

Case Report

A Case of Advanced Gastric Cancer with Para-Aortic Lymph Node Metastasis Treated with Preoperative FOLFOX Chemotherapy Followed by Radical Subtotal Gastrectomy and D2 Lymph Node Dissection

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Keywords

Gastric cancer · Para-aortic lymph node metastasis · Systemic chemotherapy · FOLFOX

Abstract

We report the case of a 73-year-old female who was diagnosed with advanced gastric cancer. Esophagogastroduodenoscopy was used to diagnose Borrmann type 3 advanced gastric cancer located at the gastric antrum. A biopsy revealed poorly differentiated adenocarcinoma. Abdominopelvic computed tomography (CT) and ¹⁸F-fluorodeoxyglucose positron emission tomography-CT (FDG-PET-CT) scans demonstrated multiple lymph node metastases, including the para-aortic lymph nodes. Systemic chemotherapy with 5-fluorouracil (5-FU), oxaliplatin, and leucovorin (FOLFOX) was initiated. An abdominopelvic CT scan taken after 4 cycles of chemotherapy showed improvement in the ulceroinfiltrative gastric lesion and marked regression of several enlarged lymph nodes. Consequently, we performed a subtotal gastrectomy with D2 lymphadenectomy. The postoperative histopathological report was early gastric carcinoma with no lymph node metastasis in the 48 resected lymph nodes. Another 4 cycles of FOLFOX chemotherapy were performed after surgery. A FDG-PET-CT scan

taken 12 months postoperatively showed no definite evidence of local recurrence or distant metastasis, and the previously noted retroperitoneal lymph nodes had disappeared. A FDG-PET-CT taken 16 months postoperatively showed multiple lymph node metastases, including the left supraclavicular lymph node. Despite 8 cycles of secondary chemotherapy with 5-FU, irinotecan, and leucovorin (FOLFIRI) and radiotherapy, the patient died 38 months after the operation.

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Introduction

Although the prognosis of gastric cancer has improved, patients with advanced gastric cancer and distant metastasis have poor outcomes and most of them die within 12 months. Systemic chemotherapy is the main treatment for stage 4 gastric cancer. Several reports have indicated that conversion surgery is effective after systemic chemotherapy. The 5-fluorouracil (5-FU), oxaliplatin, and leucovorin (FOLFOX) combination chemotherapy regimen has been established as the standard chemotherapy for colorectal cancer [1]. This regimen is also used for gastric cancer [2]. Herein, we report a case of advanced gastric cancer with para-aortic lymph node metastasis treated with a subtotal gastrectomy and D2 lymph node dissection after preoperative FOLFOX chemotherapy.

Case Presentation

A 73-year-old female who suffered from epigastric pain was diagnosed with advanced gastric cancer after an esophagogastroduodenoscopy. Esophagogastroduodenoscopy showed Borrmann type 3 advanced gastric cancer located at the gastric antrum (Fig. 1). The biopsy result was poorly differentiated adenocarcinoma. An abdominal three-dimensional computed tomography (CT) scan (Fig. 2) and ¹⁸F-fluorodeoxyglucose positron emission tomography-CT (FDG-PET-CT) scan (Fig. 3) revealed an ulceroinfiltrative gastric lesion in the mid to lower body along the lesser curvature and multiple enlarged conglomerated metastatic lymph nodes in the perigastric, gastrohepatic ligament, and the splenic hilum, and retropancreatic, portocaval, and aortocaval portions were noted. Consequently, the patient was diagnosed with cT3N3M1 gastric cancer. We decided to perform systemic FOLFOX chemotherapy. Oxaliplatin (100 mg/m²) was infused for 2 h, and 100 mg/m² folinic acid was followed by a 46-h continuous infusion of 2,400 mg/m² 5-FU. An abdominopelvic CT scan taken after 2 cycles of systemic chemotherapy showed an improving ulceroinfiltrative gastric lesion and marked regression of multiple enlarged conglomerated metastatic lymph nodes in the perigastric, gastroph hepatic, splenic hilum, retropancreatic, porta hepatis, portocaval, and aortocaval portions (Fig. 4). We performed a radical subtotal gastrectomy with D2 lymph node resection after 4 cycles of FOLFOX chemotherapy. The postoperative pathological report was early gastric carcinoma located at the center of the lesser curvature of the gastric body and moderately differentiated tubular adenocarcinoma. The depth of invasion was the muscularis mucosa (pT1a), and no metastasis was detected out of 48 resected lymph nodes. No lymphatic, venous, or perineural invasion was noted. The patient was discharged 10 days after the operation without any postoperative complications. The patient was followed with regular checkups in the outpatient department, and an additional 4 cycles of FOLFOX chemotherapy were administered. A PET-CT scan taken 12 months after the operation showed no definite evidence of local recurrence or distant metastasis and the disap-

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pearance of previously noted retroperitoneal lymph nodes (Fig. 5). The patient wanted to discontinue the FOLFOX chemotherapy due to old age-related concerns. A FDG-PET-CT scan taken 16 months after the operation showed multiple lymph node metastases, including those in the left supraclavicular, paratracheal, para-aortic, and retrocaval areas, as well as bone metastases in both femurs, the sacrum, lumbar vertebrae 4 and 5, and the left sixth rib (Fig. 6). Ultrasonography-guided fine-needle aspiration biopsy of the left supraclavicular lymph node revealed poorly differentiated metastatic adenocarcinoma. After the diagnosis of a recurrence, secondary chemotherapy with 2,400 mg/m² body surface area 5-FU, 180 mg/m² irinotecan, and 200 mg/m² leucovorin (FOLFIRI), as well as 30 Gy radiotherapy over 2 weeks was administered to the left supraclavicular lymph node and metastatic bone lesions. A total of 8 cycles of FOLFIRI chemotherapy and a total of 10,200 Gy radiotherapy were completed. Despite the secondary chemotherapy and radiotherapy, the patient died 38 months after the operation.

Discussion

A radical operation, which means complete macroscopic removal of a tumor and lymph nodes, is essential for a gastric cancer cure [3]. The 5-year overall survival of most patients with gastric cancer and a regional or distant metastasis is disappointing, and a median survival duration of >12 months has not been achieved with any chemotherapy combination [4]. However, neoadjuvant chemotherapy has been studied in cases of unresectable locally advanced gastric cancer with bulky lymph nodes [5]. Conversion surgery involves resecting previously unresectable cancer that becomes resectable because the lesion regresses after systemic chemotherapy. Some studies are available on conversion surgery for stage 4 gastric cancer [6]. Fujitani et al. [7] reported that the value of conversion surgery must be investigated in a randomized trial and that conversion surgery could be a treatment option, as no survival benefit of surgery first with a noncurable factor was shown in the REGATTA trial. The 3-year survival of patients with para-aortic node metastasis (PAN) who underwent surgery was only 5%, and tumors with PAN are almost always considered surgically incurable in western countries, according to the Japan Clinical Oncology Group (JCOG) [8]. The potential benefits of administering a chemotherapeutic regimen preoperatively include increasing the likelihood of curative resection by downsizing the tumor, eliminating micrometastasis, rapidly improving tumor-related symptoms, and determining whether the tumor is sensitive to chemotherapy [9]. FOLFOX has been the standard treatment for patients with metastatic or advanced colorectal cancers [1], and 5-FU is the main chemotherapeutic agent used to treat advanced gastric cancer, with a response rate as a single agent of 21% and a median survival rate of 6–7 months. The third-generation platinum agent oxaliplatin is an alkylating agent with the 1,2-diaminocyclohexane carrier ligand and is effective for treating advanced gastric cancer [10]. Several studies have reported that FOLFOX combination chemotherapy is effective for unresectable advanced or recurrent gastric cancer with acceptable tolerability by patients [2, 10]. In our case, an abdominopelvic CT scan showed improvement in the ulceroinfiltrative gastric lesion and marked regression of multiple enlarged conglomerated metastatic lymph nodes after administering 2 cycles of the FOLFOX regimen. Once the gastric cancer metastasized to the para-aortic lymph nodes, it is classified as M1 node cancer according to the International Union against Cancer tumor-node-metastasis classification, and extensive dissection of the nodes in this area does not improve overall or recurrence-free survival compared to that of a D2 lymphadenectomy [11]. The role of PAN dissection for

tumors treated by neoadjuvant chemotherapy is unknown. In the JCOG 9501 study, 8.5% of the patients had metastases in PANs, but excising the nodes did not improve survival compared with D2 alone [11]. In our case, PAN, which was noted on a FDG-PET-CT scan, disappeared after 3 cycles of FOLFOX chemotherapy. The pathological report after the radical subtotal gastrectomy with D2 dissection noted that the depth of tumor invasion was to the muscularis mucosa (pT1a) and the lymphatic; the venous and perineural areas were not invaded. Less than one-third of the cells were viable due to the chemotherapeutic effects. Several lymph nodes showed foam cells with fibrosis but no cancer cells in the 48 dissected nodes. The pathological response and histological tumor regression are important predictors of survival in patients with gastric cancer. The pathological response to neoadjuvant chemotherapy can be evaluated by tumor regression grade (TRG). Regression is graded as follows: TRG 4, complete regression; TRG 3, isolated cell nests; TRG 2, more residual cancer cells but fibrosis still dominant; TRG 1, residual cancer outgrowing fibrosis, and TRG 0, absence of regressive changes [12]. This grading suggests that our patient had downstaged gastric cancer after preoperative FOLFOX chemotherapy, and was classified as a TRG 2 response.

In the present case, we performed 4 courses of preoperative FOLFOX combined chemotherapy and were able to perform a radical subtotal gastrectomy with D2 lymph node dissection. The para-aortic lymph nodes were not included in the dissection, and the patient lived for 38 months. There are no established regimens, number of courses, or extent of conversion surgery for patients with stage 4 gastric cancer until now. Further studies are needed to investigate how conversion surgery can be used effectively in these patients.

Statement of Ethics

Written informed consent was obtained from the patient to publish this case report.

Disclosure Statement

There are no known conflicts of interest associated with this publication.

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Fig. 1. Esophagogastroduodenoscopy showing Borrmann type 3 gastric cancer at the antrum of the stomach.

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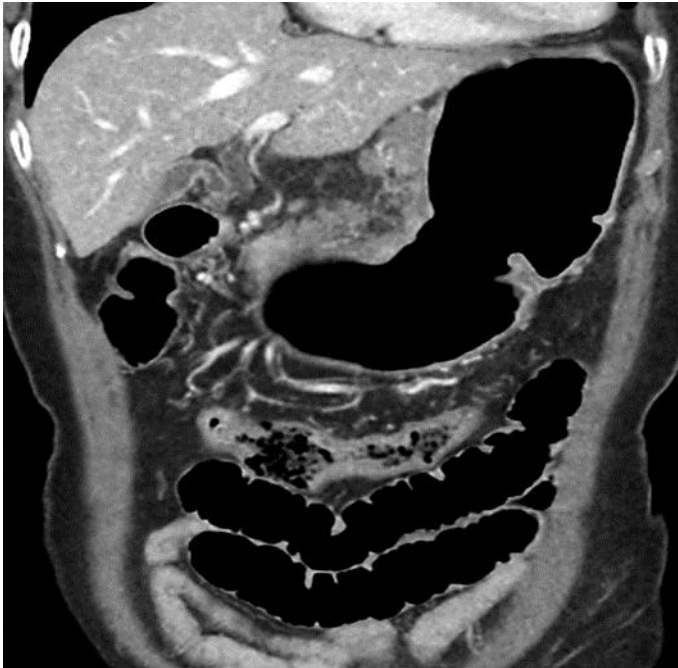


Fig. 2. Three-dimensional computed tomography of the stomach showing an ulceroinfiltrative gastric lesion in the mid to lower body along the lesser curvature with perigastric infiltration, which was diagnosed as T3 advanced gastric cancer.

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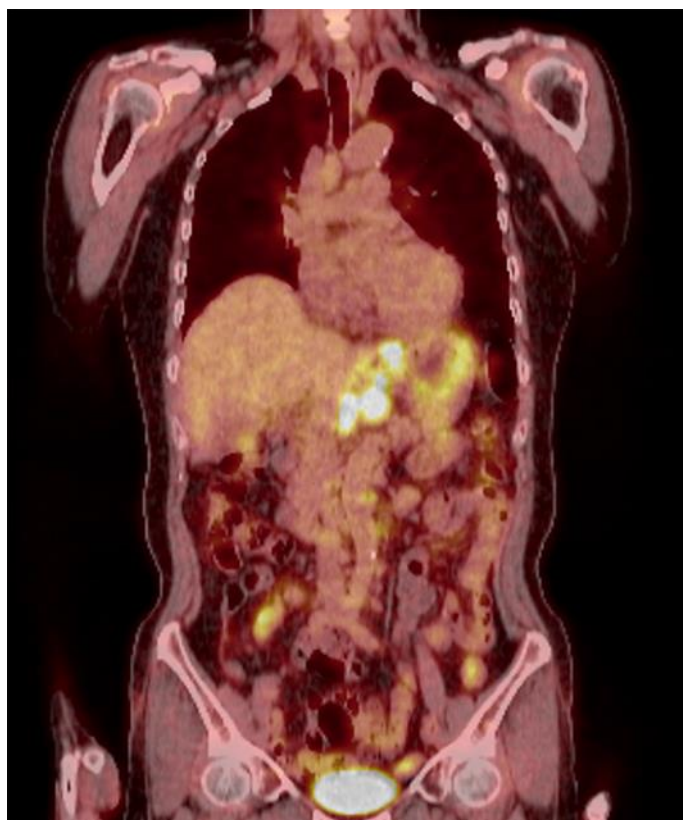


Fig. 3. Preoperative F-¹⁸fluorodeoxyglucose positron emission tomography-computed tomography scan showing metastatic lymph nodes in the left gastric, splenic hilum, left para-aortic, aortocaval, and retro-caval areas.

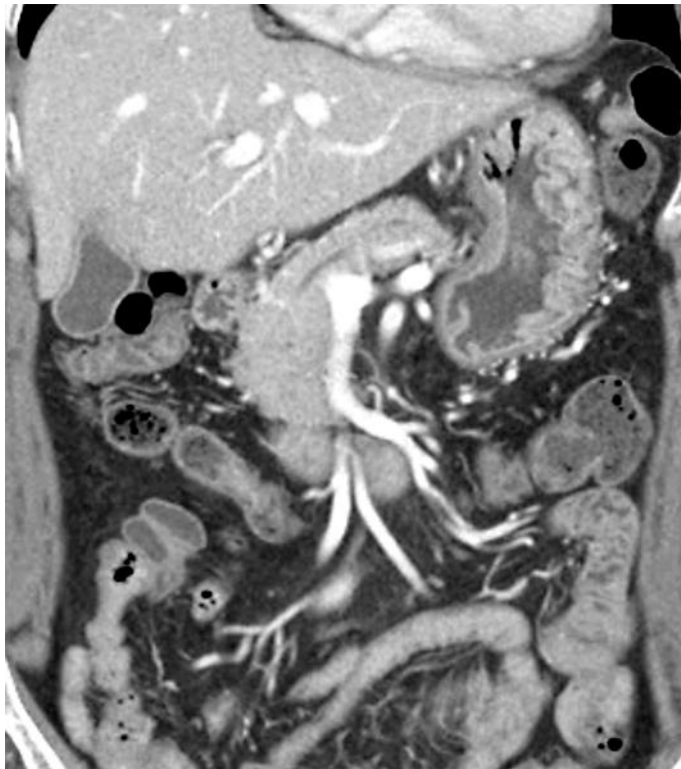


Fig. 4. Abdominopelvic computed tomography scan after 2 cycles of chemotherapy showing an interval-improved ulceroinfiltrative gastric lesion and marked regression of multiple enlarged conglomerated metastatic lymph nodes in the perigastric, gastrophepatic, splenic hilum, retropancreatic, porta hepatis, portocaval, and aortocaval portions.

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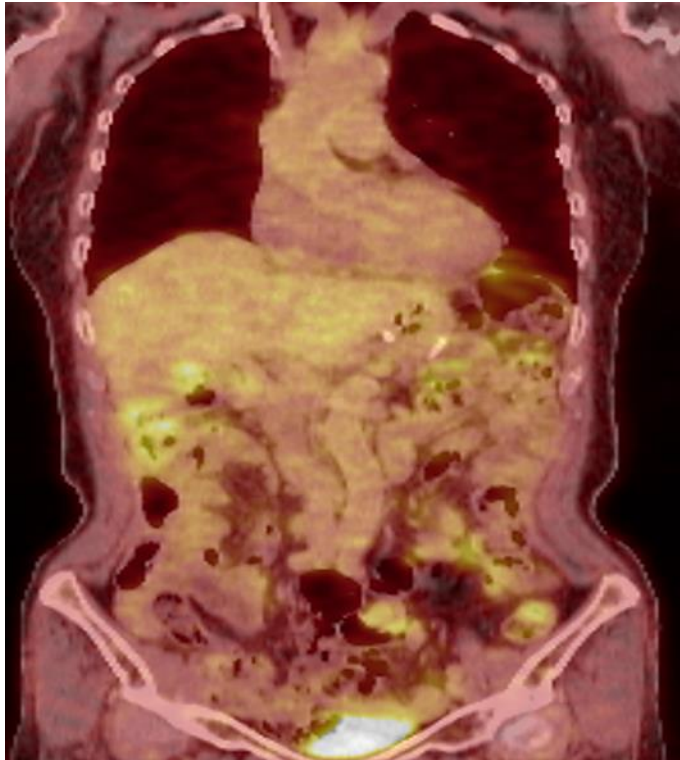


Fig. 5. F-¹⁸fluorodeoxyglucose positron emission tomography-computed tomography scan taken 12 months after the operation showing the disappearance of preoperatively noted left gastric, splenic hilum, left para-aortic, aortocaval, and retrocaval lymph nodes.

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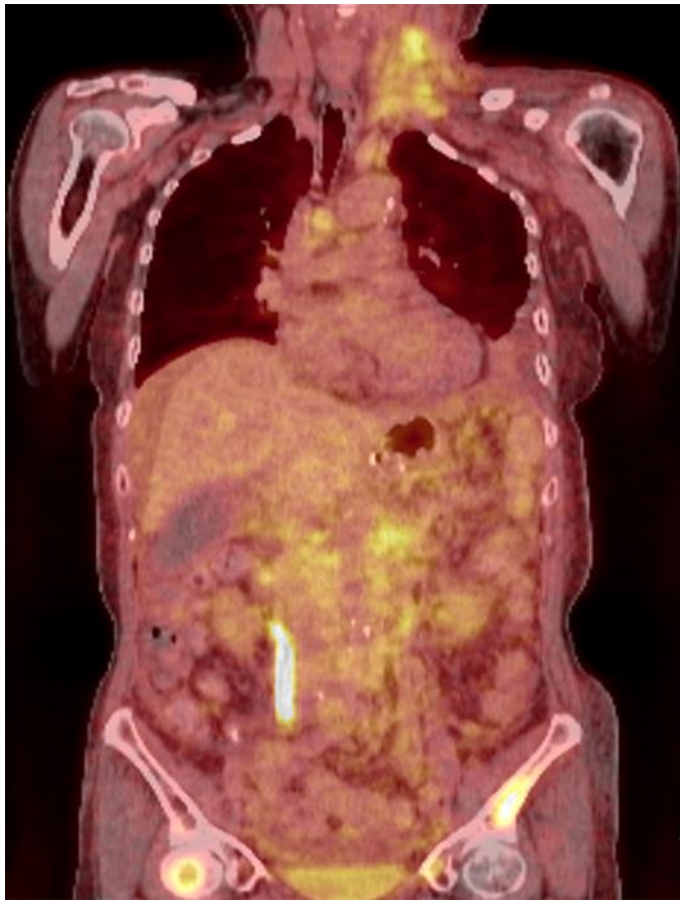


Fig. 6. Positron emission tomography-computed tomography scan taken 16 months after the operation showing multiple lymph node metastasis, including the left supraclavicular, paratracheal, para-aortic, retrocaval areas as well as a bone metastasis in both femurs, the sacrum, lumbar 4th and 5th vertebrae, and the left 6th rib.