



IS ADVANCED ALPHA-FETOPROTEIN PRODUCING GASTRIC CANCER TREATABLE?

Medical Science

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ABSTRACT

We illustrated a patient with advanced alpha-fetoprotein producing gastric cancer, who was treated with chemotherapy combined with trastuzumab, resulting in complete response in four months after therapy. It has been 5 years after his initial therapy, he is now healthy and shows no evidence of tumor recurrence. The efficacy of the trastuzumab therapy in breast cancer patients prompted studies to evaluate potential clinical benefit of the drug in patients with HER2 positive gastric cancer. The largest study, ToGA trial, has published a promising result leading FDA to approve the use of trastuzumab for HER2 positive gastric and gastroesophageal cancer. We discuss the need for the standardized assay method for HER2 status. We also bring attention to the existence of intratumoral heterogeneity in gastric cancer tissue which may cause false negative test for HER2 assay.

KEYWORDS

Alpha-fetoprotein, gastric cancer, trastuzumab, chemotherapy, intratumoral heterogeneity.

It has been known that HER2 status has become an important predictive biomarker for treatment of breast cancer with the monoclonal antibody trastuzumab¹. The efficacy of this therapy in breast cancer prompted studies to evaluate potential clinical benefit of this drug in patients with HER2 positive gastric cancer. The largest data were from ToGA trial,² composed of 3,807 gastric cancer patients from 24 countries. The ToGA trial is by far, the only well controlled studies with a target therapy in advanced gastric cancer that has been published. The end points in this study including overall survival, overall response rate and progression-free survival were all satisfactory. Therefore, FDA on October 20, 2010, approved trastuzumab to be used to treat HER2 positive advanced gastric cancer or gastroesophageal cancer.

Alpha-fetoprotein producing gastric cancer (AFP-GC) is a subtype of gastric cancer³, which has more aggressive behavior, and has been considered as having unfavorable long term survival rate, due in part to the higher propensity of liver metastasis and lymphovascular invasion, as compared with conventional gastric cancer. No standard therapy is currently available. AFP-GC with liver metastasis has a particularly dismal prognosis. Five years ago, we encountered a 54-year old man who was diagnosed as having AFP-GC with serum level AFP of 16,390 ng/ml. His gastric biopsy specimen was tested HER2 3+ using immunohistochemical method. He was treated with conventional chemotherapy combined with trastuzumab, resulting in complete clinical response. Four months after therapy, computer tomography revealed complete resolution of liver metastasis. Follow-up gastroscopy examination showed a normal mucosa at the previous tumor site (Fig 1.). For the detail clinical information and therapeutic regimens, please refer to the report earlier⁴. Five years after therapy, he is healthy without recurrence of the tumor.

To the best of our knowledge, this patient is the longest survival in the literature. The case report by Ogasawara et al⁵ was a 65-year old man, with advanced AFP-GC receiving chemotherapy combined with trastuzumab resulting in marked reduction of the tumor size in the liver, as well as in the stomach. The patient was still alive 35 months after initial therapy. Wang et al,⁶ reported a 49-year old Chinese man with locally advanced AFP-GC. He was treated with chemotherapy and trastuzumab containing regimen as neoadjuvant therapy. Subsequently, he underwent total gastrectomy with extended D2 lymph node dissection showing pathological complete response.

The published data with regard to percentage of HER2 positive gastric cancer seemed to be rather high, ranging from 6.1 to 32.0%⁷. There are several reasons for this, including the use of different antibody, the subjectivity of the pathologists' interpretation, and the different scoring system being employed, etc. Interpretation of immunohistochemical stain on gastric cancer is different from that on breast cancer. The best method is to follow the criteria issued by Hofmann et al,⁸. Another point worth mentioning is that intratumoral

heterogeneity in gastric cancer can lead to false negative result. In this respect, Ruschoff et al,⁹ recommended that ideally, at least 6-8 fragments of tumor should be present in biopsies for adequate assessment.

In this short communication, we illustrated that patients with advanced AFP-GC are treatable if their biopsy specimens are HER2 positive. However, further investigation is required with a large cohort number of patients. Giving the published data of the HER2 status in gastric cancer varies considerably, the standardized method for HER2 assay is urgently needed.

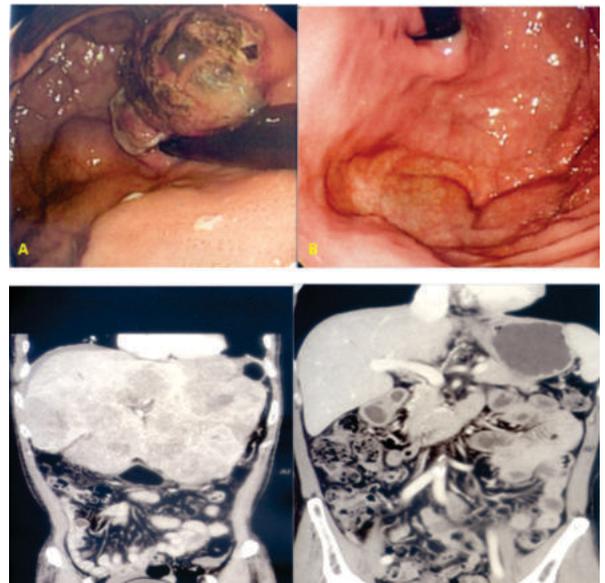


Figure 1. A. Gastroscopic examination revealed a large tumor in the stomach.

- B. After therapy, gastroscopic examination displayed a normal mucosa.
- C. Before therapy, computer tomography showed multiple metastasis in the liver.
- D. After therapy, computer tomography showed complete resolution of liver metastasis.

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