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Case Report

Chemotherapy for alpha-fetoprotein producing gastric cancers expressing human epidermal growth factor receptor 2

Kazumi Hayashi ^{a,*}, Eijiro Nagasaki ^a, Koji Nakada ^b, Miho Tamura ^a, Yasuhiro Arakawa ^a, Tadashi Uwagawa ^a, Shingo Yano ^a^a Department of Clinical Oncology and Hematology, The Jikei University School of Medicine, Tokyo, Japan^b Department of Surgery, The Jikei University School of Medicine, Tokyo, Japan

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ABSTRACT

Although, gastric cancer is one of the most common cancers worldwide, alpha-fetoprotein (AFP) producing human epidermal growth factor receptor 2 (HER2) positive gastric cancers are rare. AFP producing gastric cancer has a poor prognosis and an appropriate treatment option has not been established to date. A 75-year-old woman with AFP-producing gastric cancer was treated with S-1, an oral fluoropyrimidine derivative, chemotherapy after distal gastrectomy. Recurrence of gastric cancer was observed after 18 months and immunohistochemistry analysis showed AFP and HER2 positive gastric cancer. The patient received combination therapy containing capecitabine, cisplatin, and trastuzumab. Computed tomography scans showed regression of the lymph node metastasis. The patient's quality of life substantially improved after the treatment. Thus, the present case suggests that AFP and HER2 positive gastric cancer can be effectively treated with, capecitabine, cisplatin, and trastuzumab combination therapy.

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1. Introduction

Although, the incidence and mortality rates of gastric cancer have declined during the past decades, gastric cancer is one of the most commonly occurring cancers worldwide, particularly in Asia. In Japan, 48,632 gastric cancer patients died in 2013, and it was the second most common cause of cancer-related deaths [1].

Alpha-fetoprotein (AFP) producing gastric cancer constitutes 2.3% of all gastric cancer cases. Patients with AFP-producing gastric cancers have poor outcomes [2].

Human epidermal growth factor receptor 2 (HER2) is an established therapeutic target in breast cancer. HER2 positive breast cancer is associated with poor survival outcome and 22% of breast cancers are HER2 positive [3]. Trastuzumab, an anti-HER2 monoclonal antibody, improved the prognosis in patients with HER2 positive breast cancers [4]. HER2 overexpression is also

observed in gastric cancer and it correlates with poor outcomes and higher aggressiveness [5].

Herein, we report the case of a patient with AFP-producing gastric cancer expressing HER2, who survived without recurrence for more than 3 years after treatment with second-line combination therapy containing capecitabine, cisplatin, and trastuzumab.

2. Case report

A 75-year-old woman underwent gastroscopic examination as part of a cancer screening at our hospital. Endoscopic examination revealed a Borrmann type 3 tumor located in the pyloric region, which was diagnosed as gastric carcinoma upon histological examination of the biopsy specimen. Abdominal computed tomography (CT) showed an irregular thickening of the gastric wall and lymph node enlargement at a ventricular angle. Upon examination, the blood pressure was 114/62 mm Hg, the pulse was 89 beats per minute, and the body temperature was 36.6 °C; the respiratory assessment and the rest of the examinations showed normal results. The laboratory test results are shown in Table 1. A slight increase in the alkaline phosphatase level was observed owing to primary biliary cholangitis.

* Corresponding author. Department of Clinical Oncology and Hematology, The Jikei University School of Medicine, 3-25-8 Nishi-shimbashi Minato-ku, Tokyo 105-8461, Japan. Fax: +81-3-3436-2171.

E-mail address: kz.hayashi@gmail.com (K. Hayashi).

Table 1
Laboratory data.

White-cell count ($10^3/\mu\text{L}$)	7300
Red blood cell count ($10^6/\mu\text{L}$)	4.15
Hemoglobin (g/dL)	12.1
Hematocrit (%)	37.5
Platelet count ($10^3/\mu\text{L}$)	24.2
Aspartate aminotransferase (U/L)	44
Alanine aminotransferase (U/L)	46
Alkaline phosphatase (U/L)	541
Urea nitrogen (mg/dL)	14
Creatinin (mg/dL)	0.72
Sodium (mmol/L)	144
Potassium (mmol/L)	4.0
Calcium (mg/dL)	8.7
Total bilirubin (mg/dL)	0.7
Direct bilirubin (mg/dL)	0.1
C-reactive protein (mg/dL)	0.05

The patient underwent distal gastrectomy. The gastric tumor was examined under the microscope to determine its type. The pathological stage was determined to be IIIA (T3, N2, M0) according to the guidelines of the Japanese Gastric Cancer Association. The histological diagnosis was carcinoma with enteroblastic differentiation and the tumor cells were alpha-fetoprotein positive (Fig. 1a–b). The patient was treated with S-1 chemotherapy (80 mg/body) after surgery, and the treatment was continued for 1 year.

After 18 months, she became jaundiced and the level of AFP was as high as 237 ng/mL (normal: <5 ng/mL). Abdominal CT showed an enlargement in the lymph node of the hepatic portal region (Fig. 2a). The patient underwent percutaneous transhepatic cholangiodrainage for the treatment of obstructive jaundice, and she was diagnosed with recurrent gastric cancer.

The immunohistochemistry analysis of the tumor specimen obtained from the recurrent gastric cancer showed HER2 positivity (Fig. 1c). Therefore, the final histological diagnosis was AFP and HER2 positive gastric cancer. She received combination chemotherapy every 3 weeks with, capecitabine (1200 mg/m²

administered orally twice a day for 14 days followed by a 1 week off period), cisplatin (60 mg/m² administered intravenously on day 1), and trastuzumab (6 mg/kg administered intravenously on day 1 of the first cycle).

After the completion of 4 chemotherapy cycles, CT revealed regression of the enlarged lymph node in the hepatic portal region and the serum AFP levels returned to normal (Fig. 2b). The patient was considered to have achieved complete response (CR). After receiving 8 cycles of chemotherapy, the patient developed neutropenia, which necessitated the cessation of cisplatin. Therefore, the treatment regimen included only capecitabine and trastuzumab thereafter.

The patient has been alive for over 3 years after developing recurrent gastric cancer.

3. Discussion

AFP positive gastric cancers were reported to have poor prognoses. The 5-year survival rate and median survival period in patients with AFP positive gastric cancers were 22% and 14 months, respectively, and they had a higher incidence of lymph node metastasis, deeper invasion of the gastric wall, higher frequency of advanced stage, more marked lymphatic invasion, and higher rate of liver metastasis [6,7]. The pathological features associated with AFP positive gastric cancers are Borrmann type 2–3 advanced stage, and vascular or lymphatic channel invasion. AFP positive cancer cells were detected in the solid medullary area of the poorly differentiated adenocarcinoma consisting cuboidal or polygonal cells, and a papillary or complex glandular pattern was observed [8]. In the present case, the patient had Borrmann type 3 advanced gastric cancer that metastasized to the lymph node. The tumor cells exhibited a papillary pattern.

Several different combination therapy regimens have been reported for AFP positive gastric cancer, which included docetaxel, S-1, cisplatin, fluorouracil, etoposide, and paclitaxel [9–11]. However, there is no established treatment regimen for AFP- positive gastric

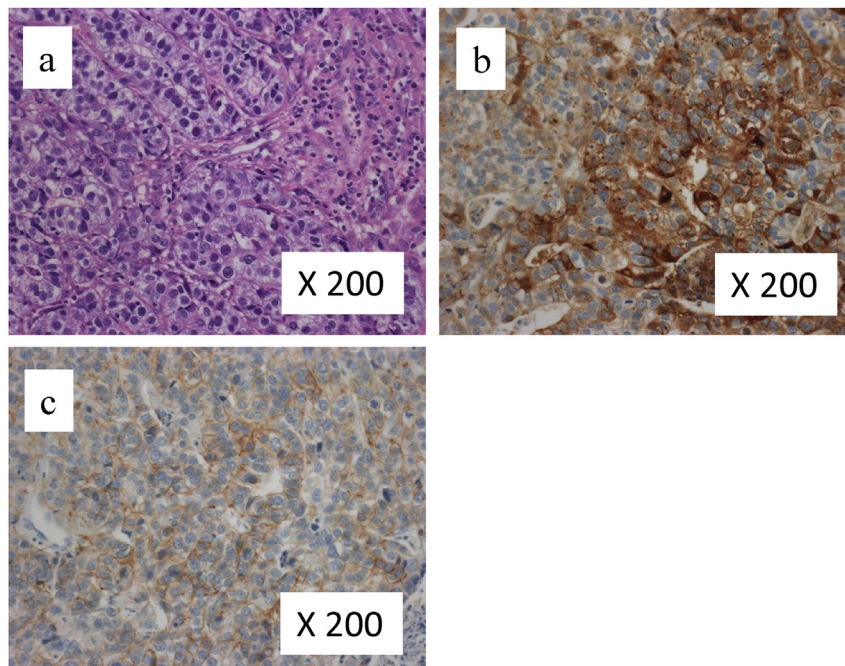


Fig. 1. Hematoxylin and eosin staining (a) showed gastric carcinoma with enteroblastic differentiation. Immunohistochemical staining was positive for alpha-fetoprotein (AFP) (b) and human EGFR-related 2 (HER2) (c).

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