

Complete Response after Treatment with UFT/LV Regimen for Liver and Lung Metastases of Rectal Cancer: A Case Report

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Abstract

A 72-year-old woman was diagnosed with Borrmann type I and II tumors in the rectosigmoid colon by colonoscopy. Whole-body Computed Tomography (CT) revealed two 1-cm masses on both lungs; however, no mass was observed in the liver. The patient underwent low anterior resection for the treatment of colorectal cancer. One month after surgery, her serum Carcinogenic Embryonic Antigen levels had doubled (283 ng/mL) compared with that at surgery; therefore, contrast-enhanced CT revealed liver metastatic lesions at segments 2 and 5. For her advanced colorectal cancer with lung and liver metastases, five cycles of chemotherapy consisting of infusional irinotecan, *I*-LV, and a bolus injection of 5-FU on day 1 followed by oral UFT and LV on days 1-7 were continued until the patient could not endure the adverse effects in the gastrointestinal tract. This regimen was chosen with the intention of reducing the infusional administration of drugs. Subsequently, an oral regimen of UFT/LV was initiated at the outpatient clinic. Twelve months later, CT revealed the disappearance of lung and liver lesions, and her serum CEA levels had returned to normal; therefore, the patient was considered to exhibit a Complete Response (CR). The chemotherapy was subsequently discontinued at the patient's request and she has maintained CR for over a year.

Keywords: Colorectal cancer, Chemotherapy, UFT/LV regimen

Introduction

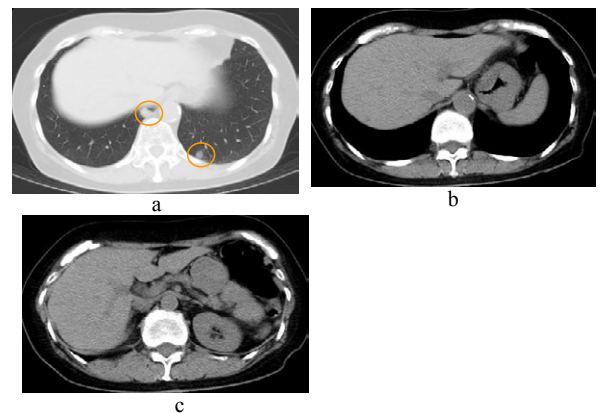
For advanced colorectal cancer, the combination of 5-FU, CPT-11, and oxaliplatin (termed as FOLFOX or FOLFIRI therapy) with the additional use of bevacizumab, is recommended as a standard therapy. Generally, 5-FU monotherapy is recommended in the treatment of relatively slowly progressing advanced colorectal cancer, which is equivalent to group 3 of colorectal cancer according to the ESMO guidelines [1]. However, the best proper use of this therapy remains to be identified. Here, we report a case of complete response after treatment with prolonged UFT/LV regimen for liver and lung metastases of rectal cancer.

Case Presentation

A 72-year-old woman visited our institution at the beginning of October 2007 with a complaint of bloody stools. She had no significant current or past medical history. Neither of her parents had a history of cancer. The following were observed on physical examination: cognitive consciousness, alert; height, 150 cm; weight, 45 kg; body mass index, 20 kg/m²; and body surface area, 1.37m². The abdomen was soft and flat with normal bowel sounds, and slight tenderness was observed over the upper abdomen. No lymph nodes were palpable, and no lumps or tumors were identified on rectal examination. Blood chemistry analyses revealed markedly increased Carcinogenic Embryonic Antigen (CEA) (105.9 ng/mL) levels.

Whole-body Computed Tomography (CT) revealed two 1-cm masses at the periphery of segment 10 on both lungs (Figure 1a); however, no mass was observed in the liver (Figure 1b and 1c). Colonoscopy revealed Borrmann type I and II tumors in the rectosigmoid colon. Biopsy specimens revealed moderately-differentiated tubular adenocarcinoma. The patient underwent low anterior and D2 lymph node resection for the colorectal cancer in mid-October 2007. With regards to masses on lungs, there was little evidence of metastases of the colorectal cancer; therefore, meticulous follow-ups by CT were scheduled without making excision at this time.

During surgery, no ascites or peritoneal dissemination was observed. The following tumors were observed in the rectosigmoid (Figure 2a) one 2×2 cm of type I tumor, one 2×2.5 cm of type II tumor, and four



Bilateral lung metastases are evident in both lower lungs (a). Liver tumors are not evident (b,c)

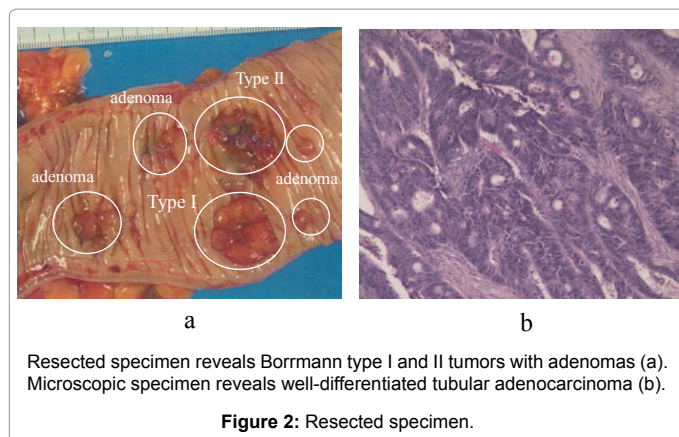
Figure 1: Noncontrast abdominal computed tomography in October 2007.

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adenomas on the oral side. Pathological examination (Figure 2b) of the type I and II tumors confirmed the diagnosis of a moderately-differentiated adenocarcinoma of pT3 (ss), ly1, and v0 and pT2 (mp), ly0, and v0, respectively. Although the postoperative course was uneventful, at 1 month after surgery, serum CEA levels had doubled (283 ng/mL) compared with those at surgery.

To evaluate recurrent versus de novo metastases, contrast-enhanced abdominal CT revealed metastatic liver lesions at segments 2 and 5. Therefore, chemotherapy using IFL/UFT [2], which consists of infusional irinotecan (198 mg), l-LV (266 mg), and a bolus injection of 5-FU (525 mg) on day 1 followed by oral UFT (400 mg) and sLV (75 mg/day) on days 1-7, was initiated. Soon thereafter, the patient was afflicted with gastrointestinal symptoms, including nausea, vomiting, and diarrhea, which was considered as grade 3 according to CTCAE ver4.0. The IFL/UFT was continued for five cycles, but the patient could not tolerate its adverse effects. In February 2008, CT revealed the appearance of a metastatic lesion in segment 7 of the liver along with the disappearance of left metastatic lesions in the lungs and a reduced lesion size in segment 1 of the liver (Figure 3b). Subsequently, considering the patient's wishes, oral chemotherapy was initiated at the outpatient clinic to control adverse effects from January 2008; UFT (300 mg/day) and LV (75 mg/day) were administered for a week day followed by 3 weekend days off at the outpatient clinic.

Thereafter, in April 2008, CT revealed the disappearance of bilateral metastatic lesions in the lungs and in segment 1 of the liver along with a reduced lesion size in segments 5 and 7 (Figure 3c). Serum CEA levels had returned to normal (2.8 ng/mL). At this time, we recommended resection of the metastatic lesions of the liver and lung, but the patient did not consent to surgical treatment. Therefore, the same oral chemotherapy regimen was continued through the outpatient clinic.

In February 2009, follow-up CT revealed the disappearance of all of the metastatic lesions (Figure 3d). In June 2012, follow-up CT revealed no metastatic lesions in the lungs and liver (Figure 3e). Moreover, fluorodeoxyglucose positron emission tomography (FDP-PET) performed in November 2012 revealed no abnormal uptakes by the lung, liver, or remaining sigmoid colon; therefore, CR was confirmed. In addition, serum CEA levels were within the normal range (2.5 ng/mL); therefore, chemotherapy was discontinued on the patient's request. Over a year has passed since the discontinuation of chemotherapy, and the patient has maintained CR without recurrence. The patient's treatment schedule and serum CEA levels are shown in Figure 4.

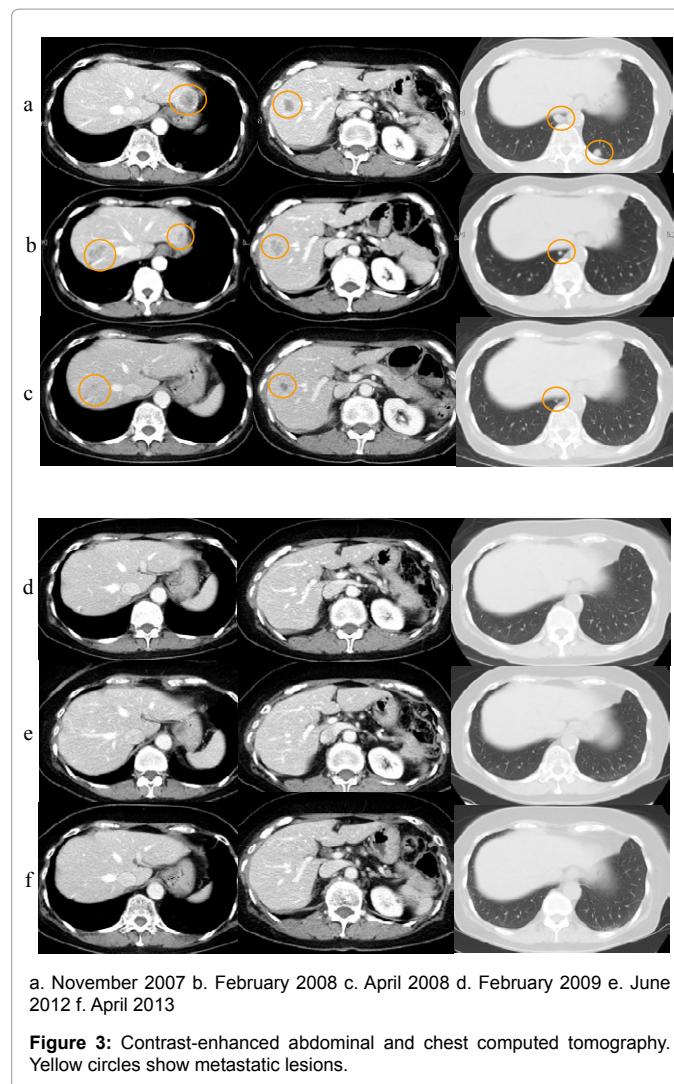
In our case, although the amount of UFT was lower than the

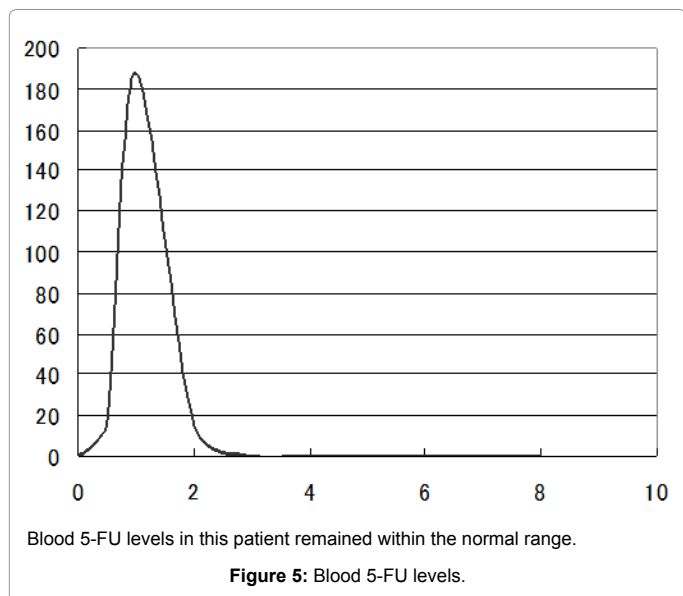
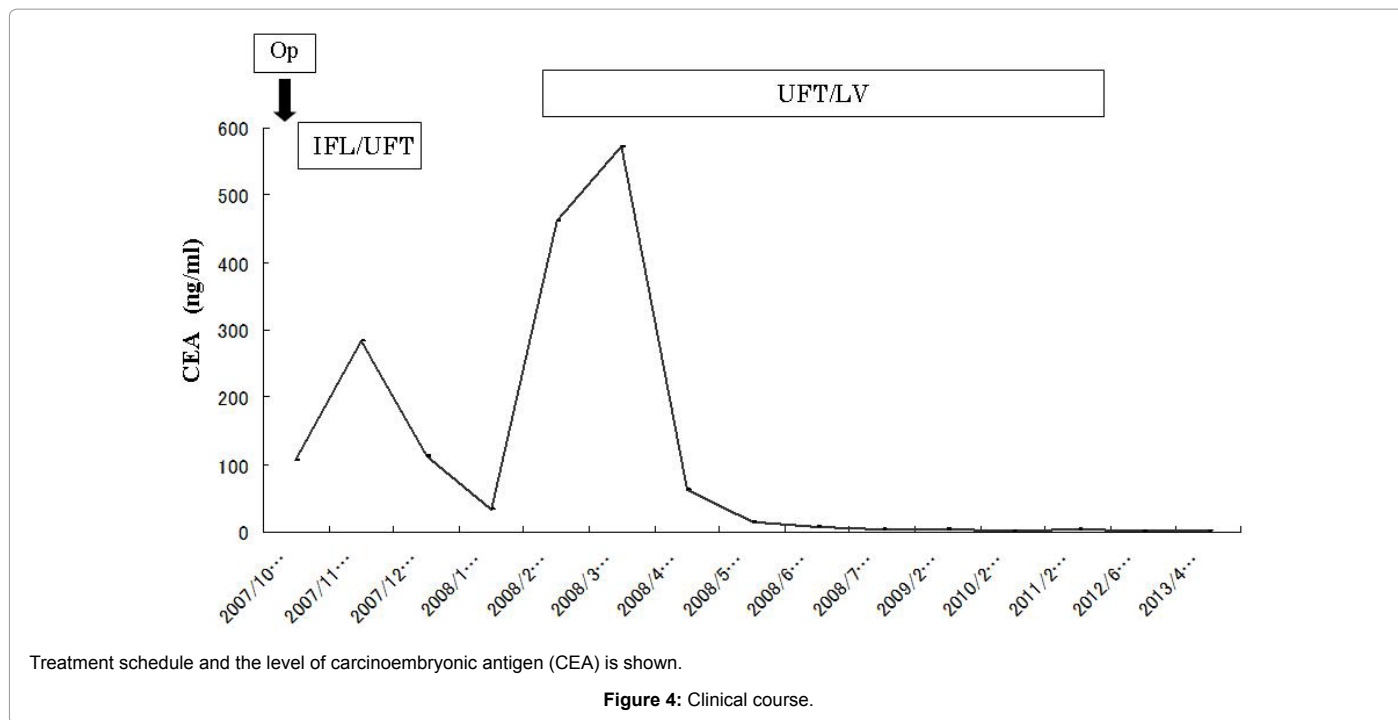
recommended amount (300mg/m²), the patient successfully achieved CR. We believed that the blood concentration of 5-FU may increase in association with a metabolic abnormality of dihydropyrimidine dehydrogenase (DPD); therefore we measured the blood concentration of 5-FU before and after its administration but found levels within the normal range (Figure 5).

Discussion

There have been a few case reports of advanced colorectal cancer in which CR was achieved using UFT/LV therapy [3]. Several CR cases included lung or liver metastases but not multiple distant metastases. It is still unclear if chemotherapy should be continued once CR is achieved. In cases in which chemotherapy is continued, a change in regimen should be considered. In cases of chemotherapy, deliberate and regular follow-ups with imaging studies and the measurement of CEA level should be conducted because there is no consensus or evidence of discontinuation of chemotherapy; further evidence is thus needed. In our case, the patient has been in CR for over a year despite discontinuing chemotherapy.

Adam et al. [4] reported that 4% of cases in which preoperative chemotherapy was administered prior to the resection of colorectal liver metastases achieved pathological CR. They also reported that the





characteristics of those cases included liver metastases of size <3 cm and CEA levels <30 ng/mL. In our case, the CEA level was markedly high before chemotherapy; however, the chemotherapy led to CR and a CEA level became within normal limits. As such, the CEA level before chemotherapy here differs from those in the other case reports.

Patients with colorectal cancer complicated by multiple lung or other distant metastases may not be candidates for surgical treatment. In our case, the number of lung and liver metastases was limited and their sizes were relatively small. Surgical treatment of the liver and lung metastases was recommended with the goal of curative resection, but the patient did not consent to surgical treatment. Despite this, the patient has been in CR without the use of anticancer agents and should

be carefully checked, with regular follow-up by imaging and blood analysis hereafter.

As a pyrimidine metabolism antagonist, 5-FU has a similar chemical structure to a metabolite that is necessary for cell division or proliferation and inhibits DNA synthesis by absorption into the cell. Moreover, it is easily metabolized in the body and has a short duration of action; therefore, its use has been limited to injections alone. On the other hand, UFT is a newly used oral agent that may have a longer duration of action. The effects and toxicity of anticancer drugs may exhibit individual variations: specifically, the action may vary if the medication is administered according to a patient's body surface area of a patient. This is probably because the actual activation of a drug-metabolizing enzyme differs among individuals. In particular, the pharmacokinetics of 5-FU-based anticancer drugs depends on the individual patient and varies with time [5]. This pharmacokinetic activity is thought to be associated with DPD levels [6]. In our patient, the measured 5-FU blood concentrations before and after its administration were within the normal range. Some underlying mechanisms regarding the successful achievement of CR after the use of lower amounts of UFT or metabolic abnormalities of DPD remain to be solved.

Conclusion

Here we presented a case of CR after treatment with an oral UFT/LV regimen for liver and lung metastases from colorectal cancer. In this case, UFT/LV therapy was efficient; moreover, the patient has maintained a successful CR after the discontinuation of chemotherapy. There may be cases in which 5-FU doses lower than the recommended amounts could effectively lead to CR through an unknown mechanism.

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