Case report

Pathological complete response after neoadjuvant chemotherapy with trastuzumab-containing regimen in gastric cancer: a case report

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Abstract

We report a 49-year-old Chinese male with locally advanced gastric adenocarcinoma achieving pathological complete response after neoadjuvant chemotherapy with trastuzumab-containing regimen. He underwent esophagogastroduodenoscopy in September 2009, which revealed a 2-cm gastric ulcer on the lesser curvature proximal to angularis. Biopsy of gastric ulcer showed moderately differentiated adenocarcinoma with overexpression of human epidermal growth factor receptor 2 (HER2) by immunohistochemistry and fluorescence in situ hybridization. Further workups with endoscopic ultrasound, computed tomography and positron emission tomography staged his cancer as T3N1M0. He received 3 cycles of neoadjuvant chemotherapy consisting of trastuzumab, oxaliplatin, docetaxel and capecitabine without severe toxicities except grade 2 diarrhea near the completion of cycle 3 requiring discontinuation of capecitabine. Afterwards, he received total gastrectomy with extended D2 lymph node dissections showing pathological complete response. He went on to receive 3 more cycles of chemotherapy postoperatively. The role of trastuzumab as a part of perioperative therapy in gastric cancer overexpressing HER2 is worth further investigation.

Introduction

Gastric cancer is the fourth most common cancer worldwide, with overall 5-year survival rate of approximate 20%, representing a significant challenge for the treating physicians. Perioperative chemotherapy has been shown to cause tumor downstaging and improve survival in patients with resectable gastric cancer. Response to neoadjuvant treatment is the most important predictor of survival after curative resection of gastric cancer.

In this case report, we describe a case of pathological complete response after neoadjuvant chemotherapy with trastuzumab-containing regimen in gastric cancer. We discuss histopathological findings and review the pertinent literatures.

Case report

A 49-year-old Chinese male with gastroesophageal reflux disease and H. Pylori infection underwent esophagogastroduodenoscopy (EGD) in September 2009, which revealed a 2-cm gastric ulcer on the lesser curvature proximal to angularis. Biopsy of gastric ulcer showed moderately differentiated adenocarcinoma. Tumor analysis for human epidermal growth factor receptor 2 (HER2) was performed by HercepTest (Genzyme, Los Angeles, CA) indicating 3+ immunohistochemistry (IHC) staining (Fig. 1). HER2 gene amplification was confirmed by fluorescence in situ hybridization (FISH) demonstrating HER2/CEP17 (chromosome enumeration probe 17) ratio of 4. Endoscopic ultrasound study indicated presence of perigastric lymphadenopathy and tumor invading through the muscularis propria. Other staging workups, including computed tomography (CT) scan of chest, abdomen and pelvis and positron emission tomography-CT (PET-CT) scan, did not reveal any distant metastasis. The clinical staging was T3N1M0,
and patient was recommended to receive neoadjuvant chemotherapy before definitive surgery. The information of ToGA trial was presented to patient [6], and patient agreed to receive trastuzumab-containing regimen: trastuzumab 6 mg/kg iv on day 1, oxaliplatin 130 mg/m² iv on day 1, docetaxel 30 mg/m² iv on day 1 and day 8, and capecitabine 625 mg/m² po bid on day 1 to day 21, every 3 weeks. He received 3 cycles chemotherapy without severe toxicities except grade 2 diarrhea near the completion of cycle 3 requiring discontinuation of capecitabine. The post-treatment imaging studies including CT scan of chest, abdomen and pelvis and PET-CT scan showed persistent mild FDG [fluorodeoxyglucose (18F)] activity involving the stomach without identifiable mass or distant metastasis.

In January 2010, he received total gastrectomy with extended D2 lymph node dissections, Roux-en-Y esophagojunostomy and cholecystectomy. Prior to surgical resection, the intraoperative EGD showed a healed scar in the original ulcerative tumor site, and laparoscopy revealed no evidence of peritoneal carcinomatosis or metastatic implants. Pathological examination of the surgical specimen indicated no residual adenocarcinoma but scar on lesser curvature with fibrosis extending into muscularis propria (Fig. 2). There were no tumor identified in 44 perigastric lymph nodes and 2 lymph nodes from porta hepatitis. He recovered uneventfully after surgery, and received 3 more cycles of chemotherapy with the same regimen with dose reduction on docetaxel and capecitabine due to gastrointestinal toxicities. He has remained free of disease after completion of chemotherapy.

Discussion

HER2 exhibits tyrosine kinase activity and functions as a growth factor receptor [7]. HER2 overexpression due to gene amplification in gastric cancer has led to aggressive clinical course and poor prognosis [8]. Trastuzumab, a monoclonal antibody against HER2, causes cell cycle arrest at G1 and exhibits antitumor activity in HER2 overexpressed gastric cancer cells [9,10]. Additionally, trastuzumab can enhance cytotoxic effects of chemotherapy in gastric cancer xenograft overexpressing HER2, when combined with capecitabine, cisplatin, or taxane [11]. Phase II studies incorporating trastuzumab with cisplatin-based regimen in patients with advanced gastric cancer overexpressing HER2 have demonstrated promising activities [12,13].

The ToGA study presented at 2009 annual meeting of American Society of Clinical Oncology has screened about 3,800 patients with advanced gastric cancer from 24 countries [14]. HER2 overexpression was detected in 22%, and the concordance rate between IHC and FISH was high at all levels of HER2 positivity [15]. There was a specific pattern of disease which correlated with HER2 overexpression. Higher rates occurred in intestinal and proximal or gastroesophageal junction cancers than in diffuse or distal gastric cancers.

Five hundred and eighty four patients tested positive for HER2 overexpression (IHC 3+ and/or FISH positive) were enrolled into ToGA study, a phase III trial comparing fluoropyrimidine (5-fluorouracil [5-FU] or capecitabine) and cisplatin chemotherapy with or without trastuzumab. Patients who received trastuzumab plus

![Figure 1 Immunohistochemical study of HER2 protein in biopsied specimen before chemotherapy](http://www.jhoonline.org/content/3/1/31)

![Figure 2 Microscopic finding of the resected specimen after chemotherapy](http://www.jhoonline.org/content/3/1/31)
The administration of trastuzumab can result in subclinical and clinical cardiac failure, and the incidence is much higher in patients receiving trastuzumab concurrently with anthracycline-containing chemotherapy regimens [21]. Instead of using ECF, we decided to use docetaxel, oxaliplatin and capecitabine in combination with trastuzumab as perioperative chemotherapy for our patient mainly due to the concern of cardiac toxicity. We have monitored our patient’s cardiac function with periodic echocardiogram evaluation, and find no evidence of cardiac failure.

Our case illustrates the first reported case of pathological complete response after neoadjuvant chemotherapy with trastuzumab-containing regimen in a patient with locally advanced gastric cancer overexpressing HER2. The use of docetaxel, oxaliplatin and capecitabine in combination with trastuzumab in this setting remains experimental, and ideally should be considered only in the context of a clinical trial. Therefore, the role of trastuzumab as a part of perioperative therapy is worth further investigation.

Consent
Written informed consent was obtained from each patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Authors’ contributions
CTH designed the paper. JW and CTH wrote the paper. WS performed endoscopic examination and biopsy. CG performed surgery. JW and GWS provided pathological evaluation. All authors read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Received: 30 July 2010 Accepted: 9 September 2010 Published: 9 September 2010

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