CASE REPORT

Management of high-grade dysplasia of the cystic duct after cholecystectomy

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SUMMARY

High-grade dysplasia (HGD) of the cystic duct margin without evidence of concurrent malignancy is a rare occurrence. We present a case of a 36-year-old woman who developed gallstone pancreatitis and subsequently underwent a laparoscopic cholecystectomy. On histopathology, she was found to have HGD at the cystic duct margin. Following evaluation, she underwent excision of the cystic duct remnant with no malignancy being present on final pathology. We present this case to discuss the management of cystic duct dysplasia in the absence of gallbladder malignancy.

BACKGROUND

Since its introduction in the late 1980s, laparoscopic cholecystectomy (LC) has become one of the most common surgical procedures and is considered the gold standard treatment for patients with symptomatic cholelithiasis.¹ Invasive malignancy is identified as an incidental finding on pathology in up to 0.8% of cholecystectomy specimens,² with this figure increasing to 2.3% in patients undergoing surgery for acute cholecystitis,³ while high-grade dysplasia (HGD) is seen in around 2.0% of cases.²

Biliary tract dysplasia is a precursor to carcinoma, and should always signal the possibility of a concurrent malignancy.^{4–7} Therefore, the presence of HGD at the cystic duct margin, even in the absence of gallbladder cancer, indicates a risk for a concomitant cholangiocarcinoma.^{6–8} There is a scarcity of data to clarify the incidence of such a presentation and thus there are no clear guidelines to follow in this situation.

We present such a case, and discuss the importance of preoperative work-up, surgical management and postoperative monitoring in the setting of HGD at the cystic duct margin after LC.

CASE PRESENTATION

A 36-year-old woman with a history of gallstone pancreatitis and previous myomectomy for uterine leiomyoma presented to our clinic 2 months after undergoing an LC at an outside institution. At the time of surgery, an intraoperative cholangiogram identified a common bile duct (CBD) stone, and after failed attempts at extraction she subsequently underwent a subsequent endoscopic retrograde cholangiopancreatography (ERCP) for stone retrieval. Her postoperative course was complicated by pancreatitis that resolved with conservative management. She was discharged on

postoperative day 5 and recovered well at home. Her pathology report revealed both low-grade and high-grade dysplasia of the cystic duct margin without any evidence of dysplasia or malignancy in the gall bladder. The patient elected to present to our institution for further surgical management.

INVESTIGATIONS

Review at our institution of the outside institution pathology slides confirmed the presence of multifocal high-grade and low-grade dysplasia involving the cystic duct margin but with no dysplasia within the gall bladder. The patient's case was reviewed at a multidisciplinary tumour board and a decision was made to perform magnetic resonance cholangiopancreatography (MRCP) and ERCP with SpyGlass visualisation to assess for cholangiocarcinoma of the intrahepatic and extrahepatic biliary tree. A CT scan was also advised to evaluate for pathology in the gallbladder bed. The CT did not identify any masses or evidence of biliary dilatation, and the MRCP revealed a normal-calibre CBD (figure 1A,B). However, imaging did identify a 3 cm tortuous cystic duct remnant with low insertion to the CBD (figure 1C).

ERCP with SpyGlass cholangioscopy revealed normal mucosa of the cystic duct and extrahepatic biliary tract (figure 1D–F). Biopsies were obtained of the blind end of the cystic duct remnant. Pathology from the cystic duct remnant did not reveal any evidence of dysplasia.

The case was further discussed in the tumour board, and due to the concern of HGD at the cystic duct margin from the previous surgery, it was decided to proceed with exploration, excision of the cystic duct and frozen section evaluation of its proximal margin. If the margin was positive, it was proposed that the external biliary tree would be excised and reconstructed.

TREATMENT

After full discussion and having obtained informed consent, the patient was taken to the operating room. The cystic duct remnant was observed (figure 2A) and dissection was performed, with application of a clip 2 mm distal to the cystic duct take-off from the CBD. The cystic duct remnant was transected and sent for frozen section pathology, this revealing no dysplasia at the proximal margin (figure 2B). A long cystic artery stump was also noted, and this was clipped proximally and resected. Haemostasis was achieved and the abdomen was closed.

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Figure 1 (A,B) CT scan and MRCP demonstrating no intrahepatic biliary dilation and no hilar mass. (C) Reformatted MRCP demonstrating a 3 cm tortuous cystic duct remnant with low insertion to the common bile duct. (D–F) ERCP with SpyGlass cholangioscopy showing normal mucosa of the proximal cystic duct (D), the cystic duct remnant tip (E), and the confluence of the right and left hepatic ducts (F). ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography.

OUTCOME AND FOLLOW-UP

The patient tolerated the procedure well and was taken to the regular nursing floor postoperatively. Her diet was advanced as tolerated and her recovery was uneventful. She was discharged on postoperative day 2. The patient returned to clinic 2 weeks postoperatively after a full recovery with no concerns. Her final pathology revealed no malignancy in the cystic duct remnant (figure 2D–F).

DISCUSSION

There is a paucity of literature on the natural history of HGD in the cystic duct after cholecystectomy, and the true incidence of this finding is unknown.⁶ However due to the known progression of dysplasia to cancer, and because of the aggressive nature and poor prognosis of biliary malignancies, it is prudent to extensively evaluate for concomitant and multifocal malignancy.^{4–7} Bickenbach *et al*⁶ reported a cholangiocarcinoma in one of five

patients with HGD at the cystic duct margin without evidence of gallbladder malignancy. Thereafter the patient underwent a bile duct resection, portal lymphadenectomy and hepatectomy including segments IVb and V, but expired 15 months later. Although this is a small case series, it sheds light on the importance of not ignoring the risk of concomitant dysplasia with cholangiocarcinoma in this population.

There is additional evidence in relation to the importance of HGD in biliary malignancies. Wakai *et al* reported carcinoma in situ/HGD at the resection margin in 13% of patients after resection of cholangiocarcinomas, and highlighted that the presence of a positive surgical margin was an important predictor of outcome in patients with extrahepatic cholangiocarcinoma.^{8,9} Furthermore, it is well known that cholangiocarcinomas and gallbladder cancers can have superficial extensions and multifocal areas of dysplasia, and so it is imperative to perform a thorough evaluation of the biliary tree when one area of dysplasia is

Figure 2 (A,B) Intraoperative demonstration of the cystic duct remnant (forceps tip) before and after resection. (C) Cystic duct remnant after resection with a suture at the proximal margin. (D–F) High-grade dysplasia.

identified. In a histological analysis reported by Sakamoto and colleagues,¹⁰ the superficial spread of malignant cells was identified in more than 10% of cases, and they suggested that a 5 mm tumour-free margin was required to improve survival. Likewise, Shirai *et al*¹¹ reported two patients with residual HGD of the cystic stump after resection for gallbladder carcinoma and both expired from recurrence at 66 and 76 months. That said there is no specific evidence for the likelihood of multifocality of HGD or indeed coexisting cholangiocarcinoma in patients with HGD alone in the cystic duct margin following cholecystectomy as the condition is very rare, or at least under-reported.

In the current report, we performed this extensive work-up for a number of reasons. The cholecystectomy was performed elsewhere and so we did not have the benefit of viewing the region ourselves intraoperatively. The CT scan was performed to exclude an obvious mass in the gallbladder fossa or the presence of metastatic disease — it had been several months between cholecystectomy and presentation to us, and this is the interval when incidental gallbladder cancers often metastasise. Granted the literature on HGD of the cystic duct is limited, we did not want to take any chances. As dysplasia of the biliary tree is often multifocal and the fact that there may be skip lesions, we performed an MRCP to evaluate in more detail. Finally as these were negative we performed an ERCP to visualise the mucosa. This imaging approach does not follow guidelines as no such evidence exists for the evaluation of HGD at the cystic duct margin and was based on discussions at our multidisciplinary meeting at each stage. We adopted this stepwise approach as at each stage we could have identified findings that precluded further investigation (local mass or metastases) and led to palliative treatment, and had these been identified we would have not excised the cystic duct. We left the ERCP to last as that is an invasive procedure. This was critical since as there was no mass on cross-sectional imaging, we needed to know that the remainder of the extrahepatic biliary tree appeared normal. Had we identified an area of HGD in the hepatic duct for example, we would have performed an excision of the extrahepatic biliary tree with lymph node dissection as opposed to simply excising the cystic duct.

Despite not seeing residual disease following extensive evaluation, we discussed the existing evidence with the patient and proceeded to excise the cystic duct taking a frozen section of the distal aspect. Had this identified HGD, a formal excision of the extrahepatic biliary tree would have been excised. In all five cases reported by the Memorial Sloan Kettering Cancer Center,⁶ all underwent further surgery despite no evidence of any radiological findings in three cases. Clearly, the decision to operate further would depend on patient factors such as existence of comorbidities or frailty, but in general for patients fit for surgery, the limited evidence would suggest that exploration and excision of the cystic duct (at least) would be advisable.

In terms of follow-up, the data in the literature are completely lacking in evidence. In this particular case, while pathology did

not show evidence of further HGD, after a long discussion with the patient regarding the lack of evidence and considering the young age at diagnosis of HGD, it was agreed that we would continue to monitor the biliary tree for 5 years as if it was a carcinoma.

Given the known progression of HGD to cancer and the grim prognosis of gallbladder cancers and cholangiocarcinoma, it is imperative to evaluate for potential malignancy when dysplasia of the biliary tree is detected.

Learning points

- ▶ High-grade dysplasia of the cystic duct margin without evidence of gallbladder malignancy after cholecystectomy is a rare finding.
- ▶ Concomitant biliary cancer is possible and radiological investigations are required to exclude it.
- ▶ Resection of the cystic duct remnant is prudent to prevent future malignant transformation.

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REFERENCES

- 1 Sain AH. Laparoscopic cholecystectomy is the current "gold standard" for the treatment of gallstone disease. *Ann Surg* 1996;224:689–90.
- 2 Solaini L, Sharma A, Watt J, *et al*. Predictive factors for incidental gallbladder dysplasia and carcinoma. *J Surg Res* 2014;189:17–21.
- 3 Lam CM, Yuen AW, Wai AC, *et al*. Gallbladder cancer presenting with acute cholecystitis: a population-based study. *Surg Endosc* 2005;19:697–701.
- 4 Sasaki R, Takeda Y, Funato O, *et al*. Significance of ductal margin status in patients undergoing surgical resection for extrahepatic cholangiocarcinoma. *World J Surg* 2007;31:1788–96.
- 5 Shingu Y, Ebata T, Nishio H, *et al*. Clinical value of additional resection of a margin-positive proximal bile duct in hilar cholangiocarcinoma. *Surgery* 2010;147:49–56.
- 6 Bickenbach KA, Shia J, Klimstra DS, *et al*. High-grade dysplasia of the cystic duct margin in the absence of malignancy after cholecystectomy. *HPB* 2011;13:865–8.
- 7 Gertsch P, Thomas P, Baer H, *et al*. Multiple tumors of the biliary tract. *Am J Surg* 1990;159:386–8.
- 8 Wakai T, Shirai Y, Moroda T, *et al*. Impact of ductal resection margin status on long-term survival in patients undergoing resection for extrahepatic cholangiocarcinoma. *Cancer* 2005;103:1210–6.
- 9 Sunkel-Laing B, Kalam A, Renfrew I, *et al*. Repeated negative biopsies in isolated high-grade cystic duct dysplasia with progression to adenocarcinoma. *Case Rep Gastroenterol* 2014;8:304–9.
- 10 Sakamoto E, Nimura Y, Hayakawa N, *et al*. The pattern of infiltration at the proximal border of hilar bile duct carcinoma: a histologic analysis of 62 resected cases. *Ann Surg* 1998;227:405–11.
- 11 Shirai Y, Yoshida K, Tsukada K, *et al*. Early carcinoma of the gallbladder. *Eur J Surg* 1992;158:545–8.

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