

Right Hemihepatectomy for Colon Cancer Metachronous Liver Metastasis in a Patient with Crohn's Disease: Case Report and Review of the Literature

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Rezumat

Hemihepatectomie dreaptă pentru metastază hepatică metacronă cu origine colonică la o pacientă cu boală Crohn: Prezentare de caz și review al literaturii

Introducere: La momentul diagnosticului 20% dintre pacienții cu cancer colorectal se prezintă în stadiul IV de boală. Boala Crohn duce la o creștere a riscului de cancer colorectal de aproximativ 20 de ori, fiind deasemenea corelată cu un prognostic nefavorabil. Scopul acestei prezentări de caz este de a ilustra rezecția unei metastaze hepatice metacronice cu origine colonică la o pacientă cu boală Crohn.

Prezentare de caz: Pacienta în vârstă de 53 de ani a fost internată în spitalul nostru pentru rezecția unei metastaze hepatice metacronice cu origine colonică. Pacienta a fost diagnosticată în urmă cu peste 10 ani cu boală Crohn și spondilită ankilopoetică. În urmă cu doi ani pacienta a prezentat o intervenție de tip Hartmann pentru un adenocarcinom de colon sigmoid, iar în urmă cu o lună o rezecție a colonului transvers cu colostomie transversă dreaptă pentru o stenoză a colostomei. Computer tomografia abdominală a relevat o metastază hepatică cu diametrul de 10/11 cm, localizată la

nivelul segmentelor 6, 7 și 8 hepatice, în contact cu venele hepatice medii și dreapta, precum și cu pediculul Glissonian drept. A fost efectuată o hemihepatectomie dreaptă, folosind manevra Pringle pentru 30 minute. Pacienta a fost externată după 12 zile, fără a dezvolta complicații postoperatorii.

Concluzii: Pacienții cu boală Crohn și metastaze hepatice de origine colorectală prezintă o provocare în practica clinică curentă. În cadrul abordului multidisciplinar, rezecția hepatică reprezintă abordul terapeutic asociat cu cele mai bune rezultate oncologice pe termen lung.

Cuvinte cheie: rezecție metacronă, metastaze hepatice, cancer colorectal, boală Crohn

Abstract

Introduction: Twenty percent of patients with colorectal cancer present stage IV disease at the time of diagnosis. The Crohn's disease increases 20 times the risk of colorectal cancer and worsens the patients' prognosis. The objective of this case report is to illustrate the surgical resection of a liver metachronous metastasis of colon cancer origin in a patient with Crohn's disease.

Case report: A 53-year old female patient was admitted to our hospital for a colon cancer metachronous liver metastasis. The patient was diagnosed for more than ten years with colonic Crohn's disease and ankylosing spondylitis. She had a Hartmann's type resection for sigmoid colon adenocarcinoma four years ago, and a secondary resection of the transverse colon with a right transverse colostomy for colonic stenosis one month before current admission. Abdominal Computed

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Tomography revealed a liver metastasis of 10/11 cm located in segments 6, 7, 8, in close contact with the right and middle hepatic veins and right Glissonian pedicle. A right hemihepatectomy was performed, using Pringle maneuver for 30 minutes. The patient was discharged after 12 days, without additional morbidities.

Conclusions: Patients with liver metastases of colorectal origin in the presence of Crohn's disease come with significant clinical challenges. Inside the multimodality approach, liver resection represents the therapeutic approach associated with the best long-term oncological results.

Key words: metachronous resection, liver metastases, colorectal cancer, Crohn's disease

Introduction

Twenty percent of patients with colorectal cancer (CRC) present stage IV disease at the time of diagnosis (1). Although the curative intent is still possible in a subgroup of these patients, the reported five-year relative survival rate is only 13% (1). The surgical approach of colorectal liver metastases (CRLMs) changes dramatically during the latest years, with a reported postoperative mortality less than 1% (2). The resectability of CRLMs is characterized by the technical possibility to remove all the visible metastases while preserving an adequate future liver remnant volume (FLRV) with its corresponding vascular supply and biliary drainage (3). Nowadays, to recruit more patients for surgical resection, neoadjuvant chemotherapy to downsize the tumors and adjunctive techniques to increase the FLRV are combined (2). In the absence of surgical resection, a median survival of less than one year was reported after diagnosis of CRLMs (4).

According to the evidence coming from tertiary centers, Crohn's disease increases 20 times the risk of colorectal cancer, up to 1.2% (5, 6), and worsens the patients' prognosis (7). Liver oligometastasis, usually defined as fewer than five nodules, should be seen as an intermediate state between localized and polymetastatic disease, with an in-between prognosis (8).

The objective of this case report is to illustrate the surgical resection of a large liver metachronous metastasis of colon cancer origin in a patient with Crohn's disease.

Case report

A 53-year old female patient was admitted to our hospital for a colon cancer metachronous liver metastasis. The patient was diagnosed for more than ten years with colonic Crohn's disease and ankylosing spondylitis. The patient had a Hartmann's type resection for sigmoid colon adenocarcinoma four years ago. The pathology exam revealed a moderately differentiated adenocarcinoma, staged as pT2N0M0. She had a secondary resection of the transverse colon with a right trans-

verse colostomy one month ago for colonic stenosis suspected to be local recurrence; this was proved to be secondary to Crohn's disease by the pathology exam. Although the liver lesion was characterized by Computed Tomography, we choose an initial colonic resection with a metachronous resection of the liver metastasis due to the presence of significant intestinal obstruction, combined with a low nutritional status of the patient, with a body mass index of 17 kg/m².

The clinical exam revealed a Karnofsky index of 70% and an ECOG index of 1. The Carcinoembryonic Antigen (CEA) was 11 ng/ml. Abdominal Computed Tomography revealed a liver metastasis of 10/11 cm located in segments 6, 7, 8, in close contact with the right and middle hepatic veins and right Glissonian pedicle (see Fig. 1). Open surgical resection was decided, using a J-shape incision. A right hemihepatectomy was performed, using Pringle maneuver for 30 minutes (see Fig. 2). The patient was discharged after 12 days, without additional morbidities.

Discussions

We presented the case of surgical resection of a large liver metachronous metastasis of colon cancer origin in a patient with severe Crohn's disease.

Although seen as a more indolent disease, the metachronous CRLMs carry a similar prognosis with the synchronous

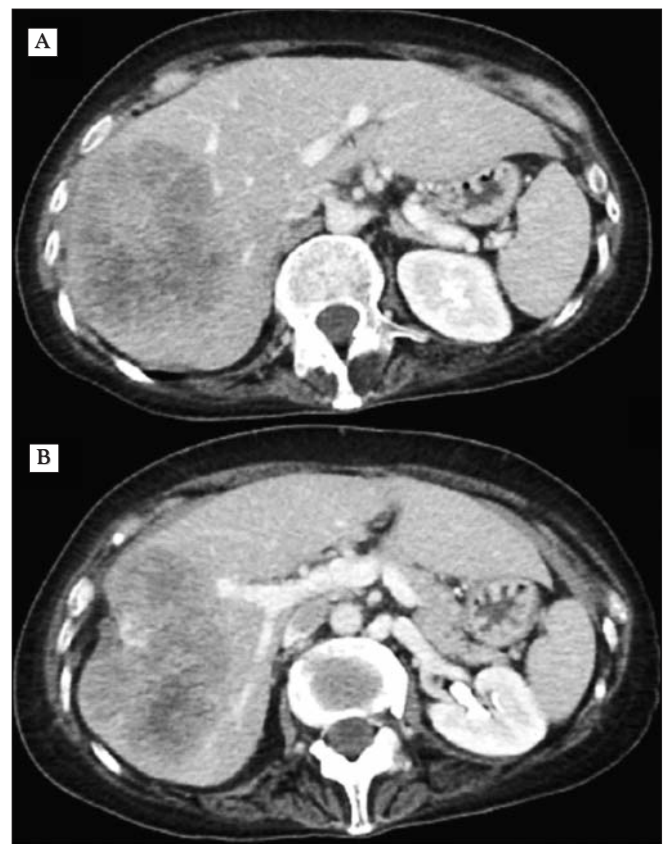


Figure 1. Computed Tomography image revealed a single colon cancer liver metastasis, located into the right hemiliver

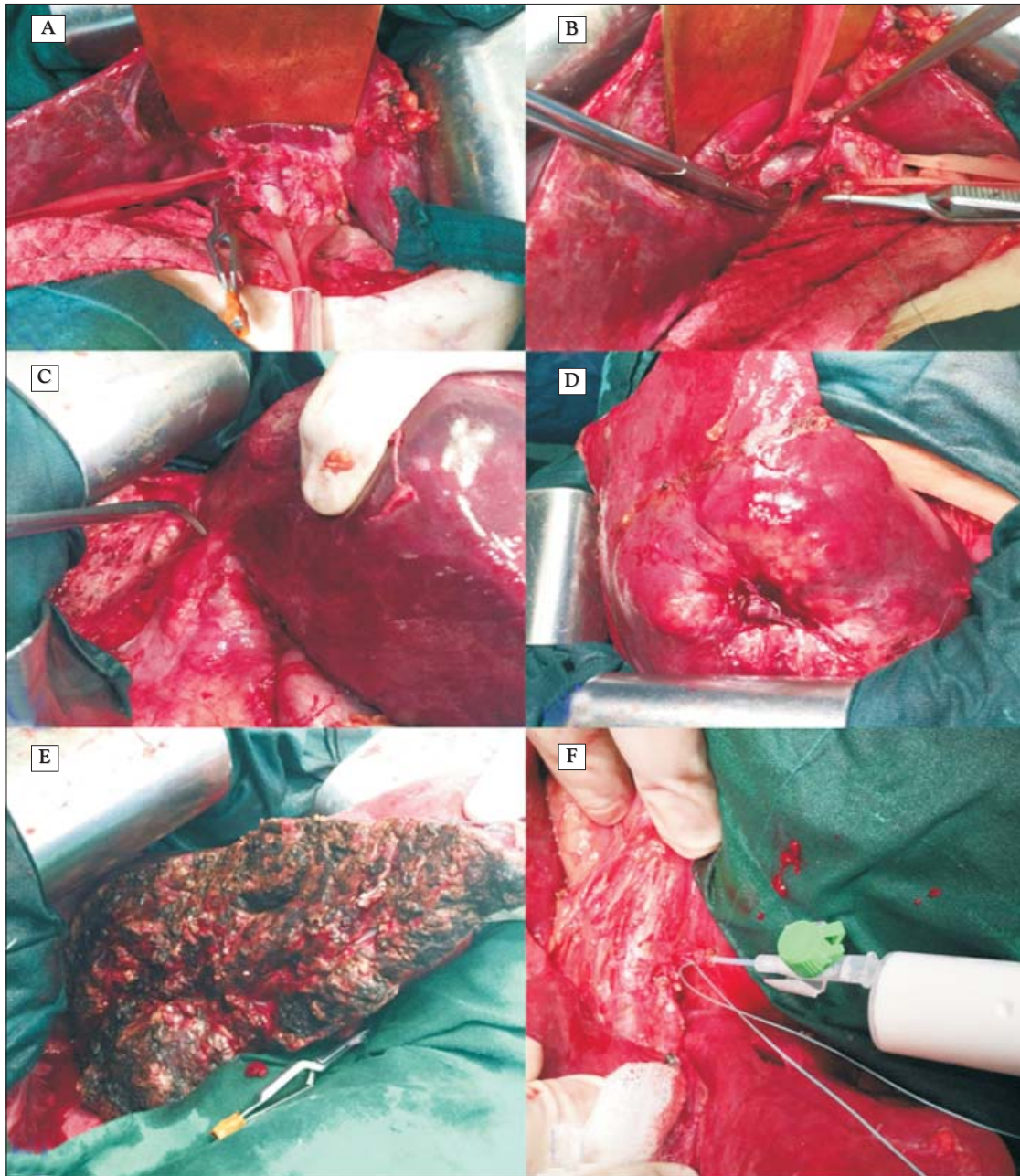


Figure 2. Intraoperative aspects. (A) Inflow control: it can be observed the right hepatic artery, common bile duct, left hepatic artery and the tourniquet used for Pringle maneuver; (B) Inflow control: it can be observed the right hepatic artery, common bile duct, and the right portal vein; (C) Outflow control: it can be observed the hepatocaval ligament (Makuuchi's ligament); (D) Electrocautery scoring of the Glisson's capsule marking the transection plane; (E) Raw transected surface of the liver; (F) White test, used to reveal the biliary leakage at the level of the transected surface of the liver

disease, as long as an R0 resection is achieved (9). The post-operative and long-term oncological outcomes were similar between the two groups even in patients with more than four lesions (10). Hackl et al. published a ten-year population-based analysis of 5772 cases of primary CRC, using data from a German tumor registry (4). CRLMs were observed in 1426 patients (24.7%). 407 patients, representing 28.5% from the CRLMs population and 7.05% of all patients, presented

metachronous disease. On multivariate analysis, there was no difference in overall survival between synchronous versus metachronous disease ($P=0.799$). Of particular importance was that resected patients with a single CRLM had a similar 10-year overall survival with non-metastatic patients (28.3% versus 29.8%, $P=ns$) (4). On the other hand, Pawlik and colleagues showed that tumor biology rather than surgical technique determine prognosis in CRLMs (see Table 1) (11).

Table 1. Differences regarding tumor marker expression between synchronous and metachronous colorectal cancer liver metastases (CRLMs) (12)

Tumor molecular marker expression	Synchronous CRLMs	Metachronous CRLMs
Increased	COX-2 mRNA TGF- α Angiopoietin-2/ Angiopoietin-1 ratio	CD 83, EGF mRNA
No differences	VEGF, angiopoietins genetic abnormalities	Ki-67 TP CD 31 CD 34 c-erb-2 ZEB2

This study coming from John Hopkins revealed that an R0 margin provide a survival benefit only in KRAS wild-type tumors (Hazard ratio 2.16, 95% CI 1.42 – 3.30, $P < 0.001$), with no impact of the margin status for tumors with KRAS mutations (R0 vs. R1 five-year overall survival 40.7% vs. 46.7%, $P = 0.348$) (11).

Historically, a 1-cm resection margin was considered associated with better outcomes following CRLMs resection (13). The current evidence showed that a margin clearance of 1-4 mm is associated with improved survival compared to R1 only for wild-type KRAS tumors (14). In cases of mutated KRAS tumors were observed no differences between R1 resections or a clearance margin of 1-4, 5-9, or ≥ 10 mm (14). As a strategy for resection, the parenchymal-sparing hepatectomy can be performed safely without compromising oncological outcomes, even for deep-placed or advanced (\geq four lesions with a diameter ≤ 50 mm) CRLMs (15, 16). Compared to major hepatectomy, the parenchymal-sparing resection is associated with a larger number of ligatures, a longer transection time, and a wider raw transected area (16).

Spelt et al. investigated the characteristics of primary tumor predictive for survival after liver resection for colon cancer metastases (17). Predictive factors for overall survival (OS) were the vascular and perineural invasion of the primary CRC tumor, the size of the largest metastasis, and severe complications after hepatic resection. The disease-free survival (DFS) was predicted by perineural invasion, the number of hepatic metastases, and preoperative CEA (17). Lymph node ratio was an independent predictive factor only for DFS (17). Serrablo et al. showed that three or more metastatic lesions, R1 resections, and less than 50% tumor necrosis are associated with a worse OS; the only independent prognostic factor in the multivariate analysis was ≥ 3 liver lesions (18). The French Colorectal Liver Metastases Working Group investigated the factors associated with recurrence after initial hepatectomy for CRLMs (19). The tumor recurrence occurred in 47.4% of 2320 included patients, with a majority of 89.1% during the first three years. The tumor recurrence was intra-hepatic, extra-hepatic, and combined in 46.2%, 31.8%, and 22%, respectively. The factors associated with recurrence after an initial hepatectomy for CRLMs were node-positive primary

CRC (HR 1.27, 95%CI 1.09-1.49), $>$ three liver metastases (HR 1.27, 95%CI 1.06-1.52) and diameter of the largest metastasis > 4 cm (HR 1.19, 95%CI 1.01-1.43) (19).

Larsen et al. evaluated the survival of patients with Crohn's disease and colorectal cancer (CD-CRC) (7). In this nationwide population-based Danish study were included 100 CD-CRC patients and 71438 patients with CRC and without CD. Although the patients with CD were younger at the time of diagnosis, the stage distribution was similar between the two groups (7). The survival rate of patients with CD-CRC was lower especially in the first year after diagnosis (54% versus 60%) (7). Another analysis of Danish medical registries, including 238 patients with CD-CRC and 107024 patients without inflammatory bowel disease showed a higher rate of stage III (21% versus 27%) and IV patients (23% versus 21%), with a lower five-year overall survival of 38% for CD-CRC compared to 41% of patients with CRC and ulcerative colitis, and 44% for CRC patients without CD (20). Dugum et al. presented 44 patients with inflammatory bowel diseases (IBD) and colorectal cancer (CRC), propensity score-matched with 176 CRC patients without IBD (21). There were no differences between the two groups regarding tumor recurrences (23% vs. 19%, $P = 0.074$), disease-free survival (Hazard ratio [HR] = 0.60, $P = 0.074$), and overall survival (HR = 0.87, $P = 0.58$) (21). An analysis of 33 patients with Crohn's disease and colorectal cancer revealed a comparable clinicopathological and molecular profile to sporadic colorectal cancer (22). Colorectal cancer in patients with Crohn's disease was BRAF (97%) and NRAS (100%) wild-type, microsatellite stable in 94% of cases and KRAS mutated in 18% of cases. A history of Crohn's disease longer than 25 years was associated with significantly shorter overall survival ($P = 0.0029$) (22).

Conclusions

Patients with liver metastases of colorectal origin in the presence of Crohn's disease come with significant clinical challenges. Inside the multimodality approach, liver resection represents the therapeutic approach associated with the best long-term oncological results.

Authors' contributions

Ionut Negoii acquisition of data, analysis and interpretation of data, drafting the article, final approval; Alexandru Runcanu interpretation of data, revising the article, final approval; Sorin Paun acquisition of data, revising the article, final approval; Mircea Beuran conception and design of the study, critical revision, final approval.

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