

CASE REPORT

## Advanced Gastric Cancer Showing Complete Remission of Metastatic Lymph Node after Chemotherapy

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A 69-year-old woman with dyspepsia and poor oral intake was diagnosed as advanced gastric cancer. Clinical staging was stage IV with inoperable status, and thus, three cycles of palliative chemotherapy with paclitaxel and cisplatin were performed. Follow up endoscopy and positron emission tomography with computed tomography (PET-CT) revealed marked decrease in the primary stomach lesion and metastatic lymph nodes. Distal gastrectomy and D2 lymph node dissection were performed with gastrojejunostomy. Later pathological examination demonstrated tumor invading submucosa. However, there was no pathologic evidence of lymph node metastasis. Only the necrotic areas without viable carcinoma cells were noted in regional lymph nodes located along the left gastric artery and common hepatic artery. Because of the excellent response to chemotherapy, R0 resection was carried out. Herein, we report a case of advanced gastric cancer showing complete remission of metastatic lymphadenopathy after palliative chemotherapy. (**Gut and Liver 2007;1:74-78**)

**Key Words:** Advanced gastric cancer; Chemotherapy; Complete response

### INTRODUCTION

Advanced gastric cancer (AGC) is the second leading cause of death related to cancer in the world.<sup>1</sup> Although surgery is the primary therapy for localized gastric cancer, only half of the patients with locally advanced gastric cancer, which comprises stages IIIA, IIIB and IV, can undergo an R0 resection and extended surgery including D2 dissection.<sup>2</sup> Prognosis is usually dismal because only 33% of all stages are resectable.<sup>3</sup> For unresectable gastric can-

cer, chemotherapy may have palliative effects in some patients. In four studies, combination chemotherapy resulted in a better quality of life and overall survival when compared with the best supportive care in patients with unresectable advanced gastric cancer.<sup>4,6</sup> Because curative resection is considered to be the best available therapy for gastric cancer, to achieve R0 resection in cases with locally advanced unresectable gastric cancer, down staging with preoperative chemotherapy followed by curative surgery may be an effective treatment modality for patients with unresectable gastric cancer.<sup>4</sup> A retrospective analysis of R0 resection was accomplished in 10 out of 27 patients with stage IV gastric cancer after undergoing preoperative S-1/DDP neoadjuvant chemotherapy.<sup>5</sup> In three Japanese case reports, down staging and curative surgery was accomplished in three patients with stage IV gastric cancer after administration of paclitaxel combined with cisplatin, TS-1 or low dose 5-fluorouracil.<sup>6-8</sup>

Herein, we report a case of stage IV gastric cancer, in which R0 resection and pathologic nodal complete response were accomplished after chemotherapy with paclitaxel and cisplatin.<sup>3</sup>

### CASE REPORT

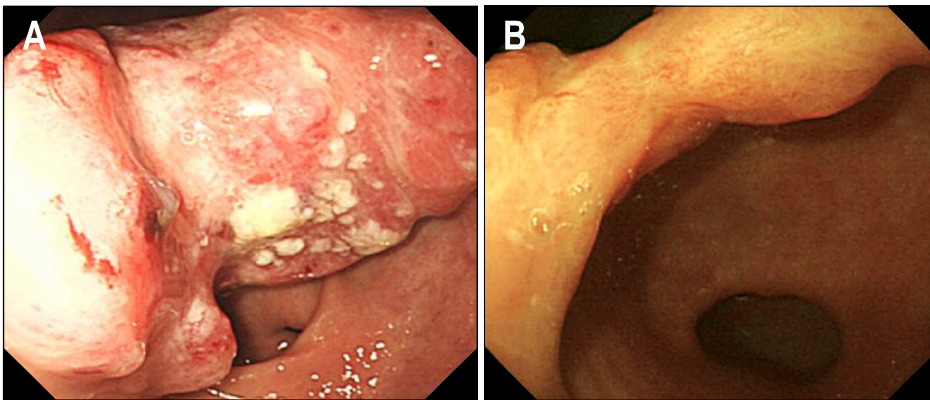
A 69-year-old woman was admitted to Severance Hospital because of dyspepsia and poor oral intake. Upper gastrointestinal endoscopy demonstrated an ulcerative lesion with irregular base, coated with dirty exudates from the prepylorus to the angle of stomach (Fig. 1A). Endoscopic biopsy revealed poorly differentiated adenocarcinoma.

Abdominal computed tomography (CT) showed massive lymphadenopathy at the left gastric, porta hepatis, porto-

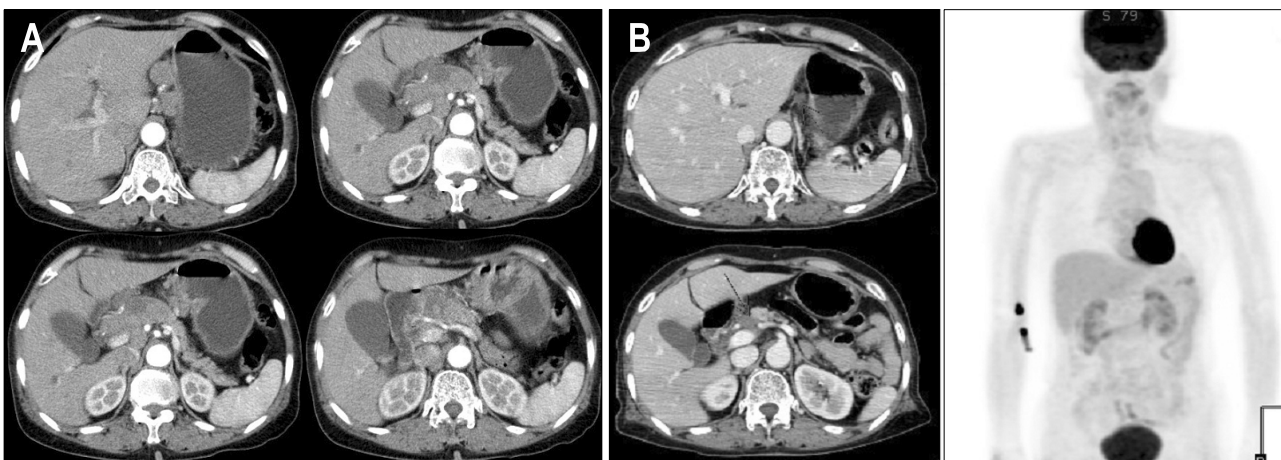
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**Fig. 1.** Findings of upper gastrointestinal endoscopy. (A) Before chemotherapy, an ulcerofungating mass with nodular surface and exudate is noted on the angle and on the lesser curvature of antrum. (B) After 3 cycles of chemotherapy, previously noted mass is replaced by slightly depressed mucosal lesion with scar.



**Fig. 2.** (A) Abdominal computed tomography (CT) before treatment reveals multiple lymphadenopathy indicating lymph node metastases at the left gastric (left upper), porta hepatis, portocaval (right upper), peripancreatic, and omental lymph nodes (left lower). The primary cancer is invading the common hepatic artery (right lower). (B) PET-CT after 3 cycles of chemotherapy shows marked decrease in size of the perigastric and hepatoduodenal ligament lymph nodes when compared to those noted on the previous abdominal CT scan (black arrows). There is no increased FDG uptake in the stomach and lymph nodes at the perigastric and hepatoduodenal ligament areas.

caval, peripancreatic and omental lymph nodes indicating lymph node metastases, including common hepatic artery invasion of the primary cancer (Fig. 2A). Physical examination revealed no specific problems. Serum level of carcinoembryonic antigen (CEA) was 166.5 ng/ml and that of the carbohydrate antigen (CA) 19-9 was 7.2 U/mL.

### 1. Neoadjuvant chemotherapy

The patient underwent combination chemotherapy for palliation, which consisted of three-week cycles of administration of cisplatin 75 mg/m<sup>2</sup> as 2 hour infusion in 150 mL of normal saline and paclitaxel 175 mg/m<sup>2</sup> as 3 hour infusion in 500 mL of 5% DW. There was no side effect during and after the first and second cycle of chemotherapy. However, grade 4 neutropenia (390/uL) and grade 4 nausea, vomiting, and hyponatremia developed after the third cycle of chemotherapy. After the completion

of three cycles of chemotherapy, follow-up gastrointestinal endoscopy demonstrated slightly depressed mucosal lesion with white atrophic changes and visible submucosal vessels in the previously noted ulcerative area. Marginal folds were slightly edematous (Fig. 1B).

Positron emission tomography with computed tomography (PET-CT) scanning did not identify the primary stomach cancer definitely. In addition, the size of the perigastric and hepatoduodenal ligament lymph nodes were markedly decreased when compared with the previous abdominal CT scan. Furthermore, there was no increased fluorodeoxyglucose (FDG) uptake in the stomach and lymph nodes at the perigastric and hepatoduodenal ligament areas (Fig. 2B).

### 2. Intraoperative findings

Surgery was recommended since the primary cancer and



Fig. 3. Gross finding of the surgical specimens. The stomach measures 22 cm along the greater curvature and 13.5 cm along the lesser curvature. There is an ill-defined pale nodular area on the serosal surface. The stomach is incised along the greater curvature, and there is an ill-defined shallow depressed lesion, measuring 2.5×2 cm. The main lesion is located in the lesser curvature side of the antrum. It is located 4.5 cm apart from the proximal resection margin and 5.5 cm apart from the distal resection margin. The remaining mucosa is slightly edematous.

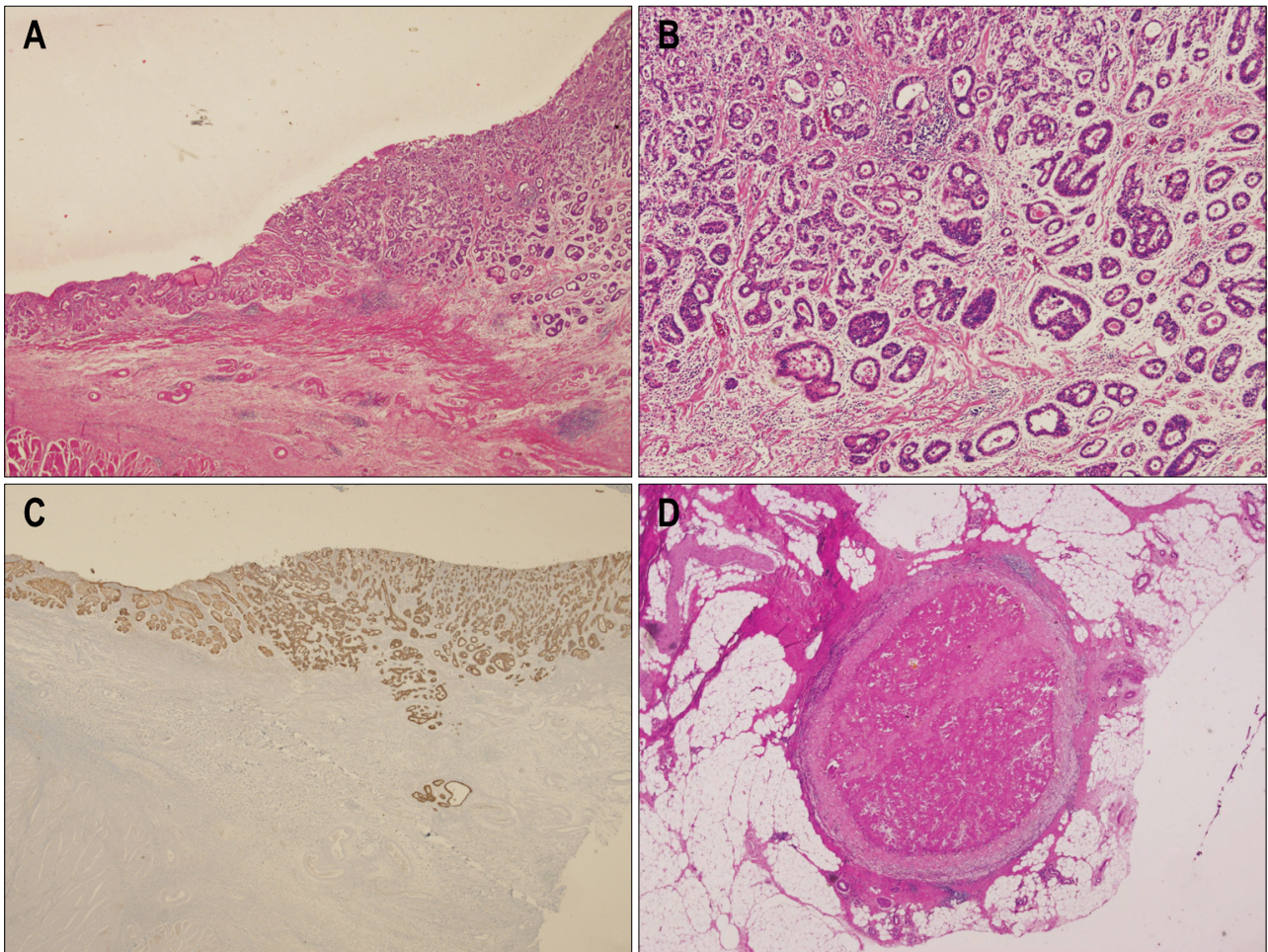


Fig. 4. Microscopic findings. (A) At low magnification, the antral mucosa is infiltrated with adenocarcinoma extending down to the submucosal layer. (B) At high magnification, the tumor glands show moderate differentiation without definite lymphovascular permeation or perineural invasion. (C) Immunohistochemical stain with cytokeratin reveals positive in tumor cells. The tumor glands are extending to the upper submucosa (sm1, invasion depth: 0.1 cm). (D) The enlarged lymph nodes are totally replaced by tumor necrosis. There is no viable tumor cell in the resected specimen.

metastatic lymph nodes showed marked decrease in size on the PET-CT scan. A subtotal gastrectomy and D2 lymph node dissection, including regional lymph nodes along the left gastric artery, common hepatic artery, and celiac artery were done. Complete omentectomy was performed with a gastrojejunostomy. The stomach was diffusely edematous and fragile. There was neither organ invasion nor peritoneal seeding. There was no palpable lesion in the rectal shelf during the surgical procedure.

### 3. Histological diagnosis

Gross examination demonstrated an ill-defined pale nodular area on the serosal surface of the stomach. When the specimen was opened along the greater curvature, an ill-defined, shallow depressed lesion was noted at the lesser curvature side of the antrum (Fig. 3). The remaining mucosa was slightly edematous.

Microscopic findings revealed a moderately differentiated tubular adenocarcinoma invading submucosa, which was detected by immunohistochemical staining for CK (AE1/AE2). The depth of the submucosa invasion was 0.1 cm (Fig. 4A-C). A total of 20 lymph nodes were dissected and evaluated by histological examination. There was no microscopic lymph node metastasis. However, necrotic areas without viable carcinoma cells were noted in No 1 (perigastric lymph node along lesser curvature), No 4 (perigastric lymph node along greater curvature), No 5 (perigastric lymph node along lesser curvature), No 7 (lymph nodes along left gastric artery), and No 8 (lymph nodes along common hepatic artery) regions, suggesting degeneration of the cancer cells (Fig. 4D). The final histological staging was T1bN0M0. The postoperative serum CEA level was 5.66 ng/mL. The patient was discharged without any postoperative complications and was followed up in the outpatient department without additional postoperative chemotherapy.

## DISCUSSION

In the present case, palliative chemotherapy was performed. Response to the chemotherapy was so dramatic that it resulted in a down staging of the cancer leading to R0 resection with pathologic nodal complete remission (CR). Two similar cases were reported in Japan. A case with pathologic nodal CR after two courses of chemotherapy with paclitaxel and TS-1 for AGC was reported.<sup>7</sup> The patient had left gastric artery lymph node metastasis with invasion to the pancreas and spleen.<sup>7</sup> Another case showed disappearance of the primary lesion and partial response of the metastatic lymph nodes in a AGC patient with peritoneal seeding after two cycle of paclitaxel and

low dose FP (5-fluorouracil and cisplatin) chemotherapy.<sup>8</sup>

Taxanes (paclitaxel and docetaxel), irinotecan and oxaliplatin are relatively new agents used for gastric cancer which demonstrated a significant activity against gastric cancer. Paclitaxel is approved in Korea as a first-line treatment for AGC. In a randomized phase II clinical trial performed in a single center, paclitaxel combined with 5FU showed a 42% response rate in metastatic gastric cancers which were naive to chemotherapy.<sup>9</sup>

It is uncommon to achieve resectability and nodal response after neoadjuvant chemotherapy in an unresectable AGC. A number of case reports on stage IV gastric cancers showed good response to chemotherapy consisting of TS-1. In their report, chemotherapy enabled possible radical resection.<sup>10-13</sup> Therefore, it has been reported that this treatment strategy may improve the prognosis in patients with AGC.

Recently, three large phase III trials were being conducted to assess the usefulness of neoadjuvant chemotherapy. The MAGIC trial in the UK compared surgery alone with ECF (epirubicin, cisplatin, and 5-fluorouracil). A multinational European trial (EORTC 40954) compared surgery alone with surgery after neoadjuvant PLF (cisplatin, leucovorin, and 5-fluorouracil). A Swiss study (SAKK 43/99) compared surgery plus preoperative TCF (taxotere, cisplatin, and 5-fluorouracil) with surgery followed by the same chemotherapy regimen.<sup>14,15</sup> Most of these clinical trials included patients with resectable AGC.

As mentioned above, fifty percent of cases were diagnosed initially as over stage III disease. Only 33% of all cases are candidates for surgical resection. For patients with unresectable AGC without distant metastasis, issue is not whether to treat with neoadjuvant chemotherapy, but rather to choose the best chemotherapeutic agents which result in down staging so that R0 resection could be performed in unresectable AGC patients. Further investigation is needed to compare the rate and degree of response to various chemotherapeutic protocols. In addition, important factors that improve outcomes in AGC need to be investigated.

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