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Case Report

A Case of Marked Response to Preoperative Chemoradiotherapy for Rectal Cancer With Para-Aortic Lymph Node Metastasis

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A 67-year-old man had rectal cancer with para-aortic lymph node metastasis. Prior to surgical resection, tegafur-uracil and leucovorin had been administered orally as chemotherapy, and radiotherapy (50.4 Gy) was applied for the rectum and para-aortic lymph nodes. Low anterior resection was then performed, followed by 45 cycles of chemotherapy in total. Enlargement of the left axillary lymph nodes was noted during treatment, but nodes shrank in response to treatment with bevacizumab + FOLFIRI (*i.e.*, irinotecan + 5-fluorouracil/leucovorin). As of the time of writing, 36 months after diagnosis, no swelling of the para-aortic lymph nodes was evident and chemotherapy was being continued. This patient was alive after achieving response to neoadjuvant therapy comprising chemotherapy and irradiation of the para-aortic lymph nodes, along with postoperative chemotherapy. This therapeutic approach of preoperative chemotherapy plus irradiation of the primary lesion and para-aortic lymph nodes has potential as an effective treatment.

Key words: Rectal cancer – Chemoradiotherapy – Para-aorta lymph node – Complete response – Bevacizumab

Radiotherapy contributes to lowering the local recurrence rate after surgical resection of rectal cancer.[1] Moreover, chemoradiotherapy that includes chemotherapy as a radiosensitizer can also reduce the local recurrence rate and increase the survival rate.[2] We report herein the case of a patient who was diagnosed with rectal cancer and para-aortic lymph node metastasis and who remains alive today after having undergone preoperative chemoradiotherapy followed by long-term postoperative chemotherapy. Numerous reports have described the use of pelvic cavity irradiation to treat rectal cancer; however, to our knowledge, the application of preoperative radiotherapy to both the pelvis and para-aortic

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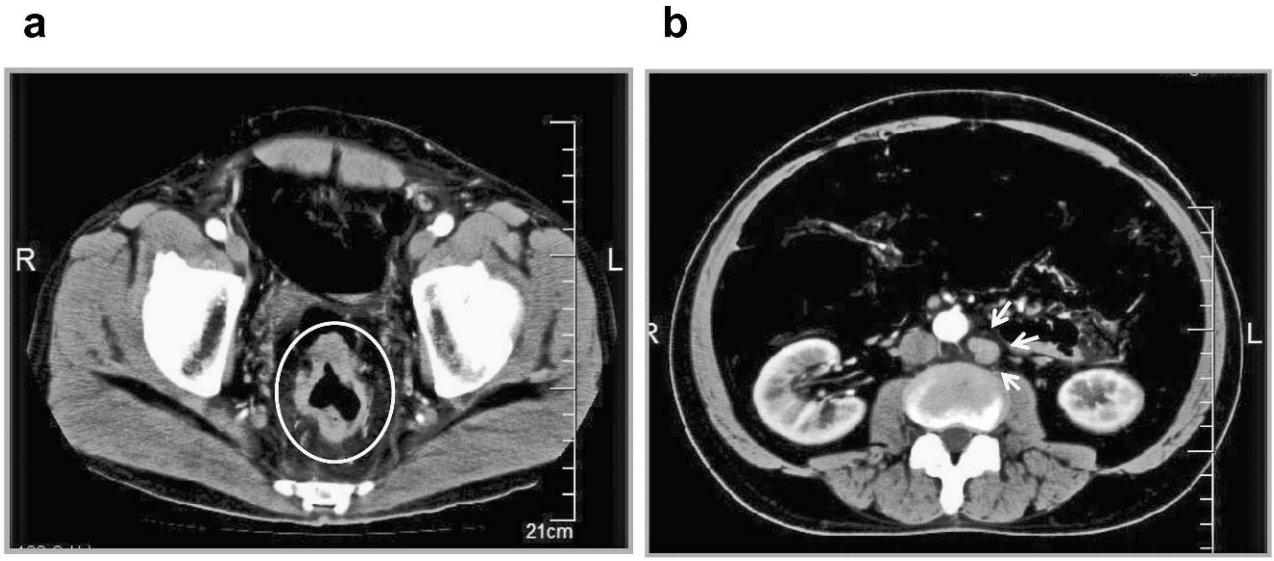

Fig. 1 CT findings. (a) CT taken prior to chemoradiotherapy, showing thickening of the rectal wall and swelling of the surrounding lymph nodes (encircled). (b) Para-aortic lymph node metastasis is also seen (arrows).

lymph nodes does not appear to have been described.

Case Report

A 67-year-old man experienced bloody stools and difficulty in defecating beginning in July 2007, and he was hospitalized for detailed testing and examination. At the time of admission, testing for tumor markers showed carcinoembryonic antigen (CEA) at 69.4 ng/mL and CA19-9 at 152.0 U/mL. Computed tomography (CT) revealed thickening of the rectal wall with swelling of the surrounding lymph nodes (Fig. 1a), along with enlargement of the para-aortic

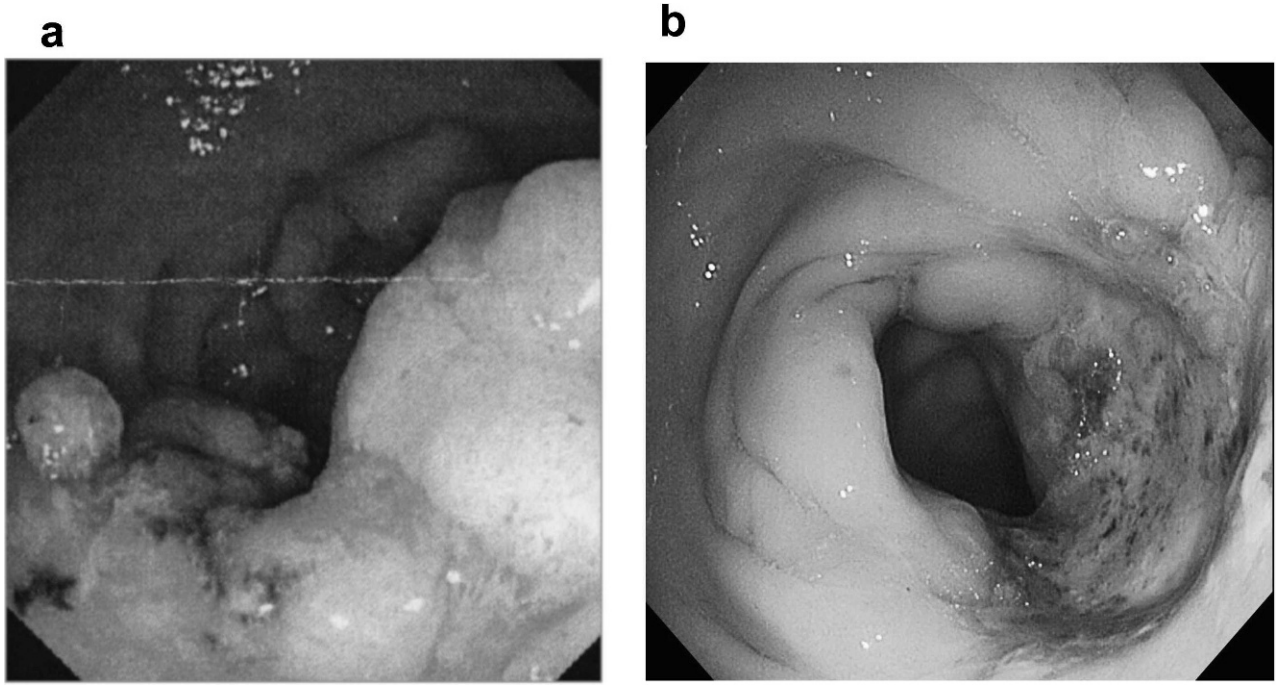

Fig. 2 Colonoscopy. (a) Lower gastrointestinal endoscopy shows a neoplastic lesion 4 cm from the anal verge. (b) After completion of the chemoradiotherapy, lower gastrointestinal endoscopy showed that the rectal tumor had shrunk in size.

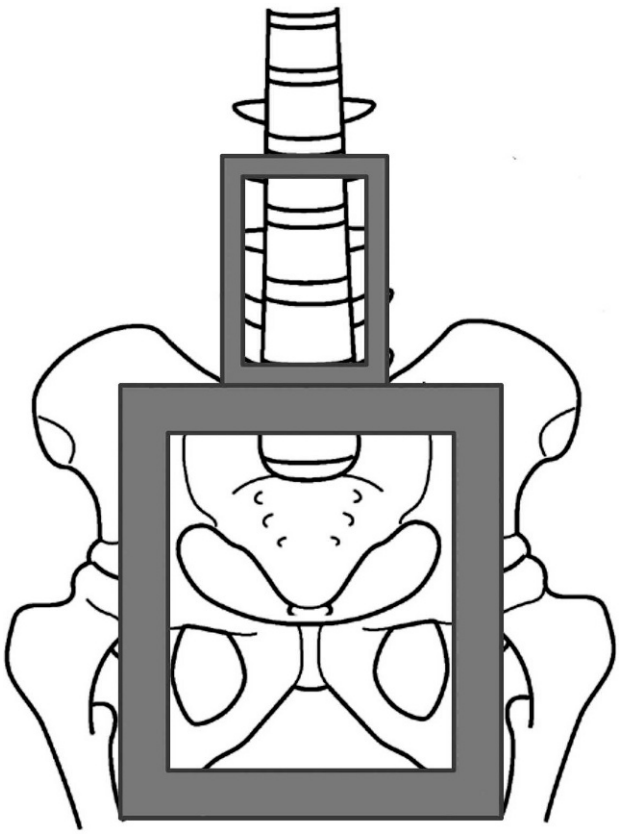

Fig. 3 The field of irradiation used in radiotherapy. The radiation field for the primary tumor in the rectum had the upper border at L5/S1. The radiation field for the para-aortic lymph nodes had the upper border at L2.

lymph nodes from the renal artery bifurcation to around the inferior mesenteric artery bifurcation (Fig. 1b). Barium enema radiography revealed a neoplastic lesion in the lower rectum. Lower gastrointestinal endoscopy found a neoplastic lesion in the rectum, 4 cm from the anal verge (Fig. 2a). Adenocarcinoma (tublar adenocarcinoma [tub2]) was identified on the basis of biopsied tissue. Prior to performing surgical resection, the patient was orally administered tegafur-uracil and leucovorin as chemotherapy, and radiotherapy (50.4 Gy) was applied to the rectum and para-aortic lymph nodes (Fig. 3). After completion of this chemoradiotherapy, endoscopic examination found that the rectal tumor had shrunk (Fig. 2b); therefore, low anterior resection was performed. Histopathologic diagnosis of the postoperative specimen identified a T2 N1 M1, stage IV tumor.

Beginning from 3 months after surgery, mFOLFOX6 (*i.e.*, oxaliplatin + 5-fluorouracil/leucovorin) monotherapy was administered twice, then administration of bevacizumab (BV) + mFOLFOX6 was started. After the fifth dose, the para-aortic lymph node metastatic lesions were judged to have been reduced in size in accordance with Response Evaluation Criteria in Solid Tumors,[3] and this was rated as a partial response. Upon completion of 15 doses, response had become a complete response (CR; Fig. 4). CR was maintained thereafter. However, frequent defecation had manifested after surgery, and perianal skin ulceration was observed. Continued administration of BV was suspected to be contributing to delayed healing of the skin wound, so the therapeutic regimen was changed to mFOLFOX6 monotherapy after the 20th dose of BV + mFOLFOX6. CT performed 2 months after BV withdrawal did not reveal any striking changes in the para-aortic lymph nodes, but enlargement of left axillary lymph nodes raised a suspicion of new metastases. Transverse colostomy was performed in February 2009. BV was withheld for a total of 4 months, then it was restarted, and a change was made to the BV + FOLFIRI combination, which was administered 25 times. No swelling of the para-aortic lymph nodes has been seen since, and the left axillary lymph nodes have shown a tendency to shrink. Figure 5 shows the time course of changes in the CEA tumor marker levels. Chemotherapy is being continued as of the time of writing, 3 years after the diagnosis of rectal cancer with para-aortic lymph node metastasis.

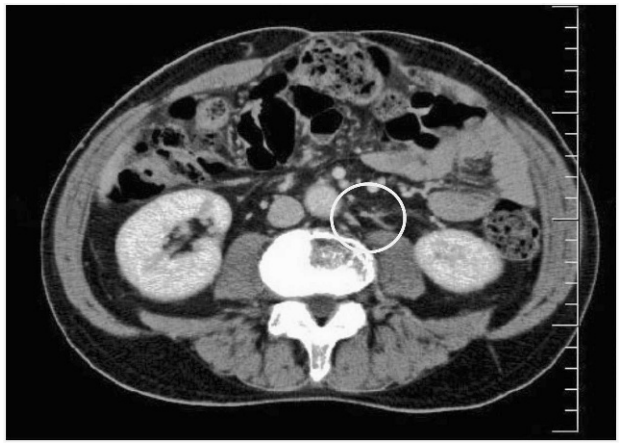

Fig. 4 CT findings. The para-aortic lymph nodes are seen to have been reduced in size (encircled) upon completion of 15 doses of BV + mFOLFOX6.

Discussion

Preoperative chemoradiotherapy is employed widely in Europe and the United States to treat rectal

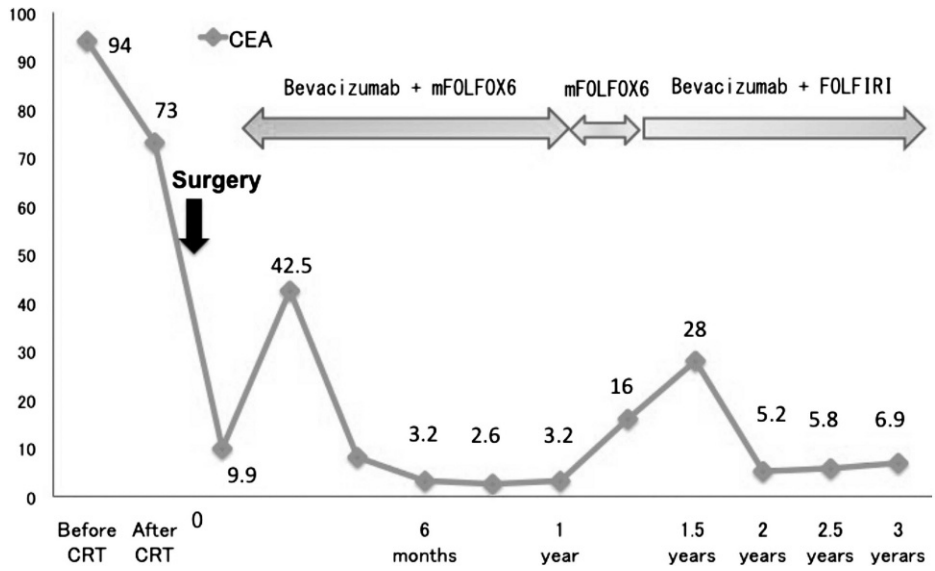

Fig. 5 Time course of changes in levels of CEA, a tumor marker.

cancer, with the objectives of expanding the indications for surgical resection by reducing the size of tumors and inhibiting local recurrence.[1,2] Previous studies have demonstrated that preoperative radiotherapy for rectal cancer lowers the local recurrence rate after surgery.[4,5] When chemotherapy is also administered, radiosensitivity of the tumor is heightened, the therapeutic effect of preoperative radiotherapy is increased, and postoperative local recurrence rate is additionally reduced.[6,7] Studies that compared the efficacy of radiotherapy alone and in combination with chemotherapy (5-fluorouracil + leucovorin) for T3 to T4 rectal cancer showed that the incidence of pathologic CR (pCR) was higher in the chemoradiotherapy group than in the radiotherapy-alone group.[6,7] In addition, postoperative 5-year local recurrence rates were lower in patients with radiotherapy combined with chemotherapy than those with radiotherapy alone.[6,7]

In the present case, the patient had advanced rectal cancer with para-aortic lymph node metastasis. Although preoperative radiotherapy or chemoradiotherapy has been shown to be effective as a neoadjuvant therapy for rectal cancer, there have been little data with regard to radiotherapy for para-aortic lymph node metastasis. Kim *et al*[11] administered stereotactic body radiotherapy, in which irradiation was performed under CT guidance, to para-aortic lymph nodes in addition to postoperative chemotherapy. They reported that, using a narrow irradiation field to treat 7 patients with para-aortic lymph node metastasis from colon cancer, no damage to normal tissues was seen, the 1-year survival rate was 100%, the 3-year survival rate was 71.4%, and the survival rate up to 37 months was increased.[11] In the present case, we performed radiotherapy for both the pelvic cavity and the para-aortic lymph node metastasis. These treatments have resulted in 3 year-survival, counting as of the time of writing. We think that this therapeutic approach of preoperative chemotherapy plus irradiation of the primary lesion and para-aortic lymph nodes has potential as an effective treatment for rectal cancer with para-aortic lymph node metastasis.

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