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Curative resection for locally advanced sigmoid colon cancer using neoadjuvant chemotherapy with FOLFOX plus panitumumab: A case report

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ABSTRACT

INTRODUCTION: FOLFOX and panitumumab combined chemotherapy plays an important role for metastatic colorectal cancer. However the usefulness of this regimen for neoadjuvant therapy is unclear.
CASE REPORT: A 67-year-old man with abdominal pain and pneumaturia was diagnosed with RAS wild-type sigmoid colon cancer with urinary bladder invasion and colovesical fistulas. Because the cancer was considered to be unresectable, a transverse-loop colostomy was performed. Colonoscopy and computed tomography revealed a marked reduction in the size of the primary tumor after six courses of FOLFOX4 (oxaliplatin, leucovorin, and 5-fluorouracil) plus panitumumab. Laparoscopic sigmoidectomy and partial cystectomy were then performed. The pathological findings based on the resected specimen showed almost complete replacement of the tumor by fibrous tissue, with only a few degenerated tumor glands persisting in the submucosa. The patient's postoperative course was uneventful and he was doing well, without disease recurrence, after 36 months of follow up.
CONCLUSION: To our knowledge, this is the first report of a successful curative resection in a patient with initially unresectable, locally advanced colorectal cancer who was treated with FOLFOX4 combined with panitumumab.

1. Introduction

Colorectal cancer (CRC) is one of the most commonly diagnosed malignancies in Japan, affecting over 100,000 individuals. It is also the third most common cancer worldwide, with up to 1 million new cases diagnosed each year [1].

Metastatic or postoperative adjuvant chemotherapy for patients with CRC is now internationally accepted as a standard therapy to improve outcome. Moreover, recent studies have demonstrated that preoperative chemotherapy improves the outcome of patients with CRC with liver metastases [2,3]. Nowadays there are some ongoing clinical trials that evaluate the efficacy of neoadjuvant approach in locally advanced colon cancer. [4–6] However, little is known about the effect and safety of preoperative chemotherapy for initially unresectable, locally advanced colon cancer without distant metastases.

Panitumumab (Pmab) is an epidermal growth factor receptor (EGFR)-targeted monoclonal antibody that has shown efficacy as monotherapy in phase III studies in patients with chemotherapy-refractory metastatic CRC [7]. It was also shown to improve patient outcome when added to standard chemotherapy, both first-line and subsequently [8].

Here we report the case of a patient with locally advanced sigmoid colon cancer with invasion of the bladder and colovesical fistulas in whom the tumor was radically resected after chemotherapy with FOLFOX4 plus Pmab.

2. Case report

A 67-year-old man was referred to our institute because of abdominal pain and pneumaturia. Colonoscopy showed a circumferential tumor of the sigmoid colon (Fig. 1a). The resulting constriction blocked passage of the endoscope. Initial computed

Abbreviations: CRC, colorectal cancer; Pmab, Panitumumab; EGFR, Epidermal growth factor receptor; CT, Computed tomography; PFS, Progression-free survival; OS, Overall survival.

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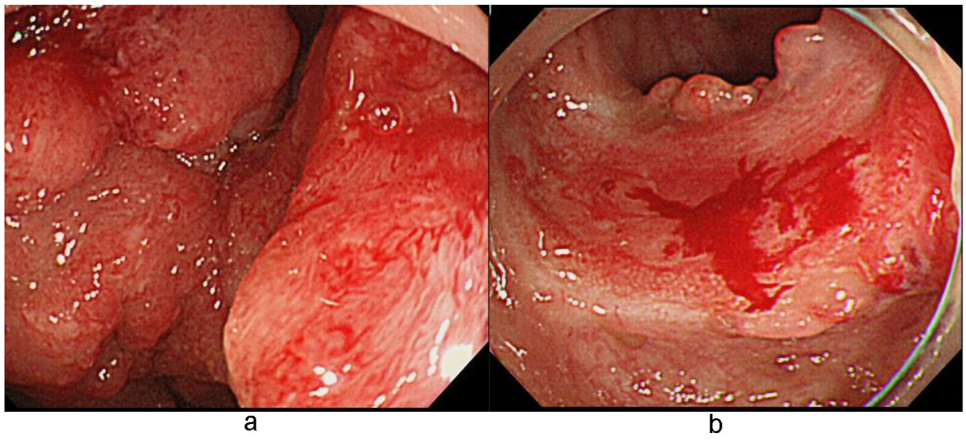

Fig. 1. (a) Colonoscopy before chemotherapy showed a circumferential tumor in the sigmoid colon, and biopsy specimens revealed moderately differentiated tubular adenocarcinoma. (b) Colonoscopy after chemotherapy showed an excellent response and the biopsies were negative for cancer cells.

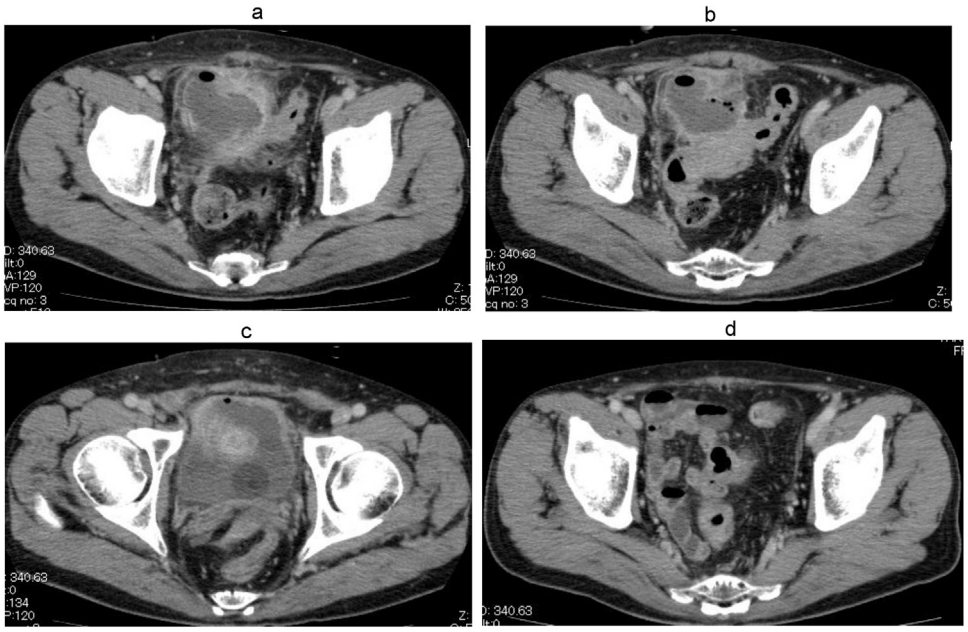

Fig. 2. (a–c)Initial computed tomography showed a circumferential thickening of the sigmoid colon wall and involving urinary bladder with a pelvic abscess and urinary air (colovesical fistula). (d) After six courses of chemotherapy showed improvement of pelvic abscess and marked reduction of the tumor.

tomography (CT) and magnetic resonance imaging showed a 4 cm × 4 cm tumor involving the urinary bladder, with a huge pelvic abscess, colovesical fistulas, and many swollen lymph nodes in the mesocolon but no distant metastasis (Fig. 2a–c).

Positron emission tomography-CT confirmed the primary tumor in the sigmoid colon and the absence of distant metastasis (Fig. 3). Microscopic examination of the tumor biopsy specimens revealed moderately differentiated tubular adenocarcinoma; the RAS status was wild-type. The patient was considered to have high-risk disease and curative resection was deemed not possible; instead, our multidisciplinary team recommended neoadjuvant chemotherapy. After undergoing a transverse-loop colostomy and improved inflammatory response caused by pelvic abscess, the patient received six courses of FOLFOX4 [oxaliplatin (85 mg/m^2 on day 1), leucovorin (100 mg/m^2 on days 1 and 2), and 5-fluorouracil (5-FU; 400 mg/m^2 as a bolus and 600 mg/m^2 as a 22-h continuous infusion on days 1 and 2)] plus Pmab (6 mg/kg) every 2 weeks. Grade 3 neutropenia, according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, developed during the last course of chemotherapy, but not febrile neutropenia

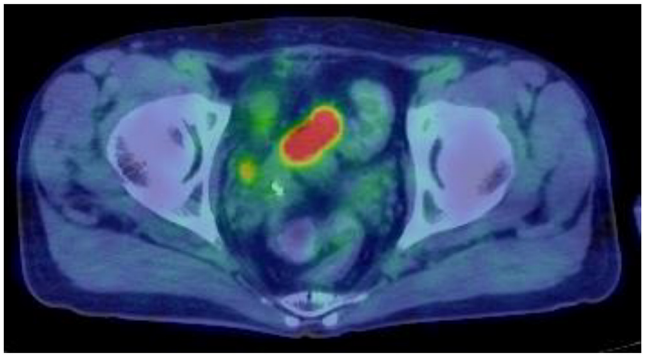

Fig. 3. PET-CT showed the primary tumor in the sigmoid colon.

or related infection. Colonoscopy and abdominal CT after systemic chemotherapy demonstrated marked tumor shrinkage, an improved pelvic abscess, and no mesocolon lymph node metastases (Figs. 1d and 2d). Biopsies of the sigmoid colon were negative for