



Pre-operative chemotherapy is the key to the next stage of gastric cancer treatment

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Currently, surgery remains the only approach to cure gastric cancer. However, improvement of prognosis by surgical resection alone is limited, and peri-operative chemotherapy is necessary (1). In recent years, several large clinical trials have shown the effectiveness of adjuvant post-operative chemotherapy for gastric cancer (2-4). In contrast, the usefulness of adjuvant pre-operative chemotherapy has not been fully demonstrated.

Wei *et al.* (2019) reported a successful gastric cancer case in which pre- and post-operative adjuvant chemotherapy was performed (5). They conducted five cycles of SOX chemotherapy, radical gastrectomy concomitant with para-aortic lymph node dissection, hyperthermic intraperitoneal chemotherapy, and six cycles of SOX adjuvant chemotherapy, with no severe adverse effects observed. The final pathological stage was ypT4N3bM1.

The clinical stage of the patient was cT4N2M0. With this initial diagnosis, the case seemed to be a resectable for an experienced surgeon. Therefore, the standard treatment strategy for this patient would be to first perform radical gastrectomy up to D2, followed by S-1 + docetaxel as adjuvant chemotherapy (4). However, if this standard therapy had been applied, this patient would have certainly died of cancer. In this case, pre-operative chemotherapy and extended radical gastrectomy were more suitable treatment strategies.

Pre-operative intensive chemotherapy for patients with tumors that are technically resectable is defined as neoadjuvant chemotherapy (NAC). Currently, the clinical significance of NAC for treating gastric cancer is not known.

The advantages of NAC include a high rate of R0 resection and high compliance (6). However, it is unclear whether these advantages are truly effective in gastric cancer. It is difficult to improve the R0 resection rate with NAC in case of gastric cancer where combined resection of invaded adjacent organs can be easily performed. Surgery for esophageal cancer is highly invasive, and the compliance of chemotherapy is reduced post-operatively (7); in contrast, the reduction in compliance after surgery for gastric cancer is not as pronounced as in esophageal cancer. Therefore, it is doubtful that small dose differences can lead to prognostic improvements. NAC also has a disadvantage in that if the cancer does not respond to the therapy, it may become unresectable. NAC should be applied to patients who are not expected to have a good prognosis after routine gastrectomy and adjuvant chemotherapy. Therefore, the usefulness of NAC in gastric cancer has been considered in cancers with bulky lymph node metastases or those with a scirrhous phenotype (8). However, the results from the clinical trial of NAC for large type 3 and type 4 gastric cancers (9) indicated that NAC had no effect in these cases (10). The clinical trial of NAC for bulky nodal metastasis is still in the planning stage, and until the results are obtained, the availability of uniform NAC for gastric cancer with cytotoxic drugs will be unclear.

In the treatment of gastric cancer, factors other than the treatment content, such as the accuracy of pre-operative diagnosis, may affect the prognosis. Unlike breast cancer, for which axillary nodal metastasis can be accurately diagnosed by needle biopsy, the diagnosis of

lymph node metastasis of gastric cancer is difficult even with the current multidetector CT scan (11,12). The pre-operative diagnosis in this case was cT4N2M0, but the final pathological diagnosis was ypT4N3bM1, and para-aortic nodal metastasis could not be diagnosed. Many of the nodal metastases of gastric cancer are microscopic metastasis, and diagnosis by CT has its own limits. From the perspective of covering the low diagnostic ability of CT, the strategy of applying NAC and super-extended nodal dissection to bulky nodal metastasis cases is worth considering.

This case eventually progressed to Stage IV. The prognosis is severe, and for some oncologists, chemotherapy is an appropriate treatment and may not be considered a surgical target. However, long-term survival cannot be expected with chemotherapy alone (13). In recent years, with advances in chemotherapy, tumors that were surgically unresectable later became resectable with the reduction or disappearance of metastatic lesions by intensive chemotherapy (14). Conversion therapy can be defined as the surgical treatment for R0 resection after chemotherapy of tumors that were originally regarded as technically or oncologically unresectable, or only marginally resectable (14,15). Recently, the result of an international joint retrospective cohort study examining the outcome of conversion therapy for gastric cancer, named CONVO-GC-1, was reported at the ASCO in 2018 (16). In the study, conversion therapy was performed in 1206 patients, and the mean survival time of R0 resected patients was 56.6 months. This outcome is much better than that in patients treated with chemotherapy alone. Conversion therapy might be a new therapeutic strategy to improve the survival of the patients, especially with R0 resection.

Unfortunately, the long-term prognosis for this patient is unknown. There is no pathological response in the article. Whether via NAC or induction chemotherapy, patients with better pathological response have been reported to have a better prognosis. When performing pre-operative chemotherapy for gastric cancer, it is expected that a method with a high response rate will lead to a good prognosis. In the future, chemotherapy for gastric cancer should also move toward molecular targeted therapy and individualized treatment, which will be useful for improving response rates and underscore the importance of pre-operative chemotherapy.

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