Ten-year follow-up after chemotherapy (S1 + cisplatin + trastuzumab) and surgery for human epidermal growth factor receptor 2-positive stage IV esophagogastric junction cancer with pathological complete response: a case report

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Case Report

Keywords: stage IV gastric cancer, chemotherapy, conversion surgery, case report

Posted Date: November 21st, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3629091/v1

Additional Declarations: No competing interests reported.

Abstract

Background:

In recent years, many reports have focused on the usefulness of conversion surgery, in which chemotherapy is given to patients with unresectable advanced gastric cancer (GC) and radical surgery is performed if resection becomes possible. However, no consensus has been reached regarding the usefulness of this strategy.

Case presentation:

A 74-year-old man was diagnosed with GC after experiencing abdominal pain. Esophagogastroduodenoscopy revealed an elevated lesion with ulceration at the esophagogastric junction (40 mm in size, type 1 gross type), and biopsy revealed well-differentiated adenocarcinoma. Chest and abdominal computed tomography showed wall thickening at the hilum and multiple enlarged lymph nodes in the left supraclavicular fossa and around the aorta from the hilum to the upper abdomen. These findings were consistent with a malignant tumor at the esophagogastric junction, and esophagogastric junction cancer was diagnosed [T3N3M1 (LYM): stage IV]. Chemotherapy was chosen, and seven courses of S1 + cisplatin (SP) + trastuzumab (HCN) were administered. The patient developed neuropathy, and two courses of S1 + HCN were administered. Approximately 10 months after the start of chemotherapy, upper gastrointestinal endoscopy and positron emission tomography/computed tomography showed that the tumor was almost gone; therefore, we decided to perform conversion surgery. The patient underwent open total gastrectomy, D2 lymph node dissection, and Roux-en-Y reconstruction. Scarring at the esophageal junction was evident on palpation of the specimen, but pathologic examination of the specimen and dissected lymph nodes showed no cancer. Postoperatively, the patient underwent 2 cycles of S1 + HCN followed by 48 cycles of HCN until the second postoperative year. No metastasis or recurrence was observed for 9 years after surgery.

Conclusions:

We have reported a case of stage IV esophagogastric junction cancer with a pathological complete response obtained by SP + HCN therapy. Conversion surgery after chemotherapy resulted in recurrence-free survival. However, further study is needed to elucidate the effect of surgery on top of chemotherapy for stage IV GC as chemotherapy continues to evolve.

Background

Although recent advances have enabled high response rates in patients with gastric cancer (GC), chemotherapy is still recommended for unresectable or recurrent GC [1]. Complete cure is considered difficult to achieve. In this study, we performed chemotherapy for esophagogastric junction cancer with

para-aortic lymph node metastasis followed by surgery after confirming a complete response. The patient achieved recurrence-free survival for 9 years after surgery with postoperative chemotherapy. We herein discuss the usefulness of conversion surgery in this case.

Case presentation

A 74-year-old man presented with the chief complaint of abdominal pain, which had been present for several months. He had been receiving medication for hypertension and atrial fibrillation. On presentation, the tumor markers carcinoembryonic antigen and carbohydrate antigen 19 − 9 were elevated (Table 1).

Table 1
Laboratory values

Complete blood count	
White blood cells	7700/μL
Red blood cells	4.85×10^{6}/μL
Hemoglobin	15.1 g/dL
Platelets	23.6×10^{3}/μL
Blood chemistry	
Total protein	6.7 g/dL
Albumin	4.0 g/dL
Total bilirubin	0.7 mg/dL
Direct bilirubin	0.0 mg/dL
Albumin	3.4 g/dL
Aspartate aminotransferase	29 IU/L
Alanine aminotransferase	19 IU/L
Lactate dehydrogenase	195 IU/L
Creatinine	0.94 mg/dL
Blood urea nitrogen	14.4 mg/dL
C-reactive protein	0.13 mg/dL
Tumor markers	
CEA	40.7 ng/mL
CA19-9	71.4 U/mL
CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19 − 9	

[Table 1 here]

Esophagogastroduodenoscopy revealed an elevated lesion with ulceration at the esophagogastric junction (40 mm in size, type 1 gross type) (Fig. 1a), and biopsy revealed well-differentiated adenocarcinoma. The HER2 score was IHC/2 + using the HercepTest. Chest and abdominal computed tomography (CT) showed wall thickening at the hilum and multiple enlarged lymph nodes in the left supraclavicular fossa and around the aorta from the hilum to the upper abdomen (Fig. 1b). Likewise, positron emission tomography (PET)-CT confirmed wall thickening at the hilum and multiple enlarged lymph nodes in the left supraclavicular fossa and around the aorta from the hilum to the upper abdomen (Fig. 1c). These findings were consistent with a malignant tumor at the esophagogastric junction, and esophagogastric junction cancer was diagnosed [T3N3M1 (LYM): stage IV]. Chemotherapy was chosen, and seven courses of S1 + cisplatin (SP) + trastuzumab (HCN) were administered; however, he developed chemotherapy-induced peripheral neuropathy, and SP was discontinued from the 8th course. Two courses of S1 + HCN were administered. Approximately 10 months after the start of chemotherapy, upper gastrointestinal endoscopy, CT, and PET-CT showed that the tumor was almost gone (Figs. 2a-c), and we decided to perform conversion surgery. At the beginning of surgery, we confirmed that the tumor was Cy0 (class I), P0 and the patient underwent open total gastrectomy, D2 lymph node dissection (Nos. 1, 2, 3, 4sa, 4sb, 4d, 5, 6, 7, 8, 9, and 11p, n = 18), and Roux-en-Y reconstruction. Scarring at the esophageal junction was evident on palpation of the specimen, but pathologic examination of the specimen and dissected lymph nodes showed no cancer (Figs. 3 and 4a-b). Postoperatively, the patient underwent 2 cycles of S1 + HCN followed by 48 cycles of HCN until the second postoperative year. Nine years after surgery, no metastasis or recurrence had been observed, and the tumor markers were almost within normal limits (Fig. 5).

Discussion and Conclusions

GC is the leading cause of morbidity and mortality in Japan, and effective treatment strategies are essential. The median survival for stage IV disease is approximately 15 months, and chemotherapy is recommended in GC treatment guidelines [1]. Although recent advances have enabled a high response rate, complete cure remains challenging. Chemotherapy has evolved over the past decade, and several options are now available. The patient in the present case was diagnosed with stage IV GC with enlarged para-aortic lymph nodes by CT and PET-CT and was treated with chemotherapy in our oncology department. Ten months later, no lesions were detected by endoscopy, CT, and PET-CT, and the patient felt that the chemotherapy had been effective. After much discussion about whether to perform surgery, we explained to the patient that we recommended conversion surgery, and he agreed. The resected specimen showed no cancer in the stomach or lymph nodes. Postoperative chemotherapy was continued, but it was terminated midway. At the time of this writing, 10 years had passed since the start of chemotherapy. We previously reported a case of long-term chemotherapy for liver metastasis that appeared after surgery for GC and disappeared [2]. In recent years, many reports have described the usefulness of conversion surgery, in which chemotherapy is given to patients with unresectable advanced GC and radical surgery is

performed if resection becomes possible [3–5]. However, no consensus on the usefulness of this strategy has yet been reached.

Although a complete response was confirmed by imaging and endoscopy in this case, surgery was deemed necessary [3], resulting in long-term recurrence-free survival. Recently, Kinoshita et al. [4] and Kano et al. [5] also reported conversion surgery for stage IV GC, and we reviewed our case as category 2 with marginally resectable metastasis. A previous report indicated that two courses of chemotherapy were acceptable, although four to six courses are usually administered, making the timing of chemotherapy before surgery difficult to determine [6]. Regarding postoperative chemotherapy, S1 alone is the preferred agent for esophagogastric junction cancer. In this case, however, the left supraclavicular and para-aortic lymph nodes were not dissected and preoperative S1 + HCN was considered. Notably, Yoshida et al. reported that chemotherapy should be continued for as long as possible after removal of the tumors, until the development of chemoresistance or uncontrollable adverse events [3]. Genome analysis has revealed a subset of patients who responded well to chemotherapy, demonstrating its effectiveness [7]. The usefulness of HCN for human epidermal growth factor receptor 2-positive GC is well known [8]; in recent years, its usefulness for GC that expresses programmed death ligand 1 [9] and claudin 18.2 [10] has also been reported, and various clinical studies are underway. This report was based on a single institution's experience; further study is needed. Such research will help to determine the course of treatment in patients with GC.

The patient said that I initially wondered if I could manage with only anticancer drugs. However, I also asked what if the anticancer drugs stopped working and I exploded. After the surgery, I remember feeling liberated. And I am grateful that I have been able to lead a normal life for about 10 years.

We have reported a case of stage IV esophagogastric junction cancer with a pathological complete response obtained by SP + HCN therapy. Conversion surgery after chemotherapy resulted in recurrence-free survival. This case suggests that chemotherapy followed by R0 resection may lead to long-term survival in patients with human epidermal growth factor receptor 2-positive stage IV esophagogastric junction cancer; however, further studies are needed to clarify the details of surgery after chemotherapy for stage IV GC, in line with the continuing evolution of chemotherapy.

Abbreviations

GC, gastric cancer

CT, computed tomography

SP, S1 + cisplatin

HCN, trastuzumab

PET, positron emission tomography

Declarations

Ethics approval and consent to participate.

Not applicable.

Consent for publication

The patient and his family provided informed consent for publication of this case report.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Competing interests

The authors declare that they have no competing interests.

Funding

None of the authors received any funding for this study.

Authors' contributions

TE and SM diagnosed the stage IV gastric cancer. TT performed the chemotherapy. TE, SM and TO performed and managed the surgery. MC performed the pathologic examination. TE was the major contributor in writing the manuscript with support from SM, TO, TT, and MC. All authors read and approved the final manuscript.

Acknowledgments

We thank Angela Morben, DVM, ELS, and Susan Furness, PhD, from Edanz (https://jp.edanz.com/ac) for editing a draft of this manuscript.

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Figures

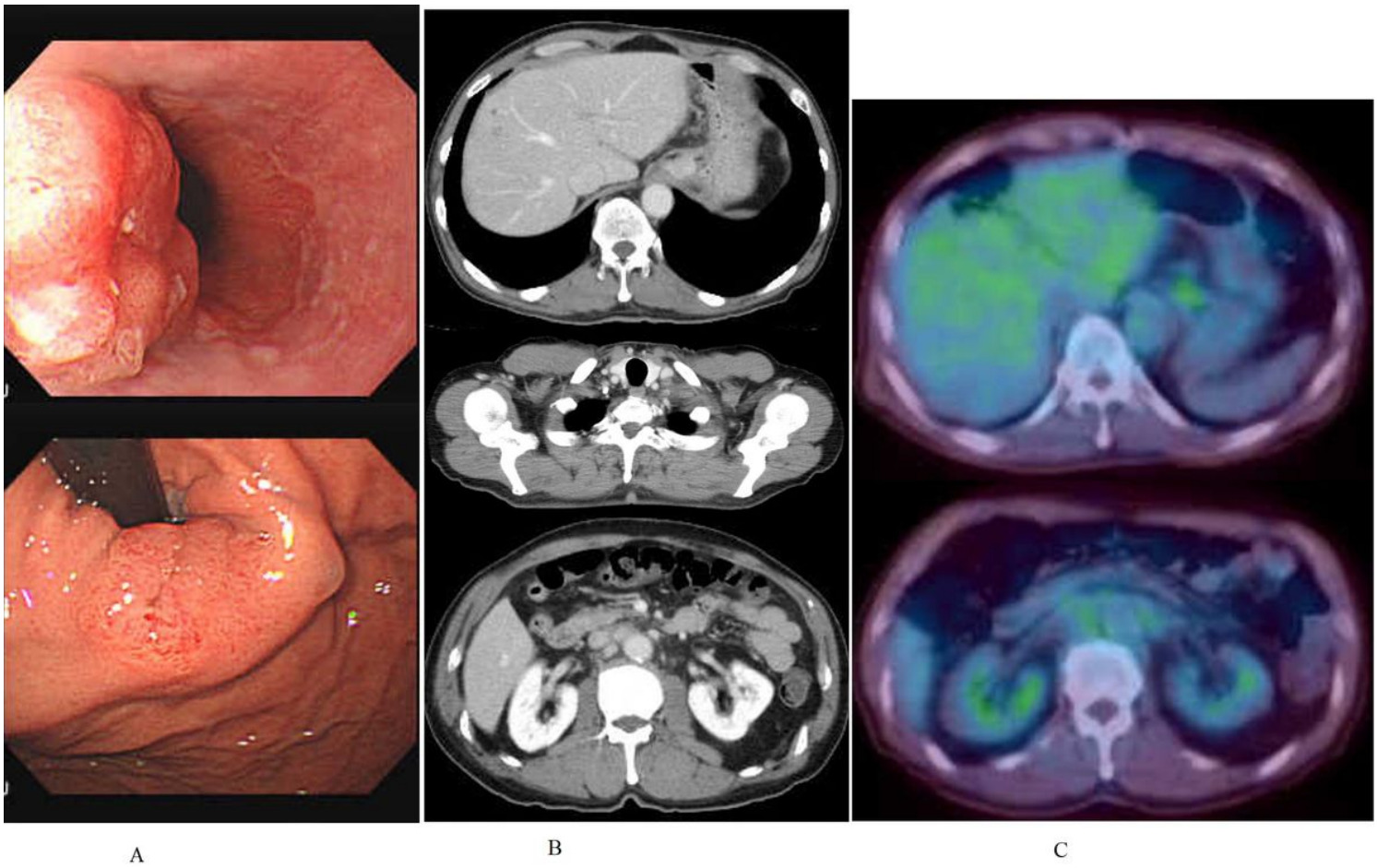

Figure 1

Images before chemotherapy. (a) Esophagogastroduodenoscopy; (b) abdominal computed tomography; (c) positron emission tomography–computed tomography.

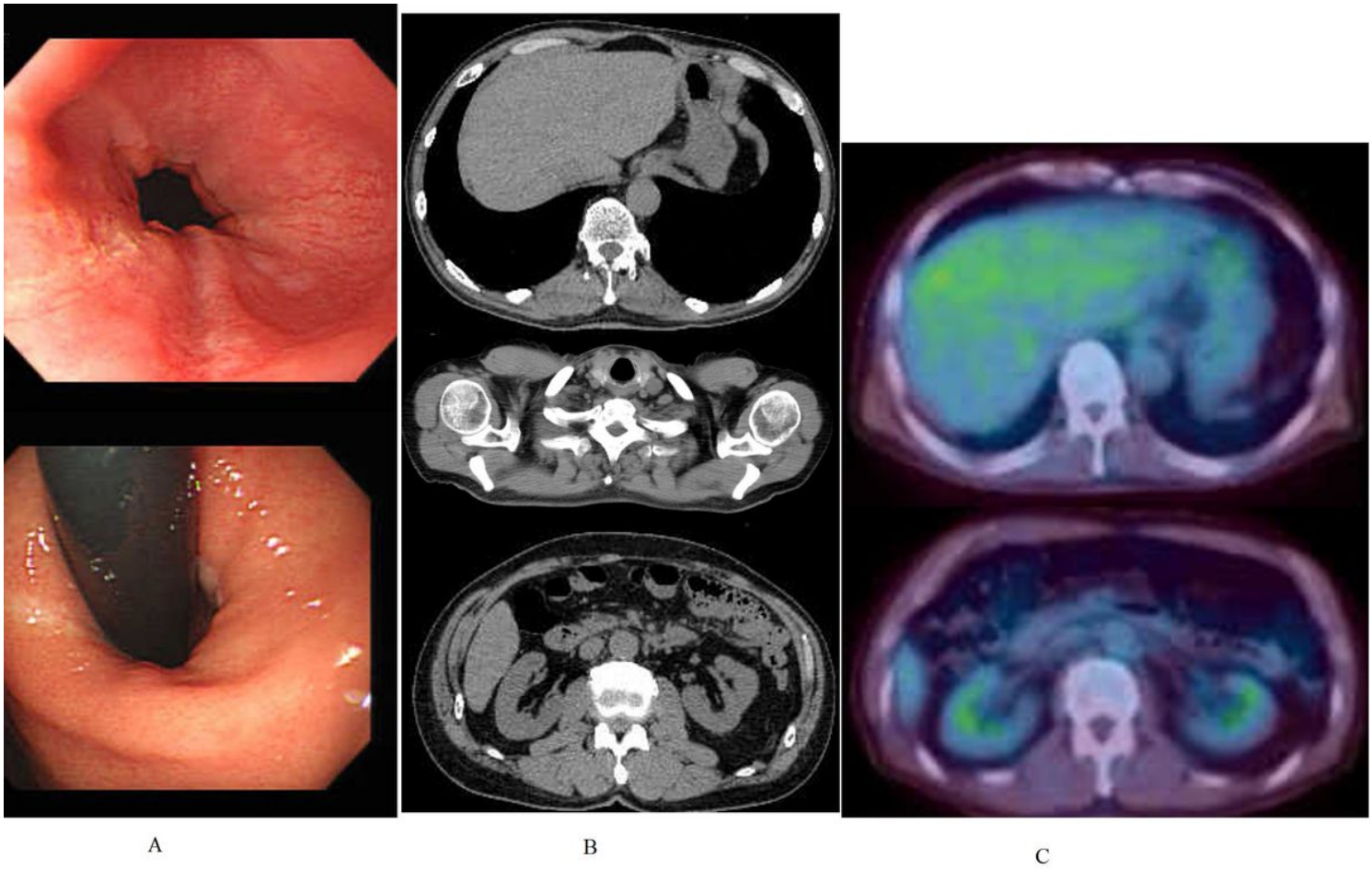

Figure 2

Images after chemotherapy. (a) Esophagogastroduodenoscopy; (b) abdominal computed tomography; (c) positron emission tomography–computed tomography.

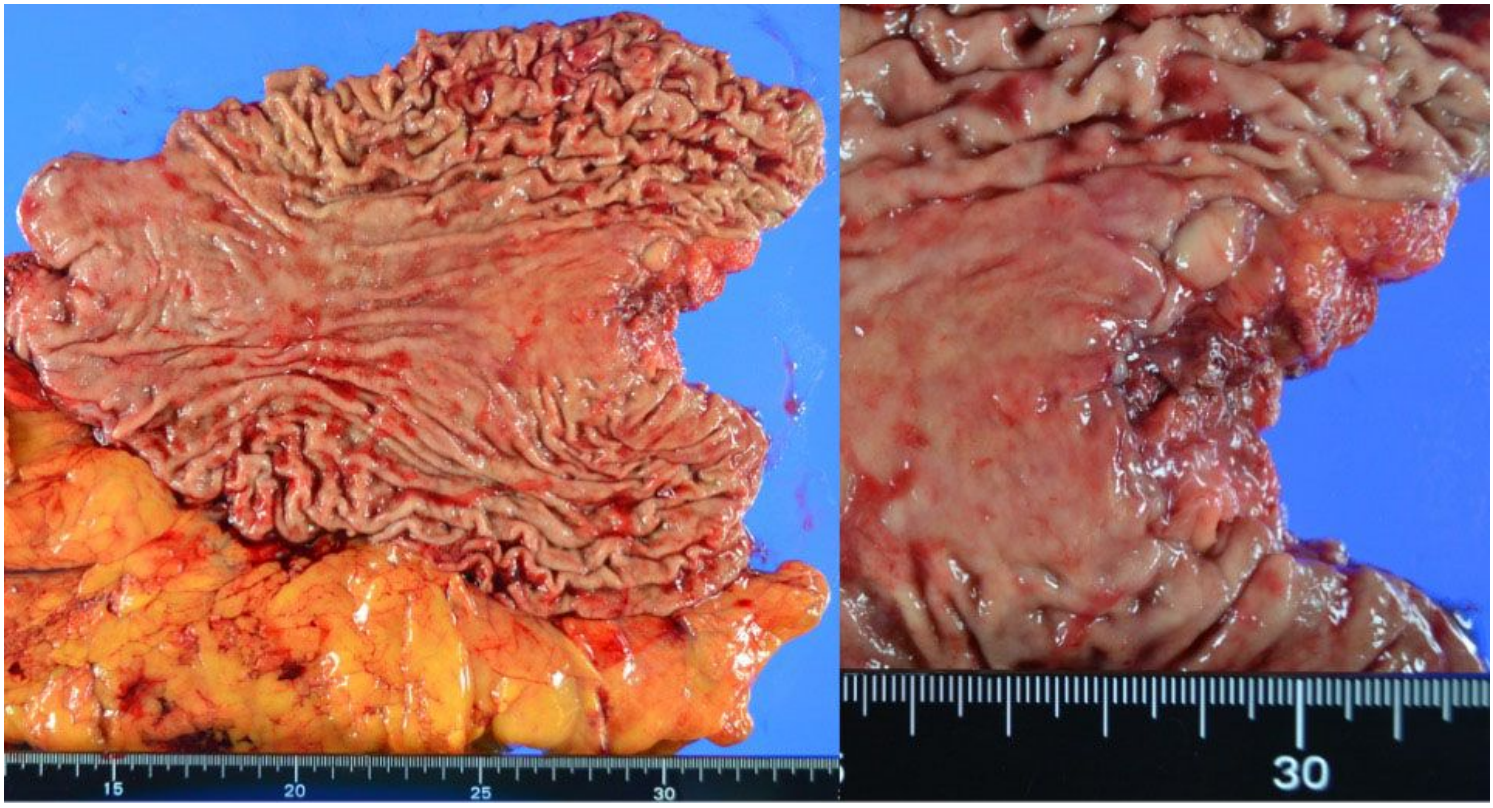

Figure 3

Resected specimens

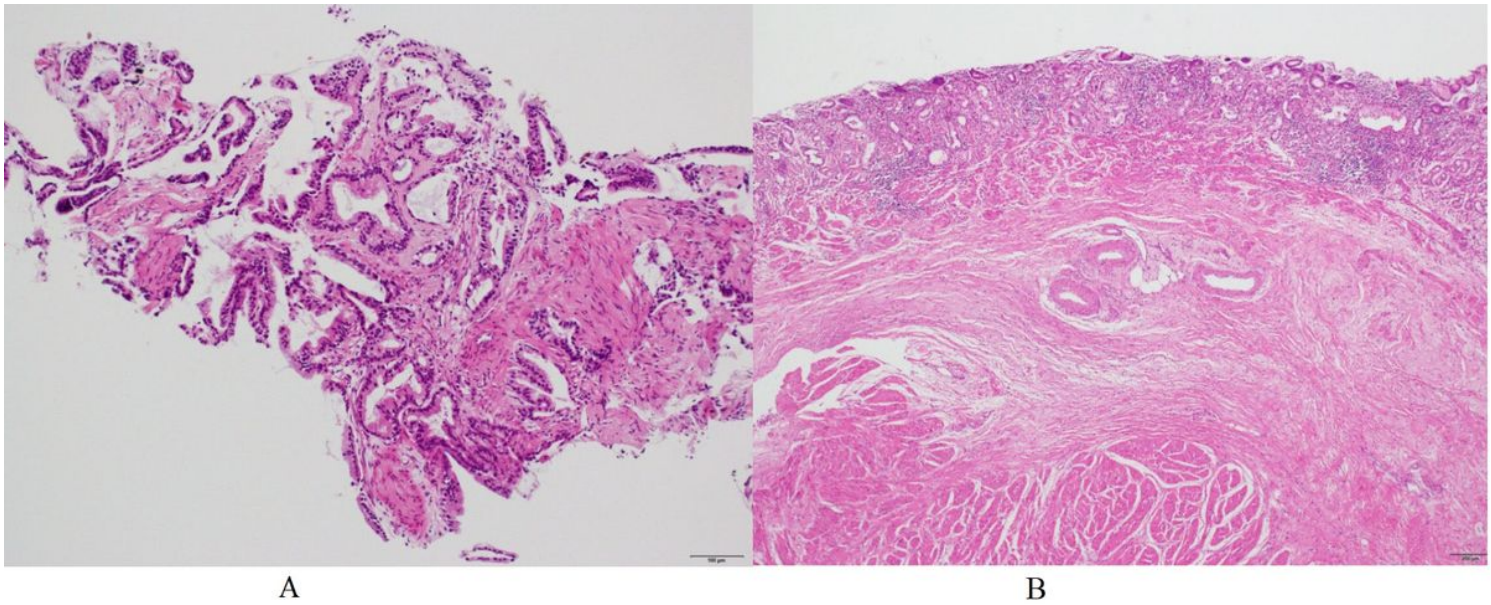

Figure 4

Pathological findings (hematoxylin and eosin stain). (a) Biopsy: papillary adenocarcinoma, well-differentiated tubular adenocarcinoma. (b) Specimen: only scar

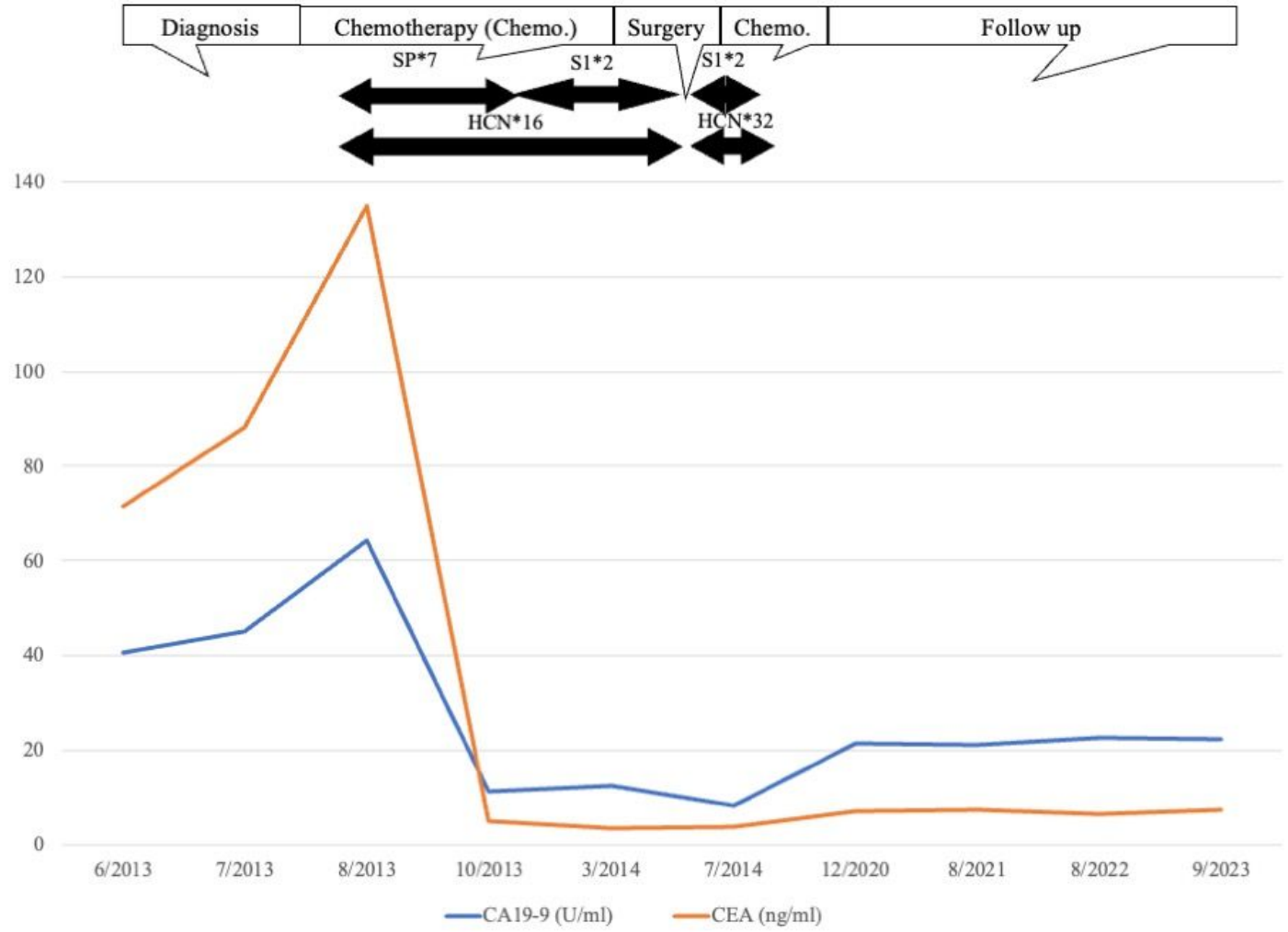

Figure 5

Time course of therapy

SP: S1 + cisplatin; HCN: trastuzumab; CEA: carcinoembryonic antigen