



Case Report

An Extreme Downstaging as a “Time Machine” for Experienced HPB Surgeon: A Case Report of a Patient with Unresectable Colorectal Liver Metastases

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Abstract

Colorectal cancer is the second leading cause of cancer death in the Western world. The present report shows a complex case of synchronous hepatic metastases from colorectal cancer and represents a further example of how a combined multimodal treatment can be successful even in patients with unresectable disease. Thanks to an excellent multidisciplinary work between oncologists, radiologists and surgeons, and thanks to an accurate preoperative study with CT scan and 3D reconstructions, it was possible to perform a radical oncologic surgery. The high surgical experience of HPB surgeons made it possible to perform this surgery successfully. The patient’s four-month follow-up shows no disease recurrence.

Keywords: Colorectal liver metastases; Conversion chemotherapy; Hepatic surgery; Resectability

Introduction

In patients with colorectal liver metastases surgical resection is the treatment of choice. Surgical resection of colorectal liver metastases (CRLM) has been widely described, with reports of five-year survival up to 58% after complete resection of the disease [1]. The goals of liver resection for CRLM are to obtain tumor-free margins and a future liver remnant (FLR) with intact vascular inflow/outflow, and biliary drainage [2]. The extent of liver surgery, and the possibility to obtain negative resection margins, can be hindered by different factors: surgical team expertise, underlying liver disease, hepatocellular/sinusoidal damage induced by chemotherapy, and the anatomic location of the metastases.

In the past, tumors located adjacent to major hepatic blood vessels (e.g., hepatic vein, portal vein) were considered unresectable, as a resection with curative intent could not be

ensured while maintaining sufficient liver remnant.

Thanks to advances in chemotherapy and surgical techniques, numerous patients with CRLM, who were deemed unresectable only a few years ago, are today surgical candidates in HPB experienced hands.

Case

A 56-year old male patient without comorbidities complained of asthenia and weight loss. He underwent abdominal ultrasonography which demonstrated multiple liver nodules. Colonoscopy showed an ulcerated circumferential mass in the left colon, causing 50% occlusion of the lumen; pathologic examination was positive for adenocarcinoma. A staging chest and abdomen CT scan was then performed showing a massive, bilobar spread of the disease to the liver (Figure 1), with parenchymal extension major than 80%, without extrahepatic localizations; the largest liver metastasis involved the emergence of the hepatic veins and the first order portal bifurcation.

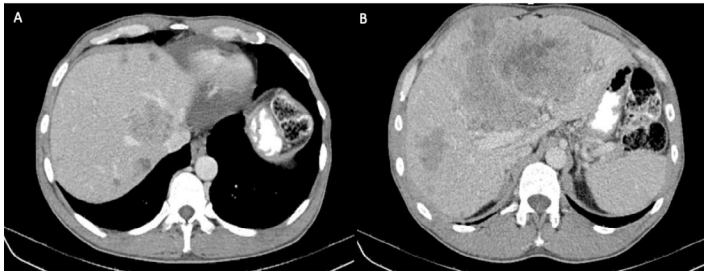


Figure 1: The first CT scan showed a massive, bilobar spread of the disease to the liver that involved the emergence of the hepatic veins (A) and the first order portal bifurcation (B).

The patient first underwent laparoscopic left colectomy with diagnostic biopsies of one of the hepatic lesions in another center. Afterward, he was referred to our center for multidisciplinary tumor board evaluation. The pathological stage was IVa (T4aN0M1a- KRAS wild type) and the patient was initially deemed unresectable due to the insufficient future liver remnant and for the aforementioned vascular reasons. A chemotherapy regimen with fluorouracil, irinotecan and leucovorin (FOLFIRI) with cetuximab was begun.

After six months of treatment, the patient was noted to have an extraordinary response to chemotherapy with a remarkable dimensional reduction of the metastases. CEA dropped from 539 ng/mL to 6,6 ng/ml. The liver was reassessed every two months until the stability of the disease was documented. After 12 cycles of Chemotherapy (Figure 2), the case was rediscussed in a multidisciplinary board and the patient was deemed eligible for surgical resection.

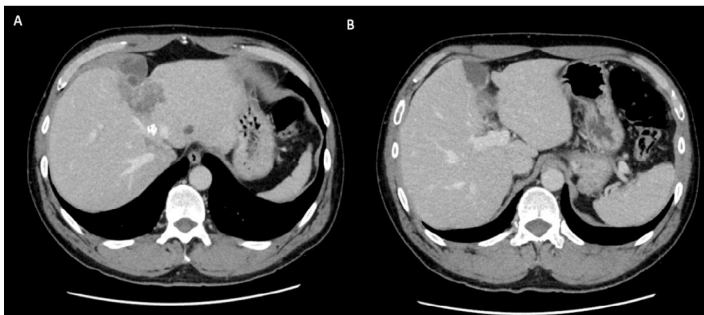


Figure 2: A CT scan after 12 cycles of chemotherapy showed an incredible response to medical treatment with right hepatic vein (A) and right portal vein (B) free from disease.

The calculated FLR was 31% and the ICG test showed an adequate liver function (R15: 4.9, PDR: 20.1). 3D reconstructions were realized as well to better understand the vascular relationship with major vessels: the main hepatic lesion (87 x 44 mm) was in close contact with the lower edge of the middle hepatic vein and the portal bifurcation, especially the left branch. The right hepatic

artery originated favorably from the superior mesenteric artery; the anterior right biliary tract appeared distant 1cm from the main lesion. The main metastasis extended from S4, coming in contact with the gallbladder, to S1. Four other smaller lesions were also identified in S2, 4, 6, 7. (Figure 3)

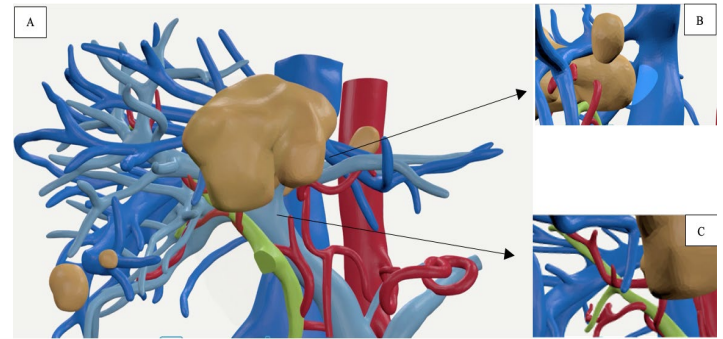


Figure 3: The preoperative 3D reconstruction (3A) was fundamental to understand the relationship of the liver injury with the surrounding vessels. In particular, the lesion partially imprinted the vena cava anteriorly (3B) and was about 1 cm from the anterior branch of the right biliary tract (3C), information not described by the radiological investigations previously performed.

No evidence of extrahepatic disease was found at exploratory laparotomy. Intraoperative liver ultrasound showed that the main lesion was in close contact with the right biliary branch of the anterior sector and with the right portal vein. A left hepatectomy (S2-3-4) extended to the anterior segments (S5-8) with previous wedge resections (S6-7) and cholecystectomy, with a tangential vena cava patch, was performed. In order to ensure R0 resection, a deep dissection of the right biliary branch was conducted, so we decided to place a transhepatic drainage to tutor the biliary tract. No postoperative complications were observed. Postoperative liver function tests normalized over the course of 1 week. A CT scan performed after ten days showed abdominal collections adjacent to the hepatic shear surfaces, a sign of normal postoperative outcome, without any clinical implications. The patient was discharged at home on postoperative day 13.

Pathologic examination demonstrated the presence of intestinal-type adenocarcinoma metastasis with tumor regression grade (Tumor Regression Grade TRG): grade 4 sec. Rubbia-Brandt (neoplasm predominant over fibrosis) in the major lesion and TRG 2 (fibrosis predominant over residual viable neoplastic tissue) and TRG 3 (neoplasm and fibrosis present in about equal measure) respectively in the atypical resections of S6 and S7. Peritumoral lympho-vascular invasion present; free resection margins on all resection. The four-month follow-up with CT scan (Figure 4) showed no recurrence of hepatic disease, the presence of collections at the site of liver resections, but without any clinical / infectious implications.

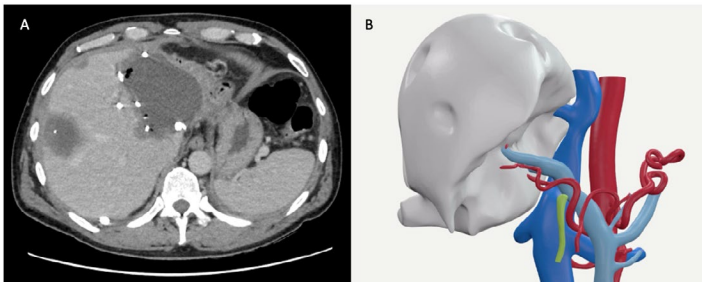


Figure 4: The four-month follow-up with CT scan (A) showed the presence of collections at the site of liver resections but without signs of residual liver disease. The 3D reconstruction (B) shows the residual liver, with initial volume increase, with partial parenchymal resection areas and vena cava patches.

Discussion

Colorectal cancer is the second leading cause of cancer death in the Western world. More than 50% of patients with Colorectal cancer develop liver metastases during the course of the disease and 90% will die from metastatic disease, with or without surgery. At the time of diagnosis of colorectal cancer, 20-25% of patients have stage IV disease and in 70-80% of cases the metastases are limited to the liver. Hepatic resection is the best treatment option for liver disease but only a minority of patients are ready for upfront surgery (20%) at the time of diagnosis.

For the remaining 80% of patients with unresectable CRLM, chemotherapy is the treatment of choice to achieve disease control, prolong survival and palliate symptoms. In some of the unresectable patients, however, a combination of cytotoxic and target-specific chemotherapy determines a downsizing of liver lesions, converting unresectable patients to resectable. The advances of chemotherapy led to the abolition of contraindication to resection in favour of technical resectability. Technical factors involve the anatomic location of the lesions, volume and function of the remnant liver [3]. According to NCCN guidelines 2020, liver resection remains the most important modality in the treatment of colorectal liver metastases. Resection must be considered feasible based on the anatomical location and extent of the disease and the maintenance of adequate liver function must be mandatory [4].

The evolution of the criteria for resectability has resulted in more patients being offered a hepatectomy. The now obsolete Ekberg contraindications (more than 4 lesions, bilobar lesions, impossibility to have a margin of at least 1 cm), have been overcome [3,5]. Since the beginning of 2000, the approach to liver resection has changed as the perspective has changed. While the original criteria for resection were based on what was removed, the new criteria are based on what would remain after performing an R0 liver resection, not only in terms of FLR but also in terms of liver function. Surgery should be undertaken with the intent of

a margin-negative resection, as patients with a positive resection margin have significantly increased risk for local recurrence as well as significantly decreased overall survival compared with margin-negative patients [6].

Preoperative chemotherapy is usually used to reduce the size of liver metastases for resection. Liver resection should not be denied to patients with stable disease after an excellent course of chemotherapy, but an adequate assessment of the FLR with preservation of vascular inflow and outflow should be made a priori. In clinical practice, the major determinants of the decision-making process are tumor and metastases status, the need for urgent / elective intervention and tumor resectability in both sites. The classic approach to surgery of synchronous liver metastases is to perform surgery on the primary tumor followed by liver resections 2-3 months later, with or without chemotherapy in the time interval between the two surgeries. Simultaneous resection of primary tumor and metastases was found to be favorable in many studies; nevertheless, a careful and cautious assessment should be made for major liver resections in patients with comorbidities, given the high risk of postoperative mortality and morbidity. However, for patients with liver metastases initially considered unresectable, there is still no consensus on what the best strategy is to lead patients to resectability.

Conclusion

A multidisciplinary team discussion with surgeons experienced in liver resection, medical oncologists, and pathologists is nowadays essential to offer the patient the best treatment option. If this concept is important for non-metastatic tumors, it is absolutely crucial in the management of patients with metastatic cancer. Resectability should be seen from a comprehensive perspective: oncological resectability (response to CT, tolerability, possible advantages/disadvantages of prolonged chemotherapy), technical resectability (FLR, anatomical location, ICG test), patient's resectability (age, comorbidity, frailty). Only with integrated oncological and surgical management can it be possible to offer the patient the best treatment for the cure of their disease. The present report shows a complex case of synchronous hepatic metastases from colorectal cancer and represents a further example of how a combined multimodal treatment can be successful even in patients with unresectable disease. The key of the success of this case is to be found in the excellent synergy between the therapeutic oncological response, a precise 3D preoperative planning and high experience on complex surgery.

Ethical approval: Due to the retrospective nature of this report and the complete anonymization of Patient's information, Ethical Review Board was deemed unnecessary. An informed consent for the treatment of personal data was signed by the Patient at the beginning of each recovery and before any invasive procedure.

Conflict of interest: There are no conflict of interests.

Author’s contributions: Sissi PALEINO and Christian COTSOGLOU made a substantial contribution to the conception and writing of the manuscript, Andrea CHIERICI to the supervision and Federica BRUNO revised it. All authors have read and approved the final version of the manuscript.

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