S-1 and oxaliplatin combined with nanoparticle albumin-bound paclitaxel adjuvant chemotherapy for advanced gastric adenocarcinoma

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To the Editor: Gastric cancer (GC) is the fifth most common malignancy and the third most common cause of cancer-related death worldwide, with >70% cases occurring in Asian populations.[1] The vast majority of patients with GC are diagnosed at an advanced stage, and the prognosis of patients with advanced GC is poor, and the mortality rate is high. Surgical resection is the cornerstone of treatment for GC. Chemotherapy, radiotherapy, targeted therapy, palliative surgery, and optimal supportive therapy have been used for the treatment of advanced GC. Conversion therapy may be a viable approach for extending overall survival. Since GC is a highly heterogeneous tumor, treatment should be performed according to its subtypes. Human epidermal growth factor receptor type 2 (HER2)-positive GC is a unique subtype of the disease, and its diagnosis and treatment strategy are different from those of HER2-negative GC. Patients with HER2-positive advanced GC can benefit from anti-HER2 therapy; however, there is currently no effective and standardized chemotherapy regimen for patients with HER2-negative advanced GC.

S-1 is an oral anti-cancer drug that consists of tegafur in combination with 5-chloro-2,4-dihydropyrimidine and potassium octreotide in a certain ratio. The regimen of conversion therapy in this study was a combination of nanoparticle albumin-bound paclitaxel (Nab-paclitaxel) and S-1 and oxaliplatin (SOX). Conversion therapy was successful with good clinical effects. Before receiving the treatment, the patient signed an informed written consent form. This case report and related images were published, with informed written consent from the patient.

A 62-year-old man was admitted with upper abdominal pain and discomfort associated with intermittent black stools for >6 months. Routine gastroscopy revealed huge ulcers on the four walls of the gastric antrum, gastric horn, and middle and lower part of the gastric body, and the base was covered with a bloody scab and pus moss, which bled easily when touched [Figure 1A]. The pathological diagnosis of endoscopic biopsy revealed poorly differentiated adenocarcinoma of the gastric antrum [Figure 1B]. Immunohistochemistry (IHC) results showed that the expression of HER2 was negative [Figure 1C and 1D], and the expression of cytokeratin pan (CKP), cytokeratin 8/18 (CK8/18), Villin, and caudal type homeobox 2 (CDX-2) was positive. The computed tomography (CT) revealed significant thickening of the gastric wall in the antrum, and a soft tissue mass shadow locally protruded into the gastric lumen. Enhanced CT revealed uneven enhancement of the lesion, scattered small lymph nodes in the hepatogastric space, and low-density filling defect shadow in the superior mesenteric vein, suggesting the formation of a tumor thrombus [Figure 1E and 1F]. The clinical final diagnosis was gastric adenocarcinoma with distant metastasis, and the imaging stage was cT4N1M1.

The patient received treatment that included SOX and Nab-paclitaxel. SOX consisted of an intravenous drip of oxaliplatin at 130 mg/m^2 on day 1 and an oral 60 mg S-1 capsule twice a day (days 1–14), repeated every 3 weeks. Nab-paclitaxel was administered at 120 mg/m^2 (iv gtt) on day 1 of each cycle for five cycles. The patient was scanned by CT before the fourth cycle of combined chemotherapy and after the fifth cycle (before surgery). The tumor and tumor thrombus were significantly reduced, and the clinical stages were cT3N1M1 and cT3N0M1, respectively [Figure 1G, 1H, 1I, and 1J]. Subsequently, the patient underwent radical distal gastrectomy and D2 lymph node dissection, followed by II anastomosis, superior mesenteric vein resection, and end-to-end anastomosis.

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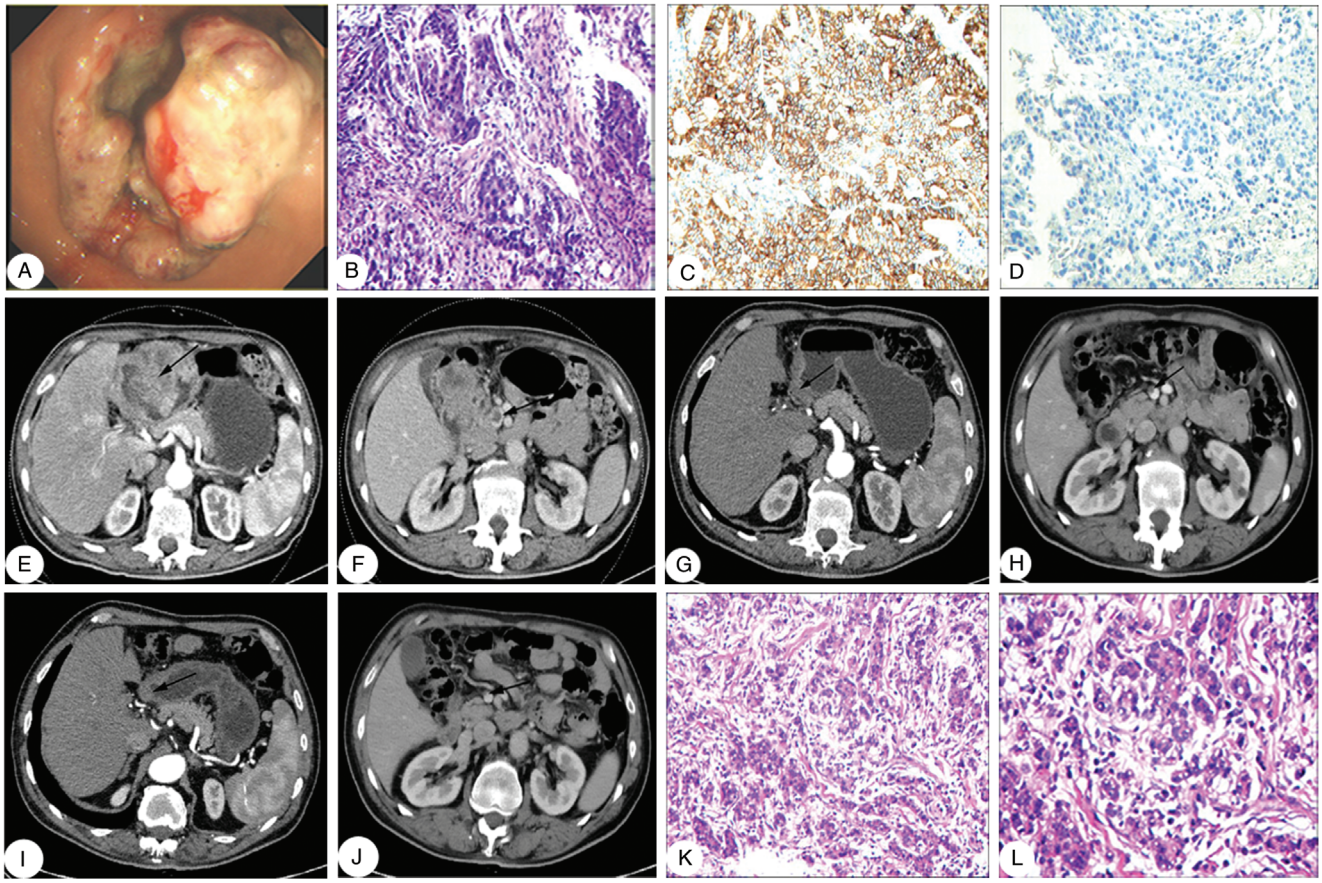

Figure 1: Imaging and pathological examination images of the patient with GC. (A) Routine gastroscopy before chemotherapy showed huge ulcers on the four walls of the gastric antrum, gastric horn, and middle and lower part of the gastric body, and the base was covered with a bloody scab and pus moss, which bled easily when touched. (B) Histopathological HE staining image of GC by preoperative endoscopic biopsy showed the poorly differentiated adenocarcinoma (original magnification ×200). (C) IHC staining results of HER2 positive control (original magnification ×200). (D) IHC staining results of GC tissue showed the expression of HER2 was negative (original magnification ×200). (E, F) The CT scans before the first cycle of Nab-paclitaxel combined with SOX chemotherapy showed significant thickening of the antral gastric wall with localized soft tissue mass shadows protruding into the gastric lumen and hypodense filling defect shadows in the superior mesenteric vein, suggesting tumor thrombosis (black arrow). (G, H) The CT scans before the fourth cycle of Nab-paclitaxel combined with SOX chemotherapy showed that the lesion and the low density filling defect in superior mesenteric vein were significantly smaller than before (black arrow). (I, J) The CT scans before the fourth cycle of Nab-paclitaxel combined with SOX chemotherapy showed that the lesion and the low density filling defect in superior mesenteric vein were significantly smaller than before (black arrow). (K) Histopathological HE staining image of postoperative GC showed the moderately differentiated adenocarcinoma (original magnification ×200). (L) Histopathological HE staining image of postoperative GC showed the moderately differentiated adenocarcinoma (original magnification ×400). GC: gastric cancer; CT: computed tomography; HE: hematoxylin-eosin; IHC: Immunohistochemistry; HER2: Human epidermal growth factor receptor type 2; Nab-paclitaxel: nanoparticle albumin-bound paclitaxel; SOX: S-1 and oxaliplatin.

During the operation, a 2-cm tumor was found on the greater curvature of the gastric antrum, and a 0.4-cm tumor thrombus was also observed on the left anterior wall of the upper segment of the superior mesenteric vein. No regional lymph node enlargement was observed. In addition, no metastatic nodules were found in the liver, parietal peritoneum, mesentery, or pelvic floor.

Post-operative pathological diagnosis revealed moderately differentiated adenocarcinoma of the gastric antrum [Figure 1K and 1L]. Lauren's classification of tumors was intestinal type, and the macroscopic type of the tumors was ulcer-type or infiltrative-type. The cancer tissue had invaded the submucosa of the gastric wall, and the tumor thrombus could be seen in the vasculature. No atypical cells were found in the nodules of superior mesenteric vein. No metastatic cancer cells were found in lymph nodes around the greater curvature of the stomach (0/3), and no cancer cells were found in other lymph nodes around the greater curvature of the stomach (0/32). The pathological tumor-node-metastasis (TNM) staging was ypT1N0M0. IHC investigation found CD31 (suggestive of vascular invasion), D2-40 (suggestive of lymphatic invasion), P53 (missense mutation), S-100 (not suggestive of neurological invasion), chromogranin A (CgA)(−), synaptophysin (Syn)(−), CD56(−), CDX-2(+), HER2(1+), postmeiotic segregation increased 2 (PMS2)(+), mutL homolog 1(MLH1)(+), human mutS homolog 2 (MSH)(+), MSH6(+), helicobacter pylori (HP)(−), and Ki-67 (Index: 70%).

After surgery, the patient received an additional three cycles of SOX and Nab-paclitaxel at the same doses as before. Abdominal CT reexamination after cessation of treatment revealed post-operative changes in the gastric malignant tumor. The residual stomach was well filled, and no thickening or enhancement was observed in the residual stomach or the wall of each anastomotic site. No enlarged lymph nodes were observed in the liver or stomach space, and no enlarged lymph nodes were observed in the retroperitoneum. In addition, gastroscopy revealed that the cardia was well opened and closed, and

no ulcers and masses were observed, and the mucosa was not abnormal.

To date, the patient has been followed up for 4 months, and no clinical manifestations have been observed.

Conversion therapy is defined as a surgical treatment aiming at an R0 resection after chemotherapy for tumors that were originally unresectable or marginally resectable for technical and/or oncological reasons. Patients with GC are usually in the advanced stage of the disease when they are diagnosed, and distant metastases are often present. For patients with advanced GC, conversion therapy may be the best treatment, which can benefit patients with advanced GC in terms of survival time.

Nab-paclitaxel is a new generation of paclitaxel drugs. Its main characteristic is that paclitaxel and human serum albumin can be combined into colloidal suspended particles with an average diameter of approximately 130 nm, so it has good water solubility, avoiding a variety of adverse reactions caused by the use of cosolvent, and it does not require pre-treatment before use. In addition, this drug can specifically adsorb cytotoxic drugs bound to albumin and collect cytotoxic drugs in tumor tissue, thereby increasing the local drug concentration and enhancing the killing effect on tumor cells.

To date, Nab-paclitaxel has shown significant clinical activity in a variety of cancers, including breast, lung, and pancreatic cancers.[2-4] An absolute randomized phase 3 clinical trial in GC revealed that weekly use of Nab-paclitaxel was non-inferior compared to weekly use of solvent-based paclitaxel.[5] The Absolute study in Japan also confirmed that second-line weekly Nab-paclitaxel regimens were not inferior to conventional weekly solvent-based paclitaxel regimens in terms of overall survival (hazard ratio = 0.97; 97.5% confidence interval = 0.76–1.23; P = 0.0085).[6] Yardley[7] reported that the uptake rate of Nab-paclitaxel was 33% higher than that of solsol-based paclitaxel. In addition, Watson *et al*[8] reported that combined Nab-paclitaxel, oxaliplatin, and 5-fluorouracil chemotherapy is an effective and promising regimen for resectable GC.

In this study, patient with advanced GC who received SOX and Nab-paclitaxel combined with chemotherapy responded well and underwent conversion surgery. Conversion therapy is a new therapeutic concept, and more clinical trials are required. Conversion therapy in GC still faces many difficulties; for example, the choice of treatment regimen and the timing of conversion surgery intervention are not clear yet and require further study. This study provides a new potential option for conversion therapy in advanced GC. For advanced GC that is not suitable for surgery, the SOX and Nab-paclitaxel combined with chemotherapy can shrink the tumor and lead to surgical treatment. However, this is only a case report. More clinical trials are needed to determine whether this chemotherapy regimen has good clinical effects in most patients with GC.

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Conflicts of interest

None.

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