



Case report

Hepatopancreatoduodenectomy for locally advanced perihilar cholangiocarcinoma: A case report and a plea not to underestimate surgical resectability

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ABSTRACT

Introduction and importance: Cholangiocarcinomas often exhibit longitudinal spread along the hepatic duct and choledocus, resulting in the impossibility to achieve complete resection through either liver resection or pancreatoduodenectomy. Hepatopancreatoduodenectomy (HPD) has been proposed as a surgical strategy to achieve complete resection, although it is burdened by very high rates of postoperative morbidity and mortality.

Case presentation: A 73-year-old patient was diagnosed with locally advanced perihilar cholangiocarcinoma extending from the right hepatic duct to the intrapancreatic choleducus; she underwent surgical evaluation in a secondary hospital without expertise in HPB surgery, and was deemed unresectable with positioning of palliative bare metal stent in the biliary tract. After second opinion evaluation at our centre, the patient was deemed resectable, and underwent HPD after right portal vein embolization. The patient is alive and without recurrence after more than six months from the intervention.

Clinical discussion: Although complex and characterized with a high burden of postoperative complications, HPD can be proposed as a curative treatment for locally advanced cholangiocarcinoma. Resectability assessment and preoperative evaluation should be managed in expert surgical centres, through a granular assessment of tumour extension and liver function. In particular, the risk of liver failure should be minimized whenever possible through future liver remnant hypertrophy strategies.

Conclusion: Hepatopancreatoduodenectomy is a feasible treatment for locally advanced cholangiocarcinoma, although it requires clinical management in high-volume and skill surgical centres, where failure to rescue from complications is less probable to occur.

1. Introduction

Cholangiocarcinoma is an aggressive and insidious disease, whose potential curative treatment still remains R0 surgical resection [1]. It is not uncommon for cholangiocarcinomas to exhibit extensive ductal spread, invading the from the hepatic bile duct confluence to the intrapancreatic bile duct [2]. Such form of local aggressiveness is difficult to treat, as complete resection through conventional procedures (i. e., major hepatectomy or pancreatoduodenectomy) is not achievable. Since its first report from Takasaki et al. in 1980 [3],

hepatopancreatoduodenectomy (HPD) has been proposed as a surgical strategy to achieve potential curative resection of longitudinally spreading cholangiocarcinomas. Although Japanese hepatobiliary surgeons have made significant contributions to HPD, its application as an effective surgical strategy remains controversial: in fact, published case series include a limited number of patients and report high postoperative morbidity and mortality rates (respectively 78.9 % and 10.3 % in the latest review) [4].

As a recent retrospective study suggests – despite the magnitude of the intervention and the high burden of complications – HPD can be

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successfully performed in high-skill hepatobiliary centres where post-operative complications can be managed with low failure-to-rescue rates [5]. As a result, taking care of a patient affected by locally advanced perihilar cholangiocarcinoma cannot be separated from a surgical resectability assessment in a high-expertise hepatobiliary referral centre.

In this manuscript we describe the case of a patient with locally advanced cholangiocarcinoma, initially deemed unresectable after evaluation in a low-volume surgical centre, which was finally treated with HPD. This case report has been reported in line with the SCARE Criteria [6].

2. Case presentation

The patient was a 73-year-old-woman with unremarkable past medical history (mild hypertension in pharmacological treatment) and good performance status (PS-ECOG 0) who presented to a secondary care hospital complaining with worsening jaundice and pruritus. An abdominal CT was performed, revealing a perihilar mass compressing the hepatic duct confluence with proximal biliary dilation and suspect involvement of the suprapancreatic choledocus. The patient then underwent bilio-pancreatic endoscopic ultrasonography and biopsy, which revealed neoplastic involvement of the right and common bile duct up to the head of the pancreas. At that time, the patient was deemed unresectable and underwent CPRE with bare self-expandable metal stent (SEMS) insertion. The procedure was complicated with mild pancreatitis treated with medical therapy. After discharge, the patient contacted our centre for a second opinion. Abdominal tomography and magnetic resonance of the liver were performed to reassess the tumour extension, which resulted stable; the patient was thus considered eligible for surgical exploration. Volumetric evaluation of the future liver remnant (segments 2-3-4) was performed, resulting 31 % of total liver volume (calculated as described by Vauthey et al. [7]). Therefore, considering the borderline volume of FLR and the possibility of cholestasis-induced liver toxicity, we decided to perform right portal vein embolization with the aim to reduce the risk of postoperative liver failure. The procedure was carried out uneventfully and led to an increase in future liver

remnant by 7 % (38 % of total liver volume). The surgical intervention was performed a month after by MR (a fully trained HPB and transplant surgeon) with the help of GF and two surgical residents. Upon laparotomy, no major contraindications for the procedure emerged. We performed an hepatectomy first approach, assessing the presence of R0 surgical margins on the left hilar plate by fresh frozen pathology. After completion of right hepatectomy and difficult extraction of the bare SEMS from the CBD, the distal margin was confirmed to be involved by neoplastic cells upon fresh frozen pathology. We then performed pancreatoduodenectomy, which resulted challenging because of the presence of a common hepatic artery arising from the SMA (Fig. 1). The reconstruction was made in a Child's fashion, with Blumgart style pancreatojejunostomy, double hepaticojejunostomy (on separated ducts for segment IV and left lobe) and gastrojejunostomy. The patient stayed in surgical intensive care unit for the first two days after the intervention and was discharged after 16 days. Postoperative course was characterized by pancreatic biochemical leak and mild ascites without laboratory signs of post hepatectomy liver failure, which were managed with medical therapy; the patient also experienced wound infection, which was managed with antibiotic therapy and negative-pressure medication. Final pathological exam on the surgical specimen demonstrated perihilar cholangiocarcinoma extending longitudinally to the intra-pancreatic choledocus, pT2 N1 (2/34) G3. Currently, the patient is alive and well without further surgical complications or signs of recurrence after more than six months from the intervention.

3. Discussion

Perihilar cholangiocarcinoma, although rare, is a disease burdened with high lethality mostly related to being often locally advanced at presentation. In fact, it frequently exhibits a pattern of perineural and periductal invasion, which leads to involvement of portal structures and hepato-duodenal lymph nodes. Complete resection is the most effective treatment for this kind of malignancy, as the role of adjuvant chemotherapy and radiotherapy remains controversial in medical literature: specifically, the studies that successfully demonstrated advantages of adjuvant chemoradiation therapy evidenced a survival benefit of only a



Fig. 1. Complete resection of right hemiliver and head of the pancreas. PD, pancreatic duct (cannulated). PV, portal vein. IVC, inferior vena cava. HA, hepatic artery arising from the superior mesenteric artery. BP, biliary plate.

few months. Resectability of perihilar cholangiocarcinomas remains limited (<50 %) due to late presentation, and should be accurately evaluated accounting tumour extension, patient status and liver function [8]. The complexity surgical treatment and clinical management mandates surgical eligibility to be assessed in high-volume and expertise centres, which are characterized by lower failure-to-rescue from surgical complications and consequently lower in-hospital and 3-months mortality [9].

This case highlights a few issues to be addressed in the management of locally advanced perihilar cholangiocarcinoma.

First, the patient was initially evaluated in a secondary care hospital with limited experience in hepato-pancreato-biliary surgery and – despite that – was deemed unresectable. Not only this decision delayed the possibility for the patient to seek care in a more appropriate surgical setting, but it led to palliative endoscopic drainage of the choledochus, which incremented the difficulty of the final intervention in our centre. This remarks the necessity for such forms of locally advanced biliary tumours to receive pre-operative clinical management and final judgement on resectability in a tertiary referral centre where multidisciplinary expertise on hepatobiliary malignancy treatment is available [5,9].

Second, the hepatectomy first approach allows for fresh frozen pathology evaluation of the intrahepatic bile duct margin, whose status – in our opinion – determines the possibility to further proceed with pancreatoduodenal resection. In fact, given the detrimental effect of R1 surgical margins on patient survival and the high rate of postoperative complications [10], HPD should be reserved for patients where the higher surgical risk can be counterbalanced with a better prognosis.

Finally, given the high-risk of potentially life-threatening complications related to the procedure, a cautious pre- and postoperative management is mandatory, both to minimize the risk where possible and to rapidly address any deviation of the postoperative course that may arise. For what concerns post-hepatectomy liver failure (PHLF), we decided to optimize liver hypertrophy even if the volume of the future liver remnant was acceptable. This decision was dictated both by the possible presence of underlying a cholestasis-induced liver injury and by the necessity to prevent PHLF with all the possible means, as the onset of this complication after HPD would be very difficult to treat, posing a high risk of postoperative death to the patient. Instead, for what concerns the risk of postoperative pancreatic fistula (POPF), it should be emphasized that the pancreatoduodenectomy in this setting frequently implies a high-risk pancreatic anastomosis, being the pancreatic gland most often soft with non-dilated pancreatic duct. Although performing total pancreatectomy may avoid the onset of POPF, it would also deprive the liver remnant of hepatotrophic factors secreted by the pancreas and further increment the extensiveness of the intervention – already demolitive per se – making this strategy unsuitable for this kind of procedure.

In conclusion, HPD represents a potential radical treatment for locally advanced perihilar cholangiocarcinoma, which can be pursued in very selected cases after a cautious multidisciplinary evaluation to assess pre- and intraoperative surgical pitfalls. Despite the magnitude of the intervention and the high risk of postoperative complications, patients can be managed in high-skill and volume hepatobiliary centres where risk mitigation strategies can be adopted, and complications can be handled without risk of failure-to-rescue.

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Ethical approval

N/A.

Consent

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Author contribution

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Matteo Ravaioli: Writing – Review & Editing, Supervision, Validation, Project administration, Funding acquisition

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The authors have no competing interests to disclose.

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