Laparoscopic Resection of Gastric Cancer in a Patient with Chronic Lymphocytic Leukemia Accompanied by Neutropenia

YUICHIRO NAKASHIMA[1,2], RYOTA NAKANISHI[1], MASAHIKO SUGIYAMA[1], KIPPEI OHGAKI[1], HIDETO SONODA[1], HIROSHI SAEKI[1], EIJI OKI[1], AYUMI MATSUYAMA[2], TAKASHI MAEDA[2], SHINICHI TSUTSUI[2], HIROYUKI MATSUDA[2], TERUYOSHI ISHIDA[2] and YOSHIHIKO MAEHARA[1]

[1]*Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Higashi-ku, Fukuoka, Japan;*
[2]*Department of Surgery, Hiroshima Red Cross Hospital and Atomic-bomb Survivors Hospital, Hiroshima, Japan*

Abstract. *Aim: We report an unusual case of early gastric cancer and T-cell-type chronic lymphocytic leukemia accompanied by severe neutropenia that was successfully treated by laparoscopic gastrectomy. Case Report: A 76-year-old female was referred to our Hospital for resection of a gastric adenoma that was suspicious for malignancy. Routine preoperative laboratory studies showed severe neutropenia and increased atypical lymphocytes in the peripheral blood. Bone marrow biopsy confirmed the diagnosis of T-cell chronic lymphocytic leukemia. One day before surgery, granulocyte colony-stimulating factor was administered. Laparoscopic-assisted distal gastrectomy was performed. The patient's postoperative course was uneventful and she was discharged after 10 days. The histopathological findings revealed well-differentiated adenocarcinoma (pT1a, pN0, and stage IA). Conclusion: Laparoscopic gastrectomy may be considered a primary approach in patients with neutropenia because it is associated with lower risk of postoperative infection and a lower mortality rate compared to open resection.*

Chronic lymphocytic leukemia (CLL) is a rare type of leukemia in Japan (about 2% of all leukemias); however, it is the most common leukemia in Western countries (1). T-cell-type chronic lymphocytic leukemia (T-CLL) is rarer still, accounting for approximately 2% of all CLL cases (2). Neutropenia is often observed in the later stages of CLL. Several studies in Western countries have demonstrated a significantly increased risk of the development of other neoplasms in patients with CLL (3, 4). These include malignant melanoma, soft-tissue sarcomas, and lung cancer. Gastric cancer has not been shown to be associated with CLL (3).

Laparoscopic-assisted distal gastrectomy (LADG) for early gastric cancer was introduced by Kitano and colleagues (5). This surgical procedure is safe, less invasive, and induces less inflammatory response than open resection. A recent report suggested that the initial inflammatory response may affect long-term outcome in gastric cancer (6). Herein, we report an unusual case of early gastric cancer and T-CLL accompanied by severe neutropenia that was successfully treated by LADG.

Case Report

A 76-year-old asymptomatic female was referred to our Hospital with a gastric adenoma suspicious for malignancy. The adenoma had been diagnosed 3 years previously. Serial monitoring of the lesion by esophagogastroduodenoscopy (EGD) revealed that the histological grade of gastric adenoma had gradually increased based on tissue biopsy.

EGD identified a polypoid lesion consisting of multiple nodules occupying the entire circumference of the antrum and gastric corpus, and the results of a final biopsy were suspicious for malignancy (Figure 1A). Upper gastrointestinal series confirmed these findings (Figure 1). Chest and pelvic computed tomography detected neither the gastric lesion, nor any enlarged lymph nodes, metastasis to distant organs, ascites, or hepatosplenomegaly.

Routine preoperative laboratory findings showed a hemoglobin concentration of 10.1 g/dl, white cell count of 8,800 /mm^3 with 3.0% neutrophils, 14.0% lymphocytes, and 76.2% atypical lymphocytes; platelet count of 140,000 /mm^3; IgG, 1,750 mg/dl [normal range (NR)=870-1700 mg/d]); IgA, 712 mg/dl (NR=110-410 mg/dl); IgM, 201 mg/dl (NR=46-

Correspondence to: Yoshihiko Maehara, Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, 3-1-1, Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan. Tel: +81 926425466, Fax: +81 926425482, e-mail: maehara@surg2.med.kyushu-u.ac.jp

Key Words: Gastric cancer, chronic lymphocytic lymphoma, neutropenia, laparoscopic-assisted distal gastrectomy.

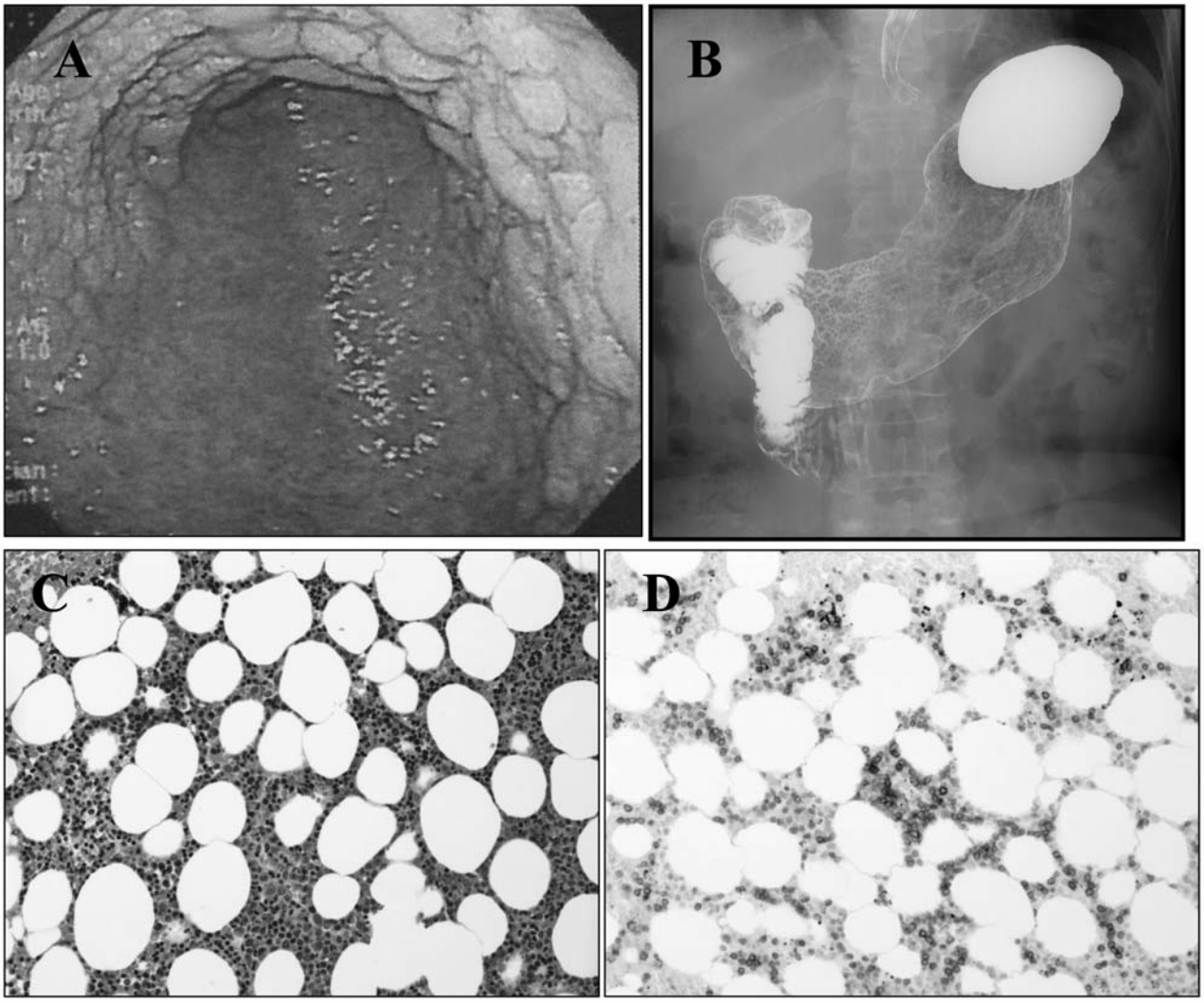

Figure 1. *Endoscopic, radiographic, and bone marrow findings. A: Upper endoscopy showed a polypoid lesion consisting of multiple nodules in the entire circumference of the gastric antrum and corpus. B: Upper gastrointestinal series showed similar findings. C: Bone marrow biopsy revealed intestinal infiltration of small lymphocytes (hematoxylin and eosin staining ×200). D: Immunohistochemistry. CD3-positive lymphocytes were increased without aggregation (×200).*

261 mg/dl); IL-2R 1114 U/ml (NR=220-530 U/ml). The patient underwent bone marrow biopsy which showed intestinal infiltration of atypical lymphocytes (Figure 1c). By immunohistochemistry, the bone marrow specimen showed increased T-lymphoid cells (CD3) and decreased B-cells (CD20, CD79 and CD23) (Figure 1d). These findings suggested a diagnosis of T-CLL. The clinical stage was Rai stage 0 and Binet stage A. According to the International Workshop on Chronic Lymphocytic Leukemia guidelines, this stage of CLL requires only monitoring without treatment (7).

One day before surgery, lenograstim (250 μg) was administered. LADG was performed with Roux-en Y reconstruction with D1 plus lymphadenectomy according to guidelines set forth in the Japanese Classification of Gastric Cancer (third English edition) (8). Operative time was 221 min and blood loss was 13 g. Pathological examination showed a 9.0 by 9.0 cm, mucosal, well-differentiated adenocarcinoma (pT1a, pN0, cH0, cP0, cM0, fStage IA) (Figure 2). There were also tubular adenomas associated with the lesion (Figure 2A-C). One adenoma showed adenocarcinoma within it, accompanied by a disturbance of cellular atypia and structural atypia (Figure 2D).

The postoperative course was uneventful, and the patient was discharged on postoperative day (POD) 10 (Figure 3). The neutrophil count was elevated postoperatively, partly attributable to surgical stress and partly to administration of

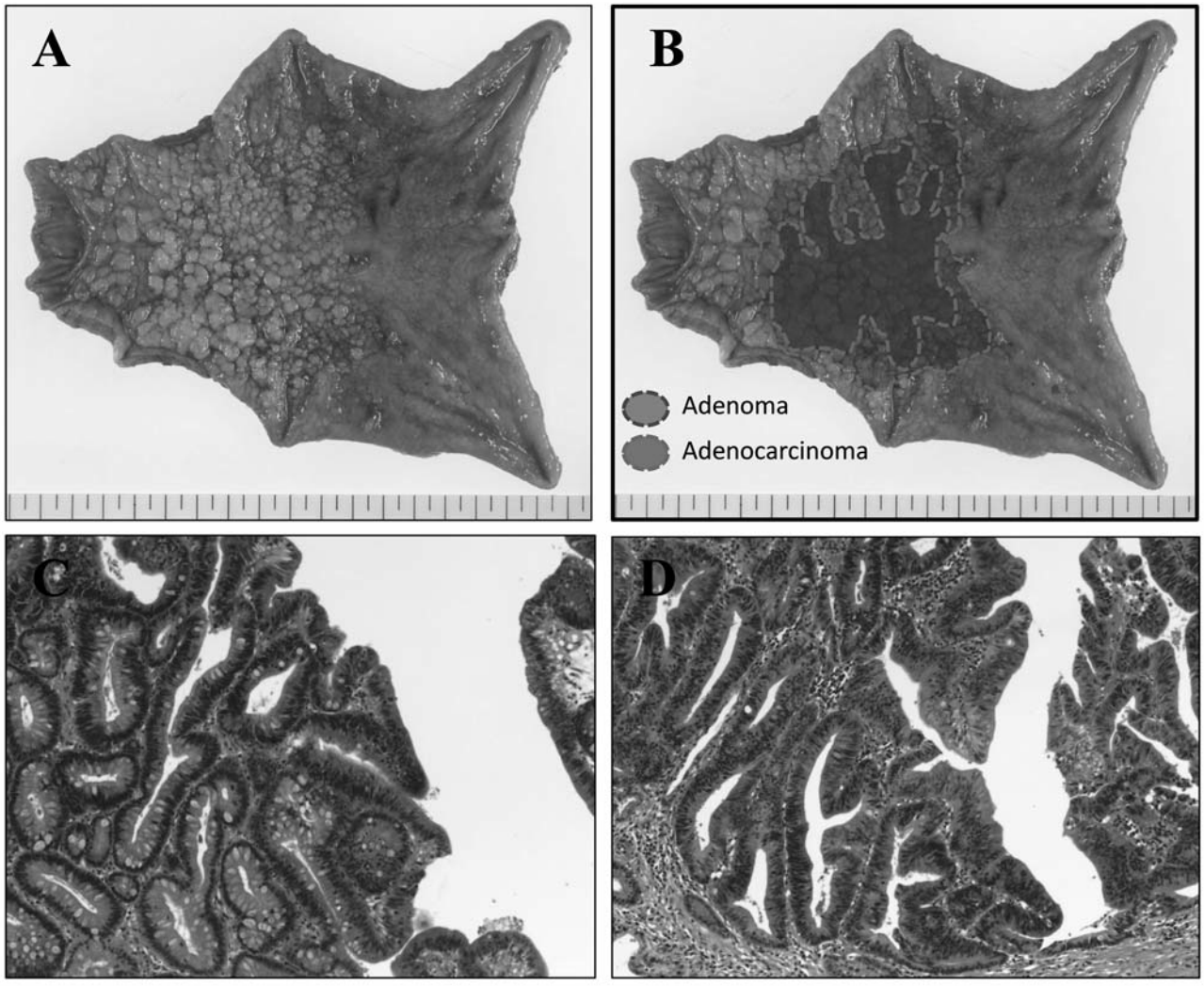

Figure 2. *Resected gastric specimen. A: Macroscopically, a 9.0 by 9.0 cm, type 0-I tumor was observed at the antrum. B: A tubular adenoma (blue area) and a well-differentiated adenocarcinoma (red area) were observed. C: Microscopically, sections from the blue area showed tubular adenoma (hematoxylin and eosin ×100). D: Microscopically, sections from the red area showed the adenocarcinoma in adenoma, accompanied by increased disturbance of cellular atypia and structural abnormalities (hematoxylin and eosin ×100).*

granulocyte colony-stimulating factor (G-CSF), but it dropped below 10,000/mm^3 on POD 5. While the patient was febrile until POD 5, secondary infection was not observed. The patient was still alive with no evidence of gastric cancer recurrence 36 month after surgery.

Discussion

In patients with CLL, an increased incidence of other malignant neoplasms has been reported (3, 4). Disease- or therapy-related immunosuppression and genetic predisposition have been identified as possible causes for this epidemiological association. Simultaneous occurrence of T-CLL and gastric adenocarcinoma, however, is a rare event. This is believed to be the first published English report of gastrectomy performed in a patient with gastric cancer accompanied by neutropenia secondary to CLL.

The reasons for this patient's unusually severe neutropenia are unclear. CLL is often associated with neutropenia, although usually only in its later stages. The causes of late-stage neutropenia are unknown, but a reduction in bone marrow mass is at least partly responsible. This was unlikely in our patient, however, as the marrow infiltration was not heavy and normal hematopoietic cell lines were not suppressed.

Abdominal surgery may result in significant morbidity or mortality in patients with neutropenia. Wade *et al*. reported on patients with hematological and solitary malignancies who developed acute abdominal pain during a neutropenic

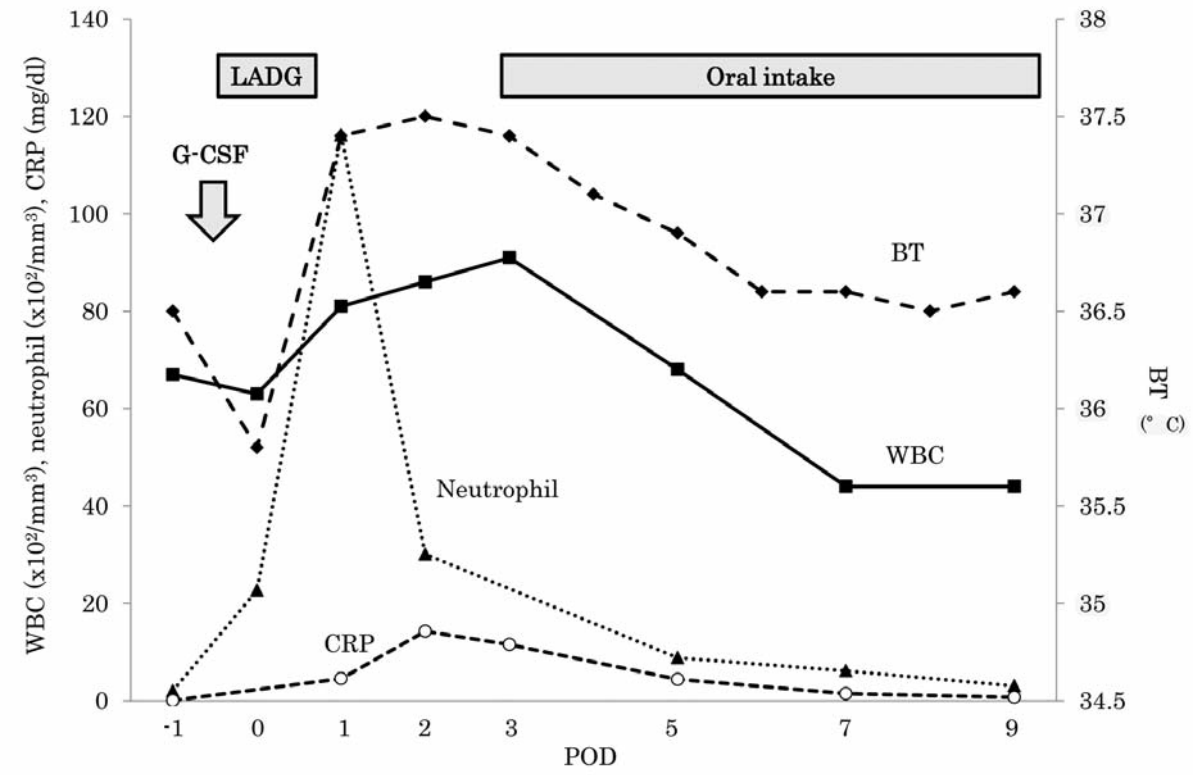

Figure 3. *Perioperative course. G-CSF: Granulocyte colony-stimulating factor, LADG: laparoscopic-assisted distal gastrectomy; WBC: White blood cell count; CRP: C- reactive protein; BT: body temperature; POD: postoperative day.*

period (9). For those undergoing operation, the 30-day postoperative mortality rate was 41%. A low neutrophil count (granulocyte count less than 1.0×10^9/l) was associated with increased mortality. Vickers reported successful treatment of wound infection in patients with neutropenia with CLL (10). G-CSF may be considered as an adjunct to antibiotic treatment in the treatment of infections due to its ability to increase the neutrophil count, thus helping would healing (10). In the case reported here, G-CSF was initiated to hasten neutrophil recovery.

Several investigators have reported that laparoscopic-assisted gastrectomy for early gastric cancer is a safe and feasible surgical procedure with acceptable short-term surgical and long-term oncological outcomes (11, 12). In the case reported here, the patient underwent LADG as it was thought that this surgical procedure would reduce postsurgical complications in our patient with neutropenia. The patient tolerated the surgery well and resumed an oral liquid diet within three days after surgery. During the four months following surgery, no adverse sequelae were observed, and the patient continues to be monitored both for recurrence and for progression of the T-CLL.

In conclusion, we experienced a rare case of gastric cancer with neutropenic T-CLL, which was successfully treated with LADG. LADG, if feasible, can be an alternative to open gastrectomy in patients with early gastric cancer with severe neutropenia, potentially reducing perioperative complications, namely secondary infections.

Conflicts of Interest

The Authors declare that they have no conflicts of interest.

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