Case report

Intraoperative indocyanine green-visualization in a difficult to localize central cholangiocarcinoma – A case report

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ABSTRACT

Introduction and importance: Near infrared fluorescence imaging with indocyanine green (ICG) can facilitate the intraoperative tumour localization and therefore a complete resection. Cholangiocarcinoma is an aggressive tumour and complete resection improves the outcome. Therefore, it is necessary to localize the tumour exactly but the translation of the preoperative imaging into the intraoperative setting can be difficult based only on sonography, computed tomography or magnetic resonance imaging.

Case presentation/clinical findings and investigations/interventions and outcome: In this case a hepatic lesion suspicious for cholangiocarcinoma was discovered accidentally. Further diagnostics were unable to prove the diagnosis, therefore right hepatectomy was recommended and performed. Preoperatively ICG was administered and near infrared imaging was used intraoperatively clearly localizing the tumour, thus facilitating the resection. The intra- and postoperative course was uneventful.

Relevance and impact: This case report supports the very promising intraoperative use of fluorescence imaging for the localization of superficial hepatic tumours. Timing and correct administration of ICG is important.

1. Introduction

1.1. Background

Cholangiocarcinoma is an aggressive entity that accounts for about 20% of primary hepatic malignancies [1]. The incidence of intrahepatic biliary tumours is rising [2]. Due to the oligosymptomatic nature of biliary tumours only one third of the patients qualify for a curative treatment at the time of diagnosis, accounting for an overall 5-year survival rate of 10% [3] Surgical resection with negative resection margins is the only curative treatment and improves the 5-year survival rate up to 40% [4]. While tumours can usually be localized with preoperative imaging such as ultrasound, computed tomography scan (CT), or magnetic resonance imaging (MRI), exact localization of the tumours intraoperatively can be very challenging.

Since the 1960’s indocyanine-green (ICG) has been established in assessing the liver function as it is exclusively metabolized in the hepatic parenchymal cells. ICG emits light at a wave length of around 835 nm when illuminated with near-infrared light and can therefore be used in fluorescence guided imaging with a tissue penetration up to 1 cm [5]. Combining these properties ICG has been established in hepatic surgery to help visualizing intrahepatic tumours and biliary structures intraoperatively [6–9]. This technique has shown to improve the outcome after resection of both primary and metastatic liver tumours [10]. In hepatocellular carcinoma patterns of fluorescence have been associated with grade of differentiation: moderately or poorly differentiated tumours showed a lower liver-to-lesion contrast when stained with ICG [8,11].

1.2. Rationale

ICG staining in hepatic surgery is a trending research topic and guidelines on the use of intraoperative fluorescence are being established. There is an ongoing debate about the exact mode of application of ICG. To support current research we present a case in which intraoperative ICG was used to localize a central intrahepatic...
cholangiocarcinoma in accordance to the recommendation by Chen et al [7]

1.3. Guidelines and literature

Feasibility and effectiveness of intraoperative ICG staining in hepatic surgery has been evaluated since 2008 [6,8,12,13]. In 2020 a consensus guideline has been published on the use of ICG in hepatic surgery [5]. This work has been reported in line with the SCARE criteria [14].

2. Case report

2.1. Patient information

In a 62-year-old Caucasian male patient routine MRI follow-up was conducted yearly due to complex renal cysts. Beside the renal cysts the patient was treated for arterial hypertension with a combination of three antihypertensive drugs. His liver was steatotic, otherwise the patient was healthy.

2.2. Clinical findings/timeline/diagnostic assessment and interpretation

As an incidental finding the MRI detected a subcapsular cystic lesion of 2.8 cm in size between the liver segments V and VIII (Fig. 1). The lesion showed no signs of malignancy and remained stable over two years. However, after 3 years a slight increase in size was noted as well as an alteration of the perfusion of the liver segments V and VIII. The bile ducts in these segments were slightly dilated. Malignancy was suspected, which was supported by contrast-enhanced sonography (CEUS) findings showing a lesion in the liver hilus of 1.7 cm in diameter with dilation of the adjacent bile ducts (Fig. 2). Laboratory findings showed an elevated CA 19–9 at 41.3 U/ml (cut-off <27 U/ml), CEA and alpha1-fetoprotein were both normal. There were no indications for cholestasis. Serologic markers for echinococci were negative.

Magnetic resonance cholangiopancreatography (MRCP) showed a slight increase of the subcapsular cystic lesion in size and - in correlation to the sonographic findings - an intrahepatic lesion of 1.7 cm was detected on the border between the liver segments V and VIII with compression of the bile ducts, suspicious for a cholangiocarcinoma.

Fig. 1. Axial T2 weighted image of the liver at initial MRI showing the subcapsular cystic lesion in liver segment V (arrow) and a normal common hepatic duct (arrowhead).
Endoscopic retrograde cholangiopancreaticography (ERCP) was performed to gather histologic samples, cholangioscopic findings showed a slight impression of the right hepatic duct but no further intraluminal findings were described. Cytologic analysis was non-diagnostic with only few normal cylindrical cells and no proof of malignant cells.

Due to the location and the above described negative cytologic findings histological confirmation of the suspected malignant tumour was not possible. The case was discussed at the interdisciplinary tumorboard and right hepatectomy was recommended. Liver function
was sufficient for a right hepatectomy as assessed via LiMAX® Test (Humedics GmbH, Berlin, Germany) with a measured value at 492 μg/h/kg (reference value for a normal liver function: >315 μg/h/kg).

2.3. Intervention

According to most recent recommendations by Chen et al. [7] 10 mg ICG (VERDYE®, Diagnostic green GmbH, Aschheim-Dornach, Germany) was administered intravenously 12 h before surgery. A standard open right hepatectomy with lymph node dissection of the hepatoduodenal ligament was performed, the intraoperative course was uneventful. After cholecystectomy the tumour could clearly be visualized with a Stryker/NOVADAQ SPY-PHI portable handheld imaging system (Stryker, Kalamazoo, MI 49002, USA) (Fig. 4a–c).

2.4. Follow-up and outcome

The postoperative course was uneventful and the patient discharged nine days after the operation with a normal length of hospital stay according to the local diagnosis related groups system (SwissDRG). Histologic analysis confirmed the diagnosis of a well-/poorly differentiated cholangiocarcinoma (pT2) with two lymph node metastases (pN1). The interdisciplinary board recommended an adjuvant chemotherapy with capecitabine over 6 months in accordance to the BILCAP trial [15].

3. Discussion

With the here presented case we demonstrate that confirming a suspicion of intrahepatic cholangiocarcinoma requires a complex diagnostic workup which maybe time consuming and expensive. In this case, histologic/cytologic samples could not be acquired due to the location of the tumour. The lesion could be localized via MRI but translation into the intraoperative was expected to be difficult. Exact determination of tumour margins is of outmost importance to ensure complete resection with negative resection margins. This improves the outcome after resection of hepatic tumours both primary and metastatic. Intrahepatic cholangiocarcinoma is an aggressive entity with a rising incidence. If not found incidentally first diagnosis usually occurs in advanced disease.

This case supports current research that fluorescence guided imaging during hepatic surgery is a safe, easily implementable and cheap method to visualize superficial intrahepatic tumours.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images during preoperative consultations. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Registration of research studies

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Guarantor

1- Till M. Hempfing
2- Thomas Steffen
CRediT authorship contribution statement

1- T. Hempfing: conceptualization, data curation, writing - original draft preparation
2- D. Husarik: resources, data curation, writing – reviewing
3- T. Steffen: idea, conceptualization, supervision, writing – reviewing and editing

Declaration of competing interest

None to declare.

References

[1] B. Moazzami, K. Majidzadeh-A, A. Dooghaie-Moghadam, et al., Cholangiocarcinoma: state of the art, J. Gastrointest. Cancer 51 (2020) 774–781.
[2] M.M. Gad, A.M. Saad, M. Faisaluddin, et al., Epidemiology of cholangiocarcinoma; United States incidence and mortality trends, Clin. Res. Hepatol. Gastroenterol. 44 (2020) 885–893.
[3] Bergquist Annika, von Seth Erik, Epidemiology of cholangiocarcinoma, Best Pract. Res. Clin. Gastroenterol. 29 (2015) 221–232.
[4] S.B. Choi, K.S. Kim, J.Y. Choi, et al., The prognosis and survival outcome of intrahepatic cholangiocarcinoma following surgical resection: association of lymph node metastasis and lymph node dissection with survival, Ann. Surg. Oncol. 16 (2009) 3048–3056.
[5] X. Wang, C.S.C. Teh, T. Ishizawa, et al., Consensus guidelines for the use of fluorescence imaging in hepatobiliary surgery, Ann. Surg. (2020), https://doi.org/10.1097/SLA.0000000000004718.
[6] M.S. Alfano, S. Molfino, S. Benedicenti, et al., Intraoperative ICG-based imaging of liver neoplasms: a simple yet powerful tool. Preliminary results, Surg. Endosc. 33 (2019) 126–134.
[7] Q. Chen, R. Zhou, J. Weng, et al., Extrahepatic biliary tract visualization using near-infrared fluorescence imaging with indocyanine green: optimization of dose and dosing time, Surg. Endosc. (2020), https://doi.org/10.1007/s00464-020-08058-6.
[8] T. Ishizawa, N. Fukushima, J. Shibahara, et al., Real-time identification of liver cancers by using indocyanine green fluorescent imaging, Cancer 115 (2009) 2491–2504.
[9] R. Sucher, M. Brunotte, D. Seebhofer, Indocyanine green fluorescence staining in liver surgery, Chirurg 91 (2020) 466–473.
[10] H.J.M. Handgraaf, L.S.F. Boogerd, D.J. Höppener, et al., Long-term follow-up after near-infrared fluorescence-guided resection of colorectal liver metastases: a retrospective multicenter analysis, Eur. J. Surg. Oncol. 43 (2017) 1463–1471.
[11] Y. Nakaseko, T. Ishizawa, A. Saito, Fluorescence-guided surgery for liver tumors, J. Surg. Oncol. 118 (2018) 324–331.
[12] T. Aski, D. Yasuda, Y. Shimizu, et al., Image-guided liver mapping using fluorescence navigation system with indocyanine green for anatomical hepatic resection, World J. Surg. 32 (2008) 1763–1767.
[13] T. Abo, A. Nanashima, S. Tobinya, et al., Usefulness of intraoperative diagnosis of hepatic tumors located at the liver surface and hepatic segmental visualization using indocyanine green-photodynamic eye imaging, Eur. J. Surg. Oncol. 41 (2015) 257–264.
[14] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, SCARE Group, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.
[15] J.N. Primrose, R.P. Fox, D.H. Palmer, et al., Capecitabine compared with observation in resected biliary tract cancer (BILCAP): a randomised, controlled, multicentre, phase 3 study, Lancet Oncol. 20 (2019) 663–673.