A case of locally advanced gastric cancer treated with nivolumab, trastuzumab, plus chemotherapy in a neoadjuvant setting

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To the Editor: Recently, the advantages of peri-operative chemotherapy in downstaging tumor and improving patient survival have been reported.[1] Herein, we report a case of gastric cancer patient receiving neoadjuvant chemotherapy along with trastuzumab and nivolumab.

A 70-year-old Chinese man was presented to our department complaining of abdominal distension and weakness in June 2017. Complete blood count showed moderate anemia (hemoglobin, 61 g/L). A gastroscopy and biopsy led to the diagnosis of a moderately to poorly differentiated adenocarcinoma, and immunohistochemistry (IHC) indicated human epidermal growth factor receptor 2 (HER2) 2+ positivity. *HER2* gene amplification was further confirmed by fluorescence *in situ* hybridization. Computed tomography revealed a mass-like lesion (67 mm × 53 mm) located on the lesser curvature, fused with regional lymph nodes and the pancreas [Figures 1A, 1D]. Besides, several swollen lymph nodes including one para-aortic lymph node 24 mm in diameter [Figure 1G] also existed. The clinical stage was determined to be T4bN3bM0 and considered unresectable. A regimen containing chemotherapy, trastuzumab, and nivolumab was then administered: trastuzumab 8 mg/kg iv bolus followed by 6 mg/kg iv every 3 weeks, oxaliplatin 150 mg iv on day 1, S-1 60 mg bid po on day 1 to day 14, and nivolumab 200 mg iv on day 8, every 3 weeks. The clinical response was classified as a partial remission according to the Response Evaluation Criteria in Solid Tumors version 1.1 [Figure 1B, 1E, and 1H]. Due to the presence of grade 2 thrombocytopenia, in cycles 3 to 4, nivolumab and trastuzumab were maintained and the chemotherapy was administered every 2 weeks: oxaliplatin 150 mg iv on day 1, S-1 40 mg bid po on day 1 to day 10. After four cycles [Figure 1C, 1F, and 1I], a total gastrectomy (D2), Roux-en-Y esophagojejunostomy along with para-aortic lymph node resection was successfully performed in October 2017. No cancer cells were identified in the dissected lymph nodes. The residual cancer in the resected specimen was diagnosed as a moderately-differentiated adenocarcinoma. IHC showed HER2 2+ positivity. The pathological stage was ypT3N0. Post-operatively, the patient received four more cycles of the same regimens. In the 16 months of follow-up, he has remained free of disease.

Furthermore, tumor mutational burden (TMB) was measured (11.1 mutations/Mb) and identified to be TMB-medium. Moreover, microsatellite instability test showed microsatellite stable phenotype. Mismatch repair (MMR) proteins were detected by IHC, which showed proficient expression of MMR proteins. IHC revealed absence of expression of programmed death-ligand 1.

Cisplatin plus S-1 is regarded as a standard first-line treatment of advanced gastric cancer (AGC) in China.[2,3] Considering the moderate anemia, physical status, and *HER2* overexpression, we chose a reduced dose of oxaliplatin, S-1, plus trastuzumab as the preferable regimen for this patient. Recently, ATTRACTION-2 study revealed the promising anti-tumor activity of nivolumab in Asian patients with advanced or recurrent gastric/gastro-esophageal junction cancer.[4] With an unclear role of nivolumab in the peri-operative therapy, we establish the possibility of combining a checkpoint inhibitor with chemotherapy and trastuzumab in treating locally AGC. Further investigation is required to explore this combination in the peri-operative setting.

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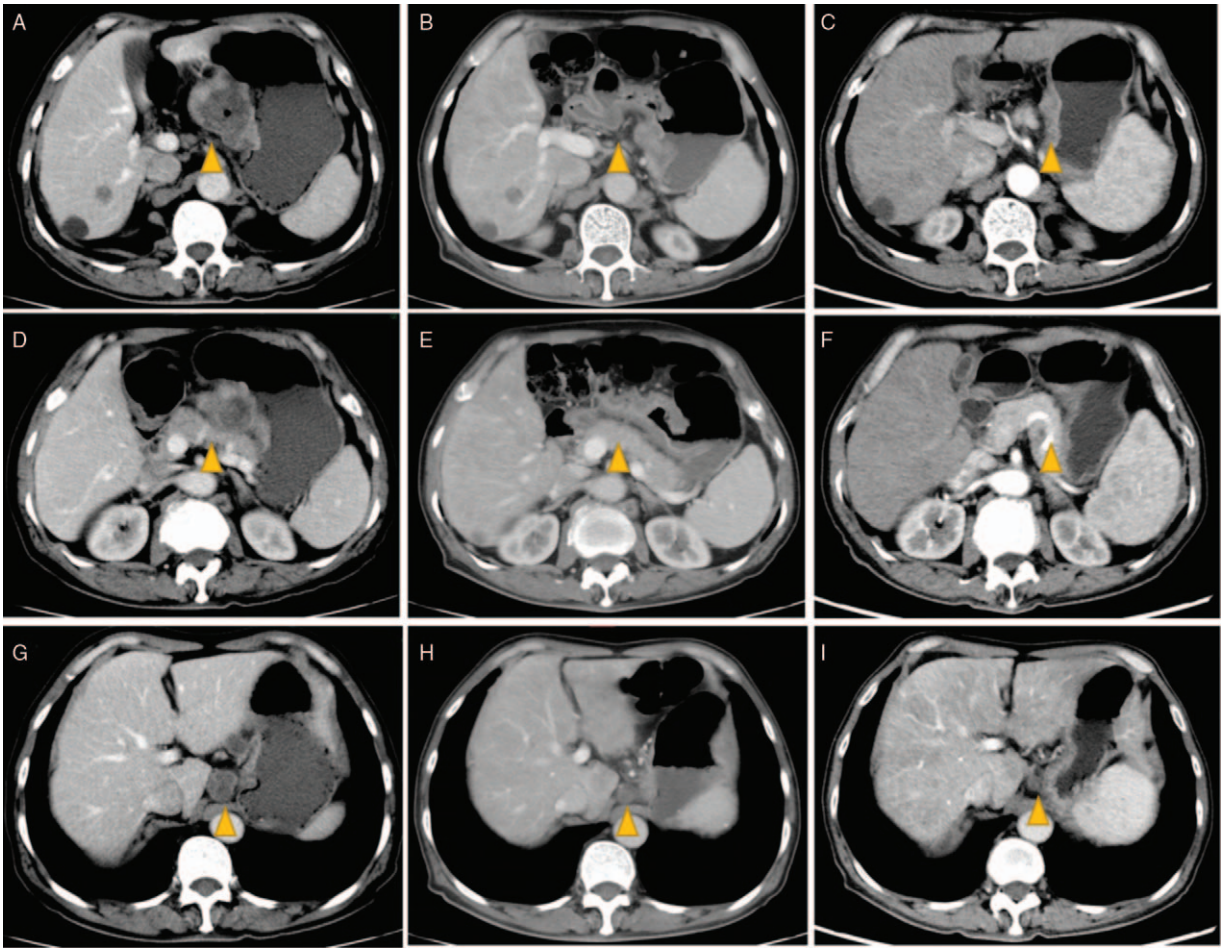

Figure 1: Computed tomography imaging before treatment, after two cycles, and at the end of treatment shows the mass located on the lesser curvature (A–C), mass fused with pancreas (D–F), and presence of an enlarged para-aortic lymph node (G–I).

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest

None.

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