should be conducted in such cases because of the lack of evidence of a desirable surgical margin as well as a definite adjuvant chemotherapy or radiation therapy.

Regarding tumor resection at the hepatoduodenal ligament, when bile duct or vessel injury occurs, there is a concern that major hepatectomy or choledochojejunostomy might be needed as additional surgery. In this case, it was not possible to clarify whether the tumor was in the liver tumor or the mesentery preoperatively, thus the ICG fluorescence imaging helped to identify the tumor's site of origin. ICG fluorescence imaging makes it easy to distinguish between the bile duct and adjacent organs in real time, which may assist in avoiding unnecessary bile duct injury and in resecting the tumor safely with minimally invasive laparoscopic surgery. We would like to suggest that the ICG fluorescence imaging technique should be actively used in such cases.

Schwannoma in the hepatoduodenal ligament is extremely rare. We identified hepatoduodenal ligament tumor intraoperatively using ICG fluorescence imaging, we were able to avoid injuring the bile duct or performing unnecessary hepatectomy. To the best of our knowledge, this is the first reported case of benign schwannoma in the hepatoduodenal ligament treated by laparoscopic surgery using ICG fluorescence imaging.

Conflicts of Interest

The Authors disclose that they have no significant relationships with, or financial interest in, any commercial companies pertaining to this article.

Authors' Contributions

All Authors examined the patients, IS, YN, JA, AK, SU, YS, MU, MS and HY investigated the specimens *via* liver needle biopsies, KT, TA, TK and MM performed the operation, KT, AE, TA, TK, TK, SM and MM discussed in graphic analysis, KT, TA, TK and MM design the study concept, KT wrote the paper. All Authors read and approved the final manuscript.

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