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CASE REPORT

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A case of pathologic complete response after neoadjuvant triplet chemotherapy for locally advanced colon cancer with mismatch repair enzyme proficiency

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ABSTRACT

Patients with potentially resectable colon cancer and expected to have negative margins should undergo resection rather than neoadjuvant chemotherapy. Recent studies have suggested that neoadjuvant immunotherapy may be an option for tumors with mismatch repair enzyme deficiency (dMMR), but standard treatment for locally advanced colon cancer with mismatch repair enzyme proficiency (pMMR) is still unclear. A 37-year-old male patient was diagnosed with clinical stage IIIC (T4b N1a M0) transverse colon cancer. Mismatch repair proteins were proficient. After 3 cycles of oxaliplatin (85 mg/m^2, day 1), irinotecan (150 mg/m^2, IV, day 1), leucovorin (200 mg/m^2, IV, day 1), and 5-fluorouracil (3000 mg/m^2, 46 hours of continuous infusion initiating from day 1), there was a remarkable reduction in the tumoral mass on the abdominal computed tomography. A right hemicolectomy was performed. A pathologic complete response was obtained. Although there is no consensus on which patients are suitable for neoadjuvant therapy in pMMR locally advanced colon cancer, triplet chemotherapy may be a reasonable option in selected patients.

Key words: complete response, colon cancer, neoadjuvant, triplet chemotherapy

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Introduction

Locally advanced colon cancer is defined as the adhesion or invasion of the primary tumor into adjacent structures and organs [1]. Patients with potentially resectable colon cancer and expected to have negative margins should undergo resection rather than neoadjuvant chemotherapy [2]. Neoadjuvant therapy for patients with locally advanced colon cancer is associated with some theoretical advantages, such as administering early effective systemic therapy that might reduce micrometastases, improving compliance with systemic therapy, and downsizing the primary tumor to provide negative surgical margins [3]. However, randomized trials have failed to verify the long-term improvement after neoadjuvant chemotherapy compared with surgery [4, 5]. Although small phase II studies have demonstrated the safety of neoadjuvant chemotherapy [6], few retrospective studies have demonstrated a survival benefit [7, 8]. Mismatch repair enzyme deficient (dMMR) colorectal cancer is responsive to programmed death-1 inhibitors in the metastatic setting. In a recent study, a pathologic complete response rate of 67% and a major pathologic response rate of 95% were ob-

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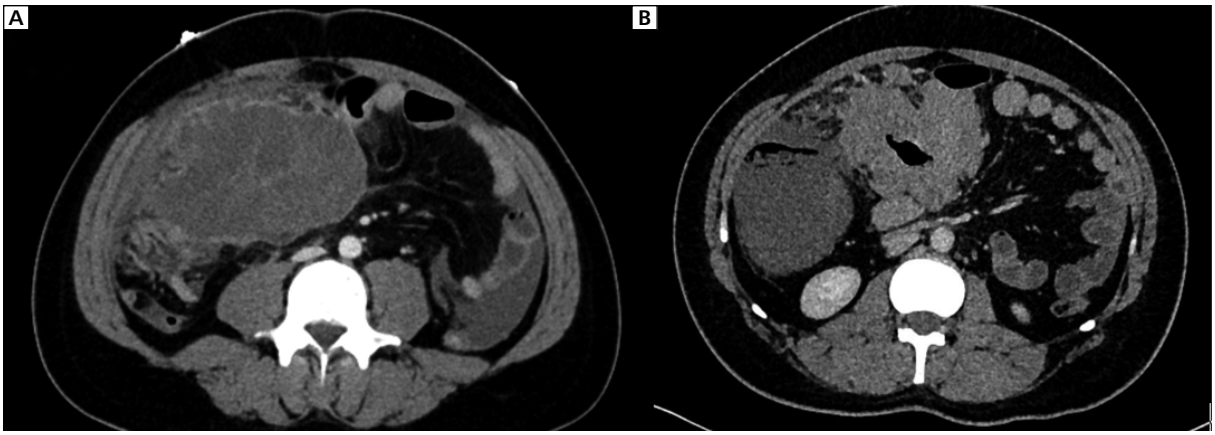

Figure 1. A–B. Malign wall thickening of the hepatic flexure and associated mass beyond the wall extending to the mesentery

tained with short-term neoadjuvant combined immunotherapy in patients with dMMR locally advanced colon cancer [9]. In another recent study, a complete response was achieved in all enrolled patients with dostarlimab in locally advanced rectal cancer with dMMR [10]. The proficient MMR (pMMR) rate is approximately 85 percent in patients with colon cancer.

Although neoadjuvant chemotherapy is not standard in locally advanced colon cancer, it could improve oncological outcomes. However, the efficacy of triplet chemotherapy is still unknown in the neoadjuvant setting in pMMR patients. We aimed to present a case with a complete pathologic response to neoadjuvant chemotherapy with mFOLFOXIRI (5-fluorouracil, leucovorin, oxaliplatin, and irinotecan) for transverse colon cancer.

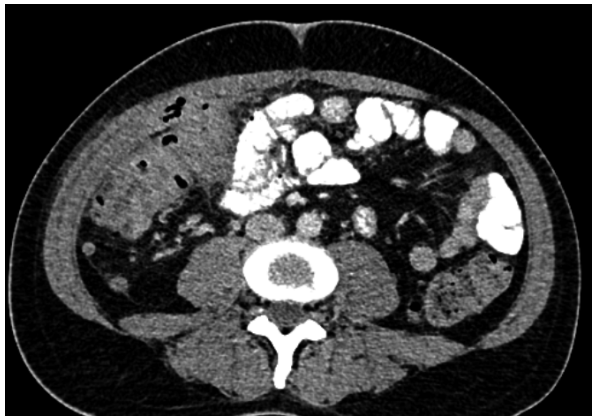

Figure 2. Abdominal tomography image after 3 cycles of triplet chemotherapy

Case presentation

A 37-year-old male patient presented with abdominal pain and fatigue. Physical examination revealed tenderness in the epigastric region and pale conjunctiva. Laboratory data showed iron deficiency anemia [hemoglobin, 9.6 g/dL, mean corpuscular volume 72 (80–100) fl, iron 21 (50–170) ug/dL, total iron binding capacity 314%, transferrin saturation 7% (20–50)]. A fecal occult blood test was positive. Carcinoembryonic antigen was 7 ng/mL. CA19.9 was 17 ng/mL. Colonoscopy showed a fragile tumor mass in the transverse colon that completely occluded the lumen. A biopsy showed colon adenocarcinoma, RAS wild type, and Braf V600E mutation status was negative. Mismatch repair proteins were proficient. Human epidermal growth factor receptor 2 was negative. Peritoneal acid examination cytology was negative. Abdominal computed tomography (CT) showed a giant 14 x12-cm mass in the right upper abdomen (Fig. 1). The tumoral mass invaded the third part of the duodenum, was close to the pancreatic uncinate process, invaded the jejunal segments, and surrounded the ileum. It was not occluding the intestines. There was a periportal 8 mm lymph node and a 1 cm lymph node in the meso of the transverse colon. There was no metastasis in the thorax CT. The patient was diagnosed with clinical stage IIIC (T4b N1a M0) transverse colon cancer. He was considered inoperable because of the extensive invasion of surrounding organs and the difficulty of margin-negative surgery. He was started on oxaliplatin (85 mg/m^2, day 1), irinotecan (150 mg/m^2, IV, day 1), leucovorin (200 mg/m^2, IV, day 1), and 5-fluorouracil (3000 mg/m^2, 46 hours of continuous infusion initiating from day 1) (FOLFOXIRI given on days 1 and 15, repeated every 4 weeks). After 3 cycles of chemotherapy, there was a remarkable reduction in the tumoral mass in the abdominal CT (Fig. 2), but also there were signs of closed perforation. A right hemicolectomy and ileotransversostomy were performed. The pathology result showed granuloma-like structures and 15 reactive lymph nodes. A pathologic complete response was obtained. There were no residual or distant metastases

in the postoperative imaging. The patient was administered 3 cycles of the adjuvant FOLFOX (days 1 and 15, every 4 weeks) regimen. The patient was disease-free in the last 20 months of follow-up.

Discussion

In the present case report, a pathologic complete response was achieved for locally advanced colon cancer after only 3 cycles of the neoadjuvant FOLFOXIRI regimen.

The standard treatment in early-stage colon cancer is surgical resection and adjuvant chemotherapy is administered according to the pathological stage. Multivisceral resection is an option for locally advanced and potentially resectable primary colon cancers. However, it has been reported that multivisceral resection might cause a longer hospital stay, delay in the start of systemic chemotherapy, and an increase in the risk of postoperative complications [11]. Neoadjuvant treatment is related to various theoretical advantages such as early administration of effective systemic therapy, downsizing the primary tumor, and improved surgery margins [4]. In 2016, neoadjuvant chemotherapy was offered as a treatment option for patients with bulky nodal disease or clinical T4b colon cancer in the National Comprehensive Cancer Network (NCCN) guidelines [12]. In the present case, a giant tumoral mass invaded the duodenum, ileum, and jejunum and was adjacent to the pancreas on the abdominal CT on admission. After 3 courses of FOLFOXIRI, there was a significant reduction in the tumoral mass, and surgical resection was performed without multivisceral resection.

The benefit of preoperative chemotherapy for patients with primary colon cancer was addressed in the phase III trial FOxTROT (T3-4N0-2, nonobstructed primary colon cancer) [13]. In the FOxTROT study, the pathologic complete response rate was 4% [13]. Preoperative chemotherapy was associated with lower rates of incomplete resection and regression of histologic staging in both the pathologic tumor and nodal stages [13]. In addition, there was a trend towards lower rates of disease recurrence at two years [13]. In studies, pathologic complete response rates of the FOLFOXIRI regimen for neoadjuvant therapy in patients with colorectal cancer ranged from 4.3% to 6.8% [14, 15] In the present case, the FOLFOXIRI regimen was preferred for complete R0 resection in the young and fit patient, and he tolerated the 3 cycles of the triplet regimen well.

The best treatment and follow-up method after neoadjuvant therapy with a pathologic complete response for colon cancer patients remains controversial. In this case, the patient received three cycles of adjuvant FOLFOX, and there was no evidence of metastasis or recurrence. Preliminary studies are showing that neoadjuvant immunotherapy may be the standard of care in patients with locally advanced colon and rectal cancer with dMMR [9, 10]. However, it suggests that neoadjuvant triplet chemotherapy may be the standard of care in patients with locally advanced colon cancer with pMMR and cT4b.

Although there is no consensus on which patients are suitable for neoadjuvant therapy in pMMR locally advanced colon cancer, triplet chemotherapy may be a reasonable option in selected patients.

Authors'scontribution

Conception: MZK, MA. Study design: MA, MKE, PFY Data collection: MA, MC, UK. Writing: MZK, PFY, MA. Editing and approval of the final draft: MZK, MA, MC, UK, PFY, MKE, MA.

Conflict of interest

Authors declare no conflict of interest.

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