Case Report

R0 resection of Stage IV HER2-positive gastric cancer after the first-line chemotherapy: a case of successful conversion therapy

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Abstract

Background: Despite the recent improvement in chemotherapy for Stage IV gastric cancer (GC), cure of this condition remains challenging. In the present report, we would like to describe a case of Stage IV GC, in which the first-line treatment achieved complete response and R0 surgical resection was successfully performed.

Case Presentation: A 64-year-old female patient presented with a chief complaint of appetite loss. Gastrointestinal endoscopy revealed Type 2 tumor at the antrum of stomach. The biopsy specimen diagnosed the patients having HER2-positive moderately differentiated adenocarcinoma of stomach. Serum level of CA19-9 was elevated to more than 12000 U/ml (normal range < 37 U/ml). Enhanced abdominal computed tomography (CT) demonstrated enlarged para-aortic lymph nodes (LNs) as well as the regional LNs, and the patient was diagnosed as having Stage IV GC. The patient underwent four courses of first-line treatment with S-1+CDDP+Trastuzumab. Consequently, the LNs and the primary tumor became undetectable. The patient underwent distal gastrostomy with dissection of regional and para-aortic LNs. Pathologically, the tumor cells were identified sparsely in the fibrotic tissue of stomach, although the tumors in LNs were completely necrotic. So far, there is no sign of tumor recurrence for more than 6 months.

Conclusion: Conversion therapy for Stage IV GC is possible, and seems clinically beneficial in selected patients.

Keywords: Conversion therapy, Stage IV, Trastuzumab, paraaortic lymph nodes

(Received: August 7, 2017; Accepted August 21, 2017)

Background

In contrast to the treatment for early gastric cancer (GC), in which endoscopic mucosal resection and/or gastrectomy with lymphadenectomy may offer cure¹, the prognosis of Stage IV GC remains dismal. Molecular targeting therapy, including trastuzumab and ramucirumab, improves the progression free survival and overall survival²,³. Nevertheless, the cure of disease by adding surgical intervention to chemotherapy remains rare, which is contrasting feature of GC to metastatic colorectal cancers. Besides, gastrectomy followed by chemotherapy does not have any survival benefit compared to chemotherapy alone for the patients with a single non-curable factor⁴. Therefore, the only hope for cure is preoperative chemotherapy followed by R0 resection.

Case presentation

A 64-year-old female patient presented to Hata-Kenmin Hospital for the treatment of appetite loss and postprandial indigestion. On physical examination, a large hard mass was noted in the upper abdomen. Her blood test revealed markedly elevated serum level of CA19-9 (> 12000 U/ml, Normal range < 37 U/ml). Gastrointestinal endoscopy revealed a Type 2 tumor at the antrum of stomach (Fig. 1A). Biopsy examination diagnosed human epidermal growth factor receptor 2 (HER-2)-positive, moderately differentiated adenocarcinoma (Fig. 1B). The following abdominal computed tomography (CT) revealed thicken gastric wall of the antrum, and enlarged regional LNs and paraaortic lymph nodes (LNs) (Fig. 1 C & D). The patient was diagnosed as having Stage IV GC due to distant metastasis of para-aortic lymph nodes.

Accordingly, she received four cycle of the first-line chemotherapy with S-1+CDDP+Trastuzumab. Level of serum CA19-9 steadily decreased to the normal range during and after chemotherapy (24.6 U/ml, Normal range
Fig. 1  (A) Endoscopic examination. The antrum of the stomach is stenotic. The observation of whole tumor is difficult.  (B) Biopsy and staining with anti-HER2 antibody revealed HER2-positive moderately differentiated adenocarcinoma of stomach. The bar is 50 µm.  (C & D) Abdominal computed tomography shows he enlarged regional LNs (No.6) and paraaortic LNs (16b1) (white arrow heads). The wall of the antrum was thickened and enhanced (C).

Fig. 2  (A & B) Abdominal CT after four courses of chemotherapy. Regional LNs nor paraaortic LNs diminished after chemotherapy (white arrow head).  (C) Intraoperative observation after paraaortic LNs dissection. 16b1 LNs are dissected in this surgical field.  (D) Microscopic observation of the primary tumor revealed residual tumor cells and surrounding fibrotic tissue. The bar is 400 µm.
< 37 U/ml). On abdominal CT, the preoperatively identified swollen LNs became undetectable, and the inflammation of the omentum and adipose tissue adjacent to gastric wall subsided (Fig. 2 A & B); clinical complete response without confirmation was diagnosed.

During the treatment, the patients had Grade 2 nausea, and the dose of S-1+CDDP was reduced by 20%. However, the patient refused further continuation of chemotherapy despite its efficacy, and chosen to undergo surgical resection. Distal gastrectomy under laparotomy, and dissection of regional and paraaortic LNs were performed (Fig. 2C). Pathological examination revealed that the majorities of the tumor was replaced by fibrotic tissue, and tumor nest was sparsely observed (Fig. 2D). No tumor cells was identified within the resected LNs but necrotic lesions. So far, 6 months has passed without any sing of tumor recurrence.

Discussion

Treatment for Stage IV GC is shifting. Yamaguchi et al reported that technically or oncologically unresectable gastric cancer still have a chance to be surgically removed after several courses of chemotherapy\(^4\). Reportedly, the median survival time of the patients undergoing R0 resection was 41.3 months, while that for the patients who could not undergo any surgical resection was 11.3 months. Despite the retrospective study and its inherited selection bias, the long-term survival observed among the patients after R0 resection is fascinating.

To facilitate and analyze conversion therapy for GC, Yoshida and colleagues recently proposed a new category system for Stage IV GC according to the possibility of surgical resection\(^5\). GC with a few paraaortic LNs metastasis (16a1 and 16b1) is classified as Category 1 (potential resectable metastasis). And the preoperative chemotherapy for such cases, termed neoadjuvant chemotherapy, results in favorable prognosis. In the present case, the distant metastases were limited to the paraaortic lymph nodes, and could be classified as Category 1 of the newly proposed classification. However, the enlargement of several paraaortic lymph nodes were observed, surgical resection did not seem best choice as an initial treatment, and the R0 resection seemed technically difficult. Therefore, we consider that the disease of the present case should be allocated to Category 2 (Marginally resectable disease) and the surgical resection in the present case falls into conversion therapy. As seen in the present case, the difficulties of categorizing the disease status lies on the heterogeneous condition of Stage IV GC, and establishing treatment strategy seems even challenging.

So far, there is no clinical trial determining the efficacy of the postoperative chemotherapy after R0 conversion therapy of Stage IV GC. The administration of agents, which is preoperatively proved effective, seemed rational. At the same time, application of postoperative treatment has to be determined in the balance of benefits, patients’ preference and its safety (adverse events). In the present case, the patients chose not to receive postoperative adjuvant chemotherapy based on the previous experience of Grade 2 nausea, which was intolerable for the patient.

In conclusion, we performed conversion therapy in a patients with initially unresectable gastric cancer due to paraaortic LNs. Based on the successful case of conversion therapy in the literature and the present case, we expect that the roll of this treatment would increase in the future.

Informed consent
The patient provided permission for publication of case report.

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