

## CASE REPORT

# Long-term survivor who underwent surgical resections of repeated peritoneal oligometastases from colon cancer : a rare case report

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**Abstract :** A 74-year-old woman underwent right hemicolectomy and partial ileal resection for ascending colon cancer with synchronous peritoneal metastasis. Histopathological examination showed moderately differentiated adenocarcinoma with mucinous component, pT4b N3 M1, and Stage IV. Postoperative chemotherapy comprising 36 courses of mFOLFOX6 with bevacizumab was administered. Twenty-two months after the surgery, computed tomography (CT) revealed a 20 mm nodular lesion adjacent to the gastric wall, and laparoscopic resection of the nodule was performed. Thirty-nine months after the second surgery, CT showed a 24 mm nodular lesion involving the liver parenchyma, and partial hepatectomy involving the nodule was performed. Histopathological examination of the nodules resected by the second and third surgeries showed the same features as the primary ascending colon cancer. The nodules were diagnosed as metachronous peritoneal metastases. The patient followed up without chemotherapy after the second and third surgery, showed no recurrence for 26 months after the third surgery. Fortunately, more than 7 years have passed since the primary tumor resection. Hence, surgical resection for synchronous and repeated metachronous peritoneal oligometastases from colon cancer can offer long-term survival. *J. Med. Invest.* 69:302-307, August, 2022

**Keywords :** colon cancer, oligometastasis, peritoneal metastasis

## BACKGROUND

Peritoneal metastasis (PM) is found in 5-13% of colorectal cancer (CRC) cases (1, 2). The prognosis of patients with CRC and PM remains poor, and the median overall survival is 10.4-34.7 months, despite the advent of systemic chemotherapy and cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) (3-10). Oligometastasis is defined as a state characterized by a limited number of metastatic lesions (11-14). Local therapies, such as surgery, radiotherapy, and radiofrequency ablation, which are indicated for CRC patients with oligometastases involving the liver, lungs, and other organs have the potential benefit of palliation on survival. However, little is known about the significance of repeated surgical resections of peritoneal oligometastases. Herein, we report a rare case of a long-term survivor who underwent surgical resection of synchronous and repeated metachronous peritoneal oligometastases from colon cancer.

## CASE PRESENTATION

A 74-year-old woman presented at our hospital with abdominal pain. Abdominal enhanced computed tomography (CT) showed a well-enhanced tumor located in the ascending colon. The low-density area around the tumor was suspected to be an intra-abdominal abscess (Fig. 1 (a)). Blood examination showed

an elevation in white blood cell count ( $15.0 \times 10^3/\mu\text{L}$ ), neutrophil count ( $13.2 \times 10^3/\mu\text{L}$ ), and CRP level (22.8 mg/dL). The serum carcinoembryonic antigen (CEA) level was slightly elevated (5.4 ng/mL) and carbohydrate antigen 19-9 (CA19-9) level was within the reference range (2.8 U/mL). She was diagnosed with ascending colon cancer and an intra-abdominal abscess due to tumor perforation ; cT4bN2M0, cStage IIIb, according to the Japanese Classification of the Colorectal Carcinoma (15). Right hemicolectomy with D3 lymphadenectomy and functional end-to-end anastomosis were performed without ileostomy because the abdominal abscess was localized around the tumor and the bowel condition was preserved. In addition, partial ileal resection was performed because a 20 mm nodular lesion, suspected to be PM, was found on the ileal wall intraoperatively. Macroscopic examination of the resected specimen showed an irregular and nodular ulcerated tumor measuring  $8 \times 6$  cm in the ascending colon (Fig. 1 (b)). Histopathological examination revealed moderately differentiated adenocarcinoma with mucinous component (Fig. 1 (c, d)). The nodular lesion on the ileal wall (Fig. 2 (a)) was pathologically diagnosed as PM (Fig. 2 (b, c)). The final diagnosis was pT4b (omentum), N3, ly1, v1, M1 (P), P2, and Stage IV according to the Japanese Classification of the Colorectal Carcinoma (15). Both RAS and BRAF statuses were wild. Postoperative chemotherapy was performed for a period of 20 months, which comprised 36 courses of mFOLFOX6 with bevacizumab according to the stop-and-go strategy (oxaliplatin 85 mg/m<sup>2</sup>, l-LV 200 mg/m<sup>2</sup>, 5-FU (5-fluorouracil) 400 mg/m<sup>2</sup> followed by a 46-hour infusion of 5-FU 2400 mg/m<sup>2</sup>, and bevacizumab 5 mg/kg on day 1, every 2 weeks).

Twenty-two months after the surgery, CT revealed a 20 mm nodular lesion adjacent to the gastric wall (Fig. 3 (a)). 18F-fluorodeoxyglucose positron emission tomography-CT (FDG PET-CT) showed high FDG accumulation in the nodular lesion without high FDG accumulation in other organs. The nodule

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was resected laparoscopically. Histopathological examination showed mucinous adenocarcinoma similar to primary ascending colon cancer (Fig. 3 (b, c, d)). She was followed up without chemotherapy due to R0-resection for solitary metastatic lesion with long disease-free interval (DFI).

Thirty-nine months after the second surgery, CT revealed a 24 mm nodular lesion involving the liver parenchyma without metastases to other organs (Fig. 4 (a)). Partial hepatectomy involving the nodule was performed. Histopathological examination demonstrated mucinous adenocarcinoma similar to primary ascending colon cancer (Fig. 4 (b, c, d)). Microsatellite instability (MSI) examination showed MSI-low or microsatellite stability. The patient has been followed-up without chemotherapy for the same reason as the second surgery and alive without recurrence for 26 months after the third surgery. Fortunately, more than 7 years have passed since the primary tumor resection.

## DISCUSSION

Herein, we describe a rare case of a long-term survivor who underwent surgical resection of synchronous and repeated metachronous peritoneal oligometastases from colon cancer. Notably, the recurrent tumors were slow-growing in nature, although the primary tumor was associated with tumor perforation, multiple lymph node metastases (N3), and synchronous peritoneal metastasis. Our case suggests that surgical resection for repeated peritoneal oligometastases can be indicated for selected patients with specific tumor histology and long disease-free interval

(DFI) and offer long-term survival without cytoreductive surgery or hyperthermic intraperitoneal chemotherapy.

In 1995, Hellman and Weichselbaum first proposed the concept of oligometastasis, which is the transitional state between localized and widespread systemic metastatic cancers (11). Local therapy for primary lesion and oligometastasis can achieve prolonged survival or even cure (16). This notion has recently been widely accepted by oncologists, and many studies have reported on various types of malignancies, mostly focusing on stereotactic radiotherapy (SRT) and stereotactic body radiotherapy (SBRT) (16-18).

Several studies have reported the significance of SRT and SBRT in patients with CRC and liver or lung oligometastases (19-22). Surgical resection of a small number of liver and/or lung metastases from CRC can yield favorable results. In contrast, systemic therapy is generally indicated for PM with widespread tumor dissemination. However, PM comprises a wide spectrum of disease phenotypes, ranging from isolated peritoneal implants to diffuse PM, which is similar to the spectrum of isolated liver metastasis to bilobar multiple liver metastases (23). Based on this phenotypic variation, the concept of oligometastases can be applied to the management of PM from CRC. Indeed, the Japanese CRC guidelines and National Comprehensive Cancer Network guidelines classify PM into localized and generalized PM and recommend surgical resection of localized PM if R0 resection can be achieved.

Recently, several authors have reported prognostic factors of PM. Shida *et al.* reported the efficacy of R0 resection of PM from CRC without CRS or HIPEC. Their study investigated 78

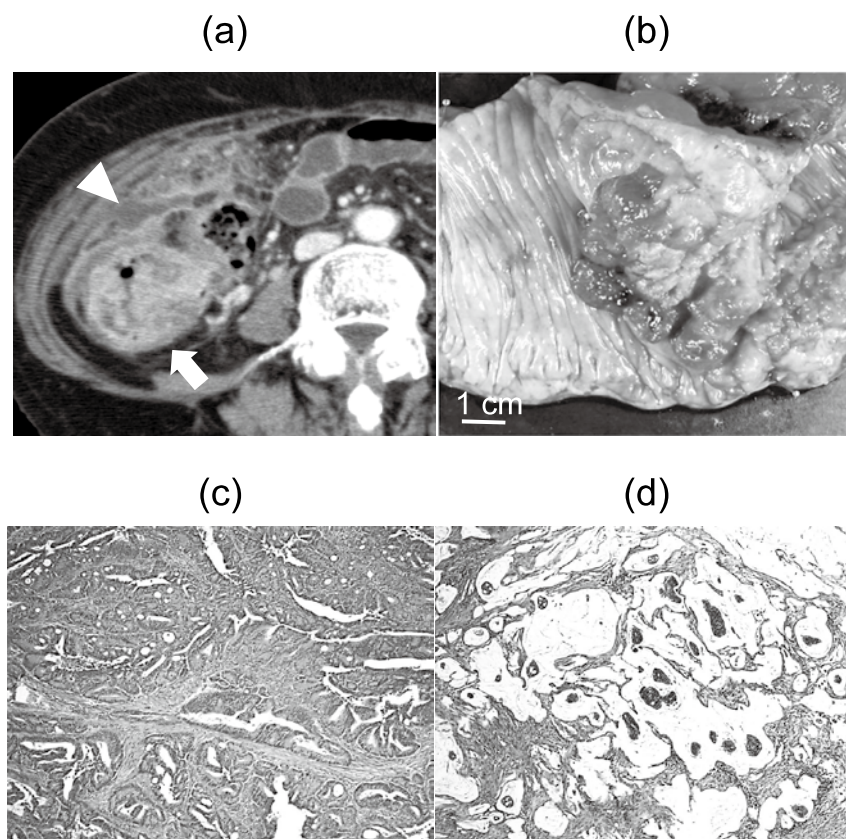


Fig. 1. (a) CT showing a well-enhanced tumor (arrow) located in the ascending colon. A low-density area around the tumor (arrowhead) was suspected of being an intra-abdominal abscess due to the tumor perforation. (b) Macroscopic image of the resected specimen by right hemicolectomy showing an irregular nodular ulcerated tumor of 8 × 6 cm in the ascending colon. (c) Histopathological image showing moderately differentiated adenocarcinoma (HE, ×40) with (d) mucinous component (HE, ×40)

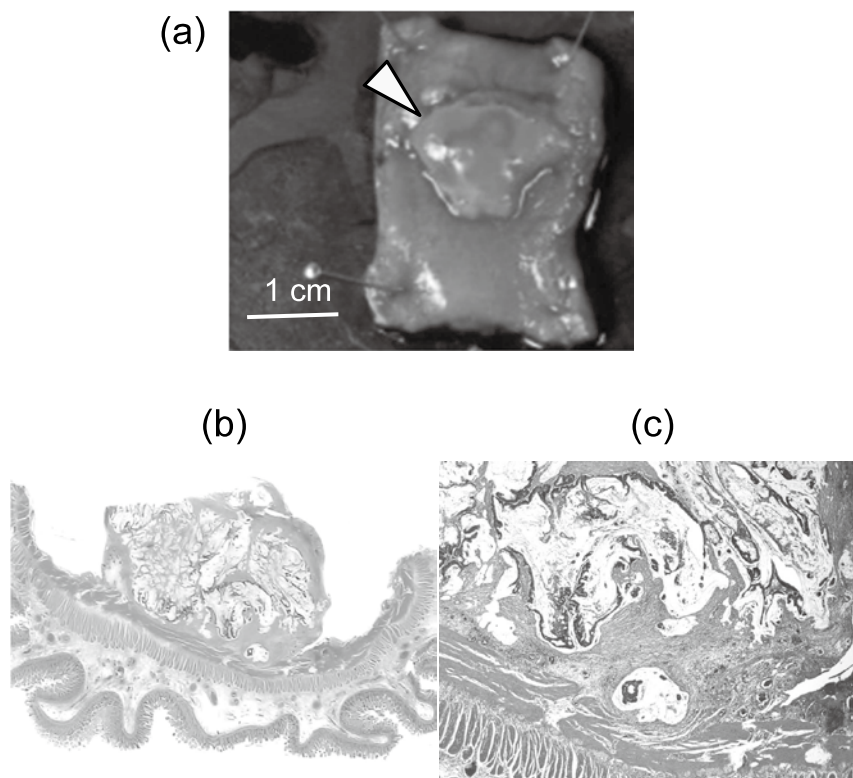


Fig. 2. (a) Macroscopic image of the resected ileum showing a 20 mm nodular lesion on the ileal serosa (arrow-head). (b, c) Histopathological image showing mucinous adenocarcinoma (b, HE, loupe image ; c, HE, ×20)

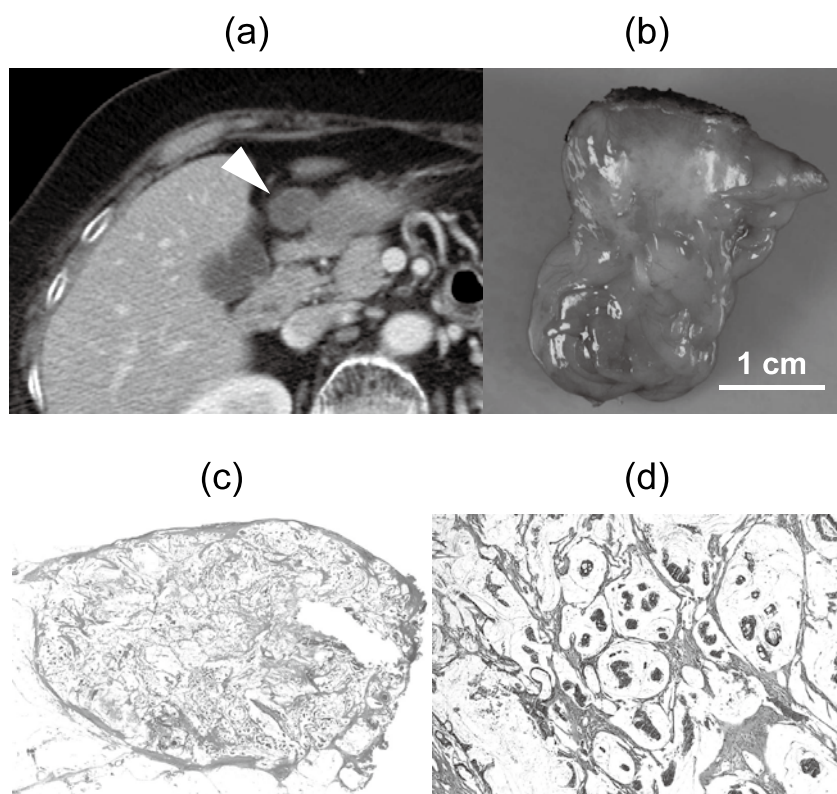


Fig. 3. (a) CT 22 months after the first surgery showing a 20 mm nodular lesion (arrow-head) adjacent to the gastric wall. (b) Macroscopic image showing a 20 mm round-shaped nodule. (c, d) Histopathological image showing mucinous adenocarcinoma (c, HE, loupe image ; d, HE, ×40)



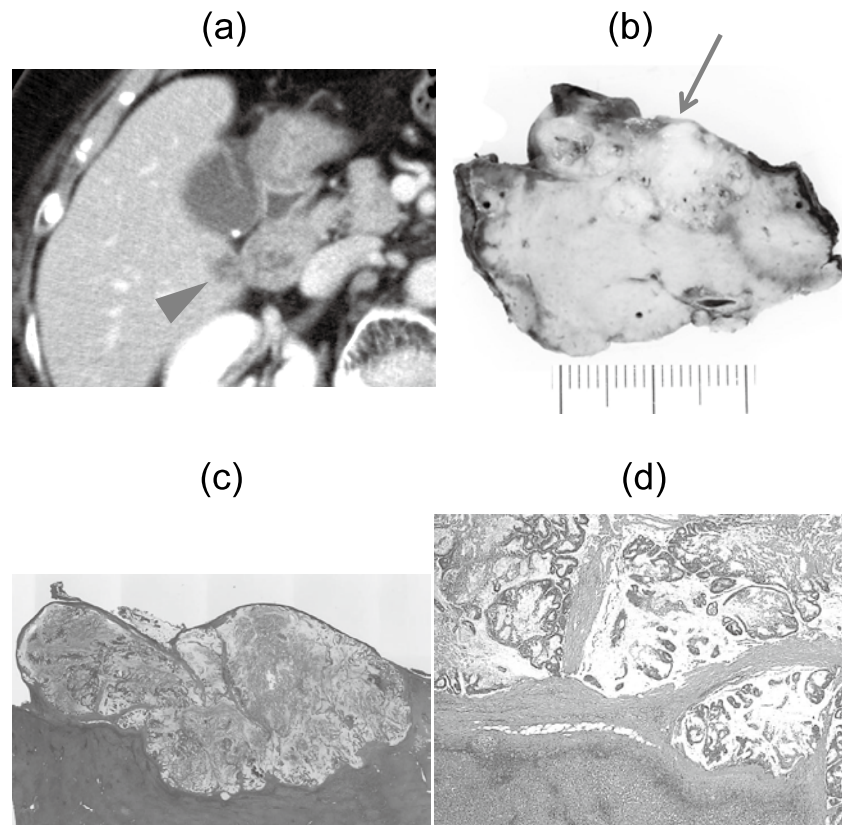


Fig. 4. (a) CT 39 months after the second surgery (partial resection of the liver) showing a 24 mm irregular nodular lesion involving liver parenchyma (arrow-head). (b) Macroscopic image showing a 24 mm irregular-shaped nodule involving liver parenchyma (arrow). (c) Histopathological image showing mucinous adenocarcinoma (c, HE, loupe image ; d, HE,  $\times 40$ )

patients with CRC and synchronous peritoneal metastasis, without other distant metastases, who underwent R0 resection. The 5-year overall-survival (OS) was 28.7% and median survival time (MST) was 33.4 months, and 17 patients survived for more than 5 years (24). Elisa *et al.* reported that the 5-year OS and MST of patients with PM from CRC treated with CRS+HIPEC were 27% and 30.1 months, respectively. They also reported that the positive prognostic factors were complete CRS, limited PM, no lymph node metastasis, and adjuvant chemotherapy (25). However, these reports did not describe the management of peritoneal recurrence after primary surgery, especially the significance of repeated surgical resection. The significance of repeated PM resection remains to be unclear. To the best of our knowledge, there is only one case report, by Komori *et al.*, in which aggressive resection for repeated PM from CRC was performed (26). The patient underwent surgical resection of a descending colon cancer and subsequently underwent four surgical resections for metachronous limited PM (DFI: 10, 9, 35, and 7 months). However, she died of diffuse PM 6 years and 7 months after the first surgery due to diffuse PM.

The present case initially had synchronous peritoneal metastasis, which was subsequently followed by metachronous peritoneal oligometastases on two occasions. She had relatively long DFI (22 and 37 months) after PM resections. Long DFI is a potential indicator of unaggressive tumor biology and a favorable prognosis (27-29). From this perspective, oligometastases with long DFIs are a favorable prognostic factor.

In the present case, histopathological examination showed that the primary tumor included a mucinous component, and the recurrent PMs resected in the second and third surgeries

were mucinous adenocarcinoma. Mucinous adenocarcinoma is a histologic subtype that accounts for 5--15% of CRCs (30-34) and is characterized by the presence of abundant extracellular mucin in at least 50% of the tumor volume (35). The mucus allows tumor cells to easily access the peritoneal cavity and regional lymph nodes, facilitating their lymphatic spread (36, 37). Consequently, a higher incidence of lymph node metastasis and PM was found compared to non-mucinous colorectal adenocarcinoma (NMCA). The reported clinicopathological features of MCA are as follow : females, younger patients, proximal colon, deeper depth of invasion, higher incidence of BRAF gene mutation and MSI, and poorer response to chemotherapy (38, 39). However, the prognosis of MCA remains controversial. Some studies have reported a poor prognosis for patients with MCA, whereas others have failed to demonstrate a significant difference in survival between patients with MCA and NMCA (32, 40-42). Due to their poorer response to chemotherapy, peritoneal oligometastases from the MCA can be an indication for surgical resection.

In conclusion, the present case has achieved over 7-year survival by surgical resections for repeated peritoneal oligometastases from colon cancer. Repeated surgical resection of peritoneal oligometastases from colon cancer can be indicated for selected patients with long DFI and offer long-term survival.

#### CONFLICT OF INTEREST

none declared

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None declared.

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