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Case Report

Complete Response of Pulmonary Metastases from Rectal Cancer to Tegafur-Uracil/Leucovorin plus Bevacizumab in an Elderly Patient: A Case Report

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Keywords
Colorectal cancer · Chemotherapy · Tegafur-uracil/leucovorin plus bevacizumab · Elderly patient · Complete response

Abstract
As a result of recent major advances in chemotherapy for metastatic colorectal cancer, the prognosis for patients with metastatic colorectal cancer has improved. However, elderly patients often cannot receive intensive therapy. There are still many problems to solve regarding treatment for elderly patients with metastatic colorectal cancer. We herein report a case of complete response of pulmonary metastases from rectal cancer to tegafur-uracil (UFT)/leucovorin (LV) + bevacizumab (Bmab) in an elderly patient. An 80-year-old woman who had undergone curative surgery for rectal cancer 5 years ago was diagnosed with pulmonary metastases. Taking into account her advanced age and low renal function (creatinine clearance: 41.2 mL/min), UFT/LV + Bmab therapy was selected. The patient received UFT (300 mg/m^2/day) and LV (75 mg/day) on days 1–5, 8–12, and 15–19 and Bmab (7.5 mg/kg) on day 1. The treatment cycle was repeated every 21 days. Following 17 courses of treatment without adverse events, a complete response was observed. Furthermore, there was no recurrence within 6 months

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after the final course of therapy. This case indicates that UFT/LV + Bmab is suitable for the treatment of elderly patients with metastatic colorectal cancer.

Introduction

As a result of recent major advances in the treatment of metastatic colorectal cancer (mCRC), including the introduction of new cytotoxic and molecular-targeted therapies, the prognosis for patients with mCRC has improved. The median overall survival of patients with mCRC who receive the standard combination therapy of doublet/triplet chemotherapy and molecular-targeted therapy has been extended to approximately 30 months [1–4]. However, these results were based on large clinical trials including only a few elderly patients. Therefore, whether or not an intensive standard regimen is suitable for elderly patients with mCRC remains unclear, and many problems persist regarding the treatment for elderly patients with mCRC.

In this situation, clinical trials of less-toxic regimens (e.g., combination of fluoropyrimidine monotherapy and antiangiogenic therapy, such as tegafur-uracil [UFT]/leucovorin [LV] + bevacizumab [Bmab] and capecitabine + Bmab) for elderly patients with mCRC have been conducted [5, 6]. The results of these clinical trials have indicated that the combination of fluoropyrimidine monotherapy and antiangiogenic therapy is an effective and well-tolerated regimen for elderly patients with mCRC.

Case Report

An 80-year-old woman who had undergone abdominoperineal resection of the rectum and lymph node dissection for stage II rectal cancer was found to have a small pulmonary nodule 5 years after the surgery (Fig. 1). Although there was a possibility that the nodule was a pulmonary metastasis, qualitative diagnosis of the nodule was difficult because the nodule was very small and equivocal. Therefore, the patient adopted a wait-and-see approach. Six months later, the patient was diagnosed with pulmonary metastases when computed tomography showed that the nodule had grown and become clearer and new pulmonary nodules had appeared (Fig. 2). Although the Eastern Cooperative Oncology Group performance status was 0 [7], the patient was 80 years old and her creatinine clearance was 41.2 mL/min; therefore, an intensive standard regimen with the possibility of severe adverse events was deemed to be inappropriate.

Given her advanced age and impaired renal function, the patient instead received UFT/LV + Bmab therapy (UFT [300 mg/m^2/day] and LV [75 mg/day] on days 1–5, 8–12, and 15–19, and Bmab [7.5 mg/kg] on day 1). The treatment cycle was repeated every 21 days. Following 17 courses of treatment without adverse events, the pulmonary metastases disappeared, and no new lesions were detected by computed tomography (Fig. 3). In addition, tumor markers such as CEA and CA19-9 were within their normal range. A complete response was observed. Furthermore, there was no recurrence within 6 months after the final course of therapy.

Discussion

In previous phase III clinical trials, combinations of doublet/triplet chemotherapies (such as FOLFOX, CapeOX, FOLFIRI, and FOLFOXIRI) and molecular-targeted therapies (such as Bmab, cetuximab, and panitumumab) were revealed to have excellent treatment outcomes (median overall survival: 24.3–41.3 months; median progression-free survival: 9.7–13.0 months; objective response rate: 53.1–65.1%) [1–4, 8]. While these intensive treatments are regarded as the standard regimens for mCRC around the world [9–11], they can cause severe adverse events. Indeed, the incidence of grade 3 or worse adverse events has been reported to be 53–91% [1–3, 12]. In elderly patients in particular, there is a high probability of severe adverse events, as elderly people often have a deteriorated internal organ function and severe comorbidities. Therefore, physicians may hesitate to treat elderly patients with this intensive standard regimen.

In previous reports, UFT/LV + Bmab and capecitabine + Bmab were reported as effective and well-tolerated treatment options for elderly patients with mCRC [5, 6]. In the present case, given the patient's advanced age and impaired renal function, the combination of fluoropyrimidine monotherapy + Bmab was deemed to be appropriate.

Nishina et al. [5] conducted a phase II study of UFT/LV + Bmab in elderly patients with mCRC and demonstrated its efficacy and safety. The overall response rate was 40%, the median progression-free survival was 8.2 months, and the median overall survival was 23 months. This treatment outcome was not markedly inferior to that using the standard regimen. Furthermore, the grade 3 or 4 toxicities observed were hypertension in 12%, fatigue in 8%, anemia in 8%, nausea in 6%, and diarrhea in 6%, indicating that the toxicity of this regimen was generally mild, even in elderly patients. These results established UFT/LV + Bmab as a suitable therapeutic option for elderly patients with mCRC.

Capecitabine + Bmab is also a therapeutic option for elderly patients with mCRC. Cunningham et al. [6] reported that the overall response rate was 19%, the median progression-free survival was 9.1 months, and the median overall survival was 20.7 months. The efficacy of capecitabine + Bmab was not inferior to that of UFT/LV + Bmab. However, an appropriate reduction of the dosage of capecitabine is necessary for patients with an impaired renal function, as an impaired renal function was reported to increase the risk of early severe toxicity [13]. In contrast, UFT/LV can be administrated at the standard dosage even in cases of mild renal dysfunction (serum creatinine levels <1.5 mg/dL) [5]. In addition, hand-foot syndrome, which may reduce the quality of life, is frequently observed when using capecitabine [6], but is rarely observed when using UFT/LV [5]. In the present case, after treatment without adverse events for 1 year, a complete response was observed.

Continuing chemotherapy without severe adverse events is indispensable for obtaining a good clinical outcome; sporadic or discontinued treatment will not lead to a good clinical outcome, even if the regimen is expected to have a strong therapeutic effect. Therefore, it is very important to choose a regimen with a relatively low risk of side effects for elderly patients.

In conclusion, the success in the present case indicates that UFT/LV + Bmab is a useful therapeutic option for elderly patients with mCRC, especially those with an impaired renal function, in terms of both its efficacy and safety.

Statement of Ethics

Written ethical approval for the publication of the present case report was obtained from the patient.

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

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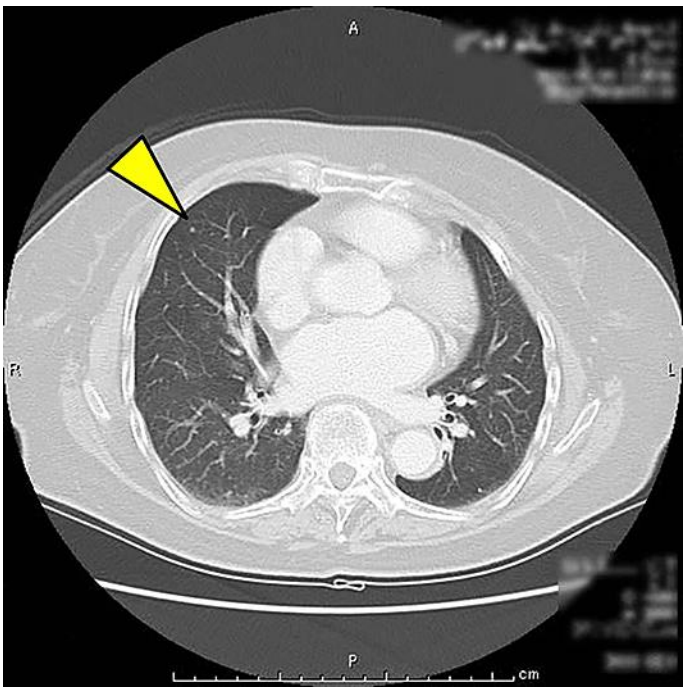

Fig. 1. Computed tomography showed a small pulmonary nodule (arrowhead; tumor diameter: 3 mm).

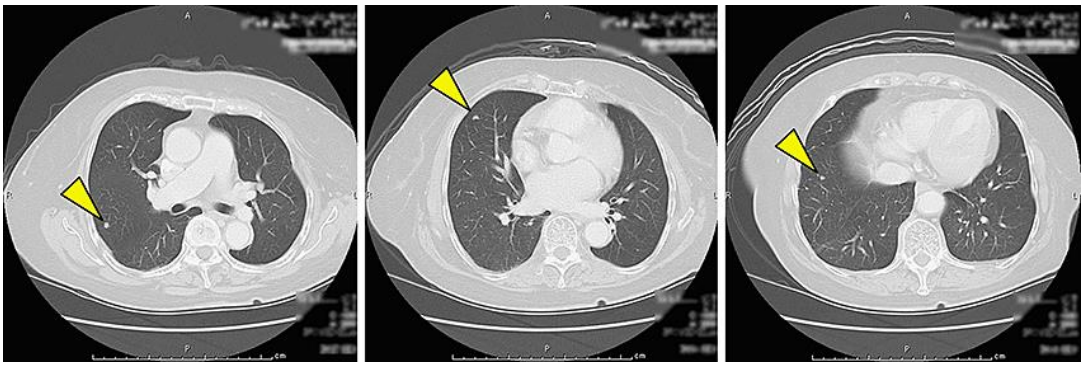

Fig. 2. Six months after the small pulmonary nodule had been detected, computed tomography showed that the nodule had grown and become clearer, and new pulmonary nodules had appeared (arrowheads; tumor diameters: 6, 7, and 5 mm, respectively).

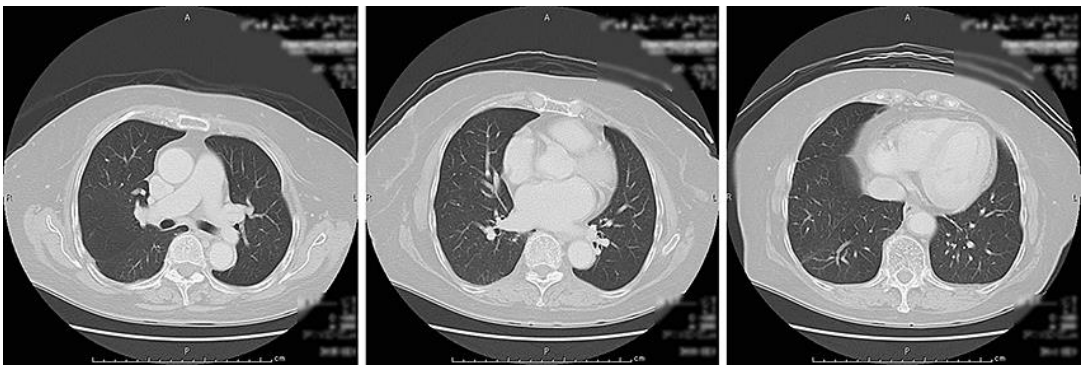

Fig. 3. After 17 courses of treatment, the pulmonary metastases had disappeared, and no new lesions were detected by computed tomography.