case report

Eur Surg (2019) 51:34–39
https://doi.org/10.1007/s10353-018-0565-6

european surgery
ACA Acta Chirurgica Austriaca

An aggressive surgical approach to rare central biliary invasion of colon cancer

Bibek Aryal · Kota Yoshikawa · Teruo Komokata · Hiroto Yasumura · Maki Inoue · Mamoru Kaieda · Yutaka Imoto

Received: 4 July 2018 / Accepted: 27 November 2018 / Published online: 14 December 2018

Summary
Background Central biliary metastasis from colorectal cancer (CRC) is a rare manifestation. Given the rarity of the lesion, cases with central biliary metastasis from CRC pose challenges in identifying the proper treatment strategy.
Methods We present a case of stage IV CRC with synchronous multiple liver metastases and central biliary invasion. We also conducted a literature search and reviewed the reports on central biliary metastasis of CRC treated by major hepatectomy combined with extrahepatic bile duct resection.
Results The patient underwent colon resection, partial hepatectomy, and transileocecal portal embolization (TIPE) as the first procedure, which was followed by an extended right hepatectomy and extrahepatic bile duct resection. Adjuvant chemotherapy was introduced, and the patient was doing well with no recurrence at 17 months after the first procedure.
Conclusion A liberal radical and aggressive resection in a multimodal treatment strategy could offer a favorable outcome in patients with a rare central biliary manifestation of CRC.

Keywords Central biliary metastasis · Colorectal cancer · Prognosis · Hepatectomy · Aggressive surgical approach

Main novel aspects

- Central biliary invasion of colorectal cancer (CRC) is an extremely rare manifestation.
- Radical and aggressive surgical approaches have a firm place in multimodal strategies for a favorable outcome in patients with biliary invasion of CRC.
- The manuscript also presents a review and summarizes the treatment strategy from the reports on central biliary invasion of CRC.

Introduction

The proportion of synchronously detected liver metastases from colorectal cancer (CRC) has been increasing recently, and only a minority of these patients are amenable to curative surgical resection [1, 2]. Simultaneous liver and colorectal resections are safe for synchronous colorectal liver metastasis (CLM; [3]). Current advancements in chemotherapy and surgical management have broadened the limitations for resection of CLM.

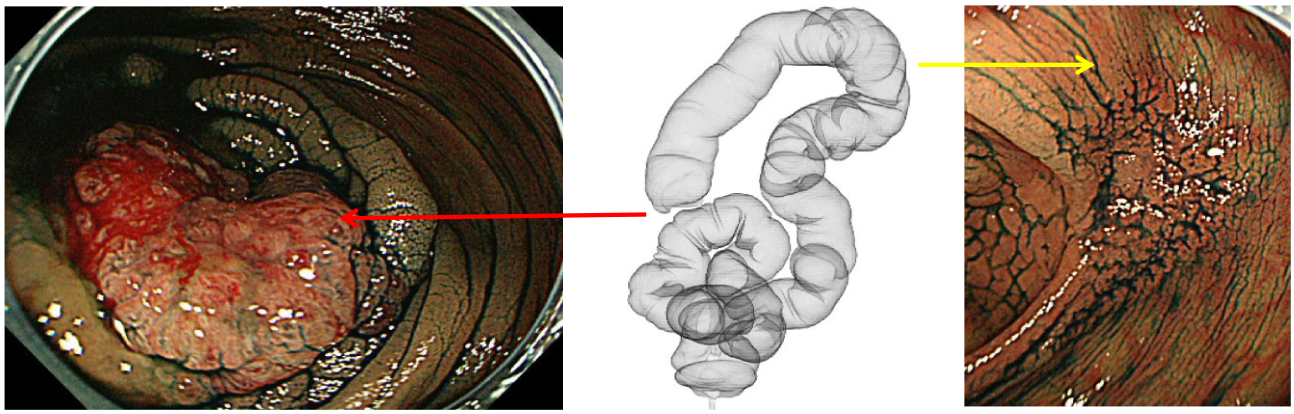
Metastatic CRC (mCRC) also invades the epithelium of hilar or intrahepatic bile ducts; the central biliary invasion of mCRC can clinically mimic perihilar cholangiocarcinoma, and sometimes obscures the therapeutic management in these patients. Herein, we report our experience of an aggressive surgical approach in a patient with central biliary metastasis of CRC.

For review, we conducted a search of the literature to identify all case reports and clinical reviews of central biliary metastasis of CRC. The search terms included “colorectal carcinoma,” “biliary metastasis,”

Author contributions The authors Bibek Aryal and Kota Yoshikawa contributed equally to the manuscript.

B. Aryal · K. Yoshikawa · T. Komokata, MD, PhD (✉) · H. Yasumura · M. Inoue · M. Kaieda
Department of Surgery, Kagoshima Medical Center, National Hospital Organization, 8-1 Shiroyamacho, Kagoshima-shi, Kagoshima 892-0853, Japan
komokata.teruo.je@mail.hosp.go.jp

B. Aryal · Y. Imoto
Cardiovascular and Gastroenterological Surgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan



a b

Fig. 1 Computed tomographic colonoscopy and colonoscopy images showing growths in the transverse colon: advanced (**a**, *red arrow*) and early (**b**, *yellow arrow*) growths

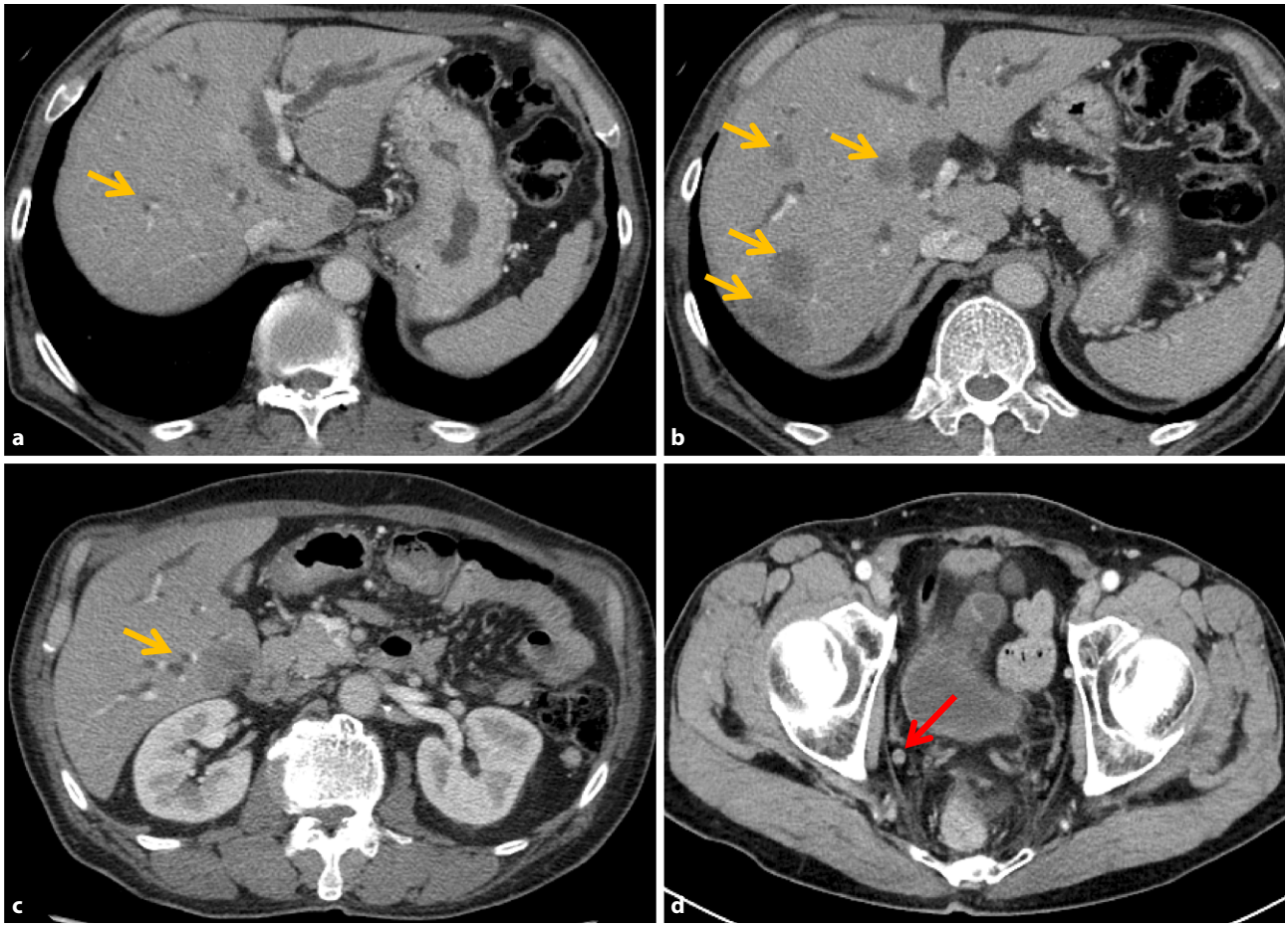


Fig. 2 Contrast-enhanced computed tomographic scan showing multiple liver metastases almost in the right lobe (**a–c**, *yellow arrows*) and a nodule of peritoneal dissemination (**d**, *red arrow*)

"hepatectomy," and "extrahepatic bile duct resection." The databases searched included PubMed and Google Scholar from January 2000 to April 2018.

Case presentation

A 67-year-old male patient presented with jaundice in a local hospital in November 2016. Laboratory investigations showed elevated total bilirubin level (T-bil: 21.0 mg/dl) and tumor markers (carcinoembryonic antigen: 92.5 ng/ml; carbohydrate antigen 19-

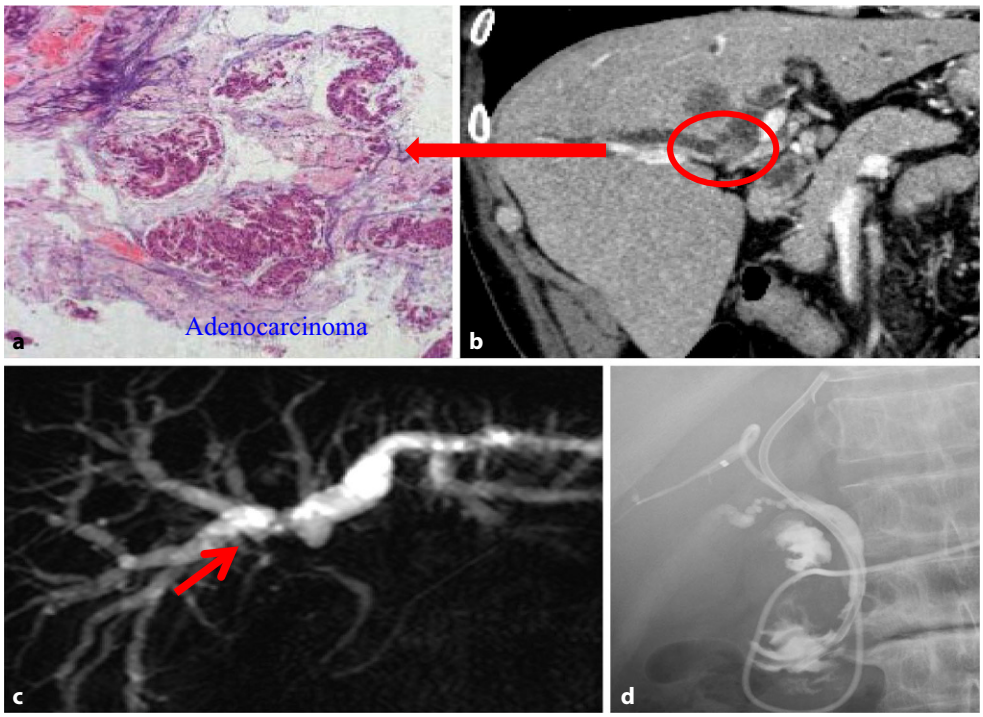


Fig. 3 Hematoxylin and eosin stain of biopsy taken from central biliary duct suggestive of adenocarcinoma (**a**, **b**). Magnetic retrograde cholangiopancreatography image showing dilatation of biliary tree (**c**; *red arrow*). Endoscopic retrograde biliary drainage and endonasobiliary drainage tubes in situ as visualized by ERCP (**d**). *ERCP* endoscopic retrograde cholangiography

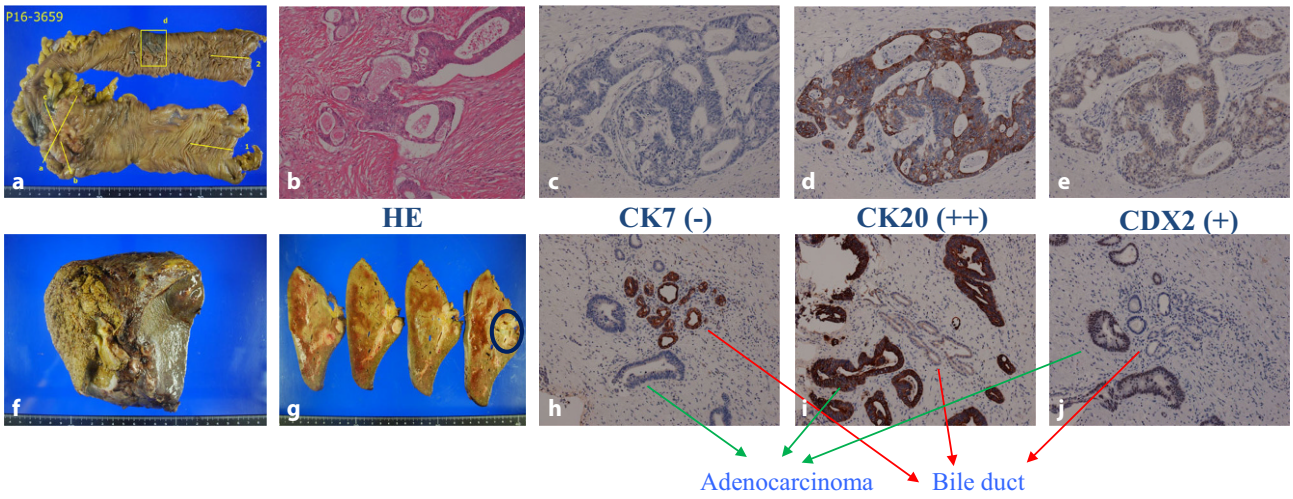


Fig. 4 Gross specimen (**a**) and hematoxylin and eosin stain (**b**) of colon cancer. Liver specimen with metastatic lesions (**f**, **g**), and biliary invasion as indicated by the *blue circle* (**g**). Immunohistochemical staining with CK7, CK20, and CDX2 for colon specimen (**c–e**), and for biliary lesion (**h–j**). Colon cancer cells and central biliary cancer cells were negative, and normal bile duct epithelium was positive, for CK7 (**c**, **h**). Colon cancer cells and central biliary cancer cells were positive, and normal bile duct epithelium was negative, for CDK20 (**d**, **i**). Colon cancer cells and central biliary cancer cells were positive, and normal bile duct epithelium was negative, for CDX2 (**e**, **j**)

9: 301 U/ml). Multiple transverse colon cancers were detected on colonoscopy and computed tomography (CT) colonography (Fig. 1). Contrast CT showed multiple metastatic lesions, mostly on the right hepatic lobe, and a nodule of peritoneal dissemination in the right pelvic space (Fig. 2). A biopsy taken from the central biliary growth revealed adenocarcinoma that was indistinguishable from colon carcinoma (Fig. 3a and b). Magnetic resonance cholangiopancreatography showed a dilated biliary tree (Fig. 3c). Endoscopic retrograde biliary drainage and endonasobiliary drainage tubes were placed (Fig. 3d). A preoperative diagnosis of stage IV transverse colon cancer (T4a, N1, M1c; American Joint Committee on Cancer [AJCC]/Union for International Cancer Control [UICC], 2017) along with perihilar cholangiocarcinoma was made, and the patient was referred to our institute for further management. On admission, the T-bil level dropped to 4.87 mg/dl. Computed tomography volumetry estimated 32% of remnant liver volume (RLV) after extended right hepatectomy, and technetium-99m galactosyl human serum albumin

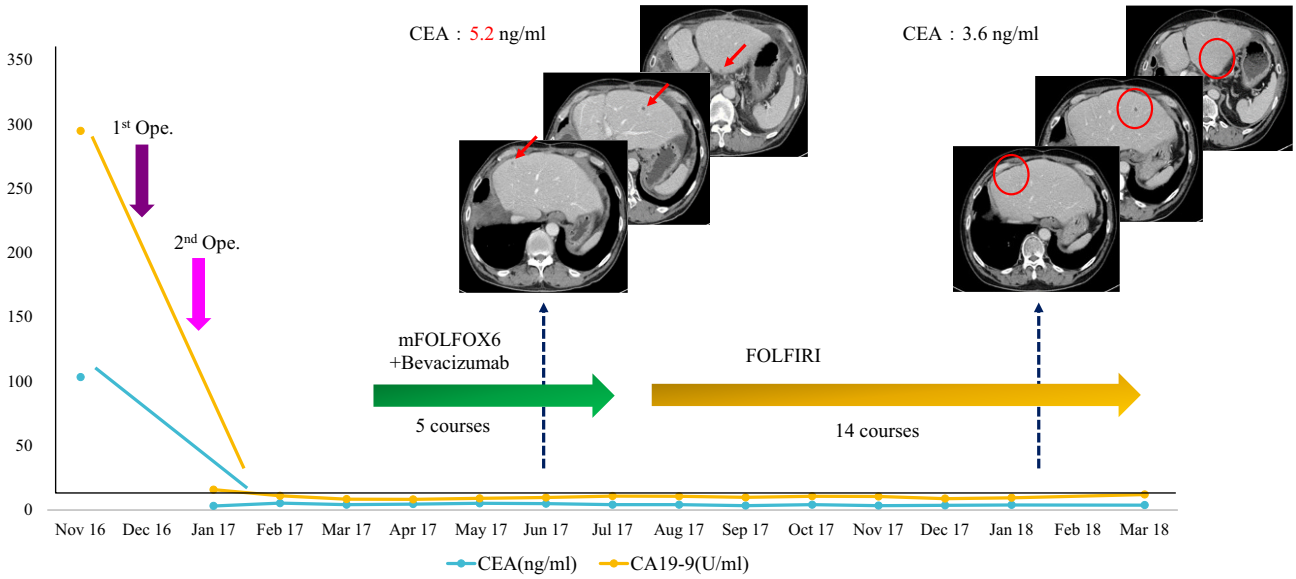


Fig. 5 Demonstration of clinical and therapeutic course. *Red arrows* indicate postresection new hepatic lesion on computed tomographic scan. *Red circles* show the remission of the hepatic lesion after switching from FOLFOX to FOLFIRI. *CEA* carcinoembryonic antigen, *CA19-9* carbohydrate antigen 19-9, *Ope*. operation

(99mTc-GSA) scintigraphy indicated a blood clearance ratio of (HH15) 0.525 (<0.6) and hepatic uptake ratio (LHL15) of 0.958 (>0.9).

The patient underwent transverse colectomy with D3 lymph node dissection, P2 (anterior right renal and right Douglas retroperitoneum) resection, along with partial resection of the Spiegel liver lobe, and transileocecal portal embolization (TIPE). On the tenth postoperative day, right renal pelvic rupture owing to possible ischemic stricture of the right ureter, due to P2 resection, was encountered, and it was treated by immediate ultrasonography-guided retroperitoneal drainage followed by the creation of a right renal fistula. Evaluation of RLV by CT volumetry conducted on the third week after the first procedure showed 39% of RLV with no new lesion on the remnant liver. The patient underwent extended right hepatectomy with extrahepatic bile duct resection and reconstruction 4 weeks after the first surgery. Additionally, right nephrectomy was performed for the irreversible damaged that occurred in the right kidney. Frozen section of the bile-duct stump was negative for cancer cells (R0) but the cut-section of the liver surface was positive. Total operation time was 9 h 56 min, and the resected liver weighed 940 g. The early postoperative course was complicated by hepaticojejunostomy leakage, which was conservatively managed.

The histopathological examination of the colon specimen revealed moderately differentiated tubular adenocarcinoma: T4a, N1, M1c (AJCC/UICC 2017; Fig. 4). Interestingly, immunohistochemical staining of both the central biliary growth and the colon cancer specimens demonstrated a similar pattern with positive CDX2 and CK20 expression and negative CK7 expression (Fig. 4c–e and h–j). Based on these pathological findings, a final diagnosis of central biliary metastasis from CRC was established.

Postoperatively, an mFOLFOX6 regimen with bevacizumab was introduced. After five cycles, recurrence of the remnant liver was suspected and the regimen was switched to FOLFIRI. The suspected metastatic lesion disappeared after ten cycles of FOLFIRI regimen. The patient has completed the 14th cycle of FOLFIRI, is on regular follow-up and doing well with no evidence of recurrence at 17 months after the first surgery. The clinical and therapeutic courses are demonstrated in Fig. 5.

Discussion

Intrahepatic bile duct invasion by mCRC is not a frequent manifestation; Estrella et al. reported the prevalence of intrabiliary growth by mCRC to range from 3.6% to 10.6% [4]. Okano et al. reviewed on a series of 149 patients undergoing liver resection for mCRC, and observed intrabiliary invasion in 42% of the hepatectomized specimens [5]. However, central or perihilar biliary invasion by mCRC is an extremely rare manifestation.

Given the rarity of the central biliary growth of CRC metastasis, no evidence-based, standard therapeutic consensus or strategy exists. The prognosis of biliary metastasis from CRC is poor with a dismal 5-year survival rate of 0% in unresectable lesions [6, 7]. Patients with biliary metastasis also tend to encounter frequent morbidities as a result of biliary obstruction. It is deemed essential to individualize surgical and therapeutic strategy to improve the prognosis in patients with biliary invasion by mCRC.

Table 1 Literature review of case reports/case series on major hepatectomy and extrahepatic bile duct resection for synchronous colorectal liver metastasis with central biliary invasion

Author	Year	Interval* (months)	Treatment	Outcome/survival
Sano et al.	2000	48	Extended left hepatectomy, caudate resection + extrahepatic bile duct resection	Alive: 83 months
Tomizawa et al.	2003	4	Extended left hepatectomy + extrahepatic bile duct resection	Died: 15 months
Wenzel et al.	2003	1	Right hepatectomy + extrahepatic bile duct resection	Alive: 12 months
Takamatsu et al.	2004	34	Left hepatectomy, wedge resection of segment VI + extrahepatic bile duct resection	Alive: 5 months
Chedid et al.	2005	1	Extended right hepatectomy, caudate resection + extrahepatic bile duct resection	Alive: 14 months
Sudo et al.	2014	55	Right hepatectomy, caudate resection + extrahepatic bile duct resection	NA
Yamaguchi et al.	2015	96	Right hepatectomy + extrahepatic bile duct resection	Alive: 38 months
Uno et al.	2016	132	Right hepatectomy, caudate resection + extrahepatic bile duct resection	Died: 56 months
Wiggers et al.	2016	NA	Left hepatectomy (n = 2), right hepatectomy (n = 8) + extrahepatic bile duct resection (n = 10)	Median survival: 19 months
Our case	2018	1	Extended right hepatectomy, caudate resection + extrahepatic bile duct resection	Alive: 17 months

NA not available
*Interval between resection of primary tumor and resection of liver/bile duct metastasis

In this report, we adopted an aggressive surgical approach in a patient who was previously considered to have an inoperable mCRC. The central biliary growth that was first mistaken for perihilar cholangiocarcinoma turned out to be a metastatic lesion from CRC, and diagnosis was established by immunohistochemistry (anti-CDX2, anti-CK20, and anti-CK7 antibodies). As observed in several other studies, immunohistochemistry remained the cornerstone for identification of metastatic biliary lesions. A two-stage hepatectomy, combined with adjuvant chemotherapy, facilitated remission of theoretically unresectable synchronous mCRC with a central biliary lesion.

Moreover, we conducted a literature review on the outcome of major hepatectomy and extrahepatic bile duct resection for CLM with central biliary invasion. Excluding our case, we found nine other reports [8–16]; six were reported from Japan [9–13, 16] including three published in Japanese ([10, 13, 16]; Table 1). The earliest reported mortality was 15 months. Wiggers et al. conducted a case-cohort analysis of patients who underwent major liver resections for CLM, and compared those with and without extrahepatic bile duct resection. In the cohort of ten patients who underwent combined major hepatectomy and extrahepatic bile duct resection, the median overall survival was 19 months [15]. The conclusion stemming from their study suggests surgical treatment in patients for whom radiological staging predicts a high chance of a radical (R0) resection. Besides, Kawakatsu et al. reported a case of intrabiliary and intrapancreatic bile duct metastasis from colorectal cancer; however, the metachronous biliary metastasis appeared 9 years after the colon resection [17]. They also adopted major hepatectomy (extended right lobectomy and caudate resection) with extrahepatic bile duct resection and the patient was reported to be well at 1 year of the last intervention.

The definition of "resectable" beholds the institutional or surgeons' surgical tradition; patients with central biliary invasion may not always be suitable candidates for curative resection because of the tumor size, multifocality, or insufficient hepatic reserve. However, a liberal resection combined with chemotherapy could merit a long-term remission in selected patients with central biliary invasion by mCRC.

Conclusion

Given the rarity of central biliary metastasis of CRC, a clear management strategy has not been established yet. The lesions present a diagnostic puzzle mimicking perihilar cholangiocarcinoma; however, immunohistochemical staining appears to be very useful in establishing a precise diagnosis. Major hepatectomy combined with extrahepatic bile duct resection in a multimodal treatment strategy seems to improve the prognosis and overall survival in suitable cases with central biliary invasion by mCRC.

Conflict of interest B. Aryal, K. Yoshikawa, T. Komokata, H. Yasumura, M. Inoue, M. Kaieda, and Y. Imoto declare that they have no competing interests.

References

1. Adam R, de Gramont A, Figueras J, et al. Managing synchronous liver metastases from colorectal cancer: a multidisciplinary international consensus. Cancer Treat Rev. 2015;41:729–41.

2. Goey KK, 't Lam-Boer J, de Wilt JH, et al. Significant increase of synchronous disease in first-line metastatic colorectal cancer trials: results of a systematic review. Eur J Cancer. 2016;69:166–77.
3. Martin R, Paty P, Fong Y, et al. Simultaneous liver and colorectal resections are safe for synchronous colorectal liver metastasis. J Am Coll Surg. 2003;197:233–41. discussion 41–2.
4. Estrella JS, Othman ML, Taggart MW, et al. Intrabiliary growth of liver metastases: clinicopathologic features, prevalence, and outcome. Am J Surg Pathol. 2013;37:1571–9.
5. Okano K, Yamamoto J, Moriya Y, et al. Macroscopic intrabiliary growth of liver metastases from colorectal cancer. Surgery. 1999;126:829–34.
6. Povoski SP, Klimstra DS, Brown KT, et al. Recognition of intrabiliary hepatic metastases from colorectal adenocarcinoma. HPB Surg. 2000;11:383–90. discussion 90–1.
7. Koh FH, Shi W, Tan KK. Biliary metastasis in colorectal cancer confers a poor prognosis: case study of 5 consecutive patients. Ann Hepatobiliary Pancreat Surg. 2017;21:57–60.
8. Chedid AD, Chedid MF, Kruel CR, et al. Extended right hepatectomy with total caudate lobe resection and biliary tree resection for a large colorectal liver metastasis involving both the right and left hepatic lobes and the umbilical fissure: a case report. Am Surg. 2005;71:447–9.
9. Sano T, Kamiya J, Nagino M, et al. Pancreatoduodenectomy after hepato-biliary resection for recurrent metastatic rectal carcinoma. J Hepatobiliary Pancreat Surg. 2000;7:516–9.
10. Sudo N, Ishikawa H, Katada T, et al. Colorectal carcinoma liver metastasis with bile duct involvement difficult to differentiate from intrahepatic cholangiocarcinoma: report of two cases. J Niigata Med Assoc. 2014;128:269–75.
11. Takamatsu S, Teramoto K, Kawamura T, et al. Liver metastasis from rectal cancer with prominent intrabile duct growth. Pathol Int. 2004;54:440–5.
12. Tomizawa N, Ohwada S, Tanahashi Y, et al. Liver metastasis of rectal cancer with intraluminal growth in the extrahepatic bile duct. Hepatogastroenterology. 2003;50:1625–7.
13. Uno M, Matsuzaki Y, Kamiya S, et al. Intrabiliary growth of metastatic adenocarcinoma 11 years after curative operation of colon cancer. Jpn J Gastroenterol Surg. 2016;49:15–21.
14. Wenzel DJ, Gaede JT, Wenzel LR. Case report. Intrabiliary colonic metastasis mimicking primary biliary neoplasia. AJR Am J Roentgenol. 2003;180:1029–32.
15. Wiggers JK, Te Riele WW, van Dongen TH, et al. Combined liver and extrahepatic bile duct resection for biliary invasion of colorectal metastasis: a case-cohort analysis and systematic review. Hepatobiliary Surg Nutr. 2016;5:350–7.
16. Yamaguchi NK, Kurumiya Y. Two resected liver metastases from rectal cancer with macroscopic intrabiliary tumor growths which collided in the right hepatic duct. Jpn J Gastroenterol Surg. 2015;48:1001–6.
17. Kawakatsu S, Kaneoka Y, Maeda A, et al. Intrapancreatic bile duct metastasis from colon cancer after resection of liver metastasis with intrabiliary growth: a case report. World J Surg Oncol. 2015;13:254.