A Case of Complete Response to S-1 plus CDDP in Early-Stage Mucosal Esophageal Cancer

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Abstract. We report a case of early-stage mucosal esophageal cancer, showing a complete response to S-1 and cis-diamminedichloroplatinum (CDDP). The patient was a 67-year-old man with synchronous double primary early-stage mucosal esophageal and advanced gastric cancer. We planned neoadjuvant chemotherapy with S-1 and CDDP for the advanced gastric cancer and endoscopic mucosal resection for the early-stage esophageal cancer. After the first course of chemotherapy, the endoscopy revealed that the esophageal cancer had become a normal mucosal lesion, and the biopsy was negative for cancer. We diagnosed a complete response to S-1 and CDDP in early-stage esophageal cancer. After two courses of chemotherapy, distal gastrectomy was performed. The patient is still alive with no sign of recurrence at 16 months after the disappearance of the original tumor. These results suggest that chemotherapy with S-1 plus CDDP may be effective in early-stage esophageal cancer.

The standard treatment for early-stage esophageal cancer is esophagectomy (1, 2). Despite advances in endoscopic therapy, the prognosis of early-stage mucosal esophageal cancer is still poor (3, 4). Several prospective trials have demonstrated that neoadjuvant chemotherapy, in conjunction with surgical intervention, confers a survival benefit for locally advanced esophageal cancer (5, 6). Tumor response to chemotherapy in early-stage esophageal cancer, however, remains to be elucidated. Complete remission of early-stage esophageal cancer with preoperative chemotherapy is rare. One such case is reported here.

Case Report

The patient was a 67-year-old man who had previously consulted his home doctor with atrial fibrillation. In January 2009, the patient was referred to the Department of Digestive Surgery, Nihon University School of Medicine, Itabashi Hospital, with esophageal and gastric tumors which were identified during a follow-up examination. Upper gastrointestinal endoscopy revealed a mid-esophageal type Iic tumor measuring 2.0 cm×1.5 cm (Figure 1a) and a type 2 tumor in the lower stomach, measuring 3.5 cm×3.5 cm (Figure 2). Biopsy specimens revealed that the esophageal tumor was a well differentiated squamous cell carcinoma and the stomach tumor was a poorly differentiated adenocarcinoma. We diagnosed synchronous double primary early-stage mucosal esophageal and advanced gastric cancer. Computed tomography, revealed multiple lymph node metastases around the stomach (Figure 3). Neoadjuvant chemotherapy with S-1 (Taiho Pharmaceutical, Tokyo, Japan) and cis-diamminedichloroplatinum (CDDP) was carried out for the advanced gastric cancer and endoscopic mucosal resection was planned for the early-stage esophageal cancer. S-1 was administered orally, at a dose of 80 mg/m² per day, for 21 days. Infusional CDDP was administered at a dose of 90 mg/m² for 90 minutes on day 8. The patient developed grade 3 diarrhoea during the first course, which resolved spontaneously after the discontinuation of chemotherapy. After the first course of chemotherapy, endoscopy was performed with the aim of carrying out endoscopic mucosal resection. However, the endoscopy revealed that the esophageal cancer had become a normal mucosal lesion (Figure 1b), and the biopsy was negative for cancer. We diagnosed a complete response to S-1 and CDDP in early-stage esophageal cancer. Due to grade 3 diarrhea in the first course, a second course of chemotherapy was carried out with an 80% dose reduction, followed by distal gastrectomy. Over the next 6 months, periodic upper gastrointestinal endoscopy was carried out to detect any further possible esophageal lesions. Currently, the patient remains on an outpatient chemotherapy consisting of S-1 at a dose of 80 mg/m² per day for 14 consecutive days followed by a 14-day, drug-free interval. A periodically performed upper gastrointestinal endoscopy, executed in December 2009, revealed no new tumor lesions. The patient was still alive at publication, with no sign of recurrence at 16 months after disappearance of the original tumor.

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Discussion

Reports of a complete response to chemotherapy in early-stage esophageal cancer are very rare. Several prospective trials have reported that complete response to chemotherapy in advanced esophageal cancer is 2.0-5.6% (5-9). However, this extremely low complete response rate may be due to the fact that the standard treatment in such cases is surgical or endoscopic mucosal resection.

Our results suggest that chemotherapy may be effective against early-stage esophageal cancer. Recently, the effect of docetaxel and CDDP plus 5-fluorouracil (DCF) in gastroesophageal cancer was reported. The overall survival time was 9.2 months. However, grade 3 or 4 treatment-related adverse events occurred in 69% of patients on DCF (5, 6). This suggests that DCF may be unsuitable for early-stage esophageal cancer due to the high rate of adverse side effects.
Chemotherapeutic regimens, including S-1, have recently produced clinical responses and survival benefits in patients with gastric cancer in Japan; even in non-resectable, advanced gastric adenocarcinoma and head and neck squamous cell carcinoma (10, 11). The efficacy of S-1 has also been demonstrated in the Adjuvant Chemotherapy Trial of TS-1 for Gastric Cancer (ACTS-GC) (12). S-1 has many advantages. These include a high efficacy, excellent tolerability, a good side effect profile, and suitability for administration in an outpatient setting. Furthermore, the combination of S-1 and CDDP has been shown to be efficacious for stage IV gastric adenocarcinoma and head and neck squamous cell carcinoma (13, 14), as well as in neoadjuvant chemotherapy for unresectable advanced gastric cancer (15, 16).

The patient was emotionally upset at the time of diagnosis of early-stage esophageal and advanced gastric cancer, which occurred during his follow-up examination. We hypothesized that administration of neoadjuvant chemotherapy for concurrent advanced gastric cancer provided the unique opportunity for a complete response to take place in his early-stage esophageal cancer.

Either chemotherapy or surgical resection, with or without esophageal preservation is usually selected as the initial treatment for advanced esophageal cancer. However, in terms of dysphagia, the functional outcome of esophagectomy is worse than that of chemotherapy (17). Furthermore, esophagectomy is associated with high mortality and morbidity rates. Surgical mortality rates have been reported as high as 5%, even at high-volume centres (18). This suggests that chemotherapy may offer functional and prognostic merits over esophagectomy in patients with early-stage esophageal cancer.

In conclusion, this case confirms the potential for complete response to S-1 plus CDDP chemotherapy in early-stage esophageal cancer. The accumulation of further such cases may enhance our understanding of this phenomenon and lead to the development of new treatment strategies for early-stage esophageal cancer.

References

