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Long-term survival of a patient with advanced gastric cancer with paraaortic lymph node metastasis who attained pathological complete response after S-1/CDDP chemotherapy: A case report



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ABSTRACT

INTRODUCTION: Gastric cancer with paraaortic lymph node (PAN) metastasis have unfavorable prognosis. There are no evidence-based preoperative chemotherapy regimens available.

CASE PRESENTATION: A 62-year-old female was diagnosed with advanced gastric cancer and PAN metastasis. We attempted S-1/CDDP chemotherapy in six courses and total gastrectomy as well as systematic dissection of regional lymph nodes and PAN. Histologically, no cancerous cells were detected in specimens. The patient has been disease-free for 5 years since the surgery.

DISCUSSION: Long-term survival case of gastric cancer with PAN metastasis attaining pathological complete response is extremely rare. It is possible that preoperative S1/CDDP with surgery might be a standard treatment strategy for gastric cancer with PANs.

CONCLUSION: We report herein a rare case of gastric cancer with PAN metastases who achieved a 5-year survival after S-1/CDDP chemotherapy and surgery.

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1. Introduction

Gastric cancer with paraaortic lymph node (PAN) metastasis is classified as distant metastasis and as Stage IV under the 7th Union for International Cancer Control (UICC^{7th}) guidelines. Furthermore, surgery for Stage IV gastric cancer is not indicated according to the Japanese gastric cancer treatment guidelines [1]. The prognosis for stage IV gastric cancer is extremely poor [2] and currently, there are no evidence-based preoperative chemotherapy regimens available. Here, we report a patient with advanced gastric cancer with PAN metastasis who showed pathologically complete response and favorable outcomes after S-1/CDDP chemotherapy.

Abbreviations: PAN, paraaortic lymph node; UICC, Union for International Cancer Control; EGD, esophagogastroduodenoscopy; CT, computed tomography; pCR, pathological complete response.

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2. Case presentation

A 62-year-old woman visited her previous doctor complaining of epigastric discomfort. She was referred to our hospital for a complete examination. She had an unremarkable medical history without anorexia and loss of weight. Her height was 156 cm, weight was 54 kg, and body surface area was 1.52 m². We measured levels of carcinoembryonic antigen (15.4 ng/mL) and carbohydrate antigen 19-9 (normal), which are tumor markers. Esophagogastroduodenoscopy (EGD) indicated the presence of a Borrmann type 3 tumor in the lesser curvature of the stomach (Fig. 1A), and histological biopsy specimens showed poorly differentiated adenocarcinoma. Abdominal computed tomography (CT) demonstrated enhanced and thickened gastric wall with multiple metastatic regional lymph nodes. Lymph nodes along the celiac artery and the lesser curvature were remarkably swollen (i.e., bulky N2) (Fig. 2A). Metastasis to PAN (No. 16a2) was also observed (Fig. 2B). We diagnosed the patient with unresectable gastric cancer (M, Less, Borrmann type 3, cT4a, cN3a, cH0, cP0, cM1, cStage IV according to UICC^{7th}) and attempted to perform treatment with S-1 (tegafur, gimestat, and otastat potassium) with CDDP (cisplatin) chemotherapy. We anticipated that the tumor would be downstaged as a result of the chemotherapy. S-1 (120 mg/body/day) was given orally twice daily for the first 3 weeks of a 4-week course. CDDP was given as an

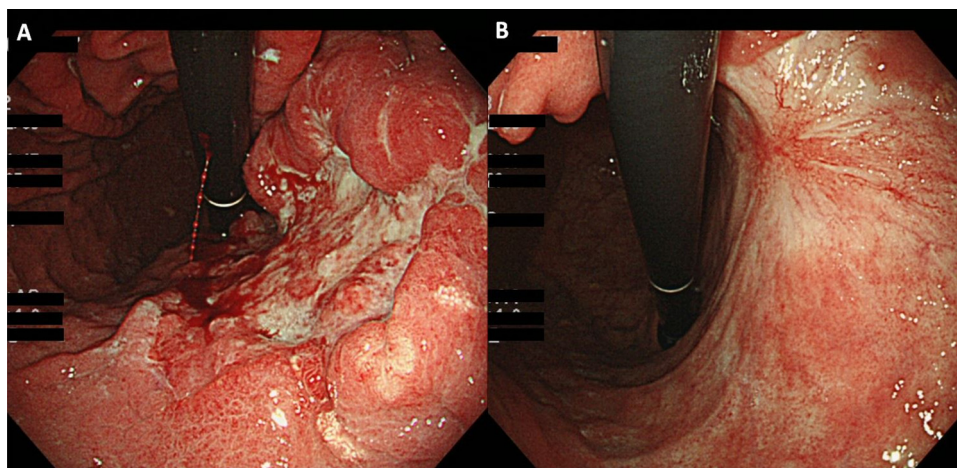


Fig. 1. (A) EGD before chemotherapy revealed Borrmann type 3 cancer in the lesser curvature of the stomach. Histological examination of the biopsy showed poorly differentiated adenocarcinoma. (B) EGD after chemotherapy showed a scar-like flat lesion in the lesser curvature of the stomach. Cancer cells were not found in the biopsy specimen.

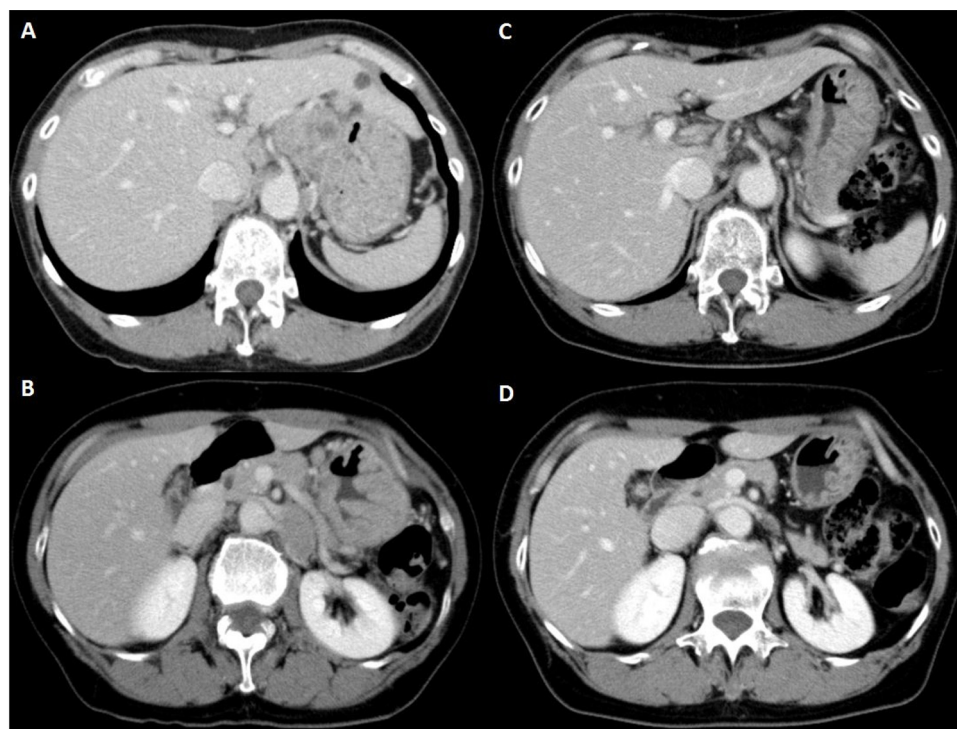


Fig. 2. Abdominal enhanced CT before chemotherapy demonstrated (A) bulky lymph nodes along the celiac artery (No.9 [33 mm]) and the lesser curvature (No.3 [42 mm]). (B) Paraaortic lymph nodes (No.16a2) were swollen (27 mm). CT after chemotherapy revealed (C) that No.9 disappeared and that No.3 shrank. (D) No.16a2 was also reduced in size.

intravenous infusion of 90 mg/body/day on day 8 of each course. She completed 6 courses of this regimen without severe adverse effects. EGD after chemotherapy demonstrated that the gastric lesion was scarred (Fig. 1B). Additionally, abdominal CT revealed a reduction in the size of the regional lymph nodes (Fig. 2C), especially the PAN (Fig. 2D); this was considered an indication for surgery. She underwent surgery 55 days after the administration of the last dose of chemotherapy. We performed total gastrectomy and D2 lymphadenectomy as well as paraaortic lymph node dissection with Roux-en-Y reconstruction. The surgery lasted for 341 min and the total blood loss was 734 ml. No macroscopic metastases were found in the liver and peritoneum, including a negative result of peritoneal washing cytology (CY0). Macroscopically, the gastric lesion in the resected specimen was scarred (Fig. 3). Histopathol-

ogy, no cancerous cells were detected in the scarred region of the stomach. The number of dissected lymph nodes was 47, and there were no metastatic lymph nodes, including PANs. The therapeutic effect of the chemotherapy was Grade 3.

The postoperative course was uneventful, and the patient was discharged from our hospital on postoperative day 14. We simply followed up her without adjuvant chemotherapy, and she remained disease-free for 5 years after surgery.

3. Discussions

Stage IV gastric cancers have an unfavorable prognosis. The Japanese gastric cancer association reported that the 5-year sur-



Fig. 3. Macroscopic findings of the resected specimen revealed a scar-like lesion in the lesser curvature of the stomach. One tick mark= one mm.

Table 1

Published cases of para-aortic lymph node metastasis with complete response to S-1/CDDP chemotherapy.

No.	Author	Year	Age/Sex	Chemotherapy	Histologic type	PAN ^a size (cm)	PAN position	Operation	Adjuvant chemotherapy	Outcome
1	Sugiki ¹¹⁾	2006	59/M	S-1 100 mg [days 1–28] CDDP 10 mg [day 1, 15] 8 cycles	por	3 × 1.5	#16a2 latero	DG + D1 + α	–	1Y alive
2	Shiraishi ¹²⁾	2007	59/M	S-1 120 mg [days 1–21] CDDP 90 mg [day 8] 2 cycles	por	2	#16a2 inter	DG + D2 +PAND ^b	–	2Y3 M alive
3	Fujisawa ¹³⁾	2007	60/M	S-1 120 mg [days 1–21] CDDP 75 mg [day 8] 2 cycles	por	2 × 1.5	#16a2 inter	DG + D2	–	1Y alive
4	Matono ¹⁴⁾	2008	67/M	S-1 120 mg [days 1–21] CDDP 25 mg [day 8] 2 cycles	tub2	–	#16a2 inter #16a2 latero	DG + D2 +PAND	S-1 120 mg/day 4weeks, q2weeks, 1Y	2Y alive
5	Oshima ¹⁵⁾	2010	59/M	S-1 120 mg [days 1–21] CDDP 93 mg [day 8] 3 cycles	por	2.5	#16a2 latero	DG + D2 +PAND	S-1 120 mg/day 4weeks, q2weeks, 1Y	6 M alive
6	Kitayama ¹⁶⁾	2015	66/M	S-1 120mg [days 1–21] CDDP 90 mg [day 8] 3 cycle	por	–	#16a2 latero	TG + D2	S-1 120 mg/day 2weeks, q1week, 1Y	2Y10 M alive
7	Our case	2017	62/F	S-1 120 mg [days 1–21] CDDP 90 mg [day 8] 6 cycle	por	2.7	#16a2 latero	TG + D2 +PAND	–	5Y

^a PAN: paraaortic lymph node.

^b PAND: paraaortic lymph node dissection.

vival rate in patients with gastric cancer are as follows: Stage IA, 92.2%; Stage IB, 85.3%; Stage II, 72.1%; Stage IIIA, 52.8%; Stage IIIB, 31.0%; and Stage IV, 14.9% [2]. Gastric cancers with PAN metastasis also have an extremely unfavorable prognosis and poor curability, with the 5-year survival rate being approximately 5% [3,4].

There are currently no evidence-based preoperative chemotherapy regimens for Stage IV gastric cancer. The S-1/CDDP is one of the first line chemotherapy regimens for Stage IV gastric cancer in Japan. In a phase II study using this regimen in patients with metastatic gastric cancer, a high response rate of 76.0% and an acceptable side-effect rate of 26.0% (Grades 3–4) were reported [5]. These results were confirmed in a phase III study (SPIRITS trial) for

metastatic gastric cancer where S-1/CDDP showed a much higher response rate of 54.0% than S-1 monotherapy, which had a response rate of 31.1% [6]. Based on the SPIRITS trial, we decided the schedule and dose of S-1 (orally twice daily 120 mg/day for the first 21 days, calculated according to the patient's body surface area >1.5 m²) and cisplatin (intravenous infusion of 60 mg/m² on day 8 of each cycle).

A standard treatment for gastric cancer with paraaortic lymph node metastasis has yet to be determined. The Japan Clinical Oncology Group (JCOG) 0405 was a phase II clinical study of preoperative S-1/CDDP chemotherapy for gastric cancer with PANs and/or bulky lymph node enlargement but no other distant metastases [7]. This was followed by gastrectomy with extended lymph node dissection

including PAN. Fifty-three patients were enrolled, and among the 51 who proved eligible, R0 resection was performed in 42 patients (82.4%). A subsequent analysis showed a good response rate of 64.7%, 3-year survival rate of 58.5% and 5-years survival rate of 52.7%. S-1/CDDP is possibly an effective regimen for preoperative chemotherapy in gastric cancer patients with PANs.

A PubMed search using key words, such as gastric cancer, PAN, S-1/CDDP, and pathological complete response (pCR), resulted in only 6 relevant well-documented cases (Table 1) [8–13]. The 7 cases consisted of 6 men and 1 woman, whose ages ranged from 59 to 67 years (mean 61.7 years). The histologic types of six-sevenths cases were poorly differentiated adenocarcinoma. The regimens of 4 cases were based on the SPIRITS trial. In all cases, the sizes of the PAN were less than 3 cm, and the PAN metastases were in No.16a2: lymph nodes between the celiac axis and lower border of the left renal vein [14]. There were no reports of a similar patient attaining a 5-year survival.

In our case, we attempted treatment using combined pre-operative S-1/CDDP chemotherapy with surgery. Consequently, pathological specimens showed no cancer cells, thereby indicating pCR. This case is rare and treatment resulted in a desirable outcome without adjuvant chemotherapy. It is possible that preoperative S1/CDDP with surgery might be a standard treatment strategy for gastric cancer with PANs.

4. Conclusions

We report herein a rare case of a patient with advanced gastric cancer with PAN metastases who achieved a 5-year survival after S-1/CDDP chemotherapy and surgery.

Declarations

This case report is compliant with the SCARE Guidelines [15].

Author's contributions

YU, KH, SS, TA, HG, and TA conceived the idea for the paper and helped draft the manuscript. TA proof read the paper. YU, KH and TA participated in the clinical treatment. All of the authors read and approved the final version of the manuscript.

Consent

When obtaining informed consent for the surgical procedure, general consent for publication and presentation was also obtained from the patient. Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Competing interests

The authors report no competing interests.

Ethics approval and consent to participate

We reported this case report in compliance with the Helsinki Declaration. We got approval of ethics committee in Anjo Kosei Hospital. The reference number in this case is C16108. My license number of clinical research is 160108.

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Guarantor

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References

- [1] JGC Association, Japanese gastric cancer treatment guidelines. 2010 (version 3), *Gastric Cancer* 14 (2011) 113–123.
- [2] A. Nashimoto, K. Akazawa, Y. Isobe, I. Miyashiro, H. Ktai, Y. Koderu, S. Tsujitani, Y. Seto, H. Furukawa, I. Oda, H. Ono, S. Tanabe, M. Kaminishi, Gastric cancer treated in 2002 in Japan: 2009 annual report of the JGCA nationwide registry, *Gastric Cancer* 16 (1) (2013) 1–27.
- [3] Y. Koizumi, A. Hara, M. Tomita, K. Sakamoto, H. Obata, T. Shiomi, S. Nakajo, K. Hashimoto, A case of advanced gastric cancer attaining histological CR of paraaortic lymph node after TS-1/CDDP neoadjuvant chemotherapy, *Gan To Kagaku Ryoho* 30 (9) (2003) 1351–1356 (In Japanese).
- [4] M. Sasako, T. Sano, S. Yamamoto, Y. Kurokawa, A. Nashimoto, A. Kurita, M. Hiratsuka, T. Tsujinaka, T. Kinoshita, K. Arai, Y. Yamamura, K. Okajima, D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer, *N. Engl. J. Med.* 359 (5) (2008) 453–462.
- [5] W. Koizumi, S. Tanabe, K. Saigenji, A. Ohtsu, N. Boku, F. Nagashima, K. Shirao, Y. Matsumura, M. Gotoh, Phase I/II study of S-1 combined with cisplatin in patients with advanced gastric cancer, *Br. J. Cancer* 89 (12) (2003) 2207–2212.
- [6] W. Koizumi, H. Narahara, T. Hara, A. Takagane, T. Akiya, M. Takagi, K. Miyashita, T. Nishizaki, O. Kobayashi, W. Takiyama, Y. Toh, T. Nagaie, S. Takagi, Y. Yamamura, K. Yanaoka, H. Orita, M. Takeuchi, S-1 Plus cisplatin versus S-1 alone for first-line treatment of advanced gastric cancer (SPIRITS trial): a phase III trial, *Lancet Oncol.* 9 (3) (2008) 215–221.
- [7] A. Tsuburaya, J. Mizusawa, Y. Tanaka, N. Fukushima, A. Nashimoto, M. Sasako, Stomach Cancer Study Group of the Japan Clinical Oncology Group: neoadjuvant chemotherapy with S-1 and cisplatin followed by D2 gastrectomy with para-aortic lymph node dissection for gastric cancer with extensive lymph node metastasis, *Br. J. Surg.* 101 (6) (2014) 653–660.
- [8] T. Sugiki, T. Inoue, E. Yanatori, H. Kamikozuru, H. Oguma, K. Takasaki, A case of advanced gastric cancer in which complete response was confirmed with resection following long-term TS-1/CDDP combined chemotherapy, *Jpn. J. Gastroenterol. Surg.* 39 (1) (2006) 38–43 (in Japanese).
- [9] O. Shiraishi, S. Hatabe, S. Ishikawa, Y. Kitano, M. Kawasaki, K. Sakai, A. Hayashibe, S. Hunai, M. Kameyama, A case of advanced gastric cancer responding to TS-1/CDDP therapy was pathological complete response, *Jpn. J. Gastroenterol. Surg.* 40 (11) (2007) 1769–1774 (in Japanese).
- [10] T. Fujisawa, W. Sano, S. Ouchi, S. Ueyama, T. Mori, D. Tsuchihashi, O. Ushikoga, M. Koyanagi, H. Yoshimura, S. Tachibana, H. Hirano, Complete histological response in gastric cancer stage IV after neoadjuvant chemotherapy including S-1 combined with CDDP—report of a case, *Gan To Kagaku Ryoho* 34 (13) (2007) 2297–2300 (in Japanese).
- [11] S. Matono, H. Horiushi, Y. Kishimoto, T. Fukumitsu, F. Yoshimura, K. Shirouzu, A case of advanced gastric cancer with para-aortic lymph node metastasis responding to neoadjuvant chemotherapy which leads to a pathological complete response, *Jpn. Surg. Assoc.* 69 (4) (2008) 815–819 (in Japanese).
- [12] N. Oshima, Y. Tanizawa, E. Bando, T. Kawamura, M. Tokunaga, N. Sugisawa, Y. Taki, Y. Motegi, N. Boku, K. Sasaki, M. Terashima, Histological complete response in a case of advanced gastric cancer treated by neo-adjuvant chemotherapy with S-1/CDDP, *Gan To Kagaku Ryoho* 37 (4) (2010) 697–701 (in Japanese).
- [13] K. Kitayama, I. Kanehara, H. Teraoka, J. Nishimura, S. Nomura, E. Noda, H. Nishino, K. Hiraskawa, A case of advanced gastric cancer responding to S-1/CDDP neoadjuvant chemotherapy, leading to a pathological complete response, *Gan To Kagaku Ryoho* 42 (1) (2015) 85–87 (in Japanese).
- [14] Japanese Gastric Cancer Association, Japanese classification of gastric carcinoma: 3rd English edition, *Gastric Cancer* 14 (2011) 101–112.
- [15] R.A. Riaz, A.F. Alexander, A. Saeta, I. Barai, S. Rajmohan, D.P. Orgill, SCARE Group, The SCARE statement: consensus-based surgical case report guidelines, *Int. J. Surg.* 34 (2016) 180–186.