

中文題目：HER-2 陽性胃癌合併腦部及腦膜轉移

英文題目：HER-2 positive gastric cancer with brain and leptomeningeal metastasis:
a case report

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Introduction:

Gastric cancer is an important health problem worldwide. Although its incidence rate decreases in recent years, it is still the fourth leading cause of cancer-related death. Distribution in the stomach about gastric cancer can be divided into cardia region and noncardia area. Noncardia gastric cancer was related to *H. pylori* infection. As for cardia gastric cancer, it has increased incidence rate in recent years, especially much higher in low-risk populations, such as USA whites. On the other hands, HER-2 plays an important role in gastric cancer. About 15% to 20% of advanced gastric cancer have overexpression or amplification of HER-2. Target therapy and immunotherapy are used to be treated in HER-2 positive. Besides, there are relatively rare reports about brain and leptomeningeal metastasis from gastric cancers and the incidence rate is about 0.16%-0.69%. Response to treatment is poor among patients with brain and leptomeningeal metastasis arising from gastric cancer. We present an advanced gastric cancer case with HER-2 positive and then with brain and leptomeningeal metastasis several months later.

Case Presentation:

This is a 37-year-old female who had suffered from abdominal fullness for 3 months. Panendoscopy showed 2 ulcerative tumors located at cardia and low-body, and the biopsy revealed poorly differentiated adenocarcinoma. Total gastrectomy, lymph node dissection and splenectomy were performed and the final pathological revealed poorly differentiated adenocarcinoma with lymphovascular permeation, perineural and aorta invasion. Immunohistochemical stains showed HER-2 positive (score 3+/3+). The pathologic stage was pT4bN3bM1.

Chemotherapy with capecitabine, oxaliplatin and trastuzumab were given for 12 courses and followed by trastuzumab maintenance therapy. Then, radiotherapy for tumor bed and regional lymph nodes was applied in 4500cGy/25fx, VMAT. However, the patient was found to have headache, blurred speech and consciousness

change after the gastric cancer was diagnosed for 19 months. Brain MRI revealed multiple brain metastasis and diffuse leptomeningeal carcinomatosis. CSF analysis showed metastatic adenocarcinoma. Radiotherapy for brain metastasis was done and capecitabine with lapatinib was given. After 20-month the gastric cancer was diagnosed, the patient expired.

Discussion:

For HER-2 positive gastric cancer patients, chemotherapy with anti-HER2 antibody(trastuzumab) is recommended to be the first-line therapy and its overall survival is significantly longer than with chemotherapy alone. Trastuzumab deruxtecan, an antibody-drug conjugate (ADC), is an anti-HER2 antibody with a cytotoxic topoisomerase I inhibitor and cleavable tetrapeptide-based linker and has been approved to treat with metastatic HER-2 positive breast cancer before. Recently, it has been approved to treat patients with advanced HER-2 positive gastric cancers. In DESTINY-Gastric 01 trial, objective response and overall survival in advanced HER-2 positive gastric cancers with trastuzumab deruxtecan were significantly higher than with chemotherapy.

In HER-2 positive breast cancers, the risk of brain metastases is higher and its incidence rate can reach 25% to 50%. However, compared to breast cancers, brain and leptomeningeal metastases from gastric cancers are rare and often < 1%. In the past studies, the relationship between HER-2 positive gastric cancers and CNS metastasis was unknown. Currently, some studies propose the hypothesis that HER-2 may have connection with CNS metastases. However, due to lack of clinical evidence, response of trastuzumab deruxtecan for HER-2 positive gastric cancer with brain and leptomeningeal metastasis remains unknown.

Conclusion:

To date, there are still few data about HER-2 positive gastric cancers with brain and leptomeningeal metastasis. Roles of HER-2 in gastric cancer are unclear. On the other hand, new ADC- trastuzumab deruxtecan may provide an anticipated hope for metastatic HER2-positive gastric cancer patients. Much more studies for treatment of HER-2 positive gastric cancers with brain and leptomeningeal metastasis are needed.