CASE REPORT

Nagoya J. Med. Sci. **78**. 501 ~ 506, 2016
doi:10.18999/nagjms.78.4.501

Aggressive resection of frequent peritoneal recurrences in colorectal cancer contributes to long-term survival

Koji Komori, Takashi Kinoshita, Oshiro Taihei, Seiji Ito, Tetsuya Abe, Yoshiki Senda, Kazunari Misawa, Yuichi Ito, Norihisa Uemura, Seiji Natsume, Jiro Kawakami, Akira Ouchi, Masayuki Tsutsuyama, Takahiro Hosoi, Itaru Shigeyoshi, Tomoyuki Akazawa, Daisuke Hayashi, Hideharu Tanaka and Yasuhiro Shimizu

Department of Gastroenterological Surgery, Aichi Cancer Center Hospital, Nagoya, Japan

ABSTRACT

We report a long-term survivor of colorectal cancer who underwent aggressive, frequent resection for peritoneal recurrences. A 58-year-old woman was diagnosed with descending colon cancer. Resection of the descending colon along with lymph node dissection was performed in September 2006. The pathological findings revealed Stage IIA colorectal cancer. The following peritoneal recurrences were removed: two in July 2007, two in the omental fat and two in the pouch of Douglas in June 2008 resected by low anterior resection of the rectum, one in the uterus and right ovarian recurrence resected via bilateral adnexectomy and Hartmann's procedure in May 2011, and one in the ascending colon by partial resection of the colon wall in December 2011. Postoperative adjuvant chemotherapy (uracil and tegafur/leucovorin, fluorouracil/levofolinate/oxaliplatin/bevacizumab, 5-fluorouracil/leucovorin/bevacizumab, irinotecan/bevacizumab, and irinotecan/panitumumab) was administered. The patient did not desire postoperative adjuvant chemotherapy after the fourth operation. The long-term survival was 6 years and 7 months.

Key Words: aggressive resection, frequent peritoneal recurrences, colorectal cancer

INTRODUCTION

Peritoneal recurrences from colorectal cancers are common, but in many cases, surgical resection is performed without preoperative recognition of multiple lesions.[1] However, single peritoneal recurrence is typically recognized, and such cases are likely to undergo complete resection. Nevertheless, there is no consensus regarding the surgical treatment of repeated peritoneal recurrences in colorectal cancer. In Japan, the Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2015 for the Treatment of Colorectal Cancer recommend that resection should be strongly considered when recurrence is observed in a single organ and complete surgical resection of the recurrent tumour is possible.[2]

Here, we report a long-term survivor of colorectal cancer who underwent aggressive, frequent

Received: July 20, 2016; accepted: September 28, 2016

Corresponding author: Koji Komori, MD

Department of Gastroenterological Surgery, Aichi Cancer Center Hospital,

1-1 Kanokoden, Chikusa-ku, Nagoya 464-8681, Japan

Tel: +81-52-762-6111, Fax: +81-52-763-5233, E-mail: kkomori@aichi-cc.jp

resection of peritoneal recurrences.

CASE PRESENTATION

The patient was a 58-year-old woman who was admitted to our hospital with lower abdominal distension. Endoscopic examination of the colorectum revealed an ulcerated, circular lesion with a clear margin in the descending colon. The patient was diagnosed with descending colon cancer. The resection of the descending colon with lymph node dissection was performed in September 2006. The pathological findings revealed Stage IIA (pSS, pN0). No adjuvant therapy was administered.

After approximately 1 year from the first primary operation, computed tomography (CT) showed one peritoneal recurrences (Figure 1 A). In July 2007, during the first recurrent operation, two peritoneal recurrences were recognized. The one in the pouch of Douglas was 8 mm in diameter and intraoperative rapid diagnosis was adenocarcinoma. The other in the left paracolic gutter was removed (Figure 1 B). After the operation, 5 cycles of oral uracil and tegafur plus leucovorin as adjunctive therapy were administered over 6 months.[3)]

After approximately 2 years from the first primary operation, CT showed two peritoneal recurrences in the paramedian region (Figure 2 A) and in the pouch of Douglas (Figure 2 B). In June 2008, in a second recurrent operation, two peritoneal recurrences were recognized in the omental fat and in the pouch of Douglas each, i.e. in all, four recurrent lesions were recognized. The two peritoneal recurrences in the omental fat were removed, and those in the pouch of Douglas were removed by low anterior resection of the rectum (Figure 2 C–E). Postoperatively, the patient was administered oral chemotherapy with uracil and tegafur plus leucovorin for approximately 6 months.

In a follow-up study, CT showed one equivocal peritoneal recurrence on the uterus and right ovarian recurrence. Subsequently, 8 cycles of modified infusional intravenous fluorouracil and levofolinate with oxaliplatin and bevacizumab; 16 cycles of 5-fluorouracil, leucovorin, and bevacizumab; 17 cycles of irinotecan and bevacizumab; and 4 cycles of irinotecan and panitumumab

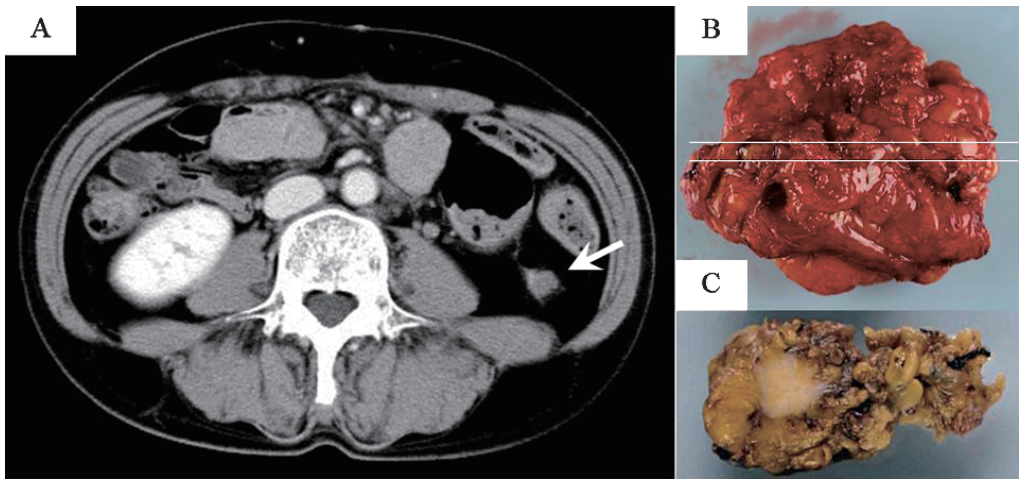

Fig. 1 Abdominal computed tomography shows a recurrent lesion in the left paracolic gutters (white arrow, A); the resected specimen (B); and the carcinoma in the cleavage plane (C).

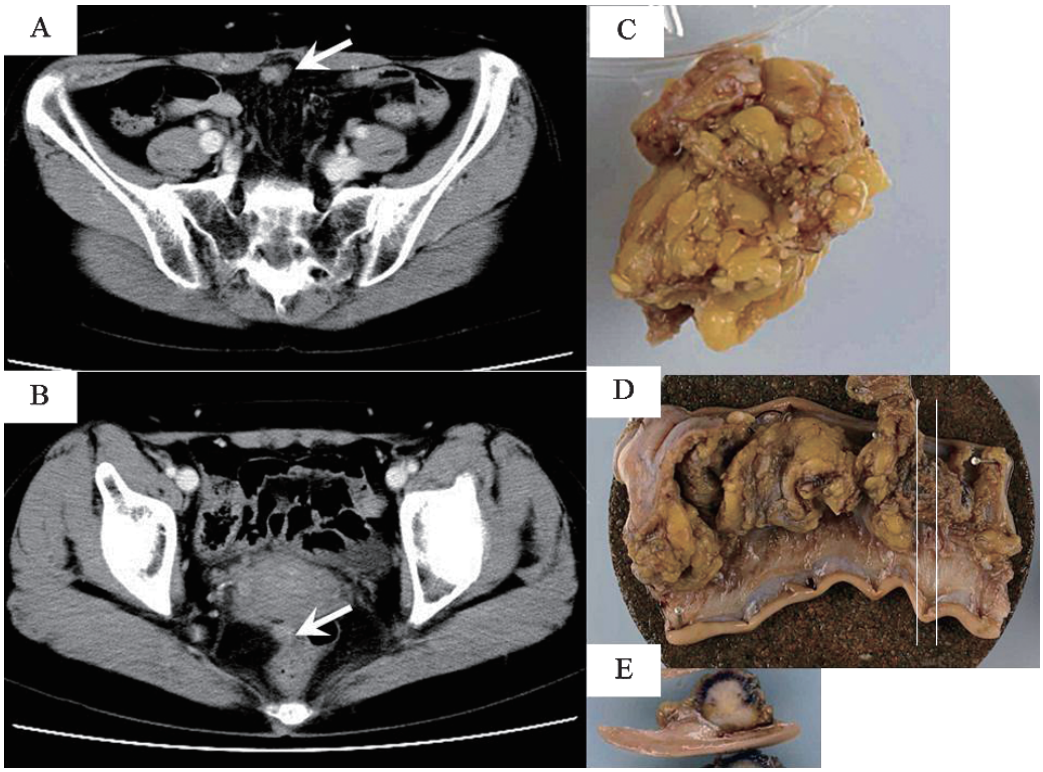

Fig. 2 Abdominal computed tomography shows a recurrent lesion in the paramedian region (white arrows, A). The resected specimens are seen (C). Abdominal computed tomography shows a recurrent lesion in the pouch of Douglas (white arrows, left lower), the resected specimen (D), and the carcinoma in the cleavage plane (E).

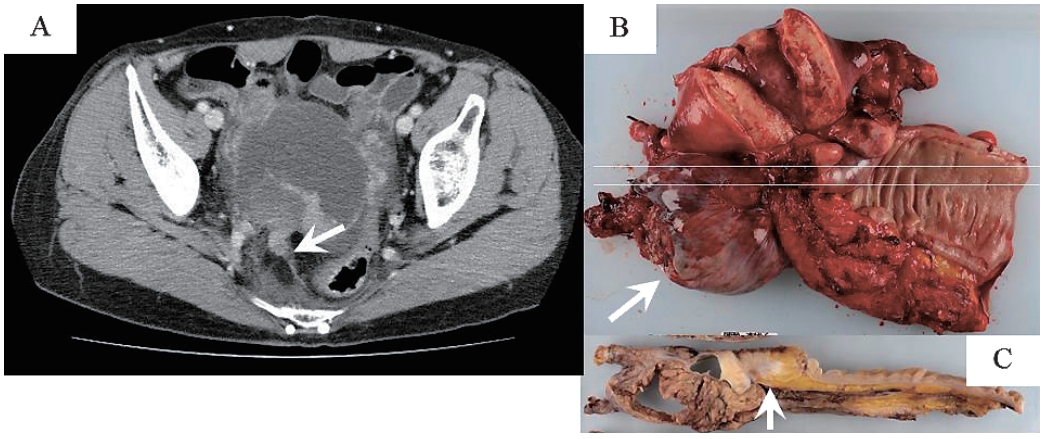

Fig. 3 Abdominal computed tomography shows right ovarian recurrence in the pelvic portion (upper white arrow, A), recurrence in the pouch of Douglas (lower white arrow, A), the resected right ovary (B), and the carcinoma in the cleavage plane (C).

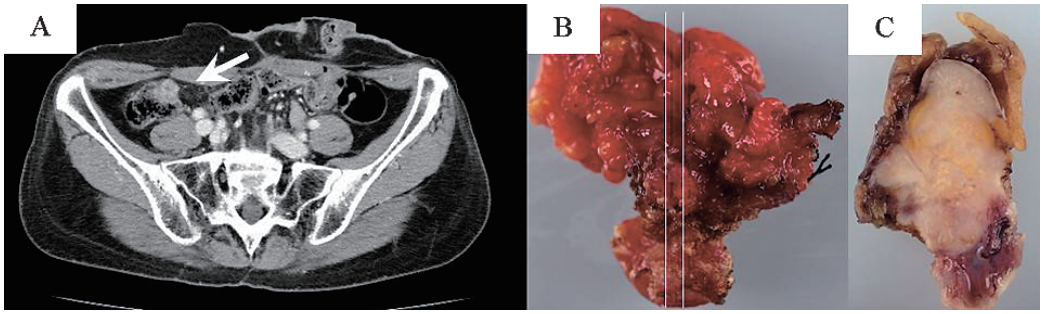

Fig. 4 Abdominal computed tomography shows a recurrent lesion attached to the ascending colon (A), the resected specimen (B), and the carcinoma in the cleavage plane (C).

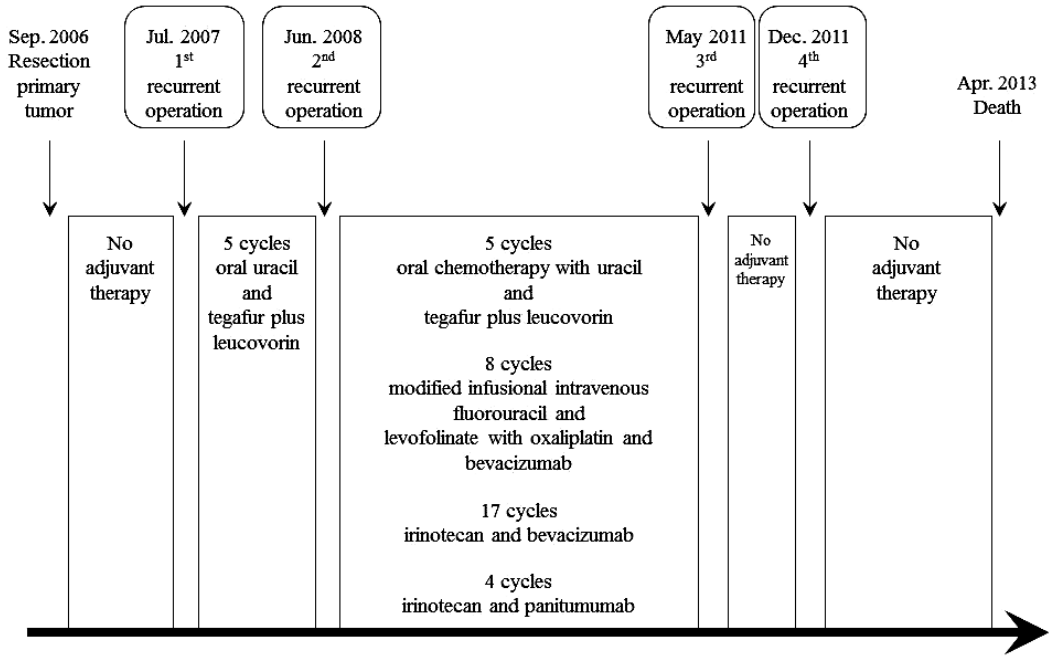

Fig. 5 This fugure shows the clinical courses.

were administered.[4) 5)] After approximately 5 years from the first operation, CT showed one peritoneal recurrence on the uterus and right ovarian recurrence (Figure 3 A). In May 2011, in the third recurrent operation, one peritoneal recurrence on the uterus and right ovarian recurrence were removed by bilateral adnexectomy and Hartmann's procedure (Figure 3 B, C). After the operation, no adjuvant therapy was administered.

After approximately 6 years from the first operation, CT showed one peritoneal recurrence in the ascending colon (Figure 4 A). In December 2011, during the fourth recurrent operation, one peritoneal recurrence in the ascending colon was removed by partial resection of the colon wall (Figure 4 B, C).

Approximately 1 year from the fourth recurrent operation, multiple peritoneal recurrent lesions

were detected on positron emission tomography. The patient did not desire further aggressive treatment. Eventually, a long-term survival of 6 years and 7 months from the first operation was obtained. The duration of "No adjuvant therapy" accounted for about 50% in all clinical courses (Figure 5).

DISCUSSION

No previous reports have described frequent resections for frequent peritoneal recurrences in colorectal cancer. In many instances, the use of chemotherapy for treating recurrences in multiple organs, e.g. liver and peritoneum, has been reported.[6] Our case is the first report to describe four resection operations for frequent peritoneal recurrences in a single patient. In this regard, it is worthwhile to describe the surgical situation and postoperative course in detail.

There are no clear guidelines regarding the optimal regimen for colorectal recurrences; however, in Japan, the JSCCR Guidelines 2015 for the Treatment of Colorectal Cancer states the following.

"If recurrence is observed in a single organ and complete surgical resection of the recurrent tumor(s) is possible, resection is strongly considered." "If recurrence is observed in more than a single organ, resection can be considered if the recurrent tumors in all of the organs are resectable; however, there is no consensus on the effects of treatment.".[2] Accordingly, in our case, a maximum of four recurrent lesions were recognized at a single time, and it was therefore thought possible to resect the same. Consequently, R0 status (no cancer) was obtained after each operation.

The postoperative course noted in this case is possibly very rare; thus, it is possible that either this patient's cancer showed low malignant potential or the frequent resection of peritoneal recurrences carried a good prognosis. The duration of "No adjuvant chemotherapy" accounted for about 50% in all clinical courses. And this evidence suggests that the frequent and multiple peritoneal recurrences could be considered an option of aggressive resection for improved long-term survival.

In recent years, the advancement of anticancer drugs led to a significant underestimation of operative treatment, but our case appreciated that the surgical resection was among the most efficacious therapeutic approach in recurrent resectable colorectal cancer. Especially in terms of an optimal time of surgical resection, our case suggested that it was better to excise as soon as possible after detection of resectable peritoneal recurrences. The aggressive frequent resection made an important contribution to prevent the patient from ileus due to compression of peritoneal recurrences during the course.

Similarly, Ozawa *et al.* reported that few patients with peritoneal carcinomatosis from colorectal cancer survive for more than 5 years, and performing R0 resection with curative intent in association with postoperative adjuvant chemotherapy should be considered in appropriately selected patients.[1]

However, most cases of peritoneal recurrence cannot be resected perfectly. In such cases, instead of complete resection, cytoreductive surgery is a potentially effective strategy. Cravioto-Villanueva *et al.* reported that cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) is feasible and safe.[7] Bretcha-Boix *et al.* reported that cytoreductive surgery combined with HIPEC is a feasible technique that might increase patient survival.[8] This treatment protocol represents a potential cure for selected patients for whom no other alternatives are available. Our hospital is not equipped with the HIPEC system; therefore, in the present case, conventional adjunctive chemotherapy was selected. If the HIPEC system were available, further

prolonged survival may be achieved.

In conclusion, we consider that in patients with colorectal cancer, the occurrence of frequent and multiple peritoneal recurrences that can be resected could be aggressively treated by surgical removal for improved long-term survival.

CONFLICTS OF INTEREST

All authors certify that they have no personal financial oinstitutional interest in the subject matter, materials, or drugs in this article.

REFERENCES

1) Ozawa H, Kotake K, Kobayashi H, Kobayashi H, Sugihara K. Prognostic factors for peritoneal carcinomatosis originating from colorectal cancer: an analysis of 921 patients from a multi-institutional database. *Surg Today,* 2014; 44: 1643–1650.
2) Watanabe T, Itabashi M, Shimada Y, Tanaka S, Ito Y, Ajioka Y, *et al.* Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for treatment of colorectal cancer. *Int J Clin Oncol,* 2015; 20: 207–239.
3) Shimada Y, Hamaguchi T, Mizusawa J, Saito N, Kanemitsu Y, Takiguchi N, *et al.* Randomised phase III trial of adjuvant chemotherapy with oral uracil and tegafur plus leucovorin versus intravenous fluorouracil and levofolinate in patients with stage III colorectal cancer who have undergone Japanese D2/D3 lymph node dissection: final results of JCOG0205. *Eur J Cancer,* 2014; 50: 2231–2240.
4) Nishina T, Takano Y, Denda T, Yasui H, Takeda K, Ura T, *et al.* A phase II clinical study of mFOLFOX6 plus bevacizumab as first-line therapy for Japanese advanced/recurrent colorectal cancer patients. *Jpn J Clin Oncol,* 2013; 43: 1080–1086.
5) Yamada Y, Takahari D, Matsumoto H, Baba H, Nakamura M, Yoshida K, *et al.* Leucovorin, fluorouracil, and oxaliplatin plus bevacizumab versus S-1 and oxaliplatin plus bevacizumab in patients with metastatic colorectal cancer (SOFT): an open-label, non-inferiority, randomised phase 3 trial. *Lancet Oncol,* 2013; 14: 1278–1286.
6) Asano T, Negita M, Uemura T, Takagi D, Hattori M, Kamiya I. A case report of advanced mucinous adenocarcinoma of the transverse colon with peritoneal dissemination effectively treated by multidisciplinary approach with a focus on FOLFOX4 therapy combined with panitumumab. *Gan To Kagaku Ryoho,* 2012; 39: 1147–1149.
7) Cravioto-Villanueva A, Cavazos M, Luna-Perez P, Martinez-Gomez H, Ramirez M. L, Solorzano J, *et al.* Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) delivered via a modified perfusion system for peritoneal carcinomatosis of colorectal origin. *Surg Today,* 2016; 46: 979–984.
8) Bretcha-Boix P, Farre-Alegre J, Sureda M, Dussan C, Perez Ruixo JJ, Brugarolas Masllorens A. Cytoreductive surgery and perioperative intraperitoneal chemotherapy in patients with peritoneal carcinomatosis of colonic origin: outcomes after 7 years' experience of a new centre for peritoneal surface malignancies. *Clin Transl Oncol,* 2010; 12: 437–442.