Surgical Resection for Local and Lateral Lymph Node Recurrence of MSI-high Cecal Cancer with the BRAF V600E Mutation

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An 84-year-old female underwent open right hemicolectomy with D3 lymph node dissection for cecal cancer, pathologically identified as pT4aN2M0 Stage IIIc and BRAF mutation-positive. Due to early recurrence of abdominal wall and right lateral lymph nodes, the patient was treated with FOLFOXIRI + Bevacizumab. Imaging after 5 courses of chemotherapy found tumor shrinkage and no new metastases. The patient did not tolerate chemotherapy well, and tumor resection was performed. Microsatellite instability (MSI) testing using multiplex polymerase chain reaction (PCR) fragment analysis revealed MSI-high status. The patient is currently recurrence-free without chemotherapy at 1 year postoperatively. BRAF-mutated colorectal cancer has a poor prognosis, and may require resection of the metastatic or recurrent tumor after comprehensive evaluation.

Key words: BRAF V600E mutation, cecal cancer, MSI-high

Case Presentation

An 84-year-old female was diagnosed with advanced cecal cancer with mild anemia, and underwent open right hemicolectomy with D3 lymph node dissection. Pathological examination showed poorly differentiated adenocarcinoma, pT4aN2aM0 pStage IIIc [6]. She was started on capecitabine plus oxaliplatin (CAPOX) as adjuvant chemotherapy. After one course of CAPOX, a follow-up abdominal computed tomography (CT) scan revealed a heterogeneous 2-cm mass in the right lower abdominal wall, suggesting local recurrence (Fig.1), although both carcinoembryonic antigen (CEA) and CA19-9 tumor markers were within normal limits. Moreover, a positron emission tomography (PET)/CT scan showed fluorine-18 deoxyglucose (FDG) accumulation in the mass on the right lower abdominal wall,
and a 1.5-cm enlarged right lateral lymph node with FDG accumulation (Fig. 2). Based on these findings, we diagnosed abdominal wall and right lateral lymph node recurrence. Genetic testing of the surgical specimen using a polymerase chain reaction (PCR)-based method revealed RAS wild-type and the BRAF V600E mutation, and FOLFOXIRI + bevacizumab was introduced as a second-line therapy following CAPOX therapy. After 5 courses without severe adverse events, a CT scan showed that the mass on the right lower abdominal wall had shrunk slightly to 1.5 cm (Fig. 3). Although there were no obvious new lesions on imaging, the patient experienced difficulty in tolerating the chemotherapy and underwent laparotomy to excise the abdominal wall mass and right pelvic lymph node. There were no intraoperative complications, the operative time was 1 hour and 53 minutes, and the estimated blood loss was 80 grams. The abdominal wall mass measured 2.8 × 1.5 cm, and the right lateral lymph node was 1.5 × 0.8 cm (Fig. 4A). Histopathologically, both tumors were diagnosed as metastasis of poorly differentiated adenocarcinoma from cecal carcinoma (Fig. 4B-D). No postoperative adjuvant chemotherapy was administered, and the patient is alive and recurrence-free one year after surgery. A later MSI test using multiplex PCR-fragment analysis revealed MSI-high status.

**Discussion**

*BRAF* mutations are found in 5-12% of patients with metastatic colorectal cancer, and *BRAF*-mutated colorectal cancer has been reported to have a poor prognosis, not only in patients with unresectable advanced recurrence but also in stage II/III patients after adjuvant chemotherapy [7]. According to the guidelines of the Japanese Society for Cancer of the Colon and Rectum and the European Society for Medical Oncology, the first-line systemic chemotherapy regimen for patients with unresectable advanced recurrent colorectal cancer with the *BRAF* V600E mutation is FOLFOXIRI + bevacizumab [1, 2]. In addition, the recommended second-line chemotherapy regimen consists of *BRAF* inhibitors: either triplet therapy with encorafenib, binimetinib and cetuximab, or doublet therapy with encorafenib and cetuximab [8].

Although it is accepted that aggressive resection improves the prognosis of liver metastases from col-
orectal cancer, the indication for surgery in patients with the *BRAF* V600E mutation remains controversial [9,10]. In our case, FOLFOXIRI+bevacizumab therapy was introduced because of early local recurrence and right lateral lymph node recurrence during adjuvant chemotherapy with CAPOX for Stage IIIc cecal cancer. Although no new lesions were found during the 5 months of chemotherapy, the patient's performance status would decrease with continued chemotherapy. Therefore, we decided to perform surgical resection because the proposed surgery was less invasive. Though it has been only one year since the surgery, the patient is now recurrence-free without chemotherapy. Even if a patient has the *BRAF* mutation-positive colorectal cancer, which is considered to have a poor prognosis, resection of metastatic or recurrent tumors after a comprehensive evaluation of the patient's general condition and tumor factors. MSI-high status might be a prognostic factor for a favorable response to treatment, including surgery, in *BRAF*-mutated colorectal cancer.

**Conclusions**

We report the case of a patient with *BRAF* mutation-positive cecal cancer with abdominal wall and right lateral lymph node recurrence, who underwent tumor resection after FOLFOXIRI+bevacizumab therapy. Even in *BRAF*-mutated colorectal cancer, which is considered to have a poor prognosis, it is worthwhile to consider resection of metastatic or recurrent tumors after a comprehensive evaluation of the patient's general condition and tumor factors. MSI-high status might be a prognostic factor for a favorable response to treatment, including surgery, in *BRAF*-mutated colorectal cancer.

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References
