CASE REPORT

Five-year survival of Advanced Esophagogastric junction cancer with achieved by complete response preoperative S-1 + CDDP combination therapy and surgical resection

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Abstract No clear consensus has been reached about the appropriate chemotherapy and/or surgery for esophagogastric junction cancer (EGJ) cancer, and no recommendations have been established. However, it is hoped that treatment of advanced gastric cancer with preoperative chemotherapy will be useful, in that it will result in down staging, increased resection rate due to tumor contraction, and avoidance of the need for multi-organ resection, and that it will thus contribute to improved prognosis. Numerous clinical studies have been carried out to date on treatment of advanced gastric cancer with multi-drug combination chemotherapy, with S-1, a pyrimidine-fluoride-based anti-tumor agent, as the principal component, and favorable results have been achieved. The present report is about a 66-year-old male who was diagnosed as having Siewert type II, stage IIIB EGJ cancer, and whose bulky tumor was treated with S-1 + CDDP (SP) preoperative chemotherapy and total gastrectomy, with the aim of achieving preoperative tumor contraction. The outcome was achievement of histological complete response, and the patient has now survived for 5 years since surgery.

Keywords Esophagogastric junction cancer · S-1 + CDDP · Neoadjuvant chemotherapy · 5-Year survival · Perioperative chemotherapy

Introduction

In recent years, the frequency of EGJ cancer has shown a tendency to increase even in Japan. However, as this cancer is located at the border between the esophagus and stomach, no clear recommendations have been established as to whether surgery and chemotherapy should be as appropriate for esophageal cancer or for gastric cancer. In addition, even in comparison with other types of gastric cancer, EGJ cancer has a poor prognosis, in connection with transfer of cancer cells in the bloodstream and lymphatic system [1, 2], and there have been no previous reports of postoperative survival of patients treated with preoperative SP chemotherapy. The present report is about one case of EGJ cancer that was treated with preoperative SP chemotherapy, resulting in histological complete response, and recurrence-free, postoperative survival for 5 years.

Case report

The patient was a 66-year-old male with the primary complaint of an unpleasant sensation when swallowing. At the initial diagnosis, the patient was 160.5 cm tall, and weighed 50.4 kg, and the results of tests and examinations were that the abdominal region was level, soft, and without pressure pain, and no masses or superficial lymph nodes were palpable. Hematology tests showed no tumor markers or other abnormal signs.

Esophagogastrroduodenoscopic findings A type-3 lesion with an associated ulcer was found, centered on the posterior wall of the cardiac region of the stomach, and the appearance was that of invasion as far as the esophagus (Fig. 1). The outcome was a diagnosis of poorly differentiated adenocarcinoma, Group 5 (Fig. 2).

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Fig. 1 Esophagogastrroduodenoscopic findings A type-3 lesion with an associated ulcer can be seen, centered on the posterior wall of the cardiac region, with invasion as far as the esophagus

Fig. 2 Histopathological findings in the endoscopic biopsy The pathological diagnosis was poorly differentiated adenocarcinoma, Group5

Thoracoabdominal computed tomography (CT) A tumor with associated contrast enhancement and wall thickening was found in the cardiac region of the stomach. In addition, a bulky tumor could be seen extending throughout the lower esophagus, abdominal esophagus, and cardiac region, and in the left crus of the diaphragm, and lymph node metastases were found around the splenic artery (Fig. 3).

Treatment progression On the basis of the above findings, a preoperative diagnosis of EGJ cancer [Siewert type II, cT4a (SE) N2M0P0H0] at stage IIIB was made in accordance with the histological efficacy judgment criteria in the Japanese Classification of Gastric Carcinoma [3]. On the basis of a clinical diagnosis, as the approach to treatment, the authors administered preoperative S-1+CDDP combination chemotherapy targeting the bulky tumor, with the aim of achieving preoperative tumor contraction. This

chemotherapy involved administration of 80 mg/m² S-1 for 3 weeks, and intravenous infusion of 60 mg/m² CDDP on day 8 after initiation of S-1 administration. Two courses of chemotherapy were completed, and the only adverse events, classified in accordance with CTCAE; version 2.0, were grade-2 appetite loss and dysgeusia. No hemotoxicity, gastrointestinal symptoms, etc., or adverse events at grade 3 or higher were found.

Efficacy judgment Judgments as to efficacy were made using the RECIST; version 1.0 [4]. The esophagogastrroduodenoscopy (EGD) findings were that the tumor was very smooth, and contracted, with the appearance of a scarred ulcer (Fig. 4). Thoracoabdominal CT showed that the tumor was associated with a certain amount of cardiac region stomach wall thickening, but the surrounding lymph nodes, and also lymph node around the splenic artery, showed marked contraction (Fig. 5), so the judgment as

Fig. 3 Thoracoabdominal CT findings A bulky tumor, invaded of the left crus of the diaphragm. It including lymph node metastases, can be seen to extend from the lower esophagus to the cardiac region of the stomach

Fig. 4 Esophagogastroduodenoscopic findings (post chemotherapy) Tumor reduced very much and became again if the surface was smooth, and it became a small ulcer

Fig. 5 Thoracoabdominal CT findings The tumor is associated with a certain amount of wall thickening in the cardiac region, but has contracted together with the surrounding lymph nodes. In addition, marked contraction of lymph node around the splenic artery can be seen

to efficacy at this time was partial response. After a rest period of approximately 3 weeks, surgery was carried out.

Findings at surgery A diagnosis of H0P0CY0 was made at ventrotomy. Total gastrectomy with splenectomy, and D2 lymph node dissection, were carried out via left

thoracolaparotomy. Postoperative progression involved no complications, and the patient was discharged from hospital on day 14 after surgery

Specimens obtained at surgery The only finding was an ulcer scar, measuring 22×24 mm, centered on the EGJ and the posterior wall of the stomach (Fig. 6).

Pathological findings We did holoblastic cleavage pathology and were diagnosed, but the viable cancer cells were not found. The diagnosis was pN0 (0/23), and was judged to be at grade 3, in accordance with the histological efficacy judgment criteria in the Japanese Classification of Gastric Carcinoma (Fig. 7) [3].

Postoperative clinical progression As prophylaxis against recurrence, postoperative chemotherapy was administered for 1 year, consisting of 6-week cycles during which 80 mg/m² S-1 was administered for 4 weeks, followed by a 2-week recovery period. No other chemotherapy was administered during the year, and at the present time, 5 years after surgery, there has been no cancer recurrence.

Fig. 6 *Surgical specimen* The only sign is scarring on the posterior wall of the gastric region. No bulky tumor can be seen

Fig. 7 *Histopathological findings* Only an ulcer scar can be seen, and there were found no viable cancer cells

Discussion

One patient was administered preoperative S-1 + CDDP combination chemotherapy for EGJ cancer, histological complete response was achieved, and he has survived for 5 years since surgery. There have been no previous reports of postoperative survival of EGJ cancer patients administered preoperative S-1 + CDDP combination chemotherapy.

Even in comparison with other types of gastric cancer, EGJ cancer has a poor prognosis, in connection with transfer of cancer cells in the bloodstream and lymphatic system [1, 2].

According to the Japanese Gastric Cancer Association's National Analysis Results Report for 2007, in patients with whom surgery was carried out, the 5-year survival rates were 91.2% at stage IA, 71.1% at stage II, 55.4% at stage IIIA, and 37.0% at stage IIIB [3]. It is clear that these outcomes are unsatisfactory. In addition, in the ACTS-GC study, carried out with D2 lymph node dissection patients, the 5-year survival rates were 84.2% at stage II, 67.1% at stage IIIA, and 50.2% at stage IIIB [5]. At stage III, there is the risk of postoperative recurrence, involving peritoneal dissemination, distant metastasis, etc., due to micrometastases present at the time of surgery. Preoperative chemotherapy is therefore carried out with the aim of reducing the numbers of micrometastases that are one of the causes of recurrence, and is followed by intensive therapy, involving resection of the remaining primary cancer and metastases.

In the Japanese Gastric Cancer Association's Gastric Cancer Treatment Guidelines [6], preoperative chemotherapy is positioned on the basis of clinical research, and although the rate of marked efficacy is low, safety has been confirmed, and it is hoped that the resection rate can be increased, and the need for multi-organ combined

resection thus avoided, by cancer down staging and tumor contraction.

There have been reported the EORTC 40954 study and the Magic study about preoperative chemotherapy for gastric cancer [7, 8]. In two Japanese studies, COMPASS [9] and JCOG0210 [10], the safety of preoperative chemotherapy was shown to be favorable.

S-1 + CDDP combination chemotherapy has been accepted as the first-line treatment for unresectable, recurrent gastric cancer since the SPIRITS study [11], and is now in wide use even in Japan as a regimen for treating gastric cancer. In other words, as the response rate in terms of anti-tumor efficacy was found to be high in the SPIRITS study, there are considered to be good prospects for use as preoperative chemotherapy for resectable, advanced gastric cancer.

The pre-treatment diagnosis for the present patient was advanced cancer with a risk of being unresectable. Treatment was administered as recommended for gastric cancer, and the preoperative chemotherapy was found to be markedly effective against both the primary cancer and the lymph node metastases. Surgery was then carried out safely. Micrometastases were suppressed by S-1 + CDDP neoadjuvant chemotherapy and postoperative oral S-1 administration, and survival for 5 years was achieved.

With respect to surgical techniques and selection of chemotherapeutic regimens for esophagogastric cancer, it will be necessary to continue to pay attention to therapeutic strategies. In particular, publication of the results with preoperative chemotherapy in the JCOG0501 study is awaited. In addition, there has recently been considerable progress with molecular-targeted drugs, and the additional effects of these in gastric cancer chemotherapy are awaited.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical.

Informed consent Informed consent was obtained from the patient for the publication of this case presentation and accompanying images.

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